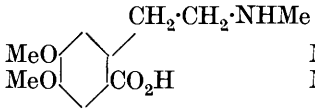
CIII.—*Synthetical Work on the* iso*Quinoline Alkaloids. Part I. Substituted* o*-Carboxyphenylethylamines.*

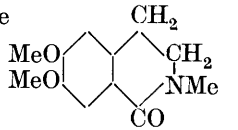
By GEORGE ALFRED EDWARDS.

THIS communication is concerned with the preparation and properties of substances obtained in a preliminary investigation of possible methods of preparing β-(4 : 5-dimethoxy-2-carboxyphenyl)ethylmethylamine (I), and of similar substances required in connexion with proposed syntheses of alkaloids of the cryptopine type.

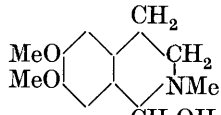
Laudanosine appeared to be a possible source of this amino-acid, since Pyman (J., 1909, **95**, 1272) had shown that the lactam, 6 : 7-dimethoxy-2-methyldihydro*iso*quinolone (II), was obtained by its oxidation. He further showed that on more gentle oxidation



(I.)

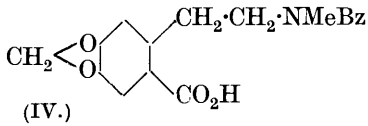


(II.)

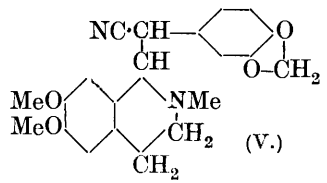


(III.)

1-hydroxy-6 : 7-dimethoxy-2-methyltetrahydro*iso*quinoline (III) was produced, and that it reacted in many respects like hydrastinine, which differs from it structurally only in containing the methylenedioxy-group in place of the two methoxy-groups. Freund (*Ber.*, 1889, **22**, 1156) found that hydrastinine gave a benzoyl derivative in which the tetrahydropyridine ring had presumably been opened, and on oxidation gave what was probably *N*-benzoyl-β-(4 : 5-methylenedioxy-2-carboxyphenyl)ethylmethylamine (IV). Attempts to benzoylate substance (III), however, resulted in the conversion of the benzoyl chloride into benzoic anhydride, the ψ-base acting merely as a catalyst.



(IV.)



(V.)

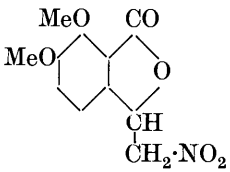
In the proposed synthesis of cryptopine, the substance (I) was to have been esterified and condensed, in presence of sodium ethoxide, with homopiperonylonitrile, $(CH_2O_2)C_6H_3{\cdot}CH_2{\cdot}CN$, or a derivative of it with a substituent in the ortho-position to the $-CH_2{\cdot}CN$ group. Attempts to prepare this nitrile from homopiperonal by Semmler and Bartelt's method (*Ber.*, 1908, **41**, 2751) gave minute yields, valueless for synthetic purposes. Interaction of piperonyl bromide

and alcoholic potassium cyanide led to *piperonyl ethyl ether*, $CH_2{:}O_2{:}C_6H_3{\cdot}CH_2{\cdot}O{\cdot}C_2H_5$. The nitrile was most conveniently prepared by condensing piperonal with hippuric acid, hydrolysing the resulting so-called azlactone to piperonylpyruvic acid (Kropp and Decker, *Ber.*, 1909, **42**, 1188; compare Buck and Perkin, J., 1924, **125**, 1680), and treating the *oxime* of this with acetic anhydride, whereby the nitrile was produced by loss of carbon dioxide and water.

