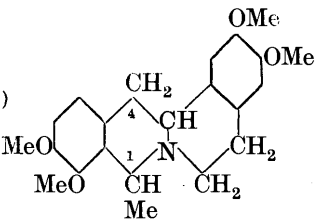
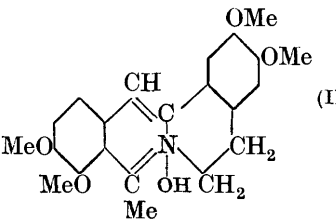
CCCXCIII.—*Synthesis of Oxydehydrocorydaline.*

By Joseph Blake Koepfli and William Henry Perkin, jun.

Corydaline, $C_{22}H_{27}O_4N$, the principal alkaloid occurring in *Corydalis cava* and *Corydalis tuberosa*, was first isolated by Wackenroder (*Berz. Jahr.*, 1826, **7**, 220); it melts at 133° and has $[\alpha]_D^{20°}$ + 300° (in chloroform). Our knowledge of the constitution of this alkaloid is very largely due to the researches of Dobbie and Lauder (J., 1902, **81**, 148), who, mainly as the result of the study of the substances obtained on oxidation and the comparison of these with the corresponding substances derived from berberine under like conditions, concluded that the constitution (I) must be assigned to corydaline.

(I.)





(II.)

This formula represents corydaline as the methyl derivative of tetrahydropalmatine containing the methyl group in the position 1.

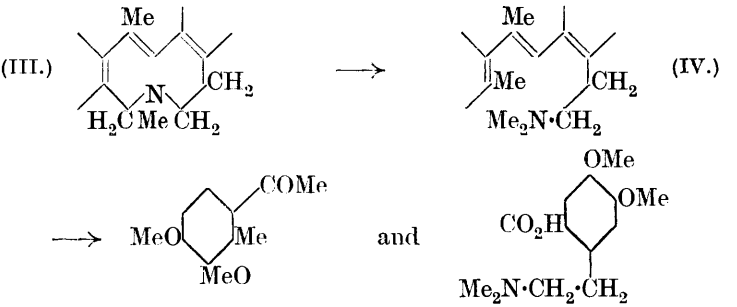
This view of the constitution of the alkaloid held the field for

several years and was also adopted by Gadamer (*Arch. Pharm.*, 1910, **248**, 205) after the careful consideration of several alternative expressions. Perhaps the most characteristic property of corydaline is its conversion by mild oxidising agents with loss of four atoms of hydrogen into the yellow base dehydrocorydaline, $C_{22}H_{25}O_5N$, which closely resembles berberine in appearance and in several of its properties and was therefore assumed to be the methylpalmatine (II) containing the methyl group again in position 1. Confirmation of this view was thought to be disclosed by the fact that, for a long time, it was not found possible to convert dehydrocorydaline chloride into derivatives corresponding with oxyberberine and dihydroberberine, and the failure to undergo this characteristic reaction was assumed to be due to the presence of the methyl group in the position 1.

However, in 1922, Gadamer and von Bruchhausen (*Arch. Pharm.*, **259**, 249) succeeded in bringing about this change by treating dehydrocorydaline acetate with sodium hydroxide, and this important result was the first clear indication that the methyl group in corydaline could not be situated in position 1. Further evidence on this point was also furnished by Späth and Lang (*Ber.*, 1921, **54**, 3074), who converted palmatine iodide, by the action of magnesium methyl iodide and subsequent reduction, into two isomeric methyltetrahydropalmatines, neither of which was identical with *dl*-corydaline. Since, however, the researches of Freund and Beck (*Ber.*, 1904, **37**, 4674) have shown that, when the Grignard reagent reacts with salts of berberine, it is the hydrogen atom (1) which becomes replaced, and it may be assumed that the salts of palmatine will behave in a similar manner, the methyltetrahydropalmatines obtained by Späth and Lang should both contain the methyl group in position 1 and one of them should be identical with *dl*-corydaline (I), which, however, is not the case. More conclusive evidence in support of this view and indicating that position 4 must be assigned to the methyl group was subsequently brought forward by von Bruchhausen (*Arch. Pharm.*, 1923, **261**, 31).

