PART II

FRIESE RERANGELEMENT OF P-AMINOPHENOL ESTERS
The phenolic ketones are prepared by various methods such as Nencki, Hoesch, Grignard, Friedel-Crafts and Fries rearrangement reactions. Out of this Fries rearrangement is convenient for preparing hydroxy phenyl ketones from phenolic esters. An attempt to avoid difficulties in the Friedel-Crafts reaction led to the discovery of the Fries reaction (Fries and Finck, Ber., 1908, 41, 4271; 1910, 43, 214). Since then considerable work has been done to prepare hydroxy phenyl ketones and also to investigate the conditions effecting the course of the reaction. Reviews on this reaction, its experimental technique, its mechanism, and its applicability and limitations towards various substituted phenolic esters have been given by various authors (A. H. Blatt, Chem. Rev., 1940, 27, 413-35; A. H. Blatt in R. Adams, "Organic Reactions", Vol. I, John Wiley & Sons, Inc., New York, 1942, p. 342; also Thomas' "Anhydrous Aluminium chloride in Organic Chemistry", Reinhold Publishing Corporation, Inc., New York, 1941, p. 696-709).

The Fries migration is of wide applicability because both the acids and phenols from which the phenol esters are prepared can be varied within extensive limits, and both are found to influence the course of Fries reaction.

Since the work of Fries (loc. cit.) several workers have investigated their reactions with various esters (aliphatic or
aromatic, saturated or unsaturated) of simple mono-, di- and tri-hydric phenols, mono- and dihydroxy naphthalenes, hydroxy anthracenes, hydroxy phenanthrenes, hydroxy biphenyls, hydroxy fluorene, etc. It has also been applied to some heterocyclic compounds like coumarone, coumarin, chromone, quinoline, etc. Effects of substituents like alkyl, halogen, carboxyl, acyl, or nitro has also been investigated. Generally ortho or para hydroxy ketones or a mixture of both is formed depending upon the experimental conditions. If the substituents are in ortho position para migration is usually favoured while if they are in meta or para, an ortho product is generally obtained. It was earlier reported that groups like carboxyl, acyl and nitro inhibit the rearrangement (Rosenmund and Schnurr, Ann., 1928, 460, 56). However, recent work by Shah and coworkers (J. Ind. Chem. Soc., 1949, 26, 235; 1952, 29, 351; 1953, 30, 915; 195, 373; 1956, 33, 249, 318), Baker (J. Chem. Soc., 1934, 1684), Brown (J. Amer. Chem. Soc., 1946, 63, 873) and Amin and Chaughuley (Sci. and Culture, 1954, 19, 614) has shown that they do not completely inhibit the transformation, though they considerably retard it.

Attempts to carry out the migration of the acyl substituted amino compounds have been either unsuccessful or the ketonic products have been obtained in poor yields (Kursanov, J. Gen. Chem., U. S. S. R., 1943, 13, 286; C. A., 1944, 38, 959; Dippy and Wood, Nature 1946, 157, 408). According to Chattaway (J. Chem. Soc., 1904, 386), the migration with monoacyl anilines
is more difficult than the migration with diacyl anilines. Recently, Julia and Baillarge, Bull. Soc. Chim., France, 1952, 19, 639; C. A., 1953, 3815) have successfully carried out the Fries reaction with O:N-diacetyl derivatives of ortho-, meta- and para-aminophenols.

The rates of formation of ortho or para hydroxy ketones in the Fries migration is also much influenced by the nature and the size of the migrating acyl group (Rosenmund and Schnurr, loc. cit.; Baltzly and Bass, J. Amer. Chem. Soc., 1933, 55, 4292; Tarbell and Fanta, ibid., 1943, 2169; Sen and coworkers, J. Ind. Chem. Soc., 1953, 30, 61; Tiwari, ibid., 1954, 31, 79).

The tendency of the formation of o-hydroxy ketones increases with the esters of higher acids even at low temperatures. However, Bell and Driver (J. Chem. Soc., 1940, 835) obtained p-isomers in the migration of phenyl stearate and palmitate along with o-isomers (see also Ralston, McCorkle and Baur, J. Org. Chem., 1940, 5, 645).

1953, 30, 269), hydrogen fluoride (Simons, Archer and Randall, 
( J. Amer. Chem. Soc., 1940, 62, 485), phosphorus pentoxide 
(Schönberg and Mustafa, J. Chem. Soc., 1943, 79), titanium 
tetrachloride (Ralston, Segebrecht and McCorkle, J. Org. Chem., 
1942, 7, 522; d'Ano and Zimmer, Chem. Ber., 1952, 85, 585; 
sodium chloride melt (Bruce, Sorrie and Thomson, J. Chem. Soc., 
1953, 2403) and concentrated sulphuric acid (Israelstan, J. S. 
African Chem. Inst., 1944, 27, 15; C. A., 1945, 2065) have also 
been used to effect the rearrangement. According to Sekera 
(Trans. Illinois State Acad. Sci., 1953, 27, 81; Br. Chem. Abstr., 
1936, AII, 55), agents other than aluminium chloride are less 
effective in the Fries transformation.

