PART I

A general method for the synthesis of substituted Homophthalic acids
Introduction

The work described in the following pages include the synthesis of certain substituted homophthalic acids, such as (I), which are required in connection with the synthesis of polycyclic hydrocarbons now in progress in these laboratories.

\[
\begin{aligned}
H_2C & \hspace{1cm} \text{CH}_2 \\
\text{H} & \hspace{1cm} \text{C} \\
\text{H} & \hspace{1cm} \text{C} \\
& \hspace{1cm} \text{CO}_2\text{H} \\
\text{CO}_2\text{H} & \hspace{1cm} \text{H} \\
\end{aligned}
\]

(I)

Several methods are now available for the preparation of homophthalic acid itself in good overall yields. For example, phthalimide on reduction with zinc dust and boiling aqueous alkali readily affords phthalide\(^1\) and when this is heated with powdered potassium cyanide\(^2\) at 200\(^\circ\)C, the product on acidification produces the half nitrile of homophthalic acid from which pure homophthalic acid is obtained on further hydrolysis in the usual way, thus:

\[
\begin{aligned}
\text{Phthalimide} & \xrightarrow{\text{Zn, alkali}} \text{Phthalide} \\
\text{Phthalide} & \xrightarrow{\text{KCN}} \text{Homophthalic acid}
\end{aligned}
\]
It is also prepared by oxidation of Indene or \( \alpha \)-hydrindone with chromic acid, but the product is usually contaminated with appreciable quantity of phthalic acid as shown below:

\[
\begin{align*}
\text{CH}_2\text{CN} & \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{CH}_2\text{CO}_2\text{K} \\
\text{CH}_2\text{CH} & \quad \xrightarrow{\text{O}} \quad \text{CH}_2\text{CO}_2\text{H} + \text{CO}_2\text{H}
\end{align*}
\]

and from O-acetyl benzoic acid by the Willgerodt method:

\[
\begin{align*}
\text{COCH}_3 & \quad \xrightarrow{(\text{NH}_4)_2\text{Sx}} \quad \text{CH}_2\text{CONNH}_2 \\
\text{CO}_2\text{H} & \quad \xrightarrow{\text{Willgerodt reaction}} \quad \text{CO}_2\text{H}
\end{align*}
\]
For obvious reasons, these methods are not, however, applicable to the preparation of the homophthalic acid derivative (I) cited above.

Perkin and Robinson\(^6\) prepared 3:4-dimethoxy homophthalic acid in a series of interesting reactions as follows:

Veratraldehyde was condensed with ethyl acetate in the presence of powdered sodium giving 3:4-dimethoxy cinnamic acid with the simultaneous hydrolysis of the corresponding ester, first formed. The latter was reduced with sodium amalgam to

\[
\text{Veratraldehyde} + \text{CH}_3\text{CO}_2\text{H}_2 \rightarrow \text{3:4-dimethoxy cinnamic acid}
\]

\[
\text{3:4-dimethoxy cinnamic acid} \rightarrow \text{3:4-dimethoxy phenyl propionic acid}
\]

give 3:4-dimethoxy phenyl propionic acid, which on ring closure with phosphoric anhydride\(^7\) in moist benzene afforded 3:4-dimethoxy-\(\alpha\)-hydrindone (II). Amylnitrite and hydrochloric acid converted the latter into the corresponding isonitroso derivative (III). This on treatment with phosphorous pentachloride underwent molecular rearrangement yielding a solid product believed to be (IV) hydrolysed to (V) with hot aqueous sodium hydroxide.
Later, Haworth repeated these experiments and showed conclusively that the product of the rearrangement of the isonitroso derivative (III) is in reality the cyano-acid (VI) and not the isomeric product (IV) as suggested by Perkin and Robinson (loc. cit.), since the substance is soluble in organic solvents and in sodium bicarbonate and is rapidly hydrolysed on warming with sodium hydroxide or dilute hydrochloric acid. This view was confirmed by the observation that alkaline hydrogen peroxide converts it into 4:5-dimethoxy homophthalamic acid (VII) which is then converted into 4:5-dimethoxy homophthalimide on heating, which is an insoluble, high melting substance, identical with the product of the reaction of heat on ammonium 4:5-dimethoxy homophthalate (VIII).
The foregoing reactions have been found to be of general application and a wide variety of methoxy-, dimethoxy- and methylenedioxy-homophthalic acids have been prepared in this way by Haworth Perkin and Stevens\(^9\), Haworth, Koepfli and Perkin\(^10\) and by Chakravarti\(^11\).

It has been shown by Dieckmann\(^12\) that one of the two methylene hydrogen atoms in the ester of the homophthalic acid can be replaced by potassium, then by the benzyl group giving \(\omega\)-benzyl homophthalic acid m.p. 164°, in the usual way.
The methylene group of homophthalimide also retains this activity as is shown by the preparation of benzylidene derivative with benzaldehyde.

In the presence of alkalis reaction readily occurs with a variety of alkyl halides, phenacyl halides, acid anhydrides or chlorides, giving the substitution products which are, however, unstable.

(R = Alkyl, Phenacyl or Acyl groups; X = methyl or ethyl)
Reference should be made in this connection to the unsuccessful attempts made by Haworth\(^1\) for the synthesis of substituted homophthalic acids of the type (I), by the action of potassium cyanide on 6:7-dimethoxy-3-phenacyl phthalide\(^2\) (IX) and its relatives, which are accessible in wide variety.

Molecular structure of (IX)

This difficulty was, however, surmounted later by Bailey and Robinson\(^3\) in a more favourable case provided by 6:7-dimethoxy-3-(3':4'-dimethoxy phenacyl) phthalide\(^4\) (X) by the action of potassium cyanide in 2-methoxy ethanol solution at 100\(^\circ\), in the presence of sodium acetate to form \(\beta-(3':4'-dimethoxy benzoyl)-\langle-(2-carboxy-3:4-dimethoxy phenyl) propionitrile (XI)

Molecular structures of (X) and (XI)
The nitrile (XI) on treatment with alkaline hydrogen peroxide gave the corresponding amide (XII), and this on further hydrolysis with hot alkali yielded the substituted homophthalic acid derivative (XIII) precisely analogous to (I). The same substance (XI) on treatment with hot hydrochloric acid in acetic acid produces a yellow compound (XIV), from which on hydrolysis from hot sodium hydroxide, the above dibasic acid (XIII) is again obtained. The structure of the nitrogenous (XIV) rests on the following synthesis:
(XIV)
Nevertheless, these interesting series of reactions leading to the ketonic dicarboxylic acid (XIII), cannot, however, have any wide application, since, they require the use of O-aldehydo-benzoic acids, which are not accessible in large variety for synthetic purposes, except, for instance, phthalaldehydic acid and opianic acid.

In the present series of experiments an excellent general method for the synthesis of substituted homophthalic acids of the type (I), has been devised, starting from substituted hydindones having the general formula (XV), and this method appears to be the most convenient for the preparation of these substances.

(XV)
The first experiment to be tried out in this connection was the action of ethyl malonate on phenyl styryl ketone in presence of catalytic amount of sodium ethoxide which resulted in the formation of the adduct (XVI) in an almost quantitative yield. This on hydrolysis and elimination carbon dioxide in the usual way gave the ketonic acid (XVII), which on reduction either by Clemmensen's method or by finely divided nickel aluminium alloy in alkaline solution afforded the monocarboxylic acid (XVIII), m.p. 108°.
The same acid (m.p. 108°) could be prepared in an inferior yield by the action of magnesium phenylethyl bromide on ethyl benzylidene malonate (XIX) after hydrolyzing and decarboxylating the resulting product (XX). The acid (XVIII) was converted into the corresponding chloride with thionyl chloride and the latter on treatment with anhydrous aluminium chloride in dry petroleum ether (b.p. 60-80°) underwent internal ring closure giving the hydrindone derivative (XV) as an almost colourless liquid, b.p. 190-195°/4 mm. This however could not be characterised by the formation of a semicarbazone or 2,4-dinitrophenyl hydrazone under the usual conditions. On treatment with methyl nitrite under the conditions described in the experimental portion it readily formed the isonitroso derivative (XXI), m.p. 110°, in a high yield. This on treatment with p-Toluene sulphonyl chloride in presence of dilute alkali underwent molecular
rearrangement yielding the cyano acid (XXII) m.p. 135°-136°.

while on hydrolysis in excess of alkali gave the substituted homophthalic acid (I), m.p. 149°-150° in a good overall yield. This readily formed its anhydride (XXIII), b.p. 200°-205°/4 mm., on boiling with acetic anhydride. The anhydride exhibits a remarkable tendency to form the isocoumarin derivative (XXIV), m.p. 104° by intramolecular Friedel Crafts acylation on treatment with the anhydrous aluminium chloride in the usual way.

m-Methoxy benzaldehyde was then condensed with acetophenone to give the corresponding chalkone derivative (XXV), m.p. 64°-65°, which on reaction with ethyl malonate
in presence of traces of sodium ethoxide and subsequent hydrolysis of the adduct (XXVI), which was not isolated, furnished the dicarboxylic acid (XXVII), m.p. 154-155°.

This on elimination of carbon dioxide in the usual way gave the ketonic acid (XXVIII), m.p. 128-129°, which on reduction by Clemmensen's method afforded the mono-carboxylic acid (XXIX).
The acid (XXIX) was converted into the corresponding chloride with phosphorous pentachloride in dry benzene and the latter on treatment with fuming stannic chloride in cold, underwent internal ring closure giving the hydrindone derivative (XXX) as a thick colourless oil, b.p. 210-212°/3 mm. 2,4-dinitrophenylhydrazone, m.p. 206-207°. It is, however, notable that the other cyclising agents such as phosphorous pentaoxide in benzene and the usual Friedel Crafts reaction with anhydrous aluminium chloride gave a very poor yield of the hydrindone derivative. On treatment with methyl nitrite and concentrated hydrochloric acid in the usual way, it readily formed the isonitroso derivative (XXXI), m.p. 160-61°, in an excellent yield. This on treatment with p-Toluene sulphonyl chloride in presence of dilute alkali, underwent molecular rearrangement, furnishing the corresponding cyano acid (XXXII), m.p. 154-155°. This on heating with hot aqueous sodium hydroxide yielded the substituted homophthalic acid (XXXIII), m.p. 175° in an overall good yield.
m-Methoxy benzaldehyde likewise, on condensation with p-methoxy acetophenone gave the corresponding substituted chalcone (XXXIV), m.p. 97-98°, which on reaction with ethylmalonate under the usual conditions and subsequent hydrolysis of the adduct (XXXV) (which was not isolated) resulted in the formation of the dicarboxylic acid (XXXVI), m.p. 141°. This
acid on decarboxylation in the usual way gave the ketonic acid (XXXVII), m.p. 138-139°, which was reduced by Clemmensen’s method to the substituted valeric acid (XXXVIII), m.p. 99°.
The acid was treated with phosphorous pentachloride in benzene to give the corresponding chloride which was then cyclised by means of anhydrous stannic chloride in benzene under cold conditions to the corresponding hydrindone derivative (XXXIX) as a pale yellow viscous oil, b.p. 230-235°/3 mm., 2,4-dinitrophenylhydrazone m.p. 188-189°, in a good yield. The hydrindone was readily converted through the agency of methyl nitrite and hydrochloric acid into the isonitroso derivative (XL), m.p. 157-158°, in a high yield. This on
treatment with p-Toluene sulphonyl chloride in the usual conditions underwent intramolecular rearrangement resulting in the formation of the nitrile (XLI), m.p. 133-135°, which was hydrolysed with hot aqueous sodium hydroxide to the substituted homophthalic acid (XLII), m.p. 137°.
Veratric aldehyde was then condensed with acetophenone, in presence of dilute caustic soda and alcohol yielding 3,4-dimethoxy chalcone (XLIII) which on treatment with ethyl malonate in presence of traces of sodium ethoxide at the room temperature resulted in the formation of the adduct (XLIV) m.p. 88-89°, in a quantitative yield. On alkaline hydrolysis it yielded the malonic acid derivative (XLV) m.p. 176°.

This acid underwent decarboxylation on heating at 170-180° furnishing the ketonic acid (XLVI) m.p. 131°, which was reduced ether by finely divided nickel aluminium alloy in alkaline solution or by Clemmensen's method to the corresponding
substituted valeric acid \((XLVII)\) m.p. 90-91°. The foregoing acid was allowed to react with powdered phosphorous pentoxide in boiling benzene resulting in the formation of the hydrindone derivative \((XLVIII)\) in colourless needles, m.p. 111-112°; 2:4-dinitrophenyl hydrazone, m.p. 241-243°. The hydrindone on reaction with methyl nitrite and concentrated hydrochloric acid in the usual way, readily furnished the isonitroso derivative \((XLIX)\) m.p. 197-198°, in a good yield.

\[ \text{(XLVI)} \]

\[ \text{(XLVII)} \]

\[ \text{(XLVIII)} \]

\[ \text{(XLIX)} \]

This was treated with \(p\)-Toluene sulphony chloride in aqueous sodium hydroxide solution to effect the Bechmann rearrangement, yielding the carboxy-nitrile \((L)\) in almost colourless needles m.p. 106-108°, which on hydrolysis with an excess of
hot aqueous caustic soda solution leads to the formation of the substituted carboxy-butyric acid (I), m.p. 149-150°.

Similarly, veratic aldehyde on reaction with p-methoxy acetophenone in dilute alkaline medium formed the trimethoxy chalcone (II), m.p. 99°, which underwent condensation with ethyl malonate on refluxing, and the resulting malonic ester derivative (which was not isolated) on hydrolysis with alcoholic potassium hydroxide gave the keto-dicarboxylic acid (III). The acid on elimination of
of carbon dioxide in the usual way resulted in the formation of the keto-butyric acid (LIV), m.p. 137-138°, which on reduction with amalgamated zinc and concentrated hydrochloric acid in boiling toluene medium gave the substituted valeric acid (LV), m.p. 88-89°. The latter on reaction with powdered
phosphorous pentaoxide in boiling benzene was converted into the corresponding hydrindone derivative (LVI) as a yellow viscous oil b.p. 250-255°/5 mm. in an average yield. This was made to react with methyl nitrite and hydrochloric acid in methyl alcohol to give readily the substituted isonitroso hydrindone (LVII), m.p. 193-194° (decomp.), in a good yield.