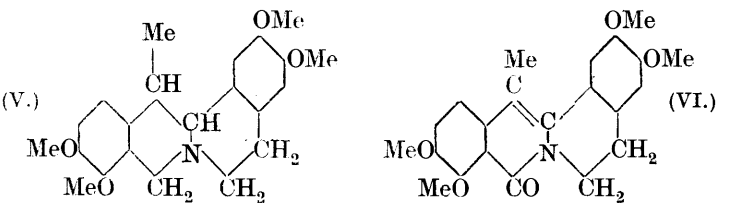
This author achieved a partial synthesis of *d*-corydaline by methylating palmatine acetone with methyl iodide and reducing the methylated product with zinc and sulphuric acid. Since the researches of Freund and Speyer (*Annalen*, 1913, **397**, 1) and Freund and Fleischer (*ibid.*, 1915, **409**, 194) have shown that, when substances of the dihydroberberine type, to which palmatine acetone is supposed to belong, interact with methyl iodide, it is the hydrogen atom in position 4 which is reactive and becomes replaced by methyl, von Bruchhausen maintains that his synthesis is strong evidence that, in corydaline, the methyl group must occupy the position 4.

More recently still, von Bruchhausen and Stippler (*Arch. Pharm.*, 1927, **265**, 152) converted corydaline methochloride into the anhydro-base (III) [compare anhydromethyltetrahydropalmatine (A), J., 1927, 2262], reduced the methosulphate of this with sodium amalgam to (IV), and showed that this substance on oxidation with permanganate yields methylacetoveratrone and, with ozone, 4 : 5-dimethoxy-2-dimethylaminoethylbenzoic acid. Not only is this interesting series of decompositions (compare J., 1916, **109**, 821), which may be represented by the partial formulæ



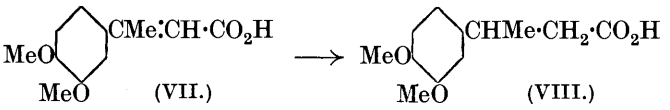
valuable general evidence of the constitution of corydaline, but, in particular, the formation of methylacetoveratrone may be taken as supporting the view that the methyl group in corydaline occupies the position 4.

This brief sketch shows that the evidence which gradually accumulated had become strongly in favour of the view that the constitution of corydaline must be represented by (V) and not by the



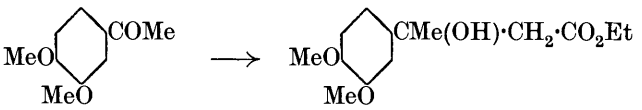
formula (I) of Dobbie and Lauder but, in order definitely to settle this matter, it seemed to us that it would be of interest to attempt to carry out a complete synthesis either of corydaline itself or of some highly characteristic derivative of the alkaloid. The derivative selected in the first place was oxydehydrocorydaline (VI), and the experience gained in the course of previous synthetical work in this group of alkaloids suggested that the best starting point for this synthesis would be β-veratrylbutyric acid (VIII). This we expected

to obtain by reducing the corresponding β-*veratrylcrotonic acid* (VII). But the acid (VII) proved difficult to prepare : among the unsuccessful attempts to obtain it may be mentioned the condensation of

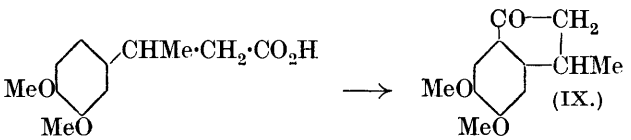


acetoveratrone with malonic acid and acetic anhydride (Massot, *Ber.*, 1894, **27**, 1225) or acetic anhydride and sulphuric acid (Meldrum, J., 1908, **93**, 598), and various processes involving the Claisen condensation.

Ultimately, acetoveratrone was found to interact readily with ethyl bromoacetate in the presence of zinc (Lindenbaum, *Ber.*, 1917, **50**, 1270) :



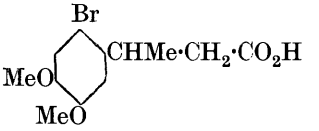
the crude ethyl β-veratryl-β-hydroxybutyrate, when distilled under reduced pressure, decomposed with the loss of water and formation of *ethyl* β-*veratrylcrotonate*. The free acid (VII), readily obtained from the ester by hydrolysis, was reduced by sodium amalgam to β-*veratrylbutyric acid* (VIII) and this, on treatment with sulphuric acid, yielded 5 : 6-*dimethoxy*-3-*methyl*-1-*hydrindone* (IX), a substance



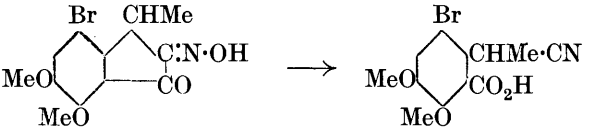
which was carefully characterised by conversion into the *oxime* and iso*nitroso*-derivative.