Ralston and coworkers (loc. cit.) have arranged various 
chlorides employed as migrating agents in the following order of 
decreasing reactivity: aluminium, ferric, titanium, stannic and 
zinc (cf. Dermer and coworkers, J. Amer. Chem. Soc., 1941, 63, 
2881).

Besides the structure of ester, other factors like the 
temperature, solvent and the amount of migrating agent also 
influence the reaction.

The effect of temperature on the Fries migration:

It was first noted by Bykmann (Chem. Weekblad, 1904, 1, 453) 
and later examined by Rosenmund and Schnurr (loc. cit.) in case 
of m-cresyl acetate and benzoate at different temperatures. They
found that low temperatures facilitate the formation of p-hydroxy ketones, while high temperatures yield o-hydroxy ones, benzoyl group requiring higher temperatures for ortho migration than the acetyl one. The temperature effect on the formation of o- or p-hydroxy ketones much depends on the nature of the acyl group and the structure of the phenol.

Szkeres and Karnay (Gazz. chim. ital., 1947, 77, 471; C. A., 1948, 3356) record an interesting observation; they got, in case of phenyl acetate, a high yield of the ortho ketone at low temperature using petroleum ether as solvent, and further found that, rise of temperature favoured the formation of the para derivative, an observation contradictory to all the previous ones.

**Effect of solvent on the Fries reaction:**

The solvent acts as a diluent in case of vigorous reactions when high temperatures are required (Groggins and Newton, Ind. Eng. Chem., 1929, 21, 369) and assures a complete homogenity of the reaction mixture thus promoting the reaction at low temperature.

Among the several solvents, nitrobenzene is one that is most generally employed. Other solvents used are s-tetrachloroethane, chlorobenzene, and carbon bisulphide, but they have little advantage over nitrobenzene.

Baltzly and Bass (loc. cit.) and Fieser and Bradsher (J. Amer. Chem. Soc., 1936, 58, 1739, 2337) observed that solvents
may effect the rate and completeness of the reaction but has no
effect on its direction. In some cases it retards or inhibits
the reaction (Calloway, Chem. Rev., 1935, 17, 327; Wali, et al.,

Ralston, McCorkle and Bauer (loc. cit.) found that solvents
have influence upon the ratio of isomers and have arranged the
solvents accordingly. With equimolecular proportion of aluminium
chloride, they can be arranged with decreasing ortho-directing
influence in the following order: 1) carbon disulphide, 2) tetra-
chloroethane, 3) petroleum ether and 4) nitrobenzene. With
excess of aluminium chloride, this order becomes as 1), 3), 2)
and 4). The extreme para-directing influence of nitrobenzene was
attributed to the directing influence of the complex formed by
aluminium chloride with nitrobenzene (Stockhaussen and Gattermann,
Ber., 1892, 25, 3521; Calloway, loc. cit.).

PRESENT WORK:

As mentioned in the Introduction, Julia and Baillarge (Bull.
Soc. chim., France, 1952, 19, 639; C. A., 1953, 47, 3815) have
studied the Fries rearrangement of C=N-diacetyl derivatives of
ortho-, meta- and para-aminophenols. As an extension of this
work, the present work has been undertaken and Fries
transformation of p-amino phenol diesters (dipropionate,
dibutyrate and dibenzoate), p-acetamino phenol esters (propionate,
butyrate and benzoate) and p-benzamino phenol esters (acetate,
propionate and butyrate) has been investigated under different conditions and best conditions for getting the maximum yields of the o-hydroxy ketones determined.

The Friedel-Crafts acylations of p-acetamino- and p-benzamino-phenols have also been carried out under the conditions of Fries migration of the corresponding esters, and the o-hydroxy ketones have been obtained in good yields.
The diacetate, dipropionate, dibutyrate and dibenzoate of p-aminophenol (A : R = -CH₃, -C₂H₅, -n-C₃H₇ and -C₆H₅) have given on Fries migration with anhydrous aluminium chloride (3.3 mols.) 2-hydroxy-5-acylamino phenyl alkyl ketones (A : R = -CH₃, -C₂H₅, -n-C₃H₇, -C₆H₅). The first two 2-acyl-4-acylamino phenols have been deacetylated using hydrochloric acid (1:1) and the corresponding 2-acyl-4-aminophenols have been obtained. 2-Benzoyl-4-benzaminophenol, resisted deacylation under these conditions.