This on treatment with freshly crystallized, p-Toluene sulphonyl chloride under the usual conditions, underwent
intramolecular rearrangement, giving the carboxy-nitrile (LVIII), m.p. 140-142°, which was hydrolysed by refluxing with aqueous sodium hydroxide for 16 hours, furnished the phosphthalic acid derivative (LIX) in fine colourless needles, m.p. 152-153°.

\[
\text{\begin{center}
\begin{tikzpicture}
\begin{scope}[scale=0.5]
\coordinate (A) at (0,0);
\coordinate (B) at (1,0);
\coordinate (C) at (1.5,0);
\coordinate (D) at (2,0);
\coordinate (E) at (2.5,0);
\coordinate (F) at (3,0);
\coordinate (G) at (3.5,0);
\coordinate (H) at (4,0);
\coordinate (I) at (4.5,0);
\coordinate (J) at (5,0);
\coordinate (K) at (5.5,0);
\coordinate (L) at (6,0);
\coordinate (M) at (6.5,0);
\coordinate (N) at (7,0);
\coordinate (O) at (7.5,0);
\coordinate (P) at (8,0);
\coordinate (Q) at (8.5,0);
\coordinate (R) at (9,0);
\coordinate (S) at (9.5,0);
\coordinate (T) at (10,0);
\coordinate (U) at (10.5,0);
\coordinate (V) at (11,0);
\coordinate (W) at (11.5,0);
\coordinate (X) at (12,0);
\coordinate (Y) at (12.5,0);
\coordinate (Z) at (13,0);
\draw (A) -- (B) -- (C) -- (D) -- (E) -- (F) -- (G) -- (H) -- (I) -- (J) -- (K) -- (L) -- (M) -- (N) -- (O) -- (P) -- (Q) -- (R) -- (S) -- (T) -- (U) -- (V) -- (W) -- (X) -- (Y) -- (Z);
\end{scope}
\end{tikzpicture}
\end{center}
\]

(LVIII)

\[
\text{\begin{center}
\begin{tikzpicture}
\begin{scope}[scale=0.5]
\coordinate (A) at (0,0);
\coordinate (B) at (1,0);
\coordinate (C) at (1.5,0);
\coordinate (D) at (2,0);
\coordinate (E) at (2.5,0);
\coordinate (F) at (3,0);
\coordinate (G) at (3.5,0);
\coordinate (H) at (4,0);
\coordinate (I) at (4.5,0);
\coordinate (J) at (5,0);
\coordinate (K) at (5.5,0);
\coordinate (L) at (6,0);
\coordinate (M) at (6.5,0);
\coordinate (N) at (7,0);
\coordinate (O) at (7.5,0);
\coordinate (P) at (8,0);
\coordinate (Q) at (8.5,0);
\coordinate (R) at (9,0);
\coordinate (S) at (9.5,0);
\coordinate (T) at (10,0);
\coordinate (U) at (10.5,0);
\coordinate (V) at (11,0);
\coordinate (W) at (11.5,0);
\coordinate (X) at (12,0);
\coordinate (Y) at (12.5,0);
\coordinate (Z) at (13,0);
\draw (A) -- (B) -- (C) -- (D) -- (E) -- (F) -- (G) -- (H) -- (I) -- (J) -- (K) -- (L) -- (M) -- (N) -- (O) -- (P) -- (Q) -- (R) -- (S) -- (T) -- (U) -- (V) -- (W) -- (X) -- (Y) -- (Z);
\end{scope}
\end{tikzpicture}
\end{center}
\]

(LIX)

3,4,3',4'-tetra methoxy chalkone was prepared according to the known method\textsuperscript{26} and refluxed with diethyl malonate in alcohol for 3 hours in presence of a little amount of sodium ethoxide, and the adduct on subsequent hydrolysis, in the usual way yielded the keto dicarboxylic acid (LX) in colourless silky needles, m.p. 180-181°. The acid on heating, underwent decarboxylation furnishing the
ketonic acid (LXI) in colourless prisms, m.p. 150-151°, which on reduction according to the method of Clemmensen, resulted in the formation of a gummy mass which was remethylated in the usual way, to give the substituted valeric acid (LXII), m.p. 107-108°. The acid was treated with powdered phosphorous pentao-
oxide in hot benzene to effect the intramolecular ring closure giving the tetramethoxy hydrindone derivative (LXIII) as a pale yellow semi solid, b.p. 260-266°C/2 mm., in about 50 per cent yield, 2,4-dinitrophenyl hydrazone, m.p. 186-187°C. This was treated with methyl nitrite and concentrated hydrochloric acid to give the isonitroso hydrindone (XLIV), m.p. 166-167°C.

![Chemical structure of LXIII](image1)

![Chemical structure of LXIV](image2)

The above isonitroso derivative was treated with p-Toluenesulphony chloride in dilute aqueous alkali to undergo the molecular rearrangement giving the corresponding nitrile (LXV) as a gummy mass which could not be purified and was directly hydrolysed in the usual way to give the substituted homophthalic acid (LXVI), m.p. 114°C.
O-veratric aldehyde on treatment with acetophenone, under the conditions described in the experimental, resulted in the formation of 2,3-dimethoxy chalcone (LXVII) as a yellow viscous oil, b.p. 225-230°/3 mm., which was allowed to condense with diethyl malonate in the usual way at room temperature and the reaction product on alkaline hydrolysis gave the keto-dicarboxylic acid (LXVIII) in fine colourless needles, m.p. 157°.
The above acid on elimination of carbon dioxide in the usual way furnished the ketonic acid (LXIX), m.p. 135°, which was reduced by amalgamated zinc and hydrochloric acid in boiling toluene to give an impure product which was purified by methylation to the monocarboxylic acid (LXX), m.p. 65°. To cyclise the foregoing acid chloride prepared from phosphorous pentachloride in the usual way, anhydrous stannic chloride was found to be the reagent of choice, giving the hydrindone (LXXI) as a colourless crystalline solid, m.p. 132-133°, in a high yield, 2,4-dinitrophenyl hydrazone, m.p. 203-204° and semicarbazone, m.p. 190°. The hydrindone was converted into the corresponding isonitroso derivative (LXXII), m.p. 121-122°, using methyl nitrite and hydrochloric acid in the usual way.
This underwent molecular rearrangement into the cyano acid (LXXIII), m.p. 156-157°, through the agency of p-Toluene sulphonyl chloride in dilute alkali, which was converted into the corresponding substituted homophthalic acid (LXXIV), m.p. 178-179° in good overall yield.

\[ \text{(LXXIII)} \]
\[ \text{(LXXIV)} \]

O-v eratic aldehyde, likewise, on condensation with p-methoxy acetophenone in the usual way, readily furnished the substituted phenyl styryl ketone (LXXV), m.p. 104-105°, which on reaction with ethyl malonate in presence of a little sodium ethoxide, and subsequent hydrolysis of the adduct resulted in the formation of the keto-dicarboxylic acid (LXXVI), m.p. 115-116°. This was decarboxylated in the usual way to give the...
ketonic acid (LXXVII), m.p. 139-140°, which on reduction according to Clemmensen's method afforded the substituted valeric acid (LXXVIII), m.p. 71-72°. This acid on treatment
with phosphorous pentachloride in benzene formed the acid chloride which under-went intramolecular ring closure by means of fuming stannic chloride in benzene, under the conditions described in the experimental, to give the hydrindone derivative (LXXIX) in colourless fine prisms, m.p. 115-116°, 2,4-dinitrophenyl hydrazone, m.p. 189-191°, and the semicarbazone, m.p. 172-173°. On treatment with methyl nitrite and concentrated hydrochloric acid in methanol, it formed the isonitroso hydrindone (LXXX), m.p. 133-134°, in a good yield. This
on reaction with p-Toluene sulphonyl chloride in presence of dilute alkali, underwent molecular rearrangement, yielding the carboxy-nitrile \( \text{LXXXI} \), m.p. 173-174°, which on heating with 10 per cent aqueous sodium hydroxide furnished the corresponding dicarboxylic acid \( \text{LXXXXII} \), in fine colourless prisms, m.p. 177-178°.

3:4-methylenedioxy chalkone \( \text{LXXXIII} \) required in this series was prepared by the action of dilute sodium hydroxide on a ethanolic solution of piperonal and acetophenone, which was allowed to react with ethyl malonate in presence of catalytic amount of sodium ethoxide in alcohol and refluxing for two hours. The adduct on subsequent hydrolysis in the usual way furnished the keto-dicarboxylic acid \( \text{LXXXIV} \), m.p.
156-157°. On elimination of carbon dioxide, it gave the ketonic acid (LXXXV), m.p. 153-154°, which was reduced according to Clemmensen's method to the corresponding monocarboxylic acid (LXXXVI), m.p. 132°. This acid was cyclised, through the
agency of phosphorus pentoxide in boiling benzene to the hydrindone derivative (LXXXVII) in colourless needles, m.p. 108-109°, 2,4-dinitrophenyl hydrazine, m.p. 220-221°, and semicarbazone, m.p. 200-201°. On treatment with methyl nitrite and hydrochloric acid in the usual manner yielded the isonitroso derivative (LXXXVIII), m.p. 176-177°. This on treatment with p-Toluene sulphonyl chloride in dilute caustic soda, underwent Beckmann transformation, giving the carboxy-nitrile (LXXXIX), m.p. 108-110°, which on heating with an excess of aqueous sodium hydroxide resulted in the formation of the substituted homophthalic acid (LXL), in almost colourless needles, m.p. 149-151°.

\[ \text{LXXXVII} \quad \text{LXXXVIII} \]

\[ \text{LXXXIX} \quad \text{LXL} \]
Piperonal, likewise on condensation with p-methoxy acetophenone under the usual conditions, readily afforded the substituted chalcone (LXLI), m.p. 135-136°, which on reaction with ethyl malonate at 100° in the usual way and the subsequent hydrolysis of the adduct with hot alcoholic potassium hydroxide, yielded the keto-dicarboxylic acid (LXLI) in fine colourless needles, m.p. 141-142°. On heating at 170-180° for 1 hour, it underwent decarboxylation to give the ketonic acid (LXIII), m.p. 154-155°, which was reduced by
means of amalgamated zinc and hydrochloric acid in boiling toluene, furnished the substituted valeric acid (LXLIV), m.p. 118-119°. The latter on cyclisation with powdered phosphorous pentaoxide in boiling benzene, lead to the formation of the hydrindone derivative (LXLV) as a yellow viscous oil, b.p. 275-280°/2 mm., which was characterized by the formation of 2:4-dinitrophenyl hydrazone, m.p. 232-233°. The action of methyl nitrite and hydrochloric acid in the usual way gave the isonitroso hydrindone (LXLVI) in pale yellow needles, m.p. 166-167°, which was converted through the agency of p-Toluenesulphonyl chloride and a solution of 10 per cent aqueous caustic soda (Beckmann rearrangement) into the cyano acid (LXLVII), m.p. 124-126°. The latter on
boiling with aqueous sodium hydroxide gave the substituted dicarboxylic acid (LXLVIII), in diamond shaped colourless prisms. m.p. 172°
Finally, propenal on treatment with acetoveratrole under the usual conditions resulted in the formation of 3:4-methyleneoxy-3':4'-dimethoxy chalcone (LXLIX), m.p. 132°. On reaction with diethylmalonate in presence of traces of sodium ethoxide in alcohol for 24 hours at 100°, and subsequent hydrolysis of the adduct, gave the keto-dicarboxylic acid (II) as a dark gummy mass which could not be induced to
crystallise. This however, on elimination of carbon dioxide in the usual way, furnished the ketonic acid (II), in light brown needles, m.p. 125°, which was reduced to the corresponding valeric acid (ILIII), m.p. 102-103°, in the usual way. It was converted into the corresponding chloride by means of phosphorous pentachloride in dry benzene, and the latter on treatment with anhydrous stannic chloride under cold conditions, underwent cyclisation, giving the hydrindone derivative (III) as a yellow viscous oil, b.p. 250-255°/2 mm., 2:4-dinitrophenyl hydrazone, m.p. 209-210°. This was converted into the isonitroso derivative (IV), m.p. 160-161°, by means of methyl nitrite and hydrochloric acid. On treating with p-Toluene sulphonyl chloride, the latter underwent
Beckmann transformation giving the carboxy nitrile (LLV), m.p. 124-126°, which was boiled with 10 per cent aqueous caustic soda solution, resulting in the formation of \( \alpha-(2\text{-carboxy-4:5\text{-methylenedioxy phenyl})-\gamma (3':4'-dimethoxy phenyl) butyric acid (LLVI) in colourless needles, m.p. 152-153°. \)
Attempts to utilize the dibasic acid (I) and/or its anhydride (XXIII) for the synthesis of polycyclic systems did not prove to be successful. Although the anhydride (XXIII) readily underwent Friedel Crafts ring closure in presence of anhydrous aluminium chloride with the formation of the isocoumarin derivative (XXIV) in a good yield, the latter could not be converted into the ketonic acid (LLVII) or into its ester. Similarly the action of magnesium methyl iodide on this isocoumarin derivative (XXIV) did not proceed in the expected way, giving the unsaturated ketone (LLVIII).
It is interesting to note that according to Turner\textsuperscript{27} the enol-lactone (LLX) under similar conditions furnishes cholestenone (LLX) in a moderate yield and also the lactone

\[ \text{Enol-lactone (LLX)} \xrightarrow{\text{MgCH}_3\text{I}} \text{(Intermediate Compound)} \]

\[ \text{Cholestenone (LLX)} \]

(LLXI) smoothly affords the unsaturated ketone (LLXII) as shown by Heard and Ziegler\textsuperscript{28}. 
The other methods of synthesis proved equally abortive. It is, however, hoped to utilize the derivatives of hydrindone (XV, XXX, XXXIX, XLVIII, LVI, LXIII, LXXI, LXXIX, LXXXVII, LXV, LLIII) encountered in the above series of investigations, for the synthesis of 1:2-benzofluorene and its derivatives.
A. Synthesis of 3', 4'-dihydro-naphtho(1', 2', 3': 4') isocoumarin.

Benzalacetophenone was obtained according to the procedure given in Practical Organic Chemistry by Vogel, 3rd. page 718. After recrystallisation from alcohol, it formed pale yellow needles, m.p. 56-57°.

β-Phenyl-γ-benzoyl butyric acid \((\text{XVII})\). - Benzalacetophenone was condensed with ethylmalonate according to known method \((\text{loc. cit.})\) and the adduct on hydrolysis and elimination of carbon dioxide was converted into β-phenyl-γ-benzoyl butyric acid, m.p. 159-160° (alcohol) \((\text{loc. cit.})\).

β-6-Diphenyl valeric acid \((\text{XVIII})\). - Method (a). - The above keto acid (30 g.) was dissolved in an aqueous solution of caustic soda (900 c.c.) of 10 per cent and heated on a water-bath at 90-95° and Nickel aluminium alloy (90 g.) \((\text{loc. cit.})\) was added in small portions (2-3 g.) with vigorous stirring. The reaction mixture was stirred for another hour at 90-95°, water being added from time to time to maintain the volume of mixture constant. The mixture was heated further with the addition of 10 per cent caustic soda solution (150 c.c.) and Nickel aluminium alloy (15 g.), as before. The hot solution was filtered and the residue washed thoroughly with water. The filtrate on cooling was acidified with concentrated hydrochloric acid with stirring, and the viscous oil which separated on standing solidified to a crystalline product. On crystallisation
from dilute acetic acid, \( \beta-5\text{-diphenyl valeric acid} \) formed colourless prisms, m.p. 108°. Yield 27 g.

0.0987 g. gave 0.2896 g. CO₂ and 0.0621 g. H₂O

Found: C, 80.1; H, 7.0

\( \text{C}_{17}\text{H}_{18}\text{O}_2 \) requires C, 80.3; H, 7.1 per cent.

\( \beta-5\text{-diphenyl valeric acid} \) was also obtained by the Clemmensen's reduction of \( \beta\text{-phenyl-\( \gamma \text{-benzoyl butyric acid} \)} \), as follows:

The foregoing keto acid (XVII) (20 g.) was heated under reflux with a mixture of Toluene (75 c.c.), 5 per cent acetic acid (50 c.c.) concentrated hydrochloric acid (50 c.c.) and amalgamated zinc (60 g.) on a sand-bath for 60 hours. Hydrochloric acid (15 c.c.) being added every 12 hours. After cooling the toluene layer was separated and washed well with water, and extracted with a 10 per cent solution of sodium carbonate. The alkaline solution was washed, acidified with hydrochloric acid to give a heavy oil, which solidified on standing. On recrystallisation from dilute acetic acid, \( \beta-5\text{-diphenyl valeric acid} \) formed colourless prisms, m.p. 108° as before. Yield 17 g.

Method (b). - Grignard reaction of phenylethyl bromide with benzylidene malonate (XIX). - Formation of ethyl-2:4-\( \beta\text{-diphenyl propyl malonate} \) (XX). - The Grignard reagent was prepared by refluxing a mixture of magnesium (2.7 g.), Iodine (0.1 g.) phenyl ethyl bromide (19.2 g.) and dry ether (200 c.c.) on the water-bath for 10 hours. Benzyl-
dene malonate (24.5 g.) prepared in the usual way (loc. cit.) was covered with dry ether (100 c.c.) and to the solution cooled in the freezing mixture, Grignard reagent prepared above was added drop by drop with shaking and the reaction mixture was left overnight in the ice chest. The Grignard complex was decomposed with a saturated solution of ammonium chloride and extracted with ether. The ethereal layer was washed several times with water and dried over anhydrous magnesium sulfate. The solvent removed and the residue fractionated under reduced pressure. Unchanged benzylidene malonate (15 g.) was recovered at 158-164°/6 mm. and finally Ethyl-2,4-diphenyl propyl malonate distilled as a colourless oil, b.p. 212-215°/6 mm. Yield 11g.