The formation of the hydrindone (IX) as the sole product of the dehydration is due to the well-known tendency to ring closure in the 6-position, para to one of the methoxy-groups. As it was necessary for the purpose of the synthesis of oxydehydrocorydaline that this should not occur but that the hydrindone formation should take place in the position 2, the 6-position was protected by the introduction of a bromine atom (Haworth, Perkin, and Stevens, J., 1926, 1764; Haworth, Koepfli, and Perkin, J., 1927, 548). 6-*Bromo*-β-*veratrylbutyric acid* (X), obtained by treating the acid (VIII) in glacial acetic acid solution with bromine, readily suffered

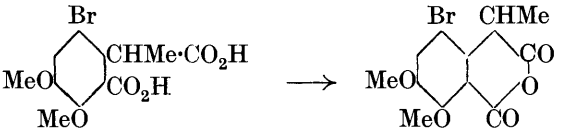
ring closure when warmed with sulphuric acid and yielded 4-*bromo*-6 : 7-*dimethoxy*-3-*methyl*-1-*hydrindone* (XI).

(X.)  (XI.)

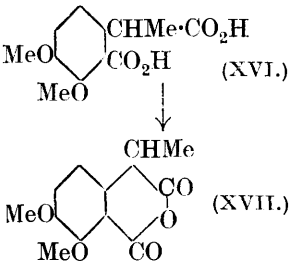
When the iso*nitroso*-derivative (XII) of this hydrindone, dissolved in sodium hydroxide, was treated with toluene-*p*-sulphonyl chloride, it underwent the Beckmann transformation and a good yield of 6-bromo-2-carboxy-3 : 4-dimethoxy-α-phenylpropionitrile (XIII) was obtained.

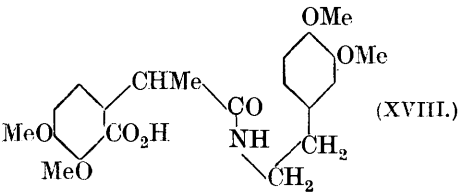
(XII.)  (XIII.)

This was converted, on hydrolysis, into 6-bromo-3 : 4-dimethoxy-α-methylhomophthalic acid (XIV), a gum from which the crystalline *anhydride* (XV) was obtained by the action of acetyl chloride.

(XIV.)  (XV.)

The anhydride was hydrolysed in alkaline solution and debrominated with sodium amalgam, and the crude 3 : 4-dimethoxy-α-methylhomophthalic acid (XVI) converted into the *anhydride* (XVII) by the action of acetyl chloride.

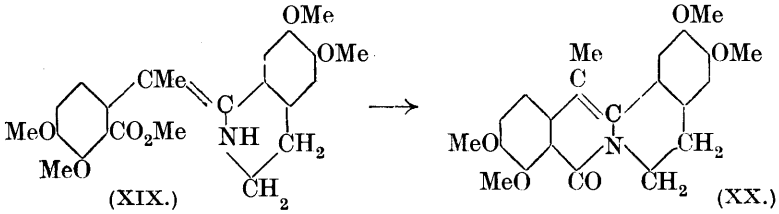




The anhydride (XVII) was now combined with β-veratrylethylamine (Haworth, Perkin, and Pink, J., 1925, **127**, 1709) by boiling the two substances together in benzene solution, the *N*-β-veratrylethyl-3 : 4-dimethoxy-α-methylhomophthalamic acid (XVIII) obtained was converted into the methyl ester, and this treated with phos-

phorus oxychloride in the expectation that methyl alcohol as well as water would be eliminated with the formation of oxydehydrocorydaline just as, for example, the methyl ester of *N*-β-veratrylethyl-3 : 4-dimethoxyhomophthalamic acid passes so easily under the same conditions directly into oxypalmatine (Haworth, Koepfli, and Perkin, J., 1927, 549).