The structures, 2-acyl-4-acylaminophenols (A : R = -CH₃, -C₂H₅, -n-C₃H₇, -C₆H₅) have been assigned to the migration products on the following grounds:

(1) The migration of the acyl group can generally take place either to ortho or para position. In the present case, the para position is occupied by the acylamino group,
while both the free ortho positions, viz., '2' and '6' are identical. Hence, the only migration products possible in these cases are 2-acyl-4-acylamino phenol, if at all the reaction is to take place.

(ii) Further, the migration products (\( A : R = -\text{CH}_3, -\text{C}_2\text{H}_5; -\text{n.} \text{C}_3\text{H}_7 \text{ and } -\text{C}_6\text{H}_5 \)) give deep blue colouration with ethanolic ferric chloride, a characteristic of a strong negative group like an acyl group present in the ortho position to the hydroxyl one.

(iii) They dissolve in dilute alkali (5.0%) with pale green colour.

(iv) All the above 2-acyl-4-acylamino phenols have been characterised by preparing their oximes, semicarbazones or in some cases 2:4-dinitrophenyl hydrazones.

Fries migration of p-aminophenol diacetate has been carried out under the conditions of Julia and Baillargé (loc. cit.). 2-Hydroxy-5-acetamino acetophenone has also been obtained by the Friedel-Crafts acetylation of p-acetaminophenol. The reaction has been carried out in absence of solvent and using anhydrous aluminium chloride (2.2 mols.) under the conditions of Fries migration, when the hydroxy ketone is formed in good yields (60.0%).

In the case of p-aminophenol dipropionate and dibutyrate, the best condition for the migration to take place smoothly is found to be at 140-45\(^{\circ}\), when the corresponding \(o\)-hydroxy ketone
is obtained in maximum yields (about 55-65.0%). However, the p-aminophenol dibenzoate required a higher temperature of 160° and a reaction period of 1.5 hours for maximum yields.

These results indicate that the acylamino group in 4-position has no inhibiting effect in Fries rearrangement reaction, 2-acyl-4-acyl-aminophenols being obtained smoothly and in good yields.

(B) FRIES ISOMERISATION OF p-ACETAMINOPHENOL ESTERS:

\[
\begin{align*}
\text{CH}_3\text{CHN} & \quad \text{CH}_3\text{CHN} \\
\text{OC-R} & \quad \text{OC-R} \\
\text{Fries migration} & \\
\text{AICl}_3 & \\
\text{CH}_3\text{CHN} & \quad \text{CH}_3\text{CHN} \\
\text{OH} & \quad \text{OH} \\
\text{CH}_3\text{CHN} & \quad \text{CH}_3\text{CHN} \\
\text{O} & \quad \text{O} \\
\text{R = -C}_2\text{H}_5; -n\text{C}_3\text{H}_7; -\text{C}_6\text{H}_5}
\end{align*}
\]

This section deals with the isomerisation of p-acetaminophenol esters, which yield the corresponding 2-acyl-4-acetaminophenols in good yields.

p-Acetaminophenol has been condensed with one molecule of each of propionic anhydride, butyryl and benzoyl chlorides and the corresponding propionate, butyrate and benzoate respectively
of p-acetaminophenol have been prepared. The Fries migrations of these esters have been investigated as in the case of p-amino-phenol diesters described before. The reactions have been carried out using anhydrous aluminium chloride (3.3 mols.) and in absence of any solvent. The structures, 2-acyl-4-acetaminophenols (B : R = -C₂H₅, -n-C₃H₇, -C₆H₅) have been assigned to the migrated products on the following grounds:

(i) The migration of the acyl group can generally take place either in ortho or para position. In the present case, the para position is blocked up by the acetamino group, while both the vacant ortho positions, viz., '2' and '6' are identical. Hence the migration can take place either in '2' or '6' position, thus giving only one product, viz., 2-acyl-4-acetaminophenol.

(ii) All the migration products (B : R = -C₂H₅, -n-C₃H₇ and -C₆H₅) give deep blue colouration with ethanolic ferric chloride, a characteristic reaction of a strongly negative group present in the vicinity of the hydroxyl group.

(iii) They dissolve in dilute alkali (5.0 %) with pale green to greenish yellow colour.

(iv) All the hydroxy ketones form the acetoxy or benzoyloxy derivatives as well as the oximes, semicarbazones or 2:4-dinitro phenyl hydrazones.

(v) The Friedel-Crafts acylation of p-acetaminophenol in absence of solvent and under the conditions of Fries migration have yielded the same 2-acyl-4-acetaminophenols,
identical with those obtained by Fries migration
(v. infra).

As in the previous case, for the propionate and the butyrate of p-acetaminophenol, the best condition for the migration to take place smoothly and in good yields has been found to be that when the mixture is heated at 140° for an hour. In this case, the o-hydroxy ketones are the only products of the migration and are obtained in good yields. However, for the migration of p-acetaminophenyl benzoate reaction temperature of 155-60° and period of 1.5 hours is required.