0.1035 g. gave 0.2827 g. CO₂ and 0.0670 g. H₂O

Found: C, 74.5; H, 7.2

C₂₂H₂₆O₄ requires C, 74.6; H, 7.3 per cent.

The foregoing malonic ester (XX) (10 g.) was heated under reflux on a water-bath with a solution of potassium hydroxide (5.5 g.) in water (6 c.c.) and alcohol (22 c.c.) for about an hour. The excess of alcohol was evaporated and the residue diluted with water. It was then extracted with ether to remove any neutral matter. The clear alkaline solution was acidified with concentrated hydrochloric acid, whereby a crystalline solid separated, which was collected and washed well with water. On recrystallization from dilute alcohol, 2,4-diphenyl propyl malonic acid (6 g.) formed fine colourless needles, m.p. 79-80°.
0.1106 g. gave 0.2940 g. CO₂ and 0.0617 g. H₂O

\[ \text{Found: C, 72.5; H, 6.2} \]

\[ \text{C}_{18}H_{16}O_{4} \text{ requires C, 72.4; H, 6.0 per cent.} \]

\( \beta-S \)-diphenyl valeric acid (XVIII). - The foregoing acid (5 g.) was decarboxylated by heating in an oil-bath at 140-150° for about an hour, until the evolution of carbon dioxide ceased. After cooling the residue was extracted with boiling 10 per cent sodium carbonate and filtered. The filtrate cooled and acidified with hydrochloric acid to give a crystalline solid, m.p. 104-106°. On recrystallisation from dilute acetic acid, \( \beta-S \)-diphenyl valeric acid formed colourless prisms, m.p. 108° as described before. Yield 3.9 g.

3-Phenylethyl hydridone (XV). - The preceding acid (XVIII) (30 g.) taken in a 100 c.c. distilling flask fitted with a baby bulb condenser and a calcium chloride guard tube, was treated with freshly distilled thionyl chloride (8.8 c.c.) at 40-50° on a water-bath with occasional shaking (until the evolution of hydrochloric acid gas ceased) for 2 hours. Excess of thionyl chloride was removed on the water pump. The crude product was dissolved in dry petroleum ether (70 c.c.) (b.p. 60-80°) and the solution added to a suspension of powdered anhydrous aluminium chloride (26 g.) in dry petroleum ether (80 c.c.) (b.p. 60-80°). The reaction mixture was heated under reflux on a water-bath for three hours, with occasional shaking. After cooling the dark brown complex was decomposed with crushed ice and concentrated hydrochloric acid. It was heated on a water-bath for half an hour to complete the decom-
position. The oily product was extracted with ether, washed successively with water, 10 per cent sodium carbonate solution and water, dried over fused calcium chloride and the solvent removed. The pure 3-Phenylethyl hydriindo (17 g.) passed over as a pale yellow viscous liquid, b.p. 190-195°/4 mm.

0.1032 g. gave 0.3273 g. CO₂ and 0.0631 g. H₂O

Found: C, 86.5; H, 6.8

C₁₇H₁₆O requires C, 86.4; H, 6.8 per cent.

3-Phenylethyl-2-isonitroso-1-hydriindo (XXI): Method (a). The preceding hydriindo (XV) (17 g.) was dissolved in methyl alcohol (15 c.c.), isoamyl nitrite (5 c.c.) (prepared according to the method given in Practical Organic Chemistry by Vogel, page 306, edition 3rd.) was added, followed by concentrated hydrochloric acid (3 c.c.). The reaction mixture was maintained at 50° on a water-bath for half an hour with vigorous shaking. After keeping overnight in the refrigerator the iso-nitroso hydriindo separated as a yellow crystalline solid. On recrystallisation from alcohol 3-Phenylethyl-2-isonitroso-1-hydriindo formed yellow prisms, m.p. 118° (decomp.). Yield 3 g.

Method (b). 3-Phenylethyl hydriindo (XV) (5 g.) was dissolved in methyl alcohol (15 c.c.) and mixed with concentrated hydrochloric acid (3 c.c.). The mixture was slightly cooled in an ice-bath and methyl nitrite gas (loc. cit.) was passed into it, until no more absorption took place. The iso-nitroso derivative gradually separated out in shining yellow crystals and on recrystallisation from alcohol it formed yellow shining prisms, m.p. 118° (decomp.). Yield 4.5 g. Most of the product was prepared according to this method.
0.1124 g. gave 0.3173 g. CO₂ and 0.0556 g. H₂O

Found: C, 77.0; H, 5.5

C₁₇H₁₅O₂N requires C, 77.0; H, 5.6 per cent.

3-Phenyl-1-O-carboxy phenyl butyronitrile (XXII). The foregoing isonitroso hydridone (XXI) (8 g.) was dissolved in 10 per cent sodium hydroxide solution (70 c.c.) and treated gradually with p-toluene sulphonyl chloride (8 g.) (freshly crystallized from petroleum ether, b.p. 40-60°) with shaking.

The reaction was completed by heating the reaction mixture on a water-bath for ten minutes. After cooling the alkaline solution was filtered and acidified with hydrochloric acid, whereby the nitrile separated as a somewhat gummy mass, which gradually solidified on standing overnight. On recrystallization from dilute alcohol, 3-phenyl-1-O-carboxy phenyl butyronitrile formed pale yellow needles, m.p. 135-136°. Yield 7.5 g.

0.1005 g. gave 0.2837 g. CO₂ and 0.0496 g. H₂O

Found: C, 77.0; H, 5.5

C₁₇H₁₅O₂N requires C, 77.0; H, 5.6 per cent.

3-Phenyl-1-(O-carboxy phenyl)butyric acid (I). The preceding nitrile (XXII) (7 g.) was dissolved in aqueous 10 per cent sodium hydroxide solution (70 c.c.) and heated under reflux on a sand-bath for about 7 hours, until the evolution of ammonia gas ceased. After cooling the alkaline solution was filtered and acidified with hydrochloric acid. The gummy mass which separated, solidified gradually on keeping and
rubbing with alcohol and petroleum ether, (b.p. 40-60°).

On recrystallisation from dilute acetic acid, 3-Phenyl-1-(O-carboxy phenyl)butyric acid formed almost colourless prisms, m.p. 149-150°. Yield 6.8 g.

0.1123 g. gave 0.2959 g. CO₂ and 0.0556 g. H₂O

Found: C, 71.8; H, 5.5
C₁₇H₁₆O₄ requires C, 71.8; H, 5.6 per cent

3-Phenyl-1-(O-carboxy phenyl)butyric acid anhydride (XXIII).— The foregoing dibasic acid (6.3 g.) was heated under reflux on a sand-bath with freshly distilled acetic acid anhydride (19 c.c.) for about 3 hours. The excess of acetic acid anhydride was removed carefully on the water pump. The residue was then distilled under reduced pressure giving anhydride (XXIII) as a slight yellow viscous mass, b.p. 200-205°/4 mm. Yield 4 g.

0.1128 g. gave 0.3146 g. CO₂ and 0.0685 g. H₂O

Found: C, 76.5; H, 5.4
C₁₇H₁₄O₂ requires C, 76.5; H, 5.3 per cent

3′,4′-Dihydro-naphtho[1′:2′:3′:4′]isocoumarin (XXIV).— A solution of the foregoing anhydride (XXIII) (3.5 g.) in dry nitrobenzene (20 c.c.) was gradually added to a suspension of powdered anhydrous aluminium chloride (6.5 g.) in nitrobenzene (40 c.c.), cooled to 0° in the freezing mixture. The reaction mixture was kept for 2 hours in the ice-bath and then left for 48 hours at the room temperature. The resulting product was decomposed with the addition of powdered ice and
hydrochloric acid. The excess of nitrobenzene was removed by steam distillation and the residue dissolved in ether. The ethereal layer was washed successively with water, 10 per cent sodium carbonate solution and again with water and dried. The ether was removed by distillation to give a crystalline solid. On recrystallisation from acetic acid (charcoal), 3'-4'-Dihydro-naphtho(1'-2';3,4)iso Coumarin formed colourless needles, m.p. 104°. Yield 3.2 g.

0.1125 g. gave 0.3386 g. CO₂ and 0.0506 H₂O

Found: C, 82.1; H, 5.0

C₁₇H₁₈O₂ requires C, 82.3; H, 4.9 per cent

All attempts to prepare the corresponding keto-acid (LLVII) were, however, unsuccessful.

B. Synthesis of 3-(2-carboxy-5-methoxy phenyl)-γ-phenyl butyric acid.

3-Methoxy chalkone (m-methoxy benzylidene acetophenone) (XXV).—Aqueous sodium hydroxide (40 c.c. of 10%) was gradually added to a solution of m-methoxy benzaldehyde (24 g.) (prepared according to the method given in Organic synthesis, Collective Volume 3rd, page 564) and acetophenone (21 g.) in alcohol (100 c.c.) with vigorous shaking. In about 5 minutes the clear solution became turbid, with evolution of heat and a heavy yellow oil separated, the shaking was continued for 2 hours and the reaction mixture left overnight in the ice chest, diluted with
water and the product extracted with ether. The ethereal layer was washed well with water and dried over fused magnesium sulphate. The solvent was removed and the residue distilled under reduced pressure. 3-Methoxy chalcone was collected as a yellow viscous oil, b.p. 200-205°/3 mm., which solidified on cooling. On recrystallisation from alcohol it formed light yellow prisms, m.p. 64-65°. Yield 35 g.

0.1132 g. gave 0.3345 g. CO₂ and 0.0611 g. H₂O

Found: C, 80.6; H, 6.0

C₁₆H₁₄O₂ requires C, 80.7; H, 5.9 per cent.

(-)-Carboxy-β-(3-methoxyphenyl)-γ-benzoyl butyric acid (XXVII):- To a solution of sodium ethoxide prepared by sodium (.25 g.) and absolute ethyl alcohol (35 c.c.), diethyl malonate (19 g.) was added followed by 3-methoxy chalcone (28 g.) with shaking, and the mixture was heated under reflux on the water-bath for about 20 minutes. The reaction product (XXVI) was hydrolysed by refluxing with a solution of potassium hydroxide (28 g.) in water (100 c.c.) and alcohol (30 c.c.) on the water-bath for an hour. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether to remove any neutral matter. The clear alkaline solution was acidified with hydrochloric acid, giving a viscous oil which solidified to a crystalline mass on cooling and standing. On recrystallisation from dilute alcohol (-)-carboxy-β-(3-methoxy phenyl)-γ-benzoyl butyric acid formed colourless needles, m.p. 154-155°. Yield 38 g.
0.1160 g. gave 0.2833 g. CO₂ and 0.0564 g. H₂O
Found: C, 66.6; H, 5.4
C₁₀H₁₈O₆ requires C, 66.7; H, 5.3 per cent

β-(3-methoxyphenyl)-γ-benzoyl butyric acid (XXVIII). - The foregoing acid (XXVII) (36 g.) was decarboxylated by heating in an oil-bath at 170-180°, until evolution of carbon dioxide ceased (1 hour). On cooling the residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The cooled alkaline solution was acidified with hydrochloric acid to give a crystalline solid. On recrystallisation from alcohol β-(3-methoxyphenyl)-γ-benzoyl butyric acid formed long colourless needles, m.p. 128-129°. Yield 30 g.

0.1012 g. gave 0.2695 g. CO₂ and 0.0556 g. H₂O
Found: C, 72.6; H, 6.1
C₁₉H₁₉O₄ requires C, 72.5; H, 6.4 per cent

β-(3-methoxyphenyl)-5-phenyl valeric acid (XXIX). - The preceding keto-acid (XXVIII) (28 g.) was reduced by heating under reflux with a mixture of Toluene (120 c.c.), 5 per cent acetic acid (60 c.c.), concentrated hydrochloric acid (50 c.c.) and amalgamated zinc (80 g.) for 48 hours. Hydrochloric acid (20 c.c.) being added every 12 hours. After cooling the toluene layer was separated, washed well with water and extracted with a 10 per cent sodium carbonate solution. The alkaline solution was acidified with hydrochloric acid to give viscous oil, which did not solidify. It was purified by dissolving in 5 per cent sodium hydroxide (250 c.c.) and treating with dimethyl sulphate (8 c.c.) at about 80° for an
hour with shaking. The alkaline solution was boiled with animal charcoal and filtered. The filtrate was acidified with hydrochloric acid to give an almost colourless semi solid (24 g.) which was collected and dried in a vacuum desiccator.

0.1228 g. gave 0.3441 g. CO₂ and 0.0796 g. H₂O
Found: C, 76.4; H, 7.2
C₁₈H₂₀O₃ requires C, 76.1; H, 7.0 per cent

5-Methoxy-3-phenylethyl-1-hydridone (XXIX). - The foregoing acid (XXIX) (5.68 g., 0.02 mole) dissolved in dry benzene (30 c.c.) was treated gradually with powdered phosphorous pentachloride (4.4 g.) with swirling and cooling in ice water. The reaction started almost immediately, which was left at room temperature, until the whole phosphorous pentachloride went into solution (1 hour). The reaction mixture was heated on a water-bath for 5 minutes and then cooled in the freezing mixture, and when benzene began to crystallize, stannic chloride (8 c.c.) mixed with dry benzene (8 c.c.) were added to it all at once. The reaction mixture was left in the freezing mixture for half an hour. Hydrochloric acid and powdered ice were added to decompose the dark coloured complex. The product was extracted with ether. The ethereal layer washed thrice with 5 per cent hydrochloric acid, water, 5 per cent sodium hydroxide solution, again with water and dried over anhydrous sodium sulphate. The solvent was removed by distillation. The residue was distilled under reduced pressure. 5-Methoxy-3-phenylethyl-1-hydridone was collected as a thick colourless oil, b.p. 210-212°. Yield 3.8 g.
0.0998 g. gave 0.2975 g. CO₂ and 0.0602 g. H₂O
  Found: C, 81.3; H, 6.7
C₁₈H₁₈O₂ requires C, 81.2; H, 6.8 per cent

2,4-dinitrophenyl hydrazone prepared in methanol on recrystal-
  lization from glacial acetic acid formed brick red needles,
m.p. 206-207°.

0.0612 g. gave 0.1981 g. CO₂ and 0.0358 g. H₂O
  Found: C, 64.5; H, 4.9
C₂₄H₂₂O₅N₄ requires C, 64.6; H, 4.9 per cent

5-Methoxy-3-phenylethyl-2-isonitroso-1-hydrindone
(XXXI).— The foregoing hydrindone (XXX) (3 g.) was dissolved
  in methyl alcohol (15 c.c.) and mixed with concentrated hydro-
  chloric acid (2 c.c.), methyl nitrite was passed into it, until
  no more absorption took place. The excess of methyl alcohol
  was evaporated, the residue was diluted with water and extrac-
  ted with ether. The ethereal solution washed with water, was
  thoroughly extracted with 5 per cent aqueous sodium hydroxide
  solution. The alkaline solution was acidified with hydrochloric
  acid whereby a light brown heavy oil separated which solidified
  on standing. On recrystallisation from dilute alcohol, 5-methoxy-
  3-phenylethyl-2-isonitroso-1-hydrindone formed shining yellow
  prisms, m.p. 160-161°. Yield 2.8 g.

0.0932 g. gave 0.2505 g. CO₂ and 0.0478 g. H₂O
  Found: C, 73.3; H, 5.7
C₁₈H₁₇O₃N₄ requires C, 73.2; H, 5.8 per cent
α-(2-carboxy-5-methoxy phenyl)-γ-phenyl butyric acid (XXXII). - The foregoing isonitroso hydrazidine (XXXI) (2.4 g.) was dissolved in aqueous 10 per cent sodium hydroxide solution (24 c.c.) and treated gradually with p-Toluene sulphonyl chloride (2.5 g.) with shaking. The reaction was completed by heating the mixture on a water-bath for about 10 minutes. After cooling the alkaline solution was filtered and acidified with hydrochloric acid to give gummy mass which solidified on standing overnight. On recrystallisation from dilute alcohol in almost colourless crystals, the nitrile (XXXII) had m.p. 154-155°. Yield 2.3 g.

