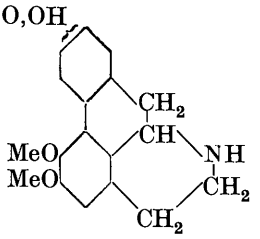
CCCCV.—*Experiments on the Synthesis of Phenolic Aporphines. Part IV. Laurotetanine.*

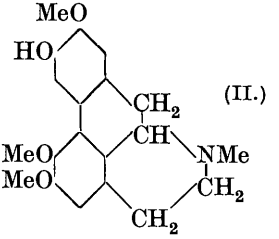
By RODERICK LANGTON DOUGLAS and JOHN MASSON GULLAND.

THE combined researches of Filippo (*Arch. Pharm.*, 1898, **236**, 601), Gorter (*Bull. Jard. bot. Buitenzorg.*, 1921, **3**, 180), Barger and Silberschmidt (J., 1928, 2919), Späth and Strauhal (*Ber.*, 1928, **61**, 2395), and Callow, Gulland, and Haworth (J., 1929, 658) allow the constitution (I) to be assigned to laurotetanine, an alkaloid which occurs in the bark of various *Lauraceæ*, particularly the

Javanese *Litsea* species. The only point of uncertainty is the position of the hydroxyl group. The solution of this problem by synthesis is twofold, since it involves the production of a phenanthra*iso*quinoline which is both a phenol and a secondary base. As this series of investigations was primarily concerned with the preparation of phenolic aporphines, it was decided in the first instance to ascertain the optimal conditions for the synthesis of 3-hydroxy-2 : 5 : 6-trimethoxyaporphine (II).

(I.)

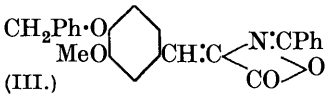


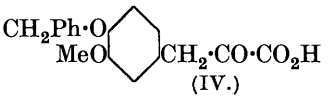


(II.)

Preliminary experiments indicated that 4-hydroxy-3-methoxyphenylpyruvic acid was too susceptible to atmospheric oxidation to permit a successful large-scale preparation of the corresponding phenylacetic acid from acetvanillin *via* the azlactone. The following procedure was therefore adopted. 5-*Keto*-2-*phenyl*-4-(4′-*benzyloxy*-3′-*methoxybenzylidene*)-4 : 5-*dihydro-oxazole* (III), prepared from benzylvanillin (Dickinson, Heilbron, and Irving, J., 1927, 1888) and hippuric acid, was hydrolysed by boiling baryta solution, and the very sparingly soluble barium salt of 4-*benzyloxy*-3-*methoxyphenylpyruvic acid* (IV) was isolated in excellent yield and decomposed with acid. During hydrolyses of the azlactone (III) under widely varied conditions with sodium hydroxide, the usual reagent, a large quantity of an amorphous substance of unknown composition was invariably produced : this greatly reduced the yield of the acid (IV), and rendered manipulation troublesome. Hydrolysis with baryta may therefore prove of considerable value in

(III.)





(IV.)

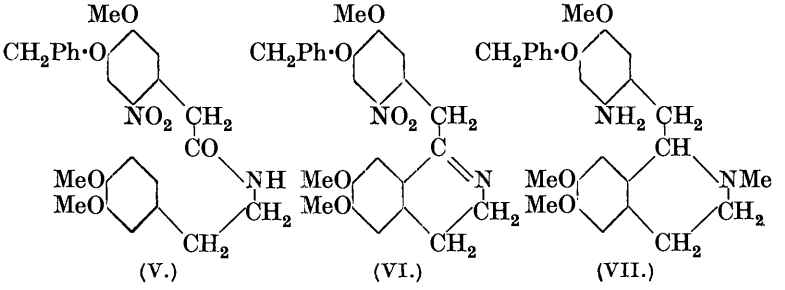
similar difficult cases, and a few examples have been examined in order to determine to what extent the method is generally applicable. The results are described in detail in the experimental section, but it may be mentioned here that the success of the method is dependent both on the low solubility of the barium salt of the keto-acid and on a moderate solubility of the barium salt of the arylidenehippuric acid.