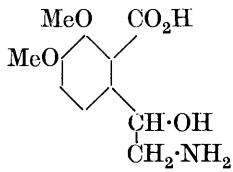
Homopiperonylonitrile condenses with the ψ-base (III) in warm alcohol. The product, 6 : 7-*dimethoxy*-1(3′ : 4′-*methylenedioxy*-ω-*cyanobenzyl*)-2-*methyltetrahydro*isoquinoline (V) does not give a benzoyl derivative under any of the normal conditions of benzoylation, and after several unsuccessful attempts to open the ring between the 1-carbon atom and the nitrogen, this line of attack was abandoned.

The direct synthesis of the required amino-acid (I) from *m*-opianic acid was next tried. The only suitable method for preparing *m*-opianic acid in the quantities required for synthetic work is that of Fargher and Perkin (J., 1921, **119**, 1724), which makes use of creosole. Only a small quantity of this being available, a preliminary investigation was made with the more readily accessible opianic acid (Edwards, Perkin, and Stoyle, J., 1925, **127**, 197), three methods of converting it into the required type of substance being examined.

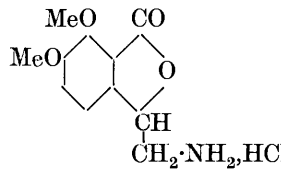
Opianic acid condensed with nitromethane to give a substance (VI) which on reduction yielded the *lactone* of β-*hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylamine hydrochloride* (VIII). The base



(VI.)



(VII.)

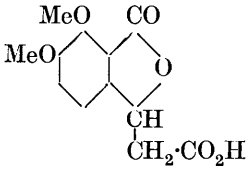


(VIII.)

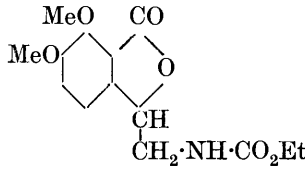
corresponding to this was formed on treatment with one molecular proportion of cold alkali, whilst hot alkali gave the amino-acid itself (VII). The latter, on being heated alone or in tetralin, lost water and ammonia, leaving a nitrogen-free, resinous substance, and treatment with reagents which attack the amino-group resulted in the formation of derivatives of the amino-lactone (VIII). The poor yields obtained by this method are probably due to the decomposition of the condensation product by the acid reducing agents.

Opianic acid condensed with malonic acid to give meconine-acetic acid (IX) (Liebermann, *Ber.*, 1886, **19**, 2290), the amide of

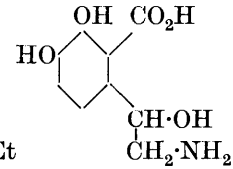
which in the Hofmann reaction, when carried out under the conditions used by Decker (*Annalen*, 1913, **395**, 291) in the preparation of substituted phenylethylamines from phenylpropionamides, gave about a 30% yield of the amino-acid (VII). The alternative Curtius reaction proceeded quite smoothly as far as the *carbamate* (X), which proved unexpectedly stable towards acid hydrolysing reagents, boiling concentrated hydrochloric acid leaving it unchanged. When the hydrolysis mixture was heated in a sealed tube at 140—150°, hydrolysis of the carbamate was accompanied by that of the two methoxy-groups, the product being β-*hydroxy*-β-(2-*carboxy*-3 : 4-*dihydroxyphenyl*)*ethylamine* (XI). This is a typical catechol derivative, giving an intense green coloration with ferric chloride and oxidising rapidly in air. It is similar in properties to the amino-acid already described. In the cold, sodium hydroxide



(IX.)



(X.)

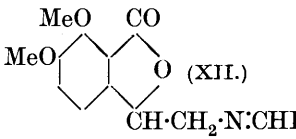


(XI.)

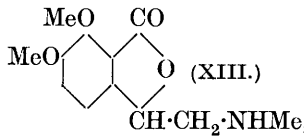
merely opened the lactone ring of the carbamate (X), but a boiling solution removed the carbethoxy-group as well. The resulting solution on careful neutralisation slowly deposited the amino-acid (VII).

Of the three methods discussed above, the Curtius reaction gives the best yield, *viz.*, 40% of the theoretical, calculated on the quantity of opianic acid taken.