As the above results clearly indicate, the acetamino group in '4' position does not inhibit the reaction, the corresponding 2-acyl-4-acetaminophenols being obtained smoothly and in overall good yields.

Friedel-Crafts Acylations of p-Acetaminophenol: Synthesis of 2-acyl-4-acetaminophenols:

The Friedel-Crafts acetylation of p-acetamino phenol has already been described in subdivision (A). In the same way, Friedel-Crafts propionylation, butyrylation and benzoylation also have been studied.

The Friedel-Crafts propionylation and butyrylation were carried out at 140° for 3 hours using anhydrous aluminium chloride (2.2 mols.) in absence of a solvent and the corresponding o-hydroxy ketones identical with those obtained by Fries migration
of \( p \)-acetamino-phenyl propionate and butyrate respectively have been obtained in good yields.

The Friedel-Crafts benzoylation is found to be successful only at 150-55° giving rise to 2-benzoyl-4-acetaminophenol in fairly good yields.

(C) FRIES ISOMERISATION OF \( p \)-BENZAMINOPHENOL ESTERS:

\[
\begin{align*}
\text{H}_5\text{C}_6\text{CHN} & \quad \text{OC-R} & \quad \text{H}_5\text{C}_6\text{CHN} \\
\text{OH} & \quad \text{R} & \quad \text{OH}
\end{align*}
\]

\( \text{Frie migration} \quad \text{AlCl}_3 \)

\( \text{R} = -\text{CH}_3; -\text{C}_2\text{H}_5; -\text{n-C}_3\text{H}_7 \)

In this section Fries isomerisation of \( p \)-benzamino phenol esters has been examined, when the corresponding 2-acyl-4-\( p \)-benzaminophenols have been obtained in fairly good yields.

\( p \)-Benzamino phenyl acetate, propionate, butyrate and benzoate have been prepared by the condensation of \( p \)-benzamino-phenol with acetic anhydride, propionic anhydride, butyryl and benzoyl chlorides respectively. The Fries transformation of
these esters have been investigated using anhydrous aluminium chloride (3.3 mols.) in absence of a solvent, and the corresponding 2-acyl-4-benzamino phenols have been obtained in good yields.

The migration products have been assigned the structures, 2-acyl-4-benzaminophenols (C : R = -CH₃, -C₂H₅, -n.C₃H₇) on the following grounds:

(i) In the Fries migration, the acyl group generally isomerises to ortho or para position. In the present case, since the para position is occupied by the benzamino group whereas both the ortho positions (viz., '2' and '6') are identical, migration can take place either in '2' or '6' position, thus giving only 2-acyl-4-benzaminophenols.

(ii) All the migration products (C : R = -CH₃, -C₂H₅ and -n.C₃H₇) give deep blue colour with ethanolic ferric chloride, this being a characteristic reaction of o-hydroxy aryl ketones.

(iii) All the hydroxy ketones dissolve in dilute alkali (5.0%) with pale green colour.

(iv) The acetyl or benzoyl derivative and oximes, semicarbazones or 2:4-dinitrophenyl hydrazones of the hydroxy ketones have been prepared.

(v) The Friedel-Crafts acylations of p-benzaminophenol have also been carried out in absence of solvent and under the conditions of the corresponding Fries migrations,
when the same 2-acyl-4-benzaminophenols identical with those obtained by Fries migration, have been produced.

In this case also, the best conditions for the Fries isomerisation of acetate, propionate and butyrate are found to be the heating of the reaction mixture at 140-45° for one hour, when maximum yield of the o-hydroxy ketones have been obtained.

It is concluded from these results that the 4-benzamino group does not inhibit the Fries migration, the corresponding 2-acyl-4-benzamino phenols being produced smoothly, and in good yields.

CONCLUSION

The Fries reaction of acetates, propionates and butyrates is best carried out at 140-45° with a reaction period of one hour. The reaction is smooth and the yields are generally 50.0—60.0 %. The corresponding Friedel-Crafts reaction also can be carried out under these conditions. Lower temperatures of 120-25° give either the unchanged ester or a mixture of the unchanged ester and the migration product; whereas higher temperatures of 160-65° or 180° give lower yields.

In case of the benzoates higher temperature 155-60° and a period of 1½ hours are required for good yields. Friedel-Crafts reaction is also successful under the same conditions.
PART II

EXPERIMENTAL

FRIES REARRANGEMENT OF p-AMINO-PHENOL ESTERS:

(A) FRIES MIGRATION OF p-AMINOPHENOL DIESTERS:

(i) Fries rearrangement of p-aminophenol diacetate:

p-Amino-phenol required for this work was prepared by the reduction of p-nitro-phenol with sodium hydrosulphite ( hydro ) in alkaline medium ( Joshi and Shah, Curr. Sci., 1949, 18, 73-74).

p-Amino-phenol diacetate:

It was prepared by heating a mixture of p-amino-phenol (11.0 g. : 1 mol. ), acetic anhydride (20.6 g. : 2 mols. ) and pyridine (3-4 drops ) on a boiling water bath for 2 hours. A white solid obtained on dilution and acidification in cold was collected, washed with dilute alkali and crystallised from ethanol, colourless thick plates, m.p. 158° (10.0 g. ). Julia and Baillargé ( Bull. Soc. chim., France, 1952, 639; C. A., 1953, 47, 3815 ) give m.p. 155° for this product.