0.1007 g. gave 0.2699 g. CO₂ and 0.0544 g. H₂O

Found: C, 73.1; H, 6.0

C₁₈H₁₈O₅N requires C, 73.2; H, 5.8 per cent

α-(2-carboxy-5-methoxyphenyl)-γ-phenyl butyric acid (XXXII). - The foregoing nitrile (XXXII) (1.5 g.) was hydrolysed by heating under reflux with a 10 per cent sodium hydroxide solution (16 c.c.) on the sand-bath, until the evolution of ammonia gas ceased (8 hours). After cooling the alkaline solution was filtered and acidified with concentrated hydrochloric acid to give a gummy product which solidified on standing. On double crystallisation from acetic acid (charcoal), α-(2-carboxy-5-methoxyphenyl)-γ-phenyl butyric acid formed fine almost colourless prisms, m.p. 175°. Yield 1.35 g.

0.1016 g. gave 0.2560 g. CO₂ and 0.0512 g. H₂O

Found: C, 68.7; H, 5.6

C₁₈H₁₈O₅ requires C, 68.8; H, 5.7 per cent
C. Synthesis of $\beta$-(2-carboxy-5-methoxy phenyl)-\(\gamma\)-(4'-methoxy-phenyl) butyric Acid.

3:4'-dimethoxy chalcone, (m-methoxy benzylidene p-methoxy acetophenone (XXXIV). Aqueous 10 per cent sodium hydroxide solution (25 c.c.) was gradually added to a solution of m-methoxy benzaldehyde (16 g.) and p-methoxy acetophenone (loc. cit.) (18 g.) with vigorous shaking at room temperature. In about 15 minutes the clear solution became turbid, with evolution of heat and a thick oil separated which solidified on cooling. The solid was collected by filtration, washed well with water and a little alcohol. On recrystallisation from alcohol, 3:4'-dimethoxy chalcone formed fine yellow needles, m.p. 97-98°. Yield 30 g.

0.1102 g. gave 0.3020 g. CO₂ and 0.0565 g. H₂O Found: C, 76.2; H, 5.7
C₁₇H₁₆O₃ requires C, 76.1; H, 5.9 per cent

$\beta$-Carboxy-\(\beta\)-(3-methoxy phenyl)-\(\gamma\)-(4'-methoxy benzyl) butyric acid (XXXVI). - To a solution of sodium ethoxide prepared from sodium (0.3 g.) and absolute alcohol (50 c.c.), diethyl malonate (16 g.) was added, followed by 3:4'-dimethoxy chalcone (26.8 g.). The reaction mixture was heated under reflux on the water-bath for 1½ hours. The reaction product (XXXV) was hydrolysed by refluxing on the water-bath, with potassium hydroxide (24 g.) dissolved in water (80 c.c.) and alcohol (25 c.c.). The excess of alcohol was removed by evaporation, the residue diluted with water
and extracted with ether to remove the neutral matter. The alkaline solution was acidified with hydrochloric acid to give a heavy oil which solidified on standing. On recrystallization from dilute alcohol, α-carboxy-β(3'-methoxy phenyl)-γ(4'-methoxy benzoyl) butyric acid formed fine colourless needles, m.p. 141°. Yield 32 g.

0.1182 g. gave 0.2791 g. CO₂ and 0.0585 g. H₂O

Found: C, 64.4; H, 5.5
C₂₀H₂₀O₇ requires C, 64.5; H, 5.4 per cent

β-(3-methoxy phenyl)-γ-(4'-methoxy benzoyl) butyric acid (XXXVII). - The foregoing acid (XXXVI) (30 g.) was decarboxylated by heating in an oil-bath at 170-180° until the evolution of carbon dioxide ceased (1 hour). On cooling the residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The filtrate on acidification with hydrochloric acid gave a crystalline solid. On recrystallization from alcohol in fine colourless prisms, β-(3-methoxy phenyl)-γ-(4'-methoxy benzoyl) butyric acid, had m.p. 138-139°. Yield 26 g.

0.1064 g. gave 0.2719 g. CO₂ and 0.0574 g. H₂O

Found: C, 69.7; H, 6.0
C₁₉H₂₀O₅ requires C, 69.5; H, 6.1 per cent

β-(3-methoxy phenyl)-γ-(4'-methoxy phenyl) valeric acid (XXXVIII). - The foregoing keto-acid (XXXVIII) (24 g.) was refluxed in an all glass apparatus with a mixture
of Toluene (75 c.c.), concentrated hydrochloric acid (30 c.c.) and amalgamated zinc (60 g.) for 60 hours. Hydrochloric acid (20 c.c.) being added every 12 hours. After cooling the toluene layer was separated, washed well with water and extracted with 10 per cent sodium carbonate solution. The alkaline extracted was acidified with hydrochloric acid to give a gummy mass which solidified on standing overnight. On recrystallisation from dilute alcohol, \( \beta-(3\text{-methoxy phenyl})-\S-(4'-\text{methoxy phenyl}) \text{ valeric acid} \) formed colourless prisms, m.p. 99°. Yield 23 g.

0.1058 g. gave 0.2812 g. \( \text{CO}_2 \) and 0.0685 g. \( \text{H}_2\text{O} \)

Found: C, 72.5; H, 7.2

\( \text{C}_{19}\text{H}_{22}\text{O}_4 \) requires C, 72.6; H, 7.0 per cent

5-Methoxy-3(4'-methoxy phenyl ethyl)-1-hydrindone (XXXIX).—The preceding acid (XXXVIII) (6.28 g.) was dissolved in dry benzene (30 c.c.) and gradually treated with phosphorus pentachloride (4.4 g.) with swirling and cooling in ice water. The reaction mixture was left for one hour at the room temperature when all phosphorus pentachloride went into solution, and then heated on a water-bath for about 5 minutes, cooled in the freezing mixture and when benzene began to crystallize, stannic chloride (8 c.c.) mixed with dry benzene (8 c.c.) added rapidly with swirling. After keeping in the freezing mixture for about 25 minutes, powdered ice and concentrated hydrochloric acid were added to decompose the dark brown complex. The organic layer was separated and the mother liquor extracted with ether. The combined organic layer washed
thrice with 5 per cent hydrochloric acid, water and 5
per cent caustic soda solution, again with water, dried over
anhydrous sodium sulphate, and the solvent removed. The
residue, a viscous oil, was distilled under reduced pressure.

5-methoxy-3(4'-methoxy phenyl ethyl)-1-hydrindone formed a
viscous yellow oil, b.p. 230-235°/3 mm. Yield 4.4 g.

0.1126 g. gave 0.3175 g. CO₂ and 0.0678 g. H₂O

Found: C, 76.9; H, 6.7

C₁₉H₂₀O₃ requires C, 77.0; H, 6.8 per cent

2:4-dinitrophenyl hydrazone prepared in methanol and crys­
tallized from acetic acid in brick red plates, m.p. 188-189°.

0.0921 g. gave 0.2131 g. CO₂ and 0.0430 g. H₂O

Found: C, 63.1; H, 5.2

C₂₅H₂₄O₆N₄ requires C, 63.0; H, 5.0 per cent

5-Methoxy-3-{4'-methoxy phenyl ethyl}-2-isonitroso-
1-hydrindone (XL).— The foregoing hydrindone (XXXIX) (4 g.)
was dissolved in methyl alcohol (30 c.c.) and concentrated
hydrochloric acid (3 c.c.) added, and the mixture was saturated
with methyl nitrite (loc.cit.), when no more was absorbed, the
excess of alcohol was removed and the residue diluted with
water. The product was extracted with ether, washed well with
water and thoroughly shaken with 5 per cent sodium hydroxide
solution. The alkaline extract was acidified with hydrochloric
acid to give a heavy oil which solidified on cooling and
standing. On recrystallization from alcohol, 5-methoxy-3-
(4'-methoxy phenyl ethyl)-2-isonitroso-1-hydrindone formed pale yellow prisms, m.p. 157-158°. Yield 3.7 g.

0.0825 g. gave 0.2127 g. CO₂ and 0.0423 g. H₂O
Found: C, 70.3; H, 5.7

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

\[\chi-(2\text{-carboxy-5-methoxy phenyl}) - \gamma-(4'\text{-methoxy phenyl})\] butyronitrile (XL). - The foregoing iso nitroso hydrindone (XL) (3 g.) was mixed with 10 per cent sodium hydroxide solution (30 c.c.) and gradually treated with p-toluene sulphonyl chloride (3 g.) (freshly crystallized from petroleum ether, b.p. 40-60°), with shaking. The reaction was completed by heating on a water-bath for 10 minutes. On cooling the alkaline solution was filtered and the filtrate acidified with hydrochloric acid to give a heavy oil which turned to a crystalline solid, on standing overnight. On crystallisation from alcohol is almost colourless needles, \[\chi-(2\text{-carboxy-5-methoxy phenyl}) - \gamma-(4'\text{-methoxy phenyl})\] butyronitrile had m.p. 133-135°. Yield 2.8 g.

0.0895 g. gave 0.2311 g. CO₂ and 0.0443 g. H₂O
Found: C, 70.4; H, 5.5

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

\[\chi-(2\text{-carboxy-5-methoxy phenyl}) - \gamma-(4'\text{-methoxy phenyl})\] butyric acid (XLI). - The preceding nitrile (XLI) (2 g.) was hydrolysed by heating under reflux on the sand-bath with a 10 per cent solution of sodium hydroxide (25 c.c.) until the evolution of ammonia gas ceased (8 hours). The
alkaline solution was cooled, filtered and acidified with hydrochloric acid to give a gummy mass, which solidified on standing overnight in the ice chest. On double crystallisation from dilute acetic acid (charcoal), $\alpha$-(2-carboxy-5-methoxy phenyl)-\(\gamma\)-(4'-methoxy phenyl) butyric acid formed colourless prismatic needles, m.p. 137°. Yield 1.9 g.

0.1074 g. gave 0.2115 g. CO₂ and 0.0570 g. H₂O

Found: C, 66.4; H, 5.9

C₁₉H₂₀O₆ requires C, 66.3; H, 5.8 per cent

D. Synthesis of $\alpha$-(2-carboxy-4:5-dimethoxy phenyl-\(\gamma\)-phenyl butyric acid.

Veratralyldene acetophenone (XLIII). - A mixture of veratric aldehyde (41.5 g.) freshly distilled acetophenone (30 g.), sodium hydroxide (13 g.) dissolved in water (170 c.c.) and alcohol (70 c.c.) was vigorously stirred for 2 hours in the ice-bath and 10 hours at the room temperature. The reaction mixture was left overnight in the ice chest. The solid which separated was collected by filtration and washed well with water. On recrystallization from alcohol veratralyldene acetophenone formed long yellow needles, m.p. 90°. Yield 65 g.

0.1029 g. gave 0.2875 g. CO₂ and 0.0537 g. H₂O

Found: C, 76.2; H, 5.8

C₁₇H₁₆O₃ requires C, 76.1; H, 5.9
Ethyl-β-(3:4-dimethoxyphenyl)-γ-benzoyl-ethyl-malonate (XLIV).—To a solution of sodium ethoxide prepared from sodium (0.2 g.) and absolute alcohol (30 c.c.), diethyl malonate (16 g.) was added followed by veratraldehyde acetophenone (26.8 g.) with vigorous shaking. In about 5 minutes the chalcone went into solution, with evolution of heat. The reaction mixture was left overnight, when it set to a solid mass. On recrystallization from alcohol, the ester (XLIV) formed fine colourless needles, m.p. 88-89°. Yield 40 g.

0.1302 g. gave 0.3207 g. CO₂ and 0.0749 g. H₂O
Found: C, 67.2; H, 6.4
C₂₄H₂₈O₇ requires C, 67.3; H, 6.5

α-Carboxy-β-(3:4-dimethoxyphenyl)-γ-benzoyl butyric acid (XLIV).—The foregoing ester (XLIV) (38 g.) was hydrolysed by heating under reflux with potassium hydroxide (24 g.) dissolved in water (80 c.c.) and alcohol (20 c.c.) on a water-bath for 1½ hours. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether to remove the neutral matter. The clear alkaline extract was acidified with hydrochloric acid to give a heavy oil which solidified on standing. On recrystallisation from dilute alcohol, α-carboxy-β-(3:4-dimethoxyphenyl)-γ-benzoyl butyric acid formed fine colourless needles, m.p. 176°. Yield 29 g.

0.1182 g. gave 0.2800 g. CO₂ and 0.0585 g. H₂O
Found: C, 64.6; H, 5.5
C₂₀H₂₀O₇ requires C, 64.5; H, 5.4 per cent.
\[ \beta-(3,4\text{-dimethoxy phenyl})-\gamma\text{-benzoyl butyric acid} \] (XLVI). The foregoing acid (XLV) (28 g.) was decarboxylated by heating in an oil-bath at 170-180° for about 1 1/2 hours, until the evolution of carbon dioxide ceased. The residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The cooled filtrate on acidification with hydrochloric acid gave a heavy oil which solidified soon. On recrystallisation from alcohol, \( \beta-(3,4\text{-dimethoxy phenyl})-\gamma\text{-benzoyl butyric acid} \) formed fine colourless needles, m.p. 131°. Yield 23 g.

0.1211 g. gave 0.3082 g. \( \text{CO}_2 \) and 0.0654 g. \( \text{H}_2\text{O} \)

Found: C, 69.4; H, 6.0

\( \text{C}_{19}\text{H}_{20}\text{O}_6 \) requires C, 69.5; H, 6.1 per cent

\[ \beta-(3,4\text{-dimethoxy phenyl})-\beta\text{-phenyl valeric acid} \] (XLVII). The preceding keto-acid (XLVI) (20 g.) was dissolved in an aqueous solution of sodium hydroxide (600 c.c. of 10%) and heated on a water-bath at 90-95°, and Nickel aluminium alloy (60 g.) (loc.cit.) was added in small portions (2-3 g.) with vigorous stirring. The reaction mixture was stirred another hour, at 90-95°, water being added from time to time to maintain the volume of the mixture constant. The mixture was heated further with the addition of 10 per cent caustic soda solution (100 c.c.) and Nickel aluminium alloy (10 g.) as before. The product worked up in the usual way to give a crystalline solid. On crystallization from alcohol,
\( \beta-(3:4\text{-dimethoxy phenyl})-5\text{-phenyl valeric acid} \) formed colourless needles, m.p. 90-91°. Yield 17 g.

0.0942 g. gave 0.2504 g. \( \text{CO}_2 \) and 0.0601 g. \( \text{H}_2\text{O} \)

Found: C, 72.5; H, 7.1

\( \text{C}_{19}\text{H}_{22}\text{O}_4 \) requires C, 72.6; H, 7.0 per cent

\( 5:6\text{-dimethoxy-3-phenyl-ethyl-1-hydrindone (XLVIII).} \)

The foregoing acid (XLVII) (10 g.) was dissolved in boiling benzene (60 c.c.) and gradually mixed with phosphorous pentoxide (40 g.), the whole being shaken thoroughly after each addition. After heating under reflux on the water-bath, the product was cooled and mixed with crushed ice to decompose the dark brown complex, and extracted with ether thoroughly. The ethereal layer was washed well with water, dilute caustic soda solution and again with water and dried over fused calcium chloride. The solvent was removed, and the residue distilled under vacuum, \( 5:6\text{-dimethoxy-3-phenyl-ethyl-1-hydrindone} \) was collected as a viscous yellow oil, b.p. 245-250°/5 mm., which solidified on standing. On recrystallisation from alcohol it formed colourless needles, m.p. 111-112°. Yield 7.5 g.