However, in the present instance, the methyl ester lost only water on treatment with phosphorus oxychloride and yielded a substance, $C_{23}H_{27}O_6N$, which was clearly 6 : 7 : 3′ : 4′-*tetramethoxy*-9-*methyl*-2′-*carbomethoxy*-3 : 4-*dihydroprotopapaverine* (XIX),* because when heated at 150—170° it yielded oxydehydrocorydaline (XX) with elimination of methyl alcohol.



It has already been pointed out (p. 2990) that oxydehydrocorydaline was first prepared by Gadamer and von Bruchhausen from dehydrocorydaline acetate by the action of sodium hydroxide, and these investigators describe it as crystallising from acetic acid in pale yellow, four-sided tablets, m. p. 228—228·5°. The substance which we obtained synthetically, after repeated crystallisation from alcohol, was nearly colourless and melted at 235—236°. We are much indebted to Dr. von Bruchhausen for kindly sending us a specimen of the oxydehydrocorydaline obtained from dehydrocorydaline acetate. After two crystallisations from alcohol, this was still pale yellow but the m. p. had risen to 234—236°, and a mixture with the synthetical substance showed no depression in melting point. There can therefore be no doubt that the two specimens are identical and that the substance obtained synthetically is in fact oxydehydrocorydaline. This synthesis of the substance clearly demonstrates that the constitution of corydaline must be that represented by formula (V).

Preliminary experiments made with the object of converting oxydehydrocorydaline into *dl*-corydaline by electrolytic reduction seem to indicate that this process does not take place so readily as the conversion of oxyberberine into tetrahydroberberine (Perkin, J., 1918, **113**, 737). When larger amounts of material are available it will be possible to decide whether the change can be brought about

* For nomenclature, see Buck, Perkin, and Stevens (J., 1925, **127**, 1462).

in this way or whether some other process of reduction must be employed.

EXPERIMENTAL.

Acetoveratrone, $C_6H_3(OMe)_2 \cdot COMe$.—Veratrole (290 g.), prepared by the action of methyl sulphate on guaiacol (Perkin and Weizmann, J., 1906, **89**, 1649), was dissolved in carbon disulphide (750 c.c.) and mixed with acetyl chloride (197 g.). Aluminium chloride (290 g.) was added to the ice-cold mixture in small portions with constant shaking, and the reaction completed by warming at 50° for a short time. The magenta-coloured crystalline mass was separated from the carbon disulphide and decomposed with ice, the whole extracted with chloroform, and the chloroform solution washed with dilute sodium hydroxide solution and with water and dried over calcium chloride. After removal of the solvent on the steam-bath, the residue was distilled under reduced pressure, acetoveratrone being obtained as a colourless oil (297 g.), b. p. 160—162°/10 mm., which crystallised on standing.

Ethyl β-Veratrylcrotonate (formula as VII).—Acetoveratrone (45 g.) and ethyl bromoacetate (50 g.) in dry benzene (280 c.c.) were placed in a 1·5-litre flask together with zinc turnings (20 g.) and heat was applied until the reaction commenced. After this had subsided, the liquid was boiled under reflux for ¾ hour, cooled, decanted from undissolved zinc, and shaken with dilute sulphuric acid. The yellow benzene solution was dried over anhydrous sodium sulphate, the solvent removed on the steam-bath, and the residual light yellow oil, consisting of crude ethyl β-veratryl-β-hydroxybutyrate (p. 2992), distilled twice under diminished pressure; the resulting *ethyl β-veratrylcrotonate* (50 g.), b. p. 195—196°/10 mm., crystallised from ligroin in large colourless prisms, m. p. 51—52° (Found: C, 67·1; H, 7·1. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

In another experiment, ethyl β-veratryl-β-hydroxybutyrate (50 g.) was refluxed in dry benzene (200 c.c.) with phosphorus oxychloride (15 c.c.) for 30 minutes. The benzene solution, which turned dark red, was washed with water and dried over sodium sulphate, and the solvent removed on the steam-bath. The dark red oil, distilled under diminished pressure, gave ethyl β-veratrylcrotonate (30 g.), and a residue which could not be distilled without decomposition. This was hydrolysed with alcoholic potassium hydroxide and the solution was diluted with water, concentrated under diminished pressure on the steam-bath, and acidified; an amorphous mass then separated which, after solution in bicarbonate, extraction with ether and chloroform, and reprecipitation, could ultimately be obtained crystalline from methyl alcohol, separating in colourless prisms, m. p. 225—226° (Found:

C, 64·8; H, 6·5; *M*, in camphor by Rast's method, 482. $C_{24}H_{28}O_8$ requires C, 64·8; H, 6·3%; *M*, 444). This *substance*, which does not appear to be reduced by sodium amalgam, is evidently produced from two molecules of veratrylhydroxybutyric acid by the elimination of two molecules of water ($2C_{12}H_{16}O_5 - 2H_2O = C_{24}H_{28}O_8$). The amount of available material was, however, so small that no further experiments were made with the substance.