The amino-acid (VII) was converted into the benzylidene compound (XII), the methiodide of which, on hydrolysis, yielded the lactone of β-*hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylmethylamine hydriodide* (XIII). On opening the lactone ring, the corresponding amino-acid was formed; it at once passed into its lactone on treatment with mineral acids or with reagents which attack the amino-group.



(XII.)

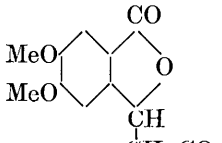


(XIII.)

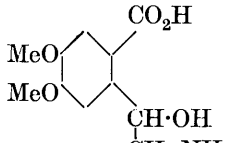
Benzenesulphonyl derivatives of the amino-acids may be prepared by treating the sodium salts with benzenesulphonyl chloride and caustic soda. The dimethylation of the product and the condensation of the ester group with the reactive methylene group in

such substances as phenylacetonitrile and phenylacetic ester will be dealt with in a later paper.

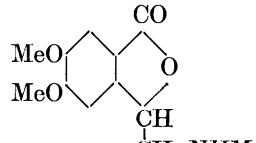
m-Opianic acid condensed best with malonic acid when dissolved in pyridine containing a trace of piperidine. The product, m-*meconineacetic acid* (XIV), was converted by the modification of the Curtius reaction already described into β-hydroxy-β-(4 : 5-dimethoxy-2-carboxyphenyl)ethylamine (XV). This was methylated



(XIV.)



(XV.)



(XVI.)

in the form of its benzylidene derivative, and the final product (derived from its lactone XVI) was precisely similar in properties to the amino-acids already described.

The quantity of creosole available proved sufficient for the production of only about 5 grams of the amino-acid. The production of this substance in quantity from *m*-meconine by another method is being investigated.

EXPERIMENTAL.

r-*Laudanosine* (*N*-methyltetrahydropapaverine) was obtained in almost quantitative yield by reducing papaverine methosulphate with zinc and alcoholic sulphuric acid. The yield obtained in Pictet and Finkelstein's process (*Ber.*, 1900, **332**, 346), *viz.*, reduction of the methiodide with tin and concentrated hydrochloric acid, is about 50%.

The solid obtained by heating papaverine (50 g.) and methyl sulphate (16 c.c.) on the water-bath for 30 minutes was dissolved in boiling water (200 c.c.), mixed with alcoholic sulphuric acid (25 c.c. of 30% solution), and the whole heated on the water-bath while zinc dust and alcoholic sulphuric acid were added alternately so that hydrogen was gently evolved. After 2½ hours, the boiling solution was filtered, the zinc washed thoroughly with boiling alcohol, and the hot solution added slowly to ammonia (350 c.c.; *d* 0·880) mixed with powdered ice. The product separated slowly as a voluminous mass of needles, and after one recrystallisation from dilute alcohol was pure, m. p. 115°.

Piperonyl Ethyl Ether.—An alcoholic solution of piperonyl bromide (Orr, Robinson, and Williams, J., 1917, **111**, 950; Robinson and Robinson, J., 1914, **105**, 1463) and excess of sodium ethoxide was warmed on the water-bath for 10 minutes and poured

into water. The *ether*, which was extracted with ether, was a pleasant-smelling oil, b. p. 130—133°/13 mm. (Found: C, 66·4; H, 6·4. $C_{12}H_{10}O_3$ requires C, 66·7; H, 6·7%).

Oxime of Piperonylpyruvic Acid.—A solution of piperonylpyruvic acid and hydroxylamine hydrochloride (1½ equivs.) in 8% aqueous sodium hydroxide (3 equivs.) was heated on the water-bath for 1 hour. According as it was acidified with acetic acid or hydrochloric acid the solution deposited the insoluble sodium salt of the oxime or the *oxime* itself. The white, flocculent precipitate of the latter was separated after 12 hours; it crystallised from alcohol in colourless needles, m. p. 174—175° (Found: N, 6·1. $C_{10}H_9O_5N$ requires N, 6·3%).