Oxidation of the acid (IV) in alkaline solution with perhydrol

afforded 4-*benzyloxy*-3-*methoxyphenylacetic acid*, which was readily converted into 6-*nitro*-4-*benzyloxy*-3-*methoxyphenylacetic acid* by nitration. The point of entry of the nitro-group was confirmed by debenzylation of this acid to 6-*nitro*-4-*hydroxy*-3-*methoxyphenylacetic acid* and subsequent methylation of this to 6-nitro-3 : 4-dimethoxyphenylacetic acid (Callow, Gulland, and Haworth, *loc. cit.*).

After some unsatisfactory attempts to deviate from the customary procedure by the use of β-3 : 4-dimethoxyphenyl-β-methoxyethylamine (Mannich and Walther, *Arch. Pharm.*, 1927, **265**, 1) instead of homoveratrylamine, 6′-*nitro*-4′-*benzyloxy*-3′-*methoxyphenylaceto*-β-3 : 4-*dimethoxyphenylethylamide* (V) was converted into the *hydrochloride* of 6′-nitro-4′-benzyloxy-3′ : 6 : 7-trimethoxy-1-benzyl-3 : 4-dihydro*iso*quinoline (VI) by the action of phosphorus pentachloride. The *methiodide* of this base was much more readily debenzylated by warm concentrated hydrochloric acid than is the isomeric 2-nitro-compound (Part III; this vol., p. 2887), this being yet another example (compare J., 1929, 658) of the neutralisation by the *o*-methoxyl of the electronic attraction of the nitro-group in the 2-position as compared with that in the 6-position.

The reduction of the methiodide was effected smoothly by zinc dust and ice-cold hydrochloric acid (*d* 1·16), and 6′-*amino*-4′-*benzyloxy*-3′ : 6 : 7-*trimethoxy*-1-*benzyl*-2-*methyltetrahydro*isoquinoline (VII) was obtained as an uncrystallisable oil, and characterised as the sparingly soluble *dipicrolonate*. Sparing solubility and a facility for crystallisation appeared to be characteristic of the dipicrolonates of aminobenzyl-*N*-methyltetrahydro*iso*quinolines (compare Part III), and this supposition has been found to be correct by the preparation of the *dipicrolonates* of 6′-amino-3′ : 4′ : 5 : 6-tetramethoxy-1-benzyl-2-methyltetrahydro*iso*quinoline, 2′-amino-3′ : 4′ : 5 : 6-tetramethoxy-1-benzyl-2-methyltetrahydro*iso*quinoline (J., 1929, 658), and 2′-amino-6 : 3′ : 4′-trimethoxy-1-benzyl-2-methyltetrahydro*iso*quinoline (J., 1928, 2083). Picrolonic acid is evidently an excellent reagent for the isolation, purification and identification of these somewhat intractable substances.



For the conversion of (VII) into 3-benzyloxy-2 : 5 : 6-trimethoxyaporphine, it was inadvisable to decompose the dipicrolonate with alkali on account of the unavoidable loss and the introduction of impurities due to atmospheric oxidation, to which the base is extremely susceptible when in alkaline media. Attempts to decompose it by shaking with chloroform and dilute sulphuric acid were unsatisfactory, because the relatively large volume of chloroform required retained much of the salt undecomposed. Finally, the dipicrolonate was decomposed by stirring with methyl alcohol containing sulphuric acid. Most (91%) of the picrolonic acid could be removed by filtration, and the diazotisation was then carried out in methyl-alcoholic sulphuric acid by means of the exact amount of concentrated aqueous barium nitrite solution. An excess of nitrous acid in this operation leads to the formation of feebly basic, tarry material. After the diazotisation, the methyl-alcoholic solution was boiled, and 3-benzyloxy-2 : 5 : 6-trimethoxyaporphine isolated as a basic oil. Debenzylation occurred slowly at room temperature in concentrated hydrochloric acid, but was rapid at 50°, and 3-hydroxy-2 : 5 : 6-trimethoxyaporphine (II) was obtained as an almost colourless phenolic and basic oil. Some colour reactions are recorded, but the description of this base will be given in a later publication.