The same compound was also obtained by heating a mixture of p-acetamino-phenol (15.0 g. : 1 mol. m.p. 168-69° : Friedlander, Ber. , 1893, 26, 178 ), acetic anhydride (10.2 g. : 1 mol. ) and pyridine (3-4 drops ) on a boiling water bath for 2 hours.
The white solid obtained on working up the reaction mixture as before crystallised from ethanol, colourless thick plates, m.p. 158° (15.0 g.).

**FRIE'S REARRANGEMENT OF p-AMINO-PHENOL DIACETATE: FORMATION OF 2-HYDROXY-5-ACETALINOACETOPHENONE:**

An intimate and well-powdered mixture of p-amino-phenol diacetate (10.0 g.: 1 mol.) and anhydrous aluminium chloride (22.0 g.: 3.3 mols.) protected from moisture was heated in an oil-bath at 140° for one and half hour. The reaction mixture began to melt at 130° with the evolution of copious fumes of hydrogen chloride. It solidified then forming a hard cake. It was cooled and treated with crushed ice and concentrated hydrochloric acid (7.0 c.c.) when a greenish solid separated. It was collected, washed with cold water and crystallised from dilute ethanol, pale green thick needles, m.p. 168° (6.0 g.). Kunckell (Ber., 1901, 34, 125) records m.p. 165° whereas Julia and Baillarge (loc. cit.) give m.p. 159-60°.

It is soluble in hot water, ethanol, methanol, acetone and acetic acid. It gives blue colour with ethanolic ferric chloride. It is insoluble in cold dilute mineral acids, but dissolves in dilute alkali with a yellowish green colour.
To an intimate and well-powdered mixture of p-acetamino-phenol (10.0 g.: 1 mol.) and anhydrous aluminium chloride (19.5 g.: 2.2 mols.), acetic anhydride (7.0 c.c.) was added cautiously when a vigorous reaction started with the evolution of copious fumes of hydrogen chloride. The initial reaction subsided in about 15 minutes after which the reaction mixture was heated on an oil bath, the temperature being raised slowly to 140° within \( \frac{1}{2} \) hour and then kept at 140-45° for 2\( \frac{1}{2} \) hours. The hard cake thus formed was then decomposed by the addition of crushed ice and concentrated hydrochloric acid (10.0 c.c.) when a yellowish green solid separated. It was collected, washed with cold water and crystallised from dilute ethanol, thick pale green needles, m.p. and mixed m.p. 168° (6.0 g.).

The acetyl derivative was prepared by heating a mixture of 2-hydroxy-5-acetaminoacetophenone (0.5 g.), acetic anhydride (1.0 c.c.) and pyridine (2-3 drops) on a boiling water-bath for 6 hours and crystallised from ethanol, thick pale yellow needles, m.p. 161-62°.

**Analysis**: 0.0984 g. substance on Kjeldahl determination required 7.2 c.c. of 0.04816 N acid.

**Found**: N, 4.93 per cent.

\( \text{C}_{14}\text{H}_{15}\text{NO}_{5} \) requires : N, 5.05 per cent.
The methoxy derivative. — It was prepared by refluxing a mixture of 2-hydroxy-5-acetamino-acetophenone (1.0 g.), dimethyl sulphate (0.5 c.c.) and anhydrous potassium carbonate (1.5 g.) in dry acetone (25.0 c.c.) on a water-bath at 60° for 12 hours. On removal of acetone a brown solid was obtained, which was collected, washed with dilute alkali and crystallized from ethanol, colourless needles, m.p. 188° (0.4 g.).

Analysis: 0.152 g. substance on Kjeldahl determination required 14.5 c.c. of 0.04816 N acid.

Found: N, 6.43 per cent.

C₁₁H₁₃NO₃ requires: N, 6.76 per cent.

DEACYTLATION OF 2-HYDROXY-5-ACETAMINO-ACETOPHENONE: FORMATION OF 2-HYDROXY-5-AMINOACETOPHENONE:

A solution of 2-hydroxy-5-acetaminoacetophenone (1.0 g.) in hot concentrated hydrochloric acid (1:1 - 25.0 c.c.) was heated under reflux on sand bath for 6 hours. It was then concentrated when 2-hydroxy-5-aminoacetophenone hydrochloride separated as a silvery white solid. It crystallized from ethanol, colourless shining plates, m.p. 231° (0.6 g.). Kunckell (Ber., 1901, 34, 125) records m.p. 158° for this compound.