Homopiperonylonitrile.—The preceding oxime was gently warmed with acetic anhydride (4 parts); the reaction, at first slow, ultimately became very violent, and water-cooling was usually necessary. The product was distilled in a vacuum; the nitrile then passed over as a golden-yellow liquid, b. p. 160°/10 mm. It quickly solidified on treatment with absolute alcohol, and on recrystallisation from dilute alcohol separated in nearly colourless needles, m. p. 49° (Medinger, *Monatsh.*, 1906, **27**, 237, gives m. p. 42°) (Found: C, 67·2; H, 4·4; N, 8·5. Calc., C, 67·1; H, 4·3; N, 8·7%).

6 : 7-*Dimethoxy*-1-(3′ : 4′-*methylenedioxy*-ω-*cyanobenzyl*)-2-*methyltetrahydro*isoquinoline (V).—1-Hydroxy-6 : 7-dimethoxy-2-methyltetrahydro*iso*quinoline (III) (Pyman, *loc. cit.*) was dissolved together with homopiperonylonitrile (1 mol.) in hot alcohol. The condensation product separated from the cooled solution in needles, which melted at 171° to a dark red liquid (Found: C, 68·8; H, 6·0. $C_{21}H_{22}O_4N_2$ requires C, 68·8; H, 6·0%). It is completely decomposed when boiled with caustic soda, and is a moderately strong base. On treatment with formaldehyde, methylal or methylene odide, high-melting bases are formed. Since these substances were obviously not of the tetrahydro*epi*berberine type, they were not further investigated.

Synthesis of β-*Hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylmethylamine.*

Reduction of Meconine-nitromethane.—Meconine-nitromethane (15 g.) was dissolved with cooling in concentrated hydrochloric acid (200 c.c.) containing stannous chloride (42 g.); much heat was generated, and the liquid soon began to deposit a yellow tin salt. After an hour, this was filtered off, washed with hydrochloric acid, dissolved in boiling water, the tin removed with hydrogen sulphide, and the filtrate evaporated to small bulk. The hydrochloride thus obtained crystallised from dilute alcohol in colourless needles, m. p.

248°, and was the *lactone* of β-*hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylamine hydrochloride* (VIII) (Found : C, 51·4; H, 5·3. $C_{11}H_{13}O_4N$,HCl requires C, 51·0; H, 5·4%).

The *picrate* of the base separated slowly in golden-yellow needles, m. p. 202—204° (decomp.), when a hot solution of the hydrochloride and picric acid in water was cooled.

Meconineacetamide.—Meconineacetic acid (Liebermann, *loc. cit.*) (40 g.) was boiled for ½ hour with thionyl chloride (130 c.c.), the acid chloride crystallising in fine needles. The excess of thionyl chloride was distilled off on a water-bath; the crystalline residue, after being washed with dry ether and dried in a steam-oven, melted at 158—159° and was sufficiently pure for immediate use.

The finely-powdered acid chloride was added slowly to aqueous ammonia (*d* 0·880; 250 c.c.) containing ice. After 1 hour, the white, amorphous product was washed with cold alkali and ether and crystallised from glacial acetic acid; it then separated in colourless masses of prisms, m. p. 223—224°. It was quite insoluble in cold alkalis, but dissolved readily, on warming, with evolution of ammonia. The latter treatment also opened the lactone ring, but all attempts to effect this change without attacking the amino-group were unsuccessful (Found : C, 57·5; H, 5·2; N, 5·6. $C_{12}H_{13}O_5N$ requires C, 57·3; H, 5·1; N, 5·6%).

The esters of meconineacetic acid may be prepared by cooling a solution of the acid chloride in the minimum amount of the hot alcohol. The methyl ester was thus obtained in colourless hexahedra, m. p. 124°, identical with that obtained by Liebermann (*loc. cit.*) by direct esterification.