β-*Veratrylcrotonic acid* (VII) was prepared by refluxing the ester (155 g.) with alcohol (500 c.c.), water (40 c.c.), and potassium hydroxide (42 g.) for 2 hours. The solution was diluted with twice its bulk of water, concentrated under diminished pressure on the steam-bath, and acidified with hydrochloric acid; the crude brown *acid* (120 g.) obtained crystallised from benzene in pointed prisms, m. p. 138—140° (Found: C, 64·7; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·8; H, 6·3%). It is sparingly soluble in water but readily soluble in the usual organic solvents with the exception of petroleum. The solution in concentrated sulphuric acid is yellow and exhibits a greenish fluorescence on standing.

The aqueous and the benzene mother-liquor (above) contain considerable quantities of a second acid which has not yet been carefully examined; it melts at 90—95° and is probably a stereoisomeride (compare Johnson and Kon, J., 1926, 2749).

β-*Veratrylbutyric Acid* (VIII).—β-Veratrylcrotonic acid (90 g.), dissolved in water (2·5 l.) and sodium hydroxide (17 g.), was treated with sodium amalgam (4 kg. of 4%) at 85—90° with mechanical stirring. After 12 hours, the cooled and filtered solution was nearly neutralised with hydrochloric acid, and a cold aqueous solution of permanganate (100 c.c. of 1%) added. After a few minutes, sulphur dioxide in excess was passed in and the white precipitate of the acid was collected, washed well, dried in a vacuum desiccator, and crystallised from benzene, separating in pointed prisms (Found: C, 64·2; H, 7·1. $C_{12}H_{16}O_4$ requires C, 64·3; H, 7·1%).

β-*Veratrylbutyric acid* melts at 84—85° and is very soluble in methyl alcohol but sparingly soluble in water or petroleum. It separates from dilute acetic acid in slender elongated prisms containing $1H_2O$: these melt at about 60—61° and lose water at 100°; the solid remaining melts at 84—85° (Found: loss at 100°, 8·3. $C_{12}H_{16}O_4,H_2O$ requires H_2O, 7·5%).

5 : 6-*Dimethoxy*-3-*methyl*-1-*hydrindone* (IX).—β-Veratrylbutyric acid (7 g.) was mixed with concentrated sulphuric acid (30 c.c.) at 60°. The temperature rose to 73° and was maintained at that for 3 minutes; the deep red solution was then poured on ice and extracted with chloroform. After being washed with sodium carbonate solution, the extract was dried over anhydrous potassium carbonate

and the solvent removed; the colourless gum obtained soon crystallised and separated from very dilute methyl alcohol, on long standing, in almost colourless prisms, m. p. 90—91° (Found: C, 69·6; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%).

This *hydrindone* is very soluble in organic solvents with the exception of petroleum. The *oxime*, prepared by the action of hydroxylamine hydrochloride and potassium acetate on an alcoholic solution of the hydrindone, is readily soluble in methyl alcohol and separates, on the addition of water, as a felted mass of colourless elongated prisms, m. p. 128—129° with previous softening (Found: N, 6·4. $C_{12}H_{15}O_3N$ requires N, 6·3%). The iso*nitroso*-derivative was prepared by the action of methyl nitrite on an alcoholic solution of the hydrindone containing a little hydrochloric acid. It separated from methyl alcohol, in which it was rather sparingly soluble, in faintly lemon-coloured prisms, m. p. 225—226° (decomp.) (Found: N, 5·6. $C_{12}H_{13}O_4N$ requires N, 6·0%).