Analysis: 0.105 g. substance gave 0.0794 g. AgCl

Found eq. wt.: 189.8

C₈H₈NO₂·HCl requires eq. wt.: 187.5
A hot solution of the above hydrochloride (1.0 g.) in water (25.0 c.c.) was made alkaline by the treatment of ammonium hydroxide solution. On removal of excess of ammonia a brown solid separated which was collected, washed with cold water and crystallised from water containing few drops of ethanol, reddish brown plates, m.p. 118° (0.6 g.). Kunckell (loc. cit.) records m.p. 110° for the same compound.

It dissolves in hot water, ethanol, methanol, acetone and acetic acid. It dissolves in dilute alkali (5.0 %) as well as in dilute mineral acids. It gives blue colour with ethanolic ferric chloride.

(ii) Fries migration of p-amino-phenol dipropionate:

The dipropionate of p-amino-phenol was prepared by heating a mixture of p-amino-phenol (10.0 g.: 1 mol.), propionic anhydride (24.0 g.: 2 mols.) and pyridine (3-4 drops) on a boiling water bath for 2 hours, and then treating it with ice-cold water containing concentrated hydrochloric acid (5.0 c.c.). The colourless solid separated was collected, washed with dilute alkali (5.0 %) and crystallised from ethanol, thick colourless plates, m.p. 165° (9.0 g.).

Analysis: 0.138 g. substance on Kjeldahl determination required 11.9 c.c. of 0.0504 N acid.

Found: N, 6.08 per cent.

C₁₂H₁₅NO₃ requires: N, 6.33 per cent.
FRIES ISOMERISATION OF p-AMINOPHENOL DIPROPIONATE: FORMATION OF 2-HYDROXY-5-PROPIONYLAMINO PROPIONPHENONE:

I. p-Aminophenol dipropionate (3.0 g.: 1 mol.) was thoroughly mixed with finely powdered anhydrous aluminium chloride (6.0 g.: 3.3 mols.) and the mixture was heated on an oil-bath at 140° for an hour. The solidified mixture was then cooled and treated with crushed ice and concentrated hydrochloric acid (5.0 c.c.), when a pale green solid separated, which was collected, washed with cold water and crystallised from dilute ethanol, thin pale green needles, m.p. 125° (1.8 g.).

Analysis: 0.126 g. substance on Kjeldahl determination required 10.9 c.c. of 0.0504 N acid.

Found: N, 6.10 per cent.

C₁₂H₁₅NO₃ requires: N, 6.33 per cent.

It is soluble in hot water, ethanol, methanol, acetone, ethyl acetate, chloroform and acetic acid, as well as in dilute alkali (5.0 %) with pale green colour, but is insoluble in dilute mineral acids. It gives dark blue colour with ethanolic ferric chloride.

II. At 160° for 1 hour. — The migration was carried out at 160° for an hour when the ortho-hydroxy ketone was obtained. It crystallised as before, m.p. 125°.

III. At 120° for 1 hour. — The Fries migration when carried
out at 120° for an hour yielded a product; it was extracted with dilute alkali (5.0%). The insoluble portion was found to be the unchanged ester (1.0 g.). The alkaline extract on working up gave the ortho hydroxy ketone crystallised as before, m.p. and mixed m.p. 125° (0.2 g.).

1) The dipropionoxy derivative. It was prepared by heating a mixture of the propiophenone (0.5 g.), propionic anhydride (1.0 c.c.) and pyridine (2 drops) on a boiling water bath for 3 hours. It was worked up as usual and the solid obtained was collected, washed and crystallised from ethanol, colourless needles, m.p. 128-29°. The mixed melting point with the original propiophenone was depressed considerably.

Analysis: 0.103 g. substance on Kjeldahl determination required 7.0 c.c. of 0.0504 N acid.

Found: N, 4.79 per cent.

C₁₅H₁₉NO₄ requires: N, 5.05 per cent.

2) Oxime. — A solution of the propiophenone (0.5 g.), hydroxylamine hydrochloride (0.5 g.) and sodium acetate (1.0 g.) in dilute ethanol were refluxed on a water bath for an hour and then left overnight at room temperature. A colourless solid was obtained which crystallised from dilute ethanol, colourless shining needles, m.p. 176-77° (decomp.).
Analysis: 0.0836 g. substance on Kjeldahl determination required 13.8 c.c. of 0.0504 N acid.

Found: N, 11.65 per cent.

C₁₂H₁₆N₂O₃ requires: N, 11.87 per cent.

3) Semicarbazone. — An ethanolic solution of the propiophenone (0.5 g.) and a solution of semicarbazide hydrochloride (0.5 g.) and sodium acetate (1.0 g.) in minimum water were mixed, refluxed for an hour and then left overnight at room temperature. A light yellow solid separated was crystallised from dilute ethanol, light yellow plates, m.p. 275° (decomp.).