Action of Sodium Hypochlorite upon the Acid Amide.—The finely-powdered acid amide, suspended in water at 60°, was shaken with exactly 1·2 mols. of sodium hypochlorite. When the solid had dissolved, the liquid was made very strongly alkaline with caustic soda, the temperature allowed to rise slowly to 85°, and, after ½ hour, the solution was cooled and made just perceptibly acid to litmus by addition of acetic acid. β-*Hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylamine* (VII) separated slowly as a microcrystalline powder, m. p. 224°. It was insoluble in all non-hydroxylic organic solvents, and very sparingly soluble in boiling alcohol or water. A solution of the crude substance in hot ammonia was filtered from insoluble impurities and boiled; as the ammonia evaporated, the amino-acid slowly separated in colourless needles, m. p. 225°. The substance is more soluble in hot solutions of such inorganic salts as copper sulphate and silver nitrate than in water, but separates from them unchanged (Found : C, 54·5; H, 6·1. $C_{11}H_{14}O_5$ requires C, 54·8; H, 6·2%).

Treatment of the amino-acid with hydrochloric acid at once converted it into the hydrochloride of the lactone (VIII), identical with the substance obtained from meconine-nitromethane. When the solid hydrochloride was treated with the theoretical quantity of 30% ice-cold caustic soda solution, it was converted into the lactone base, which is a colourless, fishy-smelling oil, very soluble in water but insoluble in non-hydroxylic solvents. The lactone ring was opened by warming with caustic soda solution for a few minutes, and the amino-acid was precipitated on making the solution just perceptibly acid to litmus with acetic acid.

The amino-acid was boiled with acetic anhydride (3 parts) for 10 minutes and the solution was then refluxed for ½ hour with its own bulk of absolute alcohol, evaporated to one-fourth its volume, and diluted with dry ether. The *acetyl* derivative of the lactone base separated in colourless needles, which crystallised from xylene in star-shaped clusters, m. p. 155° (Found: C, 58·6; H, 5·7. $C_{13}H_{15}O_5N$ requires C, 58·8; H, 5·7%).

Preparation of the Amino-acid (VII) *by means of the Curtius Reaction.*—Meconineacetyl chloride (20 g.) was added slowly to hydrazine hydrate (20 g.) cooled in ice. The resulting thick paste of meconineacetylhydrazide was thoroughly ground and, after 12 hours, dissolved in 8% hydrochloric acid (200 c.c.). A bulky, amorphous precipitate slowly separated. This was filtered off, and the filtrate cooled in ice and treated slowly with sodium nitrite (34 g. in the minimum of water). *Meconineacetyl azide* separated as a white solid (14 g.) and was washed with dry ether and dried in a vacuum desiccator. A small portion recrystallised from dry chloroform separated in colourless needles. It was comparatively stable, losing nitrogen only when heated at its melting point, 94°, for a short time (Found: N, 14·7. $C_{12}H_{11}O_5N_8$ requires N, 15·1%).

When the crude azide was boiled for ½ hour with absolute alcohol (2 parts), a violent evolution of nitrogen took place; the solution on cooling deposited crystals of the *lactone* of *ethyl β-hydroxy-β-(2-carboxy-3 : 4-dimethoxyphenyl)ethylcarbamate* (X). It crystallised from methyl alcohol in colourless cubes, m. p. 131° (Found: C, 56·9; H, 5·8; N, 4·7. $C_{14}H_{17}O_6N$ requires C, 56·9; H, 5·8; N, 4·7%).