0.1025 g. gave 0.2893 g. \( \text{CO}_2 \) and 0.0627 g. \( \text{H}_2\text{O} \)

Found: C, 77.0; H, 6.8

\( \text{C}_{19}\text{H}_{20}\text{O}_3 \) requires C, 77.0; H, 6.8 per cent

\( 2:4\text{-dinitrophenyl hydrazone} \) prepared in the usual way on crystallization from alcohol formed dark red needles, m.p. 241-243°.
0.0906 g. gave 0.2096 g. CO₂ and 0.0416 g. H₂O

Found: C, 63.1; H, 5.1

C₂₅H₂₄O₅N₄ requires C, 68.0; H, 5.0 per cent

**5:6-Dimethoxy-3-(Phenyl-ethyl)-2-isonitroso-1-hydrindone (XLIX)** - The foregoing hydrindone (XLVIII) (5 g.) was dissolved in methyl alcohol (20 c.c.) and hydrochloric acid (3 c.c.) added. The mixture was slightly cooled in an ice-bath, methyl nitrite passed into it, until no more absorption took place. The isonitroso derivative gradually separated out on cooling in yellow crystals. On recrystallisation from alcohol, 5:6-dimethoxy-3-phenyl-ethyl-2-isonitroso-1-hydrindone formed yellow plates, m.p. 197-198°. Yield 3.5 g.

0.0952 g. gave 0.2443 g. CO₂ and 0.0505 g. H₂O

Found: C, 70.0; H, 5.9

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

**<-(2-Carboxy-4:5-dimethoxy phenyl)-γ-phenyl butyronitrile (L)** - The preceding isonitroso hydrindone (XLIX) (2.5 g.) was dissolved in 10 per cent aqueous sodium hydroxide (20 c.c.) and treated gradually with p-toluene sulphonyl chloride (2.5 g.) with shaking. The reaction was completed by heating the reaction mixture on a water-bath for 15 minutes. After cooling the alkaline solution was filtered and acidified with concentrated hydrochloric acid to give the nitrile as a crystalline solid. On recrystallisation from alcohol, <-(2-carboxy-4:5-dimethoxy phenyl)-γ-phenyl butyronitrile formed almost colourless needles, m.p. 106-108°. Yield 2.1 g.
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0.1024 g. gave 0.2628 g. CO₂ and 0.0543 g. H₂O

Found: C, 70.0; H, 5.9

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

\( \text{\textit{\textit{\textit{\textit{\textit{(2-carboxy-4:5-dimethoxy phenyl) - \textgamma -phenyl butyric acid} (II).}}}} \)

The foregoing nitrile (I) (1.5 g.) was dissolved in 10 per cent aqueous sodium hydroxide solution (15 c.c.) and heated under reflux on a sand-bath for about 7 hours, until the evolution of ammonia gas ceased. After cooling the alkaline solution was filtered and the filtrate acidified with hydrochloric acid. The gummy mass which separated, solidified on standing overnight. On recrystallisation from acetic acid, \( \text{\textit{\textit{\textit{\textit{(2-carboxy-4:5-dimethoxy phenyl) - \textgamma -phenyl butyric acid}}} \)

formed colourless needles, m.p. 149-150°. Yield 1.1 g.

0.1205 g. gave 0.2925 g. CO₂ and 0.0650 g. H₂O

Found: C, 66.2; H, 6.0

C₁₉H₂₀O₆ requires C, 66.3; H, 5.8 per cent.

E. Synthesis of \( \text{\textit{\textit{\textit{\textit{(2-carboxy-4:5-dimethoxy phenyl) - \textgamma -(4'-methoxy phenyl)butyric acid} \)}} \)

3:4:4'-Trimethoxy chalcone (Veratrylaldehyde-p-methoxy acetophenone (LII). - Veratic aldehyde (41.5 g.) and p-methoxy acetophenone (37.5 g.) was dissolved in alcohol (200 c.c.) and a 10 per cent solution of sodium hydroxide (42 c.c.) was gradually added to it with shaking. The reaction mixture was left for 24 hours at the room temperature with occasional shaking. The yellow crystalline solid separated was collected by filtera-
tion and washed well with water and a little alcohol. On recrystallisation from alcohol, 3:4:4'-trimethoxy chalcone formed stout yellow needles, m.p. 93°. Yield 60 g.

0.1221 g. gave 0.3246 g. CO₂ and 0.0659 g. H₂O

Found: C, 72.6; H, 6.0

C₁₈H₁₉O₄ requires C, 72.5; H, 6.0 per cent

\(-\text{Carboxy-}\beta-(3:4-\text{dimethoxy phenyl})-\gamma-(4'-\text{methoxy benzoyl})\) butyric acid (LIII).- To a solution of sodium ethoxide prepared from sodium (0.2 g.) and absolute alcohol (30 c.c.), diethyl malonate (16 g.) was added followed by 3:4:4'-trimethoxy chalcone (LII) (29.8 g.) with shaking for an hour. The reaction mixture was left overnight at the room temperature and heated under reflux on the water-bath for 3 hours. The reaction product was hydrolysed by refluxing on the water-bath with potassium hydroxide (24 g.) dissolved in water (80 c.c.) and alcohol (20 c.c.), for an hour. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether to remove any neutral matter. The clear alkaline solution was acidified with hydrochloric acid to give a crystalline solid. On recrystallisation from dilute alcohol \(-\text{carboxy-}\beta-(3:4-\text{dimethoxy phenyl})-\gamma-(4'-\text{methoxy benzoyl})\) butyric acid formed fine colourless needles; m.p. 161-162°. Yield 30 g.

0.1029 g. gave 0.2358 g. CO₂ and 0.0490 g. H₂O

Found: C, 62.5; H, 5.3

C₂₁H₂₂O₈ requires C, 62.7; H, 5.5 per cent
\[ \beta-(3,4\text{-dimethoxy phenyl})-\gamma-(4\text{'-methoxy benzoyl}) \]
butyric acid (LIV). - The foregoing acid (LIII) (28 g.) was
decarboxylated by heating in an oil-bath at 170-180° for about
an hour. After cooling the residue was extracted with boiling
10 per cent sodium carbonate solution and filtered. On cooling
the sodio-salt of the acid separated which was acidified with
hydrochloric acid to give a colourless crystalline solid. On
recrystallization from alcohol, \[ \beta-(3,4\text{-dimethoxy phenyl})-\gamma-(4\text{'-methoxy benzoyl}) \]
butyric acid formed colourless needles, m.p. 137-138°. Yield 23 g.

0.1032 g. gave 0.2531 g. C\text{O}_2 and 0.0576 g. H\text{O}

Found: C, 66.9; H, 6.2
C\text{O}_{22}\text{H}_{22}\text{O}_6 requires C, 67.0; H, 6.1 per cent

\[ \beta-(3,4\text{-dimethoxy phenyl})-\delta-(4\text{'-methoxy phenyl}) \]
valeric acid (LV). - The above keto-acid (LIV) (20 g.) was
heated under reflux with a boiling mixture of toluene (75 c.c.),
5 per cent acetic acid (50 c.c.), concentrated hydrochloric
acid (50 c.c.) and amalgamated zinc (70 g.) for 60 hours. Hydro-
chloric acid (25 c.c.) being added every twelve hours. In
first few hours the keto-acid gradually dissolved, after 30
hours the reduced acid started separating from the toluene
layer. After cooling the separated acid was collected by fil-
teration. Further quantity of the acid was obtained by extract-
ing the toluene layer by 10 per cent sodium carbonate solution,
which was acidified with hydrochloric acid. On recrystallisa-
tion from alcohol, \[ \beta-(3,4\text{-dimethoxy phenyl})-\delta-(4\text{'-methoxy phenyl}) \]
valeric acid, m.p. 88-89°. Yield 18.5 g.
0.1239 g. gave 0.3166 g. C\(_2\)O\(_2\) and 0.0791 g. H\(_2\)O  
Found: C, 69.7; H, 7.1  
C\(_{20}\)H\(_{24}\)O\(_5\) requires C, 69.3; H, 7.0 per cent.

5\textsubscript{16}-dimethoxy-3-(4'-methoxy phenyl ethyl)-1- 
hydrindone (LVI). - The foregoing acid (LV) (10 g.) was  
dissolved in boiling benzene (60 c.c.) and treated gradually  
with phosphorous pentaoxide (50 g.) the whole being shaken  
after each addition. The reaction mixture was further refluxed  
on the water-bath for 3 hours. On cooling the product was  
mixed with powdered ice to decompose the complex. The product  
was thoroughly extracted with ether. The ethereal layer washed  
with water, 10 per cent sodium hydroxide solution and again  
with water, dried over anhydrous sodium sulphate. The solvent  
was removed and the residue distilled under reduced pressure. 
5\textsubscript{16}-dimethoxy-3-(4'-methoxy phenyl ethyl)-1-hydrindone was  
collected as a viscous yellow oil, b.p. 250-255\(^{\circ}\)/5 mm. Yield  
4.8 g. The unchanged acid (2.5 g.) was recovered from the  
alkaline washings, on acidification.

0.1071 g. gave 0.2886 g. C\(_2\)O\(_2\) and 0.0636 g. H\(_2\)O  
Found: C, 73.5; H, 6.6  
C\(_{20}\)H\(_{22}\)O\(_4\) requires C, 73.6; H, 6.7 per cent.

5\textsubscript{16}-Dimethoxy-3-(4'-methoxy phenyl ethyl)-2-isoo- 
nitroso-1-hydrindone (LVII). - The preceding hydrindone (LVI)  
(4.5 g.) was dissolved in methyl alcohol and mixed with con-  
centrated hydrochloric acid (3 c.c.) with cooling in ice. The  
mixture was saturated with methyl nitrite. On cooling the
isonitroso hydrindone separated as a yellow crystalline solid. On recrystallisation from alcohol, 5,6-dimethoxy-3-(4'-methoxy phenyl ethyl)-2-isonitroso-1-hydrindone formed shining yellow prisms, m.p. 293-194° (decomp.). Yield 3.2 g.

0.1010 g. gave 0.2499 g. CO₂ and 0.0545 g. H₂O
Found: C, 67.5; H, 6.0
C₂₀H₂₁O₅N requires C, 67.6; H, 5.9 per cent

(-{(2-carboxy-4,5-dimethoxy phenyl) - γ-(4'-methoxy phenyl) butyronitrile (LVIII). - The foregoing isonitroso hydrindone (LVII) (2.5 g.) was dissolved in aqueous 10 per cent sodium hydroxide (20 c.c.) and gradually treated with p-toluene sulphonyl chloride (2.5 g.) with shaking. The reaction was completed by heating the mixture on a water-bath for about 15 minutes, and filtered hot. On cooling, shining yellow crystals of the sodio-salt separated, which on decomposition with hydrochloric acid gave a heavy oil, which solidified on standing. On recrystallisation from dilute alcohol, (-{(2-carboxy-4,5-dimethoxy phenyl) - γ-(4'-methoxy phenyl) butyronitrile formed light yellow needles, m.p. 140-142°. Yield 2.4 g.

0.1102 g. gave 0.2727 g. CO₂ and 0.0595 g. H₂O
Found: C, 67.5; H, 6.0
C₂₀H₂₁O₅N requires C, 67.6; H, 5.9 per cent

(-{(2-carboxy-4,5-dimethoxy phenyl) - γ-(4'-methoxy phenyl) butyric acid (LIX). - The preceding nitrile (LVIII) (2 g.) was hydrolysed by heating under reflux on the sand-bath
with an aqueous 10 per cent sodium hydroxide solution (25 c.c.) for about 10 hours. After cooling the alkaline solution was filtered, and the filtrate acidified with hydrochloric acid to give a heavy oil which solidified on standing overnight in the ice chest. On recrystallization from dilute acetic acid, (-\(2\)-carboxy-4:5-dimethoxy phenyl)-\(\gamma\)-(4'-methoxy phenyl) butyric acid formed fine colourless needles, m.p. 152-153°. Yield 1.8 g.

0.1095 g. gave 0.2577 g. \(\text{CO}_2\) and 0.0591 g. \(\text{H}_2\text{O}\)

Found: C, 64.2; H, 6.0

\(\text{C}_20\text{H}_{22}\text{O}_7\) requires C, 64.2; H, 5.9 per cent

T. Synthesis of (-\(2\)-carboxy-4:5-dimethoxy phenyl)-\(\gamma\)-(3:4'-dimethoxy phenyl) butyric acid.

3:4:3:4'-Tetramethoxy chalcone.— Aqueous sodium hydroxide (25 c.c. of 10%) was added to a solution of veratraldehyde (25 g.) and acetoveratrone (27.5 g.) (prepared from veratrol according to the method given in Archiveder. pharmazie 248, 137, 1910) in alcohol (250 c.c.). After keeping at room temperature for 12 hours with occasional shaking the yellow crystalline precipitate, on recrystallisation from hot alcohol formed hexagonal yellow plates, m.p. 116-180° (loc. cit.). Yield 27 g.

\(-\text{Carboxy}-\beta-(3:4'-\text{dimethoxy phenyl})-\gamma-(3:4'-\text{dimethoxy benzoyl})\text{ butyric acid (LX).— To a solution of sodium (2 g.) in absolute alcohol (30 c.c.), diethyl malonate (11 g.) was added followed by 3:4:3:4'-tetramethoxy chalcone (22 g.).}
with shaking, and the mixture was heated under reflux on the
water-bath for 3 hours. The reaction product was hydrolysed
by refluxing with a solution of potassium hydroxide (15 g.)
in water (54 c.c.) and alcohol (20 c.c.), on a water-bath for
2 hours. The acid was isolated in the usual way. On recrysta-
llisation from dilute alcohol the acid (LX) formed colourless
silky needles, m.p. 120-121°. Yield 22 g.

0.1126 g. gave 0.2527 g. CO₂ and 0.0577 g. H₂O

Found: C, 61.2; H, 5.7

C₂₂H₂₄O₉ requires C, 61.1; H, 5.5 per cent

β-(3:4-dimethoxy phenyl)-γ-(3':4'-dimethoxy benzoyl
butyric acid (LXI). - The foregoing dicarboxylic acid (LX)
(21 g.) was decarboxylated by heating in an oil-bath at 160-
170°, for 2 hours. On cooling the residue was extracted with
boiling 10 per cent sodium carbonate solution and filtered.
The cooled alkaline filtrate was acidified with hydrochloric
acid gave a crystalline solid. The acid (LXI) on recrystall-
lation from alcohol formed colourless prisms, m.p. 150-151°.
Yield 17.5 g.

0.1007 g. gave 0.2396 g. CO₂ and 0.0571 g. H₂O

Found: C, 64.9; H, 6.3

C₂₁H₂₄O₇ requires C, 65.0; H, 6.2 per cent

β-(3:4-dimethoxy phenyl)-γ-(3':4'-dimethoxy phenyl)
valeric acid (LXII). - The preceding keto-acid (LXII) (16 g.)
was heated under reflux on a sand-bath with a mixture of amalg-
amated zinc (50 g.), toluene (75 c.c.), 5 per cent acetic acid
(37 c.c.), and concentrated hydrochloric acid (30 c.c.) for 48 hours. Hydrochloric acid (15 c.c.) being added every 12 hours. After cooling the toluene layer was separated, washed well with water and extracted with 10 per cent sodium carbonate solution. The alkaline solution was acidified with hydrochloric acid, giving a gummy mass. The product was further purified by methylation with dimethyl sulphate in the usual way, when it solidified by rubbing with ethyl acetate. On recrystallization from ethyl acetate-petroleum ether (b.p. 60-80°),

\[ \beta-(3:4\text{-dimethoxy phenyl})-5-(3':4':\text{-dimethoxy phenyl}) \text{ valeric acid} \]

for colourless fine prisms, m.p. 107-108°. Yield 13.5 g.

0.1018 g. gave 0.2512 g. CO₂ and 0.0632 g. H₂O

Found: C, 67.3; H, 6.9

\( \text{C}_{21}\text{H}_{26}\text{O}_6 \) requires C, 67.4; H, 7.0 per cent

\[ 5:6\text{-dimethoxy-3-(3':4':\text{-dimethoxy phenyl ethyl})-1-} \text{hydrindone (LXIII).} \]

The foregoing acid (LXII) (8 g.) was dissolved in boiling benzene (40 c.c.) and treated gradually with phosphorous pentoxide (40 g.), the whole being shaken after each addition. After refluxing for 3 hours on the water-bath, the product was cooled and mixed with powdered ice to decompose the phosphorous complex. The yellow suspension obtained was thoroughly extracted with ether. The ethereal layer washed successively with water, 10 per cent sodium hydroxide solution and again with water, dried over fused sodium sulphate and the solvent removed by distillation. The residue distilled under reduced pressure, the hydrindone (LXIII) formed yellow semi-solid, b.p. 260-265°/2 mm. Yield 4 g.
0.1108 g. gave 0.2872 g. CO₂ and 0.0678 g. H₂O.
Found: C, 70.7; H, 6.8
C₂₁H₄₀O₅ requires C, 70.8; H, 6.7 per cent

The 2,4-dinitrophenyl hydrazone obtained readily in the usual way, on recrystallization from acetic acid from brick red needles, m.p. 186-187°.