Experimental.

5-Keto-2-phenyl-4-(4'-benzyloxy-3'-methoxybenzylidene)-4 : 5-dihydro-oxazole (III).—A mixture of benzylvanillin (50 g.), hippuric acid (37 g.), and acetic anhydride (70 c.c.) was brought to 100° on the water-bath, mixed with powdered anhydrous sodium acetate (17 g.), and stirred until the azlactone separated. Heating was continued for 30 minutes, and the mixture was then cooled and stirred with alcohol. The solid was collected, triturated repeatedly with hot water, washed successively with alcohol and ether, and dried at 100°. The *azlactone* formed yellow needles, m. p. 195—196°, the yield being 80% of that theoretically possible (Found : N, 3·6. $C_{24}H_{19}O_4N$ requires N, 3·6%).

Hydrolyses of the Azlactone.—(i) *With sodium hydroxide solution.* The azlactone (20 g.), sodium hydroxide (6 g.), and water (50 c.c.) were heated under reflux. The colour of the azlactone was rapidly discharged, and the liquid was filled with the colourless, sparingly soluble sodium salt of *4-benzyloxy-3-methoxybenzylidenehippuric acid.* When this was collected and decomposed with dilute hydrochloric acid, the acid separated; it formed colourless needles, m. p. 210°, after two recrystallisations from glacial acetic acid (Found : N, 3·7. $C_{24}H_{21}O_5N$ requires N, 3·5%).

When the heating was prolonged, the sodium salt dissolved, forming a dark brown solution. After 6 hours this was cooled and saturated with sulphur dioxide. Benzoic acid separated, accompanied by a large amount of plastic material, which solidified to an amorphous lump. The solids were removed—in some cases with difficulty owing to their adhesive nature—and the filtrate was evaporated in an open basin with slightly more than the calculated quantity of concentrated hydrochloric acid necessary to neutralise the sodium hydroxide used. The use of a larger excess of acid caused fission of the benzyl ether and the formation of a purple tar which was always produced during hydrolyses of the non-benzylated 5-keto-2-phenyl-4-(4′-acetoxy-3′-methoxybenzylidene)-4 : 5-dihydro-oxazole. After a short time 4-benzyloxy-3-methoxyphenylpyruvic acid separated, and was collected in 54% yield when cold. This yield was decreased by the use of a larger proportion of sodium hydroxide in the hydrolysis. All attempts to crystallise the plastic by-product were unsuccessful; it was an acid, which formed a dark, tarry, sparingly soluble sodium salt.

(ii) *With barium hydroxide solution.* The azlactone (35 g.), barium hydroxide (100 g.), water (350 c.c.), and alcohol (50 c.c., to prevent frothing) were heated under reflux for 4 days. (In one experiment, the colourless solid was collected after 8 hours, but proved on examination to be the barium salt of 4-benzyloxy-3-methoxybenzylidenehippuric acid.) When no more ammonia was evolved, the solid barium salt was collected, and washed with water, leaving barium benzoate in solution. The salt was ground with dilute hydrochloric acid at 40°, and practically pure *4-benzyloxy-3-methoxyphenylpyruvic acid* (IV) separated in 90% yield. After recrystallisation from glacial acetic acid, it formed colourless needles, m. p. 179° (Found : C, 64·1; H, 5·5. $C_{17}H_{16}O_5,H_2O$ requires C, 64·2; H, 5·7%).

4-Benzyloxy-3-methoxyphenylacetic Acid.—Perhydrol (8 c.c.) was added to a well-cooled solution of the α-keto-acid (13 g.) in 2*N*-sodium hydroxide. Next day the solution was acidified with dilute sulphuric acid, and after 2 hours the crystalline precipitate was collected, and crystallised from benzene. The *acid* formed colourless prisms, m. p. 116° (Found : C, 69·9; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). It could also be crystallised in colourless needles from water, in which it is rather sparingly soluble, but some decomposition occurred at temperatures over 90°.