This carbamate was heated with concentrated hydrochloric acid (6 parts) in a sealed tube at 150° for 3 hours. The insoluble liquid thus produced was mainly methyl chloride. The aqueous liquid in the tube was boiled, filtered hot, and allowed to cool, *β-hydroxy-β-(2-carboxy-3 : 4-dihydroxyphenyl)ethylamine hydrochloride* being thus obtained in colourless needles, m. p. 262—265°. On treating

this salt with ammonium carbonate, the *amino-acid* (XI) was obtained in colourless needles, m. p. 138—140° (Found : C, 50·3; H, 5·3. $C_{19}H_{12}O_4N$ requires C, 50·7; H, 4·8%). The amino-acid dissolved readily in warm dilute acids or alkalis, but not in alkali carbonates. It did not form a lactone under the conditions obtaining in the case of the dimethoxy-compound.

The carbamate (12 g.) was dissolved in 15% sodium hydroxide solution (50 c.c.) by heating on the water-bath for ½ hour. After boiling for 5 minutes, the solution was cooled, filtered, and faintly acidified (litmus) with acetic acid. After 12 hours, the amino-acid (VII) separated as a microcrystalline powder, m. p. 224°. The yield was 7 g. from 20 g. of meconineacetic acid, *i.e.*, 40%.

From the solution obtained by boiling the amino-acid (30 g.) and benzaldehyde (60 c.c.) for 20 minutes the greater part of the excess of benzaldehyde was removed in a vacuum. The residue was mixed with boiling methyl alcohol (220 c.c.); from the filtered cooled solution the *benzylidene* derivative of the lactone base (XII) separated in slightly cream-tinged plates, m. p. 125° (Found : C, 69·2; H, 5·5. $C_{18}H_{17}O_4N$ requires C, 69·4; H, 5·5%).

The benzylidene compound was heated for 2 hours with its own weight of methyl iodide in a sealed tube at 100°. The orange liquid thus formed set, on cooling, to a mass of yellow needles, which was at once washed with carefully dried benzene and dried in a vacuum desiccator. The *methiodide* thus obtained melted at 180°. It decomposed rapidly in the air with liberation of benzaldehyde. Hydrolysis was best carried out by boiling for a short time with four parts of 95% ethyl alcohol; the filtered solution, on cooling, deposited the *lactone* of β-*hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*) *ethylmethylamine hydriodide* (XIII) in colourless prisms, m. p. 220—222°. The *hydrochloride*, prepared by boiling the hydriodide in chloroform solution with phosphorus pentachloride for 10 minutes, separated from alcohol in felted needles, m. p. 233°. The *nitroso*-compound separated in colourless needles, m. p. 108°, when a warm aqueous solution of the hydrochloride was dropped slowly into an ice-cold solution of excess of sodium nitrite (Found : C, 54·0; H, 5·2; N, 10·7. $C_{12}H_{14}O_5N_2$ requires C, 54·1; H, 5·2; N, 10·5%). From the solution obtained by shaking the hydrochloride and benzoyl chloride (1 mol.) with aqueous sodium hydroxide (2 mols.) the *benzoyl* derivative separated slowly; the large amount remaining in solution was extracted with ether. The product crystallised from a little methyl alcohol in rhombs, m. p. 106°. This substance is insoluble in cold caustic soda solution, but dissolves readily on warming (Found : C, 67·2; H, 5·7. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·5).

β-*Hydroxy*-β-(2-*carboxy*-3 : 4-*dimethoxyphenyl*)*ethylmethylamine* (VII with NHMe in place of NH_2) was obtained by heating a salt of the amino-lactone on the water-bath with a slight excess of caustic soda solution for ½ hour and just acidifying the cooled solution with acetic acid. It crystallised slowly from water in colourless plates, m. p. 190—192° (Found: C, 56·2; H, 6·8. $C_{12}H_{17}O_5N$ requires C, 56·5; H, 6·6%).