0.0882 g. gave 0.1956 g. CO₂ and 0.0421 g. H₂O
Found: C, 60.5; H, 5.3
C₂₇H₃₈O₈N₄ requires C, 60.4; H, 5.2 per cent

5:6-dimethoxy-3-(3′:4′-dimethoxy phenyl)′-2-isodinitroso-1-hydrindone (LXIV). - The foregoing hydrindone (LXIII) (3 g.) was dissolved in methyl alcohol (20 c.c.) and mixed with concentrated hydrochloric acid (2 c.c.), methyl nitrite gas passed into it, until no more absorption took place. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether. The ethereal layer, washed with water, and thoroughly extracted with a 10 per cent solution of sodium hydroxide. The cooled alkaline solution was acidified with hydrochloric acid to give the isonitroso derivative (LXIV) as a crystalline yellow solid, which, on recrystallisation from ethyl alcohol formed dull yellow prism, m.p. 166-167°. Yield 1.8 g.

0.0931 g. gave 0.2229 g. CO₂ and 0.0494 g. H₂O.
Found: C, 65.3; H, 5.9
C₂₁H₂₃O₅N requires C, 65.5; H, 6.0 per cent
\[ \text{dimethoxy phenyl butyric acid (LXVI).} \]

The foregoing iso-nitroso hydrazine (LXIV) (1.3 g.) was dissolved in 10 per cent sodium hydroxide solution (13 c.c.) and treated gradually with p-toluene sulphonyl chloride (1.3 g.) with shaking. The reaction was completed by heating on a water-bath for 10 minutes. After cooling the alkaline solution was acidified with concentrated hydrochloric acid to give a gummy mass (LXV) which could not be further purified. Yield 1.35 g. The crude nitrile (LXV) (1.2 g.) was dissolved in 10% sodium hydroxide solution (12 c.c.) and heated under reflux on a sand-bath, until the evolution of ammonia gas ceased (about 6 hours). After cooling the alkaline solution was filtered and acidified with hydrochloric acid to give a hard gummy mass which solidified on standing. On recrystallisation from dilute acetic acid \[ \text{\( \alpha \)-(2-carboxy-4:5-dimethoxy phenyl)-(3:4-dimethoxy phenyl) butyric acid} \]

formed colourless short prisms, m.p. 114°. Yield 1 g.

0.1002 g. gave 0.2296 g. CO₂ and 0.0550 g. H₂O

Found: C, 62.5; H, 6.1

C₁₂H₁₄O₈ requires C, 62.4; H, 5.9 per cent

G. Synthesis of \[ \text{\( \alpha \)-(2-carboxy-5:6-dimethoxy phenyl)-(3:4-dimethoxy phenyl) butyric acid} \]

2:3-dimethoxy chalcone (0-veratrylidene acetophenone) (LXVII). - 0-veratric aldehyde (24.9 g.) (prepared according to the method given for Veratric aldehyde in Organic Synthesis, 1936, IV, 91) and acetophenone (18 g.) was dissolved in alcohol
(120 c.c.) and a 10 per cent solution of sodium hydroxide
(38 c.c.) was gradually added to it with shaking. In about 15
minutes the clear solution became turbid, with evolution of
heat and a heavy yellow oil separated. The reaction mixture was
left overnight in the ice chest. The oily layer was extracted
with ether. The ethereal solution was washed well with water,
dried over fused magnesium sulphate. The solvent was removed
and the residue distilled under reduced pressure. 2,3-dimethoxy
chalkone was collected as a yellow viscous oil, b.p. 225-230°/3
mm. Yield 34.5 g.

0.1092 g. gave 0.3043 g. CO₂ and 0.0570 g. H₂O

Found: C, 76.0; H, 5.8

C₁₇H₁₅O₃ requires C, 76.1; H, 5.9 per cent

2-[Carboxy-β-(2,3-dimethoxy phenyl)-γ-benzoyl] butyric acid (LXVIII). - To a solution of sodium (0.3 g.)
in absolute alcohol (45 c.c.), ethyl malonate (19.5 g.) was
added followed by 2,3-dimethoxy chalkone (LXVII) (33 g.). The
reaction started immediately with evolution of heat, which
was left overnight at the room temperature. The reaction pro-
duct was hydrolysed by heating under reflux with potassium
hydroxide (27 g.) dissolved in water (60 c.c.) and alcohol
(20 c.c.) on a water-bath for an hour. The excess of alcohol
was removed by evaporation after cooling the residue was dilu-
ted with water and extracted with ether to remove any neutral
matter. The alkaline solution was acidified with hydrochloric
acid to give a heavy oil which solidified to a crystalline
mass on standing overnight. On recrystallisation from dilute
alcohol, \( \alpha \)-carboxy-\( \beta \)-(2:3-dimethoxy phenyl)-\( \gamma \)-benzoyl butyric acid formed fine colourless needles, m.p. 157°, yield 44.5 g.

0.1130 g. gave 0.2665 g. \( \text{CO}_2 \) and 0.0549 g. \( \text{H}_2\text{O} \)

Found: C, 64.3; H, 5.4

\( \text{C}_{20}\text{H}_{20}\text{O}_7 \) requires C, 64.5; H, 5.4 per cent

\( \beta \)-(2:3-dimethoxy phenyl)-\( \gamma \)-benzoyl butyric acid

(LXIX). The foregoing acid (LXVIII) (40 g.) was decarboxylated by heating in an oil-bath at 170-180°, until the evolution of carbon dioxide ceased (1 hour). On cooling the residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The cooled filtrate was acidified with hydrochloric acid, giving a gummy mass which solidified on standing. On recrystallisation from alcohol, \( \beta \)-(2:3-dimethoxy phenyl)-\( \gamma \)-benzoyl butyric acid formed short colourless prisms, m.p. 135°. Yield 35 g.

0.1138 g. gave 0.2896 g. \( \text{CO}_2 \) and 0.0615 g. \( \text{H}_2\text{O} \)

Found: C, 69.4; H, 6.0

\( \text{C}_{19}\text{H}_{20}\text{O}_5 \) requires C, 69.5; H, 6.1 per cent

\( \beta \)-(2:3-dimethoxy phenyl)-\( \delta \)-phenyl valeric acid

(LXX). The preceding keto-acid (LXIX) (32 g.) was reduced by heating under reflux with a mixture of toluene (120 c.c.), 5 per cent acetic acid (60 c.c.), concentrated hydrochloric acid (50 c.c.) and amalgamated zinc (80 g.) for 48 hours, hydrochloric acid (20 c.c.) being added every 12 hours. After cooling the toluene layer was separated, washed well with water and extracted with 10 per cent sodium carbonate solution. The
alkaline solution was acidified with concentrated hydrochloric acid to give a gummy mass which solidified on standing for several days. It was further purified by methylation with dimethyl sulphate in the usual way. On recrystallisation from dilute alcohol it formed colourless prisms, m.p. 65°. Yield 28 g.

0.0988 g. gave 0.2626 g. CO₂ and 0.0640 g. H₂O

Found: C, 72.5; H, 7.2

C₁₉H₂₂O₄ requires C, 72.6; H, 7.0 per cent

4:5-dimethoxy-3-(phenyl ethyl)-1-hydrindone (LXXI).

The foregoing acid (LXX) (6.2 g.) dissolved in dry benzene (30 c.c.) was treated gradually with powdered phosphorous pentachloride (4.4 g.) with swirling and cooling in ice water, the reaction started almost immediately, which was left at room temperature until phosphorous pentachloride went into solution (1 hour). The reaction mixture was heated on a water bath for 10 minutes and then cooled in the freezing mixture, and when benzene began to crystallize, stannic chloride (10 c.c.) mixed with dry benzene (10 c.c.) were added to it all at once. The reaction mixture was left overnight in the refrigerator. Hydrochloric acid and powdered ice were added to decompose the dark coloured complex. The product was extracted with ether. The ethereal layer washed thrice with 5 per cent hydrochloric acid, water, 5 per cent sodium hydroxide solution, again with water and dried over anhydrous sodium sulphate. The solvent was removed to give a crystalline solid. On recrystallisation from alcohol 4:5-dimethoxy-3-(phenyl ethyl)-1-hydrindone formed fine colourless prisms, m.p. 132-133°. Yield 4.2 g.
0.1020 g. gave 0.2867 g. CO₂ and 0.0624 g. H₂O

Found: C, 77.2; H, 6.8

C₁₉H₂₀O₃ requires C, 77.0; H, 6.8 per cent

The 2,4-dinitrophenyl hydrazone prepared in the usual way on recrystallisation from acetic acid, formed bright orange needles, m.p. 203-204°.

0.0986 g. gave 0.2281 g. CO₂ and 0.0444 g. H₂O

Found: C, 65.1; H, 5.0

C₂₅H₂₄O₆N₄ requires C, 63.0; H, 5.0 per cent

The semicarbazone which was readily obtained in the usual way separated from alcohol in almost colourless prisms, m.p. 190°.

0.0971 g. gave 0.2417 g. CO₂ and 0.0572 g. H₂O

Found: C, 67.9; H, 6.6

C₂₆H₂₃N₃O₃ requires C, 68.0; H, 6.5

4:5-dimethoxy-3-(phenyl ethyl)-2-isonitroso-1-hydrindone (LXXI) — The foregoing hydrindone (LXXI) (2-5 g.) was dissolved in methyl alcohol (40 c.c.) and mixed with concentrated hydrochloric acid (2 c.c.), methyl nitrite gas was passed into it, until no more absorption took place. The methyl alcohol was evaporated, the residue a yellow crystalline mass was diluted with water and extracted with ether. The ethereal layer was washed well with water, and thoroughly extracted with 5 per cent sodium hydroxide. The alkaline solution was acidified with hydrochloric acid to give a gummy mass
which solidified on standing. On recrystallisation from alcohol (charcoal), the isonitroso derivative (LXXII), m.p. 121-122°. Yield 1.9 g.

0.0982 g. gave 0.2724 g. CO₂ and 0.0521 g. H₂O

Found: C, 70.1; H, 5.9

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

(-{2-carboxy-5:6-dimethoxy phenyl}-γ-phenyl) butyronitrile (LXXIII). - The preceding isonitroso hydridone (LXXII) (1.5 g.) was dissolved in 10 per cent sodium hydroxide solution (15 c.c.) and treated gradually with p-toluene sulphonyl chloride (1.6 g.) with shaking. The reaction was completed by heating the reaction mixture on water-bath for about 10 minutes. After cooling the alkaline solution was filtered and acidified with hydrochloric acid whereby the nitrile separate as a somewhat gummy mass which solidified to a yellow crystalline product on standing. On recrystallisation from dilute alcohol (-{2-carboxy-5:6-dimethoxy phenyl}-γ-phenyl) butyronitrile formed pale yellow nodules, m.p. 156-157°. Yield 1.4 g.

0.0894 g. gave 0.2298 g. CO₂ and 0.0483 g. H₂O

Found: C, 70.1; H, 6.0

C₁₉H₁₉O₄N requires C, 70.2; H, 5.8 per cent

(-{2-carboxy-5:6-dimethoxy phenyl}-γ-phenyl) butyric acid (LXXIV). - The foregoing nitrile (LXXIII) (1.1 g.) was dissolved in 10 per cent sodium hydroxide solution (12 c.c.) and heated under reflux on a sand-bath for about
8 hours, until the evolution of ammonia gas ceased. After cooling the alkaline solution was filtered, and acidified with concentrated hydrochloric acid to give a fine pale yellow crystalline solid. On double crystallisation from acetic acid (charcoal) the dibasic acid (LXXIV) formed light yellow shining plates, m.p. 178-179°. Yield 1 g.

0.1122 g. gave 0.2724 g. CO₂ and 0.0596 g. H₂O

Found: C, 66.2; H, 5.9
C₁₉H₂₀O₆ requires C, 66.3; H, 5.8 per cent

H. Synthesis of \( \alpha\)-(2-carboxy-5:6-dimethoxy phenyl) -\( \gamma\)-[4'-methoxy phenyl] butyric acid.

\( 2:3:4\)'-trimethoxychalkone (0-veratraldehyde-p-methoxy acetophenone) (LXXV). - Aqueous 10 per cent sodium hydroxide solution (25 c.c.) was gradually added to a solution of 0-veratric aldehyde (16.6 g.) and p-methoxy acetophenone (15 g.) in alcohol (80 c.c.) with shaking. In about 10 minutes the clear solution became turbid, with evolution of heat and a heavy yellow oil separated which solidified on standing. The solid was collected by filtration and washed well with water and a little alcohol. On recrystallization from alcohol, \( 2:3:4\)'-trimethoxychalkone formed clusters of yellow needles, m.p. 104-105°. Yield 25 g.

0.1202 g. gave 0.3184 g. CO₂ and 0.0659 g. H₂O

Found: C, 72.3; H, 6.1
C₁₈H₁₈O₄ requires C, 72.5; H, 6.0 per cent

\( \alpha\)-(Carboxy-\( \beta\)-(2:3-dimethoxy phenyl) -\( \gamma\)-(4'-methoxy benzoyl) butyric acid (LXXVI). - To a solution of sodium
ethoxide prepared from sodium (0.2 g.) and absolute alcohol (40 c.c.), diethylmalonate (12 g.) was added followed by 2:3-4'-trimethoxy chalkone (LXXV) (22.5 g.) and the mixture was shaken vigorously at the room temperature. In about 5 minutes the chalkone went into solution with evolution of heat and left overnight. The reaction product was hydrolysed by heating under reflux on the water-bath with potassium hydroxide (18 g.) dissolved in water (60 c.c.) and alcohol (20 c.c.), for one hour. The excess of alcohol was removed on the water-bath, the residue diluted with water and extracted with ether. The clear alkaline solution on acidification with hydrochloric acid gave a thick oil which solidified to a crystalline mass on standing for 2 days. On recrystallisation from dilute alcohol, $\alpha$-carboxy-$\beta$-(2:3-dimethoxy phenyl)$-\gamma$-(4'-methoxy benzoyl) butyric acid formed fine colourless needles, m.p. 115-116°. Yield 25 g.