6-Nitro-4-benzyloxy-3-methoxyphenylacetic Acid.—A solution of 4-benzyloxy-3-methoxyphenylacetic acid (65 g.) in glacial acetic acid (500 c.c.) was stirred mechanically and cooled as thoroughly as possible without allowing the solvent to solidify. Nitric acid

(*d* 1·42; 40 c.c.) was added gradually from a dropping funnel, and a mauve-coloured precipitate separated. 15 Minutes after all the nitric acid had been added, the mixture was poured into a large volume of water, and the yellow solid was collected, washed, dried, and crystallised from alcohol. *6-Nitro-4-benzyloxy-3-methoxyphenylacetic acid* (58 g.) formed yellow needles, m. p. 222° (Found : N, 4·1. $C_{16}H_{15}O_6N$ requires N, 4·4%). The sodium salt crystallised in colourless hair-fine needles from 2*N*-sodium hydroxide solution, in which it was sparingly soluble.

6-Nitro-4-hydroxy-3-methoxyphenylacetic Acid.—A mixture of 6-nitro-4-benzyloxy-3-methoxyphenylacetic acid (0·5 g.), acetic acid (5 c.c.), and concentrated hydrochloric acid (5 c.c.) was boiled under reflux for 10 minutes, water was added, and the benzyl chloride removed by distillation in steam. The *acid* separated from the solution on cooling, and, when recrystallised from water containing a drop of hydrochloric acid, formed long yellow needles : these softened at 110° and melted at 170—171° after being dried in a vacuum desiccator, but melted at 184° after being dried at 100° (Found : N, 6·3. $C_9H_9O_6N$ requires N, 6·2%). The solution in sodium hydroxide was orange-red, and no colour was developed with alcoholic ferric chloride. Methylation was effected by shaking with methyl sulphate and warm sodium hydroxide solution until the colour was discharged. Acidification precipitated 6-nitro-3 : 4-dimethoxyphenylacetic acid, which, after recrystallisation from benzene, melted at 206—207° alone or mixed with an authentic specimen.

6′-Nitro-4′-benzyloxy-3′-methoxyphenylaceto-β-3 : 4-dimethoxyphenylethylamide (V).—When a suspension of 6-nitro-4-benzyloxy-3-methoxyphenylacetic acid (17·2 g.) and phosphorus pentachloride (25 g.) in chloroform was agitated gently for 20 minutes, the acid passed into solution in the form of the acid chloride, which cannot be isolated from the interaction of the acid and thionyl chloride. This solution was added gradually to a vigorously stirred and well-cooled mixture of homoveratrylamine (12 g.), chloroform (50 c.c.), and sodium hydroxide (250 c.c. of 2*N* and 400 c.c. of water). The stirring was continued for 20 minutes, the chloroform layer separated, and the aqueous layer extracted with chloroform. The combined chloroform solutions were washed with dilute hydrochloric acid and with water, dried, and evaporated, and the residual solid was dissolved in the minimum of boiling acetone (reflux) and treated with charcoal. When the filtrate was cooled, the amide (12 g.) separated in crystalline condition suitable for the next stage. When recrystallised from methyl alcohol, *6′-nitro-4′-benzyloxy-3′-methoxyphenylaceto-β-3 : 4-dimethoxyphenylethylamide* formed yellow

needles, m. p. 168° (Found : C, 64·9; H, 5·8. $C_{26}H_{28}O_7N_2$ requires C, 65·0; H, 5·8%).