β-*Hydroxy*-β-(2-*carboxy*-4 : 5-*dimethoxyphenyl*)*ethylmethylamine* (XV *with* NHMe *in place of* NH_2).

m-*Meconineacetic Acid*.—*m*-Opianic acid (28 g.), malonic acid (35 g.), piperidine (30 drops), and pyridine (100 c.c.) were heated on a water-bath for 6 hours. After boiling for a few minutes, the mixture was cooled and poured into 16% hydrochloric acid (300 c.c.); the product, which separated slowly in clusters of needles, crystallised well from a little glacial acetic acid in colourless needles, m. p. 230—231° (Found: C, 56·8; H, 5·0. $C_{12}H_{12}O_6$ requires C, 57·1; H, 4·8%).

m-*Meconineacetyl Chloride*.—*m*-Meconineacetic acid was boiled for ½ hour with twice its weight of thionyl chloride, the excess of solvent was removed in a vacuum, and the yellow, syrupy product was made to crystallise by treatment with dry ether. It separated from dry xylene in colourless prisms, m. p. 103—104°.

m-*Meconineacetamide* was prepared in exactly the same way as meconineacetamide. It separated from much alcohol in clusters of needles, m. p. 240—241° (Found: N, 5·6. $C_{12}H_{13}O_5N$ requires N, 5·6%).

Ethyl m-*meconineacetate* was produced when the acid chloride was dissolved in a little hot ethyl alcohol, and the product allowed to cool. It separated in fine needles, m. p. 133°. The same substance was obtained by direct esterification (Found: C, 59·8; H, 5·8. $C_{14}H_{16}O_6$ requires C, 60·0; H, 5·8%). The *methyl* ester separated from methyl alcohol in colourless plates, m. p. 129°.

m-Meconineacetic acid was converted by the method already described into m-*meconineacetyl azide*. This separated as a gummy substance which crystallised from chloroform in clusters of needles, m. p. 100° with evolution of nitrogen (Found: N, 14·8. $C_{12}H_{11}O_5N_3$ requires N, 15·1%). Treatment with alcohol converted this into the *lactone* of *ethyl* β-*hydroxy*-β-(2-*carboxy*-4 : 5-*dimethoxyphenyl*)*ethylcarbamate*, which separated in glistening plates with a pale brown tinge, m. p. 177—178° (Found: C, 56·9; H, 5·8; N, 4·7. $C_{14}H_{17}O_6N$ requires C, 56·8; H, 5·6; N, 5·0%). Hydrolysis of this with four times its weight of 12% aqueous caustic soda gave a clear solution which, on being cooled and just acidified with acetic acid, deposited β-*hydroxy*-β-(2-*carboxy*-4 : 5-*dimethoxyphenyl*)*ethylamine*

(XV) in fine, hexagonal prisms, m. p. 204—205° (Found : C, 54·5; H, 6·0. $C_{11}H_{14}O_5N$ requires C, 54·8; H, 6·2%). The acid readily formed a *benzylidene* compound in the manner described above, which crystallised from methyl alcohol in colourless needles, m. p. 146° (Found : C, 69·1; H, 5·7. $C_{18}H_{17}O_4$ requires C, 69·4; H, 5·5%). When quite dry, the latter added on methyl iodide in the manner already described, and the *methiodide* was hydrolysed on treatment with hot dilute alcohol to the *lactone* of *β-hydroxy-β-(2-carboxy-4 : 5-dimethoxyphenyl)ethylmethylamine* (XVI), which crystallised from ethyl alcohol in colourless prisms, m. p. 230—231°. Treatment of this with caustic soda solution opened the lactone ring and produced the amino-acid, which was purified by boiling its solution in ammonia until no more crystals separated. It was thus obtained in needles, m. p. 199—204° (decomp.) (Found : C, 56·9; H, 6·8. $C_{12}H_{17}O_5N$ requires C, 56·5; H, 6·6%).

The author wishes to thank Professor W. H. Perkin, F.R.S., for many helpful suggestions, and the Advisory Council of the Department of Scientific and Industrial Research for a grant which enabled him to carry out the greater part of this investigation.

THE DYSON PERRINS LABORATORY, OXFORD. KING'S COLLEGE, LONDON.

[*Received, January 4th,* 1926.]