Analysis: 0.0768 g. substance on Kjeldahl determination required 21.7 c.c. of 0.0504 N acid.

Found: N, 19.94 per cent.

C₁₃H₁₈N₄O₃ requires: N, 20.14 per cent.

DEPROPYONYLATION OF 2-HYDROXY-5-PROPIONYLAMINO PROPIOPHENONE:

FORMATION OF 2-HYDROXY-5-AMINO PROPIOPHENONE:

A mixture of 2-hydroxy-5-propionylamino propiophenone (1.0 g.) and concentrated hydrochloric acid (1:1 - 50.0 c.c.) was heated under reflux on a sand bath for 6 hours. It was then concentrated when on cooling the hydrochloride separated as a colourless lustrous solid, which crystallised from ethanol, colourless lustrous plates, m.p. 220° (0.6 g.).
Analysis: 0.116 g. substance gave 0.0848 g. AgCl

Found eq. wt.: 196.3

C₉H₁₁NO₂.HCl requires eq. wt.: 201.5

The aqueous solution of the hydrochloride (0.5 g. in 25.0 c.c.), on treatment with ammonium hydroxide, gave 2-hydroxy-5-amino propiophenone, which crystallised from dilute ethanol, pale brown needles, m.p. 106-08° (0.2 g.).

Analysis: 0.122 g. substance on Kjeldahl determination required 14.3 c.c. of 0.0504 N acid.

Found: N, 8.26 per cent.

C₉H₁₁NO₂ requires: N, 8.48 per cent.

It is soluble in the usual solvents, dilute alkali (5.0 %) and dilute mineral acids. It gives dark blue colouration with ethanolic ferric chloride.

(iii) Fries migration of p-aminophenol dibutyrate:

Preparation of p-aminophenol dibutyrate. — A mixture of p-aminophenol (10.0 g.: 1 mol.), n-butyryl chloride (20.0 g.: 2 mols.) and pyridine (3-4 drops) was heated on a boiling water-bath for 2 hours. A colourless solid was obtained on working up; it crystallised from ethanol, colourless shining plates, m.p. 128° (11.5 g.).
Analysis: 0.132 g. substance on Kjeldahl determination required 9.9 c.c. of 0.0504 N acid.

Found: N, 5.29 per cent.

C_{14}H_{19}NO_{3} requires: N, 5.62 per cent.

FRIES ISOMERISATION OF p-AMINOPHENOL DIBUTYRATE: FORMATION OF 2-HYDROXY-5-BUTYRYLAMINO BUTYROPHENONE:

I. An intimate mixture of p-aminophenol dibutyrate (3.0 g.: 1 mol.) and well powdered anhydrous aluminium chloride (4.6 g.: 3.3 mols.) was heated on an oil-bath at 140° for an hour. It was decomposed as usual by treating it with crushed ice and concentrated hydrochloric acid (5.0 c.c.) when dirty green solid separated; it was crystallised from dilute ethanol, thin greenish yellow needles, m.p. 90° (1.5 g.).

Analysis: 0.116 g. substance on Kjeldahl determination required 8.9 c.c. of 0.0504 N acid.

Found: N, 5.41 per cent.

C_{14}H_{19}NO_{3} requires: N, 5.62 per cent.

It is soluble in the common organic solvents. It dissolves in dilute alkali (5.0 %) but is insoluble in dilute mineral acids. It gives blue colour with ethanolic ferric chloride.

II. At 160° for 1 hour. — The above migration yielded the desired ketone which crystallised as before, m.p. 90° (1.3 g.).

III. At 120-25° for 1 hour. — This migration also gave the
orthohydroxy ketone, crystallised as before, m.p. 90° (1.35 g.).

IV. At 100° for 1 hour. — When the migration was carried out in a boiling water bath (at 100°) for one hour, only the unchanged dibutyrate was obtained (2.0 g.) and no ketone could be isolated.

1) The acetox,y derivative. — It was prepared by heating the butyrophenone (0.5 g.) with acetic anhydride (2.0 c.c.) and pyridine (2 drops) on a boiling water-bath for an hour. It crystallised from ethanol, colourless needles, m.p. 75°.

Analysis: 0.1012 g. substance on Kjeldahl determination required 6.5 c.c. of 0.0504 N acid.

Found: N, 4.52 per cent.

\(C_{16}H_{21}NO_4\) requires: N, 4.81 per cent.

2) Oxime, prepared by the usual method, crystallised from dilute ethanol, colourless needles, m.p. 170° (decomp.).

Analysis: 0.0794 g. substance on Kjeldahl determination required 11.6 c.c. of 0.0504 N acid.

Found: N, 10.30 per cent.