6′-*Nitro*-4′-*benzyloxy*-3′ : 6 : 7-*trimethoxy*-1-*benzyl*-3 : 4-*dihydro*iso*quinoline* (VI).—The preceding amide (2 g.) was added to a well-cooled solution of phosphorus pentachloride (2 g.) in chloroform (12 c.c.), and immediately brought into solution by shaking. The mixture was kept at room temperature for 7 days protected from moisture, ice was added, and the solvent and phosphorus oxychloride were removed by distillation under reduced pressure at 40°. The resulting gum soon solidified, the liquid was decanted, and the solid dissolved in hot methyl alcohol (15 c.c.) and mixed with hot 2*N*-hydrochloric acid (30 c.c.). The hot solution was filtered (charcoal), and on cooling, the filtrate deposited 6′-*nitro*-4′-*benzyloxy*-3′ : 6 : 7-*trimethoxy*-1-*benzyl*-3 : 4-*dihydro*iso*quinoline hydrochloride* as yellow needles, which were collected, washed with water, and dried in a vacuum desiccator; on being heated, it lost water of crystallisation and softened at 95—105°, hardened again, and melted at 210° (Found : loss at 100°, 10·1. $C_{26}H_{26}O_6N_2,HCl,3H_2O$ requires loss, 9·8%. Found in dried material : Cl, 6·8. $C_{26}H_{26}O_6N_2,HCl$ requires Cl, 7·1%).

The base separated as an oil when aqueous ammonia was added to a solution of the hydrochloride in methyl alcohol. It was taken up in much ether, in which it was sparingly soluble, and the solution was dried rapidly with potassium carbonate and concentrated. The base separated in colourless prisms, m. p. 155—156°, which dissolved readily in benzene, chloroform, and hot methyl and ethyl alcohols. Chloroform was not a suitable solvent for the extraction of the base, since the latter became contaminated with products of atmospheric oxidation. In subsequent preparations, therefore, the suspension in dilute aqueous ammonia from the decomposition of the hydrochloride was seeded, and the base gradually crystallised in colourless needles, m. p. 154°, which were dried and used for the next preparation without being recrystallised from alcohol, since that operation caused atmospheric oxidation to take place.

The methiodide. On the first occasion on which the methiodide was prepared, it separated in bright yellow crystals when the base (1 g.) and an excess of methyl iodide were heated under reflux on the water-bath for 6 hours. The mixture was cooled and the crystals were collected, washed with ether (yield, 1·2 g.), and recrystallised from methyl alcohol. The *methiodide* formed bright yellow, transparent plates, m. p. 196—197° (Found in material dried at 100° : C, 53·2; H, 4·9. Found in material dried in a vacuum desiccator : C, 50·8; H, 5·2. $C_{27}H_{29}O_6N_2I$ requires C, 53·6; H, 4·8%. $C_{27}H_{29}O_6N_2I,2H_2O$ requires C, 50·6; H, 5·2%).

In subsequent preparations under the same conditions, the crude methiodide separated in pale greenish-yellow crystals, and formed straw-coloured, non-transparent tablets, m. p. 202°, when crystallised from methyl alcohol (Found in material dried in a vacuum desiccator : C, 50·9; H, 5·0%). Further small quantities were obtained by concentrating the methyl iodide mother-liquors.

6′-*Amino*-4′-*benzyloxy*-3′ : 6 : 7-*trimethoxy*-1-*benzyl*-2-*methyltetrahydro*isoquinoline (VII).—Zinc dust was added gradually to a suspension of the methiodide (4·5 g.) in hydrochloric acid (*d* 1·16; 70 c.c.), care being taken to prevent any rise in temperature above 0°. After 3 hours the solution, which had become almost colourless, was filtered from excess of zinc, covered with a layer of ether, and made alkaline with concentrated aqueous ammonia in an atmosphere of nitrogen. Any rise in temperature was again avoided. The base was taken up by repeated extraction with ether in a stream of nitrogen, but in spite of these precautions much oxidation took place and the aqueous layer became deep blue. The combined ethereal extracts were washed with water, dried with sodium sulphate, and evaporated, leaving the base as a brown gum (2·32 g.; 70%). This was dissolved in hot alcohol (50 c.c.) and mixed with picrolonic acid (3 g.) in hot alcohol (200 c.c.). On scratching or, better, seeding, the hot solution deposited the *dipicrolonate*; after several hours it was collected, washed, and dried in a vacuum desiccator; yield, 91% (Found : C, 55·1; H, 5·1; N, 13·8. $C_{27}H_{32}O_4N_2,2C_{10}H_8O_5N_4,2H_2O$ requires C, 55·6; H, 5·1; N, 13·8%). When recrystallised from methyl alcohol–acetone, it formed yellow needles, m. p. 193—194°. It was very sparingly soluble in hot alcohol, but dissolved easily in acetone. The base diazotised readily and then coupled with alkaline β-naphthol to form a crimson precipitate of an azo-dye.