0.1046 g. gave 0.2397 g. CO2 and 0.0527 g. H2O

Found: C, 62.5; H, 5.5
C21H22O8 requires C, 62.7; H, 5.5 per cent

$\beta$-(2:3-dimethoxy phenyl)$-\gamma$-(4'-methoxy benzoyl) butyric acid (LXXVII). - The preceding dicarboxylic acid (LXXVI) (22 g.) was decarboxylated by heating in an oil-bath at 160-170° for about an hour. After cooling the residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The cooled alkaline solution was acidified with hydrochloric acid to give a heavy oil which solidified to a crystalline mass. On recrystallisation from alcohol, $\beta$-(2:3-dimethoxy
phenyl) - γ-(4'-methoxy benzoyl) butyric acid formed shining
colourless prisms, m.p. 139-140°. Yield 20 g

0.1063 g. gave 0.2619 g. CO₂ and 0.0574 g. H₂O

Found: C, 67.2; H, 6.6

C₂O₂H₂₂O₆ requires C, 67.0; H, 6.1 per cent

\[ \beta-(2,3\text{-dimethoxy phenyl})-\gamma-(4'-\text{methoxy phenyl})\] valeric acid (LXXVIII). - The foregoing keto-acid (LXXVII)
(18 g.) was heated under reflux on the sand-bath, with a mix-
ture of toluene (50 c.c.), water (40 c.c.), concentrated hydro-
chloric acid (50 c.c.) and amalgamated zinc (60 g.) for 50 hours.
Hydrochloric acid (25 c.c.) being added every 12 hours. After
cooling the aqueous layer was separated and extracted with ether.
The combined organic extracts were added to aqueous 10 per
cent sodium hydroxide (180 c.c.), and the solvents removed by
steam distillation. The product was purified by remethylation
with dimethyl sulphate in the usual way, to give a heavy oil
which solidified on standing. On recrystallisation from petro-
leum ether (b.p. 80-100°), \( \beta-(2,3\text{-dimethoxy phenyl})-\gamma-(4'-\text{methoxy phenyl})\) valeric acid formed silkly colourless needles,
m.p. 71-72°. Yield 16 g

0.1134 g. gave 0.2895 g. CO₂ and 0.0704 g. H₂O

Found: C, 69.6; H, 6.9

C₂O₂H₂₄O₅ requires C, 69.8; H, 7.0 per cent

4:5-dimethoxy-3-(4'-methoxy phenyl ethyl)-1-hydroin-
done (LXXIX). - The foregoing acid (LXXVIII) (679 g.) dissolved
in dry benzene (30 c.c.) was treated gradually with powdered phosphorous pentachloride (4.5 g.) with swirling and cooling in ice water. The reaction started almost immediately, which was left at room temperature until all phosphorous pentachloride went into solution (1 hour). The reaction mixture was heated on a water-bath for 5 minutes, cooled in the freezing mixture and when benzene began to crystallize, stannic chloride (7 c.c.) mixed with dry benzene (7 c.c.) added rapidly with shaking. The reaction mixture was left in the freezing mixture for about 25 minutes. The complex was decomposed by adding hydrochloric acid and powdered ice. A small amount of ether was also added to facilitate the separation of the layers, and the whole extracted with ether. The ethereal layer was washed in the usual way. The solvents removed by distillation to give a mass of crystalline solid. On recrystallization from alcohol, 4:5-dimethoxy-3-(4'-methoxy phenyl ethyl)-1-hydrindone formed fine colourless prisms, m.p. 115-116°. Yield 4.8 g.

0.1058 g. gave 0.2851 g. CO₂ and 0.0647 g. H₂O

Found: C, 73.5; H, 6.8
C₂₀H₂₂O₄ requires C, 73.6; H, 6.7 per cent

The 2:4-dinitrophenyl hydrazone obtained readily in the usual way, on recrystallization from ethanol in fine bright red needles, m.p. 189-191°.

0.0803 g. gave 0.1811 g. CO₂ and 0.0376 g. H₂O

Found: C, 61.5; H, 5.2
C₂₆H₂₆O₇N₄ requires C, 61.6; H, 5.1 per cent
The semicarbazone which was readily obtained separated from alcohol in fine colourless prisms, m.p. 172-173° (shrinks at 150°).

0.0799 g. gave 0.1925 g. CO₂ and 0.0474 g. H₂O

Found: C, 65.7; H, 6.6

C₁₁H₁₀N₂O₃ requires C, 65.6; H, 6.5 per cent

4,5-dimethoxy-3-(4'-methoxy phenyl ethyl)-2-isonitroso-1-hydrindone (LXXIX). - The above hydrindone (LXXIX) (3.3 g.) was dissolved in methyl alcohol (50 c.c.) and mixed with concentrated hydrochloric acid (2.3 c.c.). The mixture was saturated with methyl nitrite and when no more was absorbed, the excess of alcohol was removed and the residue diluted with water, and extracted with ether. The ethereal layer washed well with water, was thoroughly extracted with 5 per cent aqueous sodium hydroxide solution. The alkaline solution was neutralized with hydrochloric acid, the gummy mass which separated, solidified on standing with petroleum ether (b.p. 40-60°). On recrystallization from a mixture of benzene-petroleum ether, 4,5-dimethoxy-3-(4'-methoxy phenyl ethyl)-2-isonitroso-1-hydrindone formed light yellow needles, m.p. 133-134°.

Yield 2.7 g.

0.1014 g. gave 0.2506 g. CO₂ and 0.0529 g. H₂O

Found: C, 67.4; H, 5.8

C₂₀H₂₁O₃N requires C, 67.6; H, 5.9 per cent
\(-\{2\text{-carboxy}-5\text{-6-dimethoxy phenyl}\}-\gamma\text{-}4\text{-methoxy phenyl} \text{ butyronitrile (LXXXI)}\). The foregoing imino nitroso hydrindone (LXXXI) (2.2 g.) was dissolved in aqueous 10 per cent sodium hydroxide solution (22 c.c.) and treated gradually with p-toluene sulphonyl chloride (2.4 g.). The reaction mixture was shaken for about 10 minutes and then heated on a water-bath for 10 minutes. On cooling the alkaline solution was filtered and the filtrate acidified with hydrochloric acid to give a gummy mass which solidified to a yellow crystalline solid on standing. On recrystallisation from alcohol in light brown prisms, the nitrile (LXXXI) had m.p. 173-174°. Yield 2.2 g.

0.1170 g. gave 0.2896 g. CO₂ and 0.0611 g. H₂O

Found: C, 67.5; H, 5.8
C₂₀H₂₁O₅N requires C, 67.6; H, 5.9 per cent

\(\langle 2\text{-carboxy-5\text{-6-dimethoxy phenyl}}\rangle -\gamma\text{-}4\text{-methoxy phenyl} \text{ butyric acid (LXXXII)}\). The preceding nitrile (LXXXI) (1.8 g.) was hydrolysed by heating under reflux on the sand-bath, with 10 per cent aqueous sodium hydroxide solution (20 c.c.), for about 8 hours. After cooling the alkaline solution was filtered and acidified with hydrochloric acid to give a yellow crystalline solid. On recrystallisation from alcohol (charcoal), \(\langle 2\text{-carboxy-5\text{-6-dimethoxy phenyl}}\rangle -\gamma\text{-}4\text{-methoxy phenyl} \text{ butyric acid} \) formed fine colourless prisms, m.p. 177-178°. Yield 1.6 g.

0.1218 g. gave 0.2863 g. CO₂ and 0.0647 g. H₂O

Found: C, 64.1; H, 5.9
C₂₀H₂₂O₇ requires C, 64.2; H, 5.9 per cent
I. **Synthesis of \( \alpha-(2\text{-carboxy-4:5\text{-methylenedioxy phenyl})} - \gamma\text{-phenyl butyric acid.} \)**

**3:4-methylenedioxy chalcone (Piperonylendene acetophenone) (LXXXIII).** - Aqueous 10 per cent sodium hydroxide solution (30 c.c.) was gradually added to a solution of 3:4-methylenedioxy benzaldehyde (Piperonal) (30 g.) and acetophenone (24 g.) in alcohol (150 c.c.) with vigorous shaking. In about 5 minutes the clear solution became hazy, with evolution of heat and a solid separated. The reaction mixture was left overnight at the room temperature, and the solid collected by filtration, washed well with water and a little alcohol. On recrystallisation from alcohol it formed yellow needles, m.p. 122°. Yield 50 g.

\( \alpha\text{-Carboxy-}\beta-(3:4\text{-methylenedioxy phenyl}) - \gamma\text{-benzoyl butyric acid (LXXXIV).} \)** - To a solution of sodium ethoxide prepared from sodium (0.4 g.) in absolute alcohol (60 c.c.), diethyl malonate (31 g.) was added, followed by 3:4-methylenedioxy chalcone (LXXXIII) (48 g.) with shaking, and the mixture was heated under reflux on the water-bath for 2 hours. The reaction product was hydrolysed by refluxing with a solution of potassium hydroxide (48 g.) in water (160 c.c.) and alcohol (40 c.c.), on the water-bath for an hour. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether to remove any neutral matter. The clear alkaline solution was acidified with hydrochloric acid, and the solid which separated was collected. On recrystallisation from alcohol, \( \alpha\text{-carboxy-}\beta-(3:4\text{-methylenedioxy phenyl}) - \gamma\text{-benzoyl butyric acid.} \)
butyric acid formed fine colourless needles, m.p. 156-157°. Yield 60 g.

0.1047 g. gave 0.2465 g. \( \text{CO}_2 \) and 0.0414 g. \( \text{H}_2\text{O} \)

\[ \text{Found: C: 64.2; H: 4.4} \]

\( \text{C}_{19}\text{H}_{16}\text{O}_7 \) requires C, 64.0; H, 4.5 per cent

\[ \beta-(3:4\text{-methyleneedioxy phenyl})-\gamma\text{-benzoyl butyric acid} \]

The foregoing acid (LXXXIV) (58 g.) was decarboxylated by heating in an oil-bath at 170-180° for an hour. On cooling the residue was extracted with 10 per cent sodium carbonate solution and filtered. The alkaline filtrate was acidified with hydrochloric acid, whereby a crystalline solid separated. On recrystallization from dilute acetic acid \( \beta-(3:4\text{-methyleneedioxy phenyl})-\gamma\text{-benzoyl butyric acid} \) formed short colourless needles, m.p. 153-154°. Yield 45 g.

0.0955 g. gave 0.2427 g. \( \text{CO}_2 \) and 0.0446 g. \( \text{H}_2\text{O} \)

\[ \text{Found: C: 69.3; H: 5.2} \]

\( \text{C}_{19}\text{H}_{16}\text{O}_7 \) requires C, 69.2; H, 5.1 per cent

\[ \beta-(3:4\text{-methyleneedioxy phenyl})-8\text{-phenyl valeric acid} \]

The preceding keto-acid (LXXXV) (40 g.) was reduced by heating under reflux with a mixture of toluene (150 c.c.) 5 per cent acetic acid (75 c.c.), concentrated hydrochloric acid (50 c.c.) and amalgamated zinc (120 g.), for 60 hours, hydrochloric acid (25 c.c.) being added every 12 hours after cooling the toluene layer was separated, washed with water and extracted with a 10 per cent solution of sodium carbonate. The alkaline solution on acidification with hydrochloric acid gave.
a gummy mass which solidified on standing. On recrystallisation from alcohol, 4-(3,4-methylenedioxy phenyl)-8-phenyl valeric acid formed slightly coloured needles, m.p. 132°. Yield 28 g.

0.1002 g. gave 0.2651 g. CO₂ and 0.0559 g. H₂O

Found: C, 72.4; H, 6.2

C₁₈H₁₈O₄ requires C, 72.5; H, 6.0 per cent

5:6-methylenedioxy-3-phenyl ethyl-1-hydrindone (LXXVII). - The foregoing acid (LXXXVI) (8 g.) was dissolved in dry boiling benzene (50 c.c.) and powdered phosphorous pentoxide (40 g.) was added to it in 3 lots, with vigorous shaking after each addition. The reaction mixture was heated under reflux on a water-bath for 3 hours. After cooling, powdered ice was added to decompose the phosphorous complex, and the product was extracted with ether. The ethereal layer was washed with water, 10 per cent sodium hydroxide, again with water and dried. The solvent was removed and the residue distilled under reduced pressure. 5:6-methylenedioxy-3-phenyl ethyl-1-hydrindone, b.p. 220-225°/2 mm, on recrystallisation from alcohol formed colourless needles, m.p. 108-109°. Yield 4.5 g.

0.1217 g. gave 0.3457 g. CO₂ and 0.0613 g. H₂O

Found: C, 77.0; H, 5.6

C₁₈H₁₆O₃ requires C, 77.1; H, 5.7 per cent

The 2:4-Dinitro-phenyl hydrazone obtained readily in the usual way separated from alcohol in bright red needles, m.p. 220-221°.
0.0941 g. gave 0.2157 g. CO₂ and 0.0353 g. H₂O.

Found: C, 62.6; H, 4.2

\( \text{C}_24\text{H}_{20}\text{O}_6\text{N}_4 \) requires C, 62.6; H, 4.3 per cent

The semicarbazone prepared in the usual way on recrystallisation from alcohol formed colourless needles, m.p. 200°-201°.

0.0889 g. gave 0.2204 g. CO₂ and 0.0456 g. H₂O.

Found: C, 67.6; H, 5.7

\( \text{C}_19\text{H}_{19}\text{O}_3\text{N}_3 \) requires C, 67.7; H, 5.6 per cent

5:6-methylenedioxy-3-phenyl ethyl-2-isonitroso-1-hydrindone (LXXXVIII). - The foregoing hydrindone (LXXXVII) (3 g.) was dissolved in methyl alcohol (30 c.c.) and mixed with concentrated hydrochloric acid (2.5 c.c.), methyl nitrite was passed into it, until no more absorption took place. The excess of methyl alcohol was evaporated, the residue diluted with water and extracted with ether. The product was isolated in the usual way to give a yellow crystalline solid. On recrystallisation from alcohol, 5:6-methylenedioxy-3-phenyl ethyl-2-isonitroso-1-hydrindone formed light yellow needles, m.p. 176-177°. Yield 2.4 g.

0.0991 g. gave 0.2537 g. CO₂ and 0.0446 g. H₂O.

Found: C, 69.8; H, 5.0

\( \text{C}_{18}\text{H}_{15}\text{O}_4\text{N} \) requires C, 69.9; H, 4.9 per cent

\( \alpha\)-(2-carboxy-4:5-methylenedioxy phenyl)-\( \gamma\)-phenyl butyronitrile (LXXXIX). - The preceding isonitroso hydrindone (LXXXVIII) (2 g.) was dissolved in aqueous 10 per cent
sodium hydroxide solution (20 c.c.) and treated gradually with p-toluene sulphonyl chloride (2 g.) with shaking. The reaction was completed by heating the mixture on a boiling water-bath for about 10 minutes. After cooling the alkaline solution was filtered and the filtrate acidified with hydrochloric acid to give a yellow crystalline solid. On recrystallization from dilute alcohol, \(-\text{(-carboxy-4:5-methylene dioxy phenyl)}-\gamma\text{-phenyl butyric nitrile}\) formed pale yellow needles, m.p. 108-110°. Yield 1.9 g.

0.0855 g. gave 0.2198 g. CO₂ and 0.0362 g. H₂O

Found: C, 70.1; H, 4.7

C₁₈H₁₄O₄N requires C, 69.9; H, 4.9 per cent

\(-\text{(-carboxy-4:5-methylene dioxy phenyl)}-\gamma\text{-phenyl butyric acid (LXXI). - The foregoing nitrile (LXXXIX) (1.4 g.) was hydrolysed by heating under reflux on a sand-bath, with a 10 per cent solution of sodium hydroxide (15 c.c.) for about 8 hours. After cooling the alkaline solution was filtered and the filtrate acidified with hydrochloric acid to give a gummy mass, which was extracted with ether. The ethereal solution was washed with water and diluted with petroleum ether (b.p. 60-80°) to separate the tarry matter. The clear ether solution was decanted and the solvent evaporated to give a light yellow crystalline solid. On recrystallization from dilute acetic acid (charcoal), \(-\text{(-carboxy-4:5-methylene dioxy phenyl)}-\gamma\text{-phenyl butyric acid}\) formed almost colourless short needles, m.p. 149-151°. Yield 1.1 g.
J. Synthesis of \( \alpha-(2\text{-carboxy}\cdot-4\text{-methylenedioxy phenyl})\cdot\gamma\cdot-4\text{-methoxy phenyl butyric acid} \)

3:4-methylendioxy-4'-methoxy chalcone (piperonylledene-p-methoxy acetophenone (LXXI). - Aqueous 10 per cent solution of sodium hydroxide (15 c.c.) was gradually added to a solution of pieronal (15 g.) and p-methoxy acetophenone (15 g.) in alcohol (75 c.c.) with vigorous shaking. In about 10 minutes the reaction mixture became warm and a yellow crystalline solid started separating, which was left for 24 hours at room temperature. The solid was collected and washed well with water and a little alcohol. On recrystallization from hot benzene, it formed long yellow needles, m.p. 135-136°. Yield 25 g.

\[ \text{0.1121 g. gave 0.2968 g. CO}_2 \text{ and 0.0494 g. H}_2\text{O} \]
\[ \text{Found: C, 72.2; H, 4.9} \]
\[ \text{C}_{17}\text{H}_{14}\text{O}_4 \text{ requires C, 72.3; H, 5.0 per cent} \]

\( \alpha\text{-Carboxy-}\beta\cdot(3:4\text{-methylendioxy phenyl})\cdot\gamma\cdot-(4'\text{-methoxy benzoyl}) \) butyric acid (LXXXI). - To a solution of sodium (0.3 g.) in absolute alcohol (45 c.c.), diethyl malonate (12 g.) was added, followed by the above chalcone (LXXI) (21 g.) with shaking. The mixture was heated under reflux for 2 hours. The adduct was hydrolysed by refluxing with a solution of potassium hydroxide (18 g.) in water
(60 c.c.) and alcohol (20 c.c.), for an hour. The excess of alcohol was removed the residue diluted with water and extracted with ether. The clear alkaline solution was acidified to give a heavy oil which solidified on standing. On recrystallisation from dilute ethanol, \( \alpha \)-carboxy-\( \beta \)-(3:4-methylene dioxy phenyl) \(-\gamma\)-(4'-methoxy benzoyl) butyric acid formed fine colourless needles, m.p. 141-142°. Yield 24 g.