6-*Bromo*-β-*veratrylbutyric Acid* (X).—β-Veratrylbutyric acid (75 g.) was dissolved in glacial acetic acid (150 c.c.) and acetic anhydride (50 c.c.) at 0° and mechanically stirred while bromine (55 g.) in glacial acetic acid (50 c.c.) was slowly added. The product was poured into water containing a little sulphurous acid. The almost colourless oil (100 g.) obtained gradually solidified; after being washed, it was dried in a desiccator and a portion was crystallised from acetic acid and a little water, separating in colourless stout prisms, m. p. 106—107° (Found: C, 47·5; H, 5·0. $C_{12}H_{15}O_4Br$ requires C, 47·5; H, 5·0%). This *bromo-acid* is very soluble in organic solvents with the exception of petroleum and may be crystallised from a mixture of this and benzene.

4-*Bromo*-6 : 7-*dimethoxy*-3-*methyl*-1-*hydrindone* (XI).—6-Bromo-β-veratrylbutyric acid (10 g.) was treated with concentrated sulphuric acid (50 c.c.) at 75° for 5 minutes and the orange-red solution was then poured on ice and extracted with chloroform. After being washed with sodium carbonate solution, the extract was dried over anhydrous potassium carbonate, and the solvent removed. The light green gum obtained partly crystallised when rubbed with a glass rod. After draining on porous porcelain and several crystallisations from dilute methyl alcohol, the *bromohydrindone* was obtained in lemon-coloured, flat prisms (2 g.), m. p. 82—83° (Found: C, 50·5; H, 4·6. $C_{12}H_{13}O_3Br$ requires C, 50·5; H, 4·6%). The *oxime* separated from methyl alcohol in stout prisms, m. p. 187—188° (Found: N, 4·5. $C_{12}H_{14}O_3NBr$ requires N, 4·7%).

4-*Bromo*-2-iso*nitroso*-6 : 7-*dimethoxy*-3-*methyl*-1-*hydrindone* (XII).—A solution of the bromohydrindone (5 g.) in methyl alcohol (30 c.c.) and concentrated hydrochloric acid (2 c.c.) was saturated

with methyl nitrite, the temperature being maintained at 35°. The yellow solution obtained slowly deposited crystals of the *iso*nitroso-derivative, which separated from alcohol, in which it was but slightly soluble, in small, pale yellow, elongated prisms (3·5 g.), m. p. 217° (decomp.) (Found : N, 4·3. $C_{12}H_{12}O_4NBr$ requires N, 4·4%). The acid mother-liquor, on being concentrated in a vacuum, deposited a crystalline substance (1 g.), which separated from methyl alcohol in colourless prisms, m. p. 155—156°, but was not further examined.

6-*Bromo*-3 : 4-*dimethoxy*-α-*methylhomophthalic Anhydride* (XV). —The *iso*nitroso-derivative (3·7 g.) was dissolved in water (25 c.c.) and sodium hydroxide (1·7 g.), toluene-*p*-sulphonyl chloride (2·7 g.) added to the deep red solution, and the mixture well shaken. On raising the temperature gradually to 50°, all went into solution, and at 60° the liquid became colourless. It was cooled, filtered, and acidified and the colourless syrupy 6-bromo-2-carboxy-3 : 4-dimethoxy-α-phenylpropionitrile (XIII), which did not crystallise, was extracted with ether. After removal of the solvent, the gummy nitrile was gently boiled with aqueous sodium hydroxide (50 c.c. of 8%) for 3 hours or until evolution of ammonia could no longer be detected. The filtered and well-cooled solution deposited, on addition of hydrochloric acid, crude 6-bromo-3 : 4-dimethoxy-α-methylhomophthalic acid (XIV) as a sticky mass; this was extracted with ether, and the ethereal solution dried over anhydrous sodium sulphate and evaporated. The colourless gummy acid was refluxed on the steam-bath with excess of acetyl chloride for ½ hour, the excess of acetyl chloride removed under diminished pressure, and the pale yellow *anhydride* (XV) crystallised from dry benzene, separating in minute, colourless, flat prisms (2·8 g.), m. p. 128—129° (Found : C, 45·7; H, 3·5. $C_{12}H_{11}O_5Br$ requires C, 45·7; H, 3·5%).