A reduction carried out at 40—50° with the same reagents yielded a gum which did not diazotise and couple, and had probably suffered debenzylation. In an attempt to avoid the aerial oxidation which complicates the ether extraction described above, the base was reduced as before in cold acid, and in the same solution was diazotised and treated with copper powder. Ultimately a small amount of a non-phenolic chlorine-free gum was obtained, which formed a *picrolonate* as minute yellow needles, m. p. 245° (Found : N, 16·6%). The analysis is not in agreement with that required by any obvious product.

Dipicrolonates of Aminobenzyl-N-*methyltetrahydro*isoquinolines.—These separated at once in crystalline form when hot alcoholic solutions of the bases and picrolonic acid were mixed. They were recrystallised from alcohol. 6′-*Amino*-3′ : 4′ : 5 : 6-*tetramethoxy*-1-

*benzyl-2-methyltetrahydro*isoquinoline *dipicrolonate* formed yellow clusters of radiating needles, m. p. 150° (decomp.) (Found: N, 15·0. $C_{21}H_{28}O_4N_2,2C_{10}H_8O_5N_4,2H_2O$ requires N, 15·0%). *2′-Amino-3′ : 4′ : 5 : 6-tetramethoxy-1-benzyl-2-methyltetrahydro*isoquinoline *dipicrolonate* formed yellow, sack-shaped prisms, m. p. 201° (decomp.) (Found: N, 15·2. $C_{21}H_{28}O_4N_2,2C_{10}H_8O_5N_4,2H_2O$ requires N, 15·0%). *2′-Amino-6 : 3′ : 4′-trimethoxy-1-benzyl-2-methyltetrahydro*isoquinoline *dipicrolonate* formed short, stout, yellow prisms with wedge-shaped ends, showing much cross-twinning, m. p. 207° (decomp.) (Found: N, 15·6. $C_{20}H_{26}O_3N_2,2C_{10}H_8O_5N_4,2H_2O$ requires N, 15·5%).

3-Benzyloxy-2 : 5 : 6-trimethoxyaporphine and 3-Hydroxy-2 : 5 : 6-trimethoxyaporphine (II).—The picrolonate (1·9 g.) of the base (VII) was ground with a cold mixture of concentrated sulphuric acid (1 c.c.) and methyl alcohol (20 c.c.), and the precipitated picrolonic acid (0·9 g.; 91%) was collected and washed with a little methyl alcohol. The filtrate and washings contained the base together with a little picrolonic acid, and were cooled in ice and diazotised by the gradual addition of the calculated amount of barium nitrite in concentrated aqueous solution. The diazonium salt solution was kept in the ice-chest for several hours, the barium sulphate removed by filtration, and the filtrate boiled gently under reflux for 30 minutes; during this treatment the colour changed from green to brown. The solution was cooled, neutralised to Congo-red paper by the addition of sodium acetate solution, and the methyl alcohol was removed under reduced pressure at 40°. The resulting yellow solution contained a small amount of brown solid, which was removed by filtration (charcoal), and the filtrate was made alkaline with ammonia and extracted repeatedly with ether. The extract was shaken with sodium hydroxide solution and then with water, dried, and evaporated, leaving 3-benzyloxy-2 : 5 : 6-trimethoxyaporphine as a brown oil (0·52 g.; 64%), which dissolved readily in dilute acetic acid. The picrate, picrolonate, chloroplatinate, and hydriodide were amorphous.