0.1208 g. gave 0.2764 g. CO₂ and 0.0500 g. H₂O

Found: C, 62.4; H, 4.6
C₁₂H₁₈O₈ requires C, 62.2; H, 4.7 per cent

\( \beta \)-(3:4-methylene dioxy phenyl)-\( \gamma \)-(4'-methoxy benzoyl) butyric acid (LXLIII). - The above acid (LXLII) (22 g.) was decarboxylated by heating in an oil-bath at 170-180°, for an hour. After cooling the residue was extracted with boiling 10 per cent sodium carbonate solution and filtered. The filtrate was acidified with hydrochloric acid to give a crystalline solid. On recrystallisation from acetic acid, \( \beta \)-(3:4-methylene dioxy phenyl)-\( \gamma \)-(4'-methoxy benzoyl) butyric acid formed fine colourless needles, m.p. 154-155°. Yield 19.5 g.

0.1163 g. gave 0.2841 g. CO₂ and 0.0576 g. H₂O

Found: C, 66.6; H, 5.5
C₁₉H₁₈O₆ requires C, 66.7; H, 5.3 per cent

\( \beta \)-(3:4-methylene dioxy phenyl)-\( \gamma \)-(4'-methoxy benzoyl) valeric acid (LXLIV). - The foregoing keto-acid (LXLII) (18 g.) was reduced by heating under reflux on the sand-bath
with a mixture of amalgamated zinc (50 g.), toluene (40 c.c.), 5 per cent acetic acid (40 c.c.) and concentrated hydrochloric acid (40 c.c.), for 48 hours. Concentrated hydrochloric acid (15 c.c.) being added every 12 hours. After cooling the toluene layer was separated and the mother liquor extracted with ether. The combined organic layer, after washing well with water, was extracted with 10 per cent sodium carbonate solution. The alkaline extract was acidified with hydrochloric acid, whereby a crystalline solid separated. On recrystallization from acetic acid, \( \beta \)-(3,4-methylenedioxy phenyl) - \( \alpha \)-(4′-methoxy phenyl) valeric acid formed short colourless prisms, m.p. 118-119°. Yield 16 g.

0.0920 g. gave 0.2342 g. CO₂ and 0.0497 g. H₂O

Found: C, 69.4; H, 6.0
C₁₉H₂₀O₅ requires C, 69.5; H, 6.1 per cent

5,6-methylenedioxy-3(4′-methoxy phenyl ethyl)-1-
hydrindone (LXLV). - The foregoing acid (LXLIV) (10 g.) was dissolved in boiling benzene (50 c.c.) and treated gradually with phosphorous pentaoxide (50 g.). After refluxing on the water-bath for 3 hours, the product was cooled and mixed with crushed ice to decompose the complex. The pale yellow suspension obtained was thoroughly extracted with ether. The ethereal layer washed with water, dilute sodium hydroxide and again with water, and dried. The solvent was removed and the residue distilled under reduced pressure. 5,6-methylenedioxy-3(4′-methoxy phenyl ethyl)-1-hydrindone was collected as a viscous yellow oil, b.p. 275-280°/2 mm. Yield 5.6 g.
The 2,4-dinitrophenyl hydrazone formed readily on crystallisation from acetic acid, had m.p. 232-233°.

0.0856 g. gave 0.1918 g. CO₂ and 0.0339 g. H₂O
Found: C, 61.1; H, 4.4
C₂₅H₂₈O₁₇N₄ requires C, 61.2; H, 4.5 per cent

**5:6-methylenedioxy-3(4'-methoxy phenyl ethyl)-2-iso-nitroso-1-hydrindone (LXLVI).** - The above hydrindone (LXLV) (4 g.) was dissolved in methyl alcohol (24 c.c.) and mixed with concentrated hydrochloric acid (2.5 c.c.) and saturated with methyl nitrite. The excess of alcohol was evaporated and the residue after dilution with water was extracted with ether. The ethereal layer was washed well with water and extracted 10 per cent sodium hydroxide solution. The alkaline extract was acidified with hydrochloric acid to give a yellow crystalline solid. On recrystallisation from ethanol, 5:6-methylenedioxy-3-(4'-methoxy phenyl ethyl)-2-isonitroso-1-hydrindone formed pale yellow needles, m.p. 166-167°. Yield 3.4 g.

0.1017 g. gave 0.2514 g. CO₂ and 0.0467 g. H₂O
Found: C, 67.4; H, 5.1
C₁₉H₁₇O₂₅N requires C, 67.3; H, 5.0 per cent
\( \alpha-(2\text{-carboxy-4,5\text{-methylenedioxy phenyl}})\gamma-(4'\text{-methoxy phenyl})\text{butyro nitrile (LXLVII)} \). The foregoing iso-nitroso hydridone (LXLVI) (2.5 g.) was mixed with 10 per cent sodium hydroxide solution (25 c.c.) and gradually treated with p-toluene sulphony chloride (2.5 g.) with shaking. The reaction was completed by heating the mixture on the water-bath for 10 minutes. After cooling the alkaline solution was filtered and acidified with hydrochloric acid to give a gummy mass which solidified on standing. On recrystallization from dilute alcohol, \( \alpha-(2\text{-carboxy-4,5\text{-methylenedioxy phenyl}})\gamma-(4'\text{-methoxy phenyl})\text{butyro nitrile} \) formed almost colourless crystals, m.p. 124-126°. Yield 2.2 g.

0.0836 g. gave 0.2057 g. CO₂ and 0.0391 g. H₂O

Found: C, 67.1; H, 5.2

\( C_{19}H_{17}O_5N \) requires C, 67.3; H, 5.0 per cent

\( \alpha-(2\text{-carboxy-4,5\text{-methylenedioxy phenyl}})\gamma-(4'\text{-methoxy phenyl})\text{butyric acid (LXLVIII)} \). The preceding nitrile (2 g.) was dissolved in 10 per cent sodium hydroxide solution (25 c.c.) and heated under reflux on the sand-bath for about 8 hours. The alkaline solution was cooled and filtered, and the filtrate was acidified with hydrochloric acid to give a gummy mass which solidified on standing. On double crystallization from acetic acid (charcoal), \( \alpha-(2\text{-carboxy-4,5\text{-methylenedioxy phenyl}})\gamma-(4'\text{-methoxy phenyl})\text{butyric acid} \) formed diamond shaped colourless prisms, m.p. 172°. Yield 1.9 g.

0.1106 g. gave 0.2579 g. CO₂ and 0.0508 g. H₂O

Found: C, 63.6; H, 5.1

\( C_{19}H_{19}O_7 \) requires C, 63.7; H, 5.0 per cent
K. Synthesis of \( \alpha \)-[2-carboxy-4,5-methylene dioxy phenyl] \( \gamma \)-[3',4'-dimethoxy phenyl] butyric acid

3,4-methylene dioxy-3',4'-dimethoxy chalcone (Piperonylidene acetoveratrone (LXLIX)). - An aqueous solution of sodium acetate (25 c.c.) was gradually added to a solution of piperonal (15 g.) and acetoveratrone (18 g.) in alcohol (80 c.c.) with vigorous shaking. The reaction mixture was left overnight at room temperature and the crystalline yellow solid which separated was collected by filtration and washed well with water and alcohol. On recrystallisation from alcohol 3,4-methylene dioxy-3',4'-dimethoxy chalcone formed yellow plates, m.p. 132°. Yield 23 g.

0.1183 g. gave 0.2997 g. CO\(_2\) and 0.0554 g. H\(_2\)O

Found: C, 69.1; H, 5.2
C\(_{18}\)H\(_{16}\)O\(_5\) requires C, 69.2; H, 5.1 per cent

\( \beta \)-[3,4-methylene dioxy phenyl] \( \gamma \)-[3',4'-dimethoxy benzoyl] butyric acid (LLI). - To a solution of sodium (0.2 g.) in absolute ethyl alcohol (40 c.c.), diethyl malonate (11 g.) was added, followed by the above chalcone (LXLIX) (20.8 g.) with shaking and heated under reflux on the water-bath for about 24 hours. The reaction product was hydrolysed by refluxing on the water-bath with a solution of potassium hydroxide (16 g.) in water (55 c.c.) and alcohol (20 c.c.) for an hour. The excess of alcohol was removed, the residue diluted with water and extracted with ether. The clear alkaline solution was acidified with hydrochloric acid to give a dark coloured semi solid which could not be induced to
101 crystallise. The crude acid (LL) (16 g.) was decarboxylated by heating in an oil-bath at 170-180° for 2 hours. After cooling the residue was extracted with boiling 10 per cent aqueous sodium carbonate solution and filtered. The alkaline filtrate was acidified to give a crystalline solid. On recrystallisation from acetic acid, $\beta$-($3:4$-methyleneoxy phenyl)-$\gamma$-($3:4$'-dimethoxy benzoyl) butyric acid formed fine light brown needles, m.p. 125°. Yield 12.5 g.

0.1014 g. gave 0.2391 g. CO₂ and 0.0593 g. H₂O

Found: C, 64.3; H, 6.5

C₂₀H₂₀O₇ requires C, 64.5; H, 6.4 per cent

$\beta$-($3:4$-methyleneoxy phenyl)-$\gamma$-($3:4$'-dimethoxy phenyl) valeric acid (LLIII). - The preceding keto-acid (LLI) (11 g.) was reduced by heating under reflux with a mixture of toluene (60 c.c.) 5 per cent acetic acid (30 c.c.), concentrated hydrochloric acid (30 c.c.) and amalgamated zinc (80 g.) for 60 hours. Hydrochloric acid (10 c.c.) being added every 12 hours. After cooling the toluene layer was separated, washed well with water and extracted with 10 per cent aqueous sodium carbonate solution. The alkaline solution was acidified with hydrochloric acid to give a semi solid which was further purified by methylation, in the usual way. On recrystallisation from petroleum ether (b.p. 80-100°), $\beta$-($3:4$-methyleneoxy phenyl)-$\gamma$-($3:4$'-dimethoxy phenyl) valeric acid formed stout colourless prisms, m.p. 102-103°. Yield 9.5 g.
0.1002 g. gave 0.2465 g. CO₂ and 0.0559 g. H₂O.
Found: C, 67.1; H, 6.42
C₂O₂H₂O₆ requires C, 67.9; H, 6.1 per cent

5:6-methylenedioxy-3-(3':4'-dimethoxy phenyl ethyl)-1-hydrindone (III).

- The foregoing acid (III) (7.2 g.) dissolved in dry benzene (30 c.c.) was gradually treated with powdered phosphorous pentachloride (4.4 g.) with swirling and cooling in ice water, the reaction started almost immediately, which was left at room temperature until phosphorous pentachloride went into solution (1 hour). The reaction mixture was heated on a water-bath for 10 minutes, cooled in the freezing mixture and when benzene began to crystallize, stannic chloride (10 c.c.) mixed with dry benzene (10 c.c.) were added to it all at once. The reaction mixture was left overnight in the ice chest. Hydrochloric acid and powdered ice were added to decompose the complex. The product was worked up in the usual way. After removing the solvents the residue was distilled under reduced pressure, 5:6-methylenedioxy-3(3':4'-dimethoxy phenyl ethyl)-1-hydrindone was collected as a viscous pale yellow oil, b.p. 250-255°/2 mm. Yield 4.5 g.

0.1162 g. gave 0.3004 g. CO₂ and 0.0606 g. H₂O.
Found: C, 70.5; H, 5.8
C₂O₂H₂O₅ requires C, 70.6; H, 5.9

The 2:4-dinitrophenyl hydrazone prepared in the usual way on recrystallization from acetic acid in brick-red needles, bad m.p. 209-210°.
0.0852 g. gave 0.1878 g. CO₂ and 0.0353 g. H₂O

Found: C, 60.1; H, 4.6

C₂₆H₂₄O₆N₄ requires C, 65.0; H, 4.6 per cent

5:6-methylenedioxy-3(3′:4′-dimethoxy phenyl) ethyl

2-isonitroso-1-hydrindone (LLIV). - The foregoing hydrindone (LLIII) (1 g.) was dissolved in methyl alcohol (18 c.c.) and mixed with concentrated hydrochloric acid (2 c.c.), methyl nitrite gas passed into it, until no more absorption took place. The excess of alcohol was evaporated, the residue diluted with water and extracted with ether. The ethereal layer was washed well with water and extracted with a 10 per cent solution of sodium hydroxide. The cooled alkaline solution was acidified whereby the isonitroso hydrindone separated as a yellow crystalline solid. On recrystallization from dilute ethyl alcohol, 5:6-methylenedioxy-3(3′:4′-dimethoxy phenyl)-2-isonitroso-1-hydrindone formed pale yellow needles, m.p. 160-161°. Yield 1.95 g.

0.1102 g. gave 0.2622 g. CO₂ and 0.0516 g. H₂O

Found: C, 64.9; H, 5.2

C₂₀H₁₉O₆N₂ requires C, 65.0; H, 5.1 per cent

α-(2-carboxy-4:5-methylenedioxy phenyl)-γ-(3′:4′-dimethoxy phenyl) butyro nitrile (LLV). - The preceding isonitroso hydrindone (LLIV) (1.6 g.) was dissolved in aqueous 10 per cent sodium hydroxide solution (16 c.c.) and treated gradually with p-toluene sulphonyl chloride (1.6 g.) with shaking. The reaction was completed by heating on a water-
bath for 10 minutes. After cooling the alkaline solution was filtered and acidified with concentrated hydrochloric acid to give a yellow crystalline solid. On recrystallisation from dilute alcohol \(-\{(2\text{-carboxy-4,5-methylenedioxy phenyl})-\gamma-(3',4'-\text{dimethoxy phenyl})\text{ butyronitrile}\}\) formed pale yellow needles, m.p. 124-126°. Yield 1.4 g.

0.0906 g. gave 0.2165 g. CO₂ and 0.0432 g. H₂O

Found: C, 65.1; H, 5.3

C₂₀H₁₉O₆N requires C, 65.0; H, 5.1 per cent

\(-\{(2\text{-carboxy-4,5-methylenedioxy phenyl})-\gamma-(3',4'-\text{dimethoxy phenyl})\text{ butyric acid (LLVI)\}. The above nitrile (LLV) (1.1 g.) was dissolved in aqueous 10 per cent sodium hydroxide solution (11 c.c.) and heated under reflux on the sand-bath for about 8 hours. After cooling the alkaline solution was filtered and acidified with hydrochloric acid to give a brownish semi solid, which solidified on standing. \(-\{(2\text{-carboxy-4,5-methylenedioxy phenyl})-\gamma-(3',4'-\text{dimethoxy phenyl})\text{ butyric acid\} on recrystallisation from dilute alcohol (charcoal) in colourless needles, m.p. 152-153°. Yield 0.95 g.

0.1215 g. gave 0.2754 g. CO₂ and 0.0558 g. H₂O

Found: C, 61.8; H, 5.1

C₂₀H₂₀O₈ requires C, 61.9; H, 5.2 per cent
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