3 : 4-*Dimethoxy*-α-*methylhomophthalic Anhydride* (XVII).—The bromo-anhydride just described (2 g.) was dissolved in a little dilute aqueous sodium hydroxide, and the yellow solution warmed for a few minutes on the steam-bath until colourless. It was then diluted with water (100 c.c.) and heated on the steam-bath with sodium amalgam (100 g. of 4%) for 6 hours until a small filtered test portion showed only a faint cloudiness on treatment with hydrochloric acid. The whole was then acidified, extracted several times with ether, saturated with ammonium sulphate, and again repeatedly extracted, and the combined extracts were carefully dried over anhydrous sodium sulphate. The colourless gummy 3 : 4-dimethoxy-α-methylhomophthalic acid remaining after evaporation of the ether was refluxed with excess of acetyl chloride for ½ hour. After removal of the excess of acetyl chloride under diminished pressure,

the pale brown 3 : 4-*dimethoxy*-α-*methylhomophthalic anhydride* (XVII) was dissolved in boiling dry benzene and the solution was decolorised with norite and concentrated; the anhydride then separated in colourless prisms (1·2 g.), m. p. 131—133° (Found: C, 60·8; H, 5·1. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%).

6 : 7 : 3′ : 4′-*Tetramethoxy*-9-*methyl*-2′-*carbomethoxy*-3 : 4-*dihydroprotopapaverine* (XIX).—3 : 4-Dimethoxy-α-methylhomophthalic anhydride (1·5 g.) and β-veratrylethylamine (1·3 g.) were refluxed together in dry benzene (30 c.c.) for 2 hours. The well-cooled, pale yellow solution was extracted with aqueous sodium hydroxide (25 c.c. of 5%) and the orange-yellow alkaline liquid was extracted with ether and then made acid with hydrochloric acid. The precipitated, colourless, gummy *N*-β-veratrylethyl-3 : 4-dimethoxy-α-methylhomophthalamic acid (XVIII) was dried in a desiccator, and the brittle amorphous solid obtained, which could not be crystallised, was dissolved in a solution of sodium bicarbonate (0·7 g.) in water (10 c.c.). Addition of silver nitrate (3 g. in 10 c.c. of water) to the filtered solution precipitated the silver salt, which was washed once with water, dried in a vacuum over phosphoric oxide, and refluxed with methyl iodide (3 c.c.) in dry ether (50 c.c.) for 12 hours. The filtered ethereal solution was evaporated to dryness and the crude gummy methyl ester (2 g.) was gently boiled with freshly distilled phosphorus oxychloride (20 c.c.) for 10 minutes. The excess of oxychloride was removed by distillation under reduced pressure, the residue warmed with water (60 c.c.), and the clear solution made alkaline with sodium hydroxide; the orange amorphous precipitate which then separated crystallised from methyl alcohol in colourless prisms (1·1 g.), m. p. 136—137° with previous softening (Found: C, 66·7; H, 6·5. $C_{23}H_{27}O_6N$ requires C, 66·8; H, 6·5%). This *substance*, the properties of which show that it has the constitution (XIX), is soluble in dilute acids and precipitated unchanged by alkalis. It does not appear to be readily hydrolysed by methyl-alcoholic sodium hydroxide.

Oxydehydrocorydaline (XX).—When the methyl ester (XIX) just described (1 g.) was heated in a test-tube at 150—170° for 10 minutes, the colourless substance, after melting, turned yellow, evolution of methyl alcohol could be detected, and the residue became quite dry and apparently crystalline. The substance was dissolved in much boiling alcohol, in which it was very sparingly soluble; almost colourless, cube-like prisms separated on slow cooling, and a further quantity was obtained by concentrating the mother-liquor. After recrystallisation, the substance (0·5 g.) melted at 235—236° and a micro-analysis gave C, 69·0; H, 6·0, whereas $C_{22}H_{23}O_5N$ requires C, 69·2; H, 6·0%. This substance is insoluble in dilute acids or

alkalis, but dissolves readily in warm glacial acetic acid, and crystallises unchanged on the addition of water. It is soluble in sulphuric acid (50%), on warming, and the addition of a drop of concentrated nitric acid produces an almost black coloration, which changes to deep wine-red in a few minutes and then very slowly fades to yellow. There could be no doubt that this substance, which has properties so very similar to those of oxyberberine, is oxydehydrocorydaline (XX), and this view was confirmed, as has already been explained in the introduction (p. 2994), by direct comparison with a specimen of oxydehydrocorydaline from corydaline for which we are indebted to Dr. von Bruchhausen.

THE DYSON PERRINS LABORATORY,
OXFORD.

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