The base (0·5 g.) and concentrated hydrochloric acid (10 c.c.) were warmed at 50° for 30 minutes; oily drops of benzyl chloride were perceptible in the brown liquid. An equal volume of water and some charcoal were added, and the pale yellow filtrate was covered with a layer of ether and made alkaline with ammonia. Several extractions with ether removed the product, but much oxidation took place and the aqueous layer rapidly became deep green. The ether, which showed a faint blue fluorescence, was washed, dried, and distilled, leaving 3-hydroxy-2 : 5 : 6-trimethoxyaporphine as an almost colourless gum, which dissolved readily in

sodium hydroxide solution and in dilute acetic acid. With concentrated sulphuric acid a green coloration was developed, becoming reddish-brown at 100° : with nitric acid, the colour was orange-red. A solution in Mandelin's reagent was at first dull green, then sepia, claret, and finally violet-brown. A solution in Fröhde's reagent was at first colourless, then yellow, and became pale orange-brown at 100°.

Hydrolyses of Azlactones by Barium Hydroxide.—The aldehydes were converted into azlactones by standard methods, and in each case the azlactone (5 g.), barium hydroxide (20 g.), water (70 c.c.), and alcohol (10 c.c., to prevent frothing) were heated in an oil-bath under reflux until no more ammonia was evolved. The mixture was cooled, and the residual barium salt collected, washed with water, and decomposed by grinding with dilute hydrochloric acid. The crude arylpyruvic acid was collected and dried in a vacuum.

Aldehyde.	M. p. of crude arylpyruvic acid.	M. p. recorded in literature.	Yield %.
Piperonal	210°	215° (corr.) a.	85
Benzaldehyde	155	164 b.	25
Anisaldehyde	181	186 c.	23
Vanillin	—	—	Nil
m-Hydroxybenzaldehyde	—	—	,,
p-Hydroxybenzaldehyde	—	—	,,

a. Kropp and Decker, *Ber.*, 1909, **42**, 1188.
b. Bettziecke and Menger, *Z. physiol. Chem.*, 1927, **172**, 56.
c. Erlenmeyer and Wittenberg, *Annalen*, 1905, **337**, 294.

The unsuccessful hydrolysis of the azlactone of an *o*-nitro-aldehyde is recorded in Part III (this vol., p. 2890). The hydrolysis of the azlactone derived from *p*-nitrobenzaldehyde in the present conditions yielded no α-keto-acid, whilst the hydrolysis of the azlactone corresponding to *m*-nitrobenzaldehyde yielded only *m*-nitro-α-benzamidocinnamic acid (see below).

5-*Keto*-4-m- *and* -4-p-*nitrobenzylidene*-2-*phenyl*-4 : 5-*dihydro-oxazole.*—A mixture of *m*-nitrobenzaldehyde (5 g.), hippuric acid (6 g.), acetic anhydride (10 c.c.), and powdered anhydrous sodium acetate (3 g.) was heated on the water-bath until the azlactone separated. Water was added, and the heating continued for 30 minutes. The solid was collected, triturated with hot water, and recrystallised from alcohol. 5-*Keto*-4-m-*nitrobenzylidene*-2-*phenyl*-4 : 5-*dihydro-oxazole* (76% yield) separated in cream-coloured needles, m. p. 174° (Found : N, 9·7. $C_{16}H_{10}O_4N_2$ requires N, 9·5%).

5-*Keto*-4-p-*nitrobenzylidene*-2-*phenyl*-4 : 5-*dihydro-oxazole*, prepared from *p*-nitrobenzaldehyde in an exactly similar manner, formed yellow needles, m. p. 233° (Found : N, 9·7. $C_{16}H_{10}O_4N_2$ requires N, 9·5%).

m-*Nitro-α-benzamidocinnamic Acid.*—The azlactone (5 g.) was heated with barium hydroxide under the conditions detailed above until the evolution of ammonia had apparently ceased (4 days). The barium salt was collected and decomposed, and the solid crystallised from dilute acetic acid. The *acid* formed colourless needles, m. p. 223—224° (Found : C, 61·5; H, 3·7. $C_{16}H_{12}O_5N_2$ requires C, 61·5; H, 3·8%).

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[*Received, August 26th*, 1931.]