\(C_{14}H_{20}N_3O_3\) requires: N, 10.60 per cent.

(iv) Fries migration of p-aminophenol dibenzoate:

Preparation of p-aminophenol dibenzoate. — A mixture of p-aminophenol (10.0 g.), benzoyl chloride (26.0 g.) and pyridine (3-4 drops) was heated on a boiling water bath for
2 hours. On usual treatment ash coloured solid separated, which was crystallised from acetic acid, tiny colourless needles, m.p. 233° (18.0 g.) (m.p. 231° according to Auwers and Sonnenstuhl, Ber., 1904, 37, 3940).

**Fries Migration of p-Aminophenol Dibenzoate : Formation of 2-Hydroxy-5-Benzamino Benzophenone :**

I. An intimate mixture of p-aminophenol dibenzoate (3.0 g.: 1 mol.) and anhydrous aluminium chloride (4.2 g.: 3.3 mols.) was heated in an oil bath at 160° for 1.5 hours. On working up the cooled reaction mixture as before, a brown solid separated, which was collected, and crystallised from ethanol, brown needles, m.p. 160° (1.8 g.).

**Analysis:** 0.148 g. substance on Kjeldahl determination required 8.6 c.c. of 0.0504 N acid.

Found: N, 4.10 per cent.

C₂₀H₁₅N₀₃ requires: N, 4.42 per cent.

It is soluble in the usual solvents. It dissolves in dilute alkali (5.0%) but is insoluble in dilute mineral acids. It gives a dirty blue colour with ethanolic ferric chloride solution.

II. At 180° for 1.5 hours. — The above migration when carried out at 180° for 1.5 hours gave the ketone crystallised as before, m.p. 160° (1.8 g.).
III. At 140° for 1.5 hours. — When the migration was carried out at 140° for 1.5 hours gave the alkali soluble o-hydroxy ketone, brown needles, m.p. 160° (0.5 g.) and the alkali insoluble original dibenzoate, colourless needles, m.p. 233° (1.0 g.).

**THE FRIEDEL CRAFTS BENZOYLATION OF p-BENZALINOPHENOL: FORMATION OF 2-HYDROXY-5-BENZALINO BENZOPHENONE:**

An intimate and well-powdered mixture of p-benzaminophenol (3.0 g.: 1 mol.) and anhydrous aluminium chloride (4.2 g.: 2.2 mols.), and benzoyl chloride (2.0 c.c.) were after the vigorous reaction subsided heated on an oil-bath at 160° for 3 hours. It was then worked up as usual when a brown solid separated which crystallised from ethanol, brown needles, m.p. and mixed m.p. 160° (1.5 g.).

(1) **The acetyl derivative**, prepared by acetic anhydride-pyridine method, crystallised from ethanol, light brown needles, m.p. 146°.

*Analysis*: 0.1032 g. substance on Kjeldahl determination required 5.3 c.c. of 0.0504 N acid.

*Found*: N, 3.62 per cent.

*C_{22}H_{17}NO_{4} requires*: N, 3.90 per cent.

(2) **Oxime** prepared by the usual method, crystallised from dilute ethanol, light grey needles, m.p. 305°.
Analysis: 0.0852 g. substance on Kjeldahl determination required
9.8 c.c. of 0.0504 N acid.

Found: N, 8.11 per cent.

\( C_{20}H_{16}N_2O_3 \) requires: N, 8.43 per cent.

(3) Semicarbazone, prepared as before, crystallised from dilute ethanol, colourless tiny needles, m.p. 300°.

Analysis: 0.098 g. substance on Kjeldahl determination required
20.3 c.c. of 0.0504 N acid.

Found: N, 14.62 per cent.

\( C_{21}H_{18}N_4O_3 \) requires: N, 14.97 per cent.

(B) FRIES ISOMERISATION OF p-ACETAMINOPHENOL ESTERS:

(1) Fries rearrangement of p-acetaminophenyl propionate:

The propionate of p-acetaminophenol was prepared by heating a mixture of p-acetaminophenol (10.0 g.), propionic anhydride (8.3 g.) and pyridine (3-4 drops) on a boiling water-bath for 2 hours. On usual treatment, a colourless solid separated, which crystallised from ethanol, colourless plates, m.p. 130° (9.0 g.).

Analysis: 0.1442 g. substance on Kjeldahl determination required
13.2 c.c. of 0.0504 N acid.

Found: N, 6.46 per cent.

\( C_{11}H_{13}NO_3 \) requires: N, 6.76 per cent.
FRIES TRANSFORMATION OF \( p \)-ACETAMINOPHENYL PROPIONATE : FORMATION OF 2-HYDROXY-5-ACETAMINO PROPIOPHENONE :

I. The propionyl ester (3.0 g. : 1 mol.) and anhydrous aluminium chloride (6.4 g. : 3.3 mols.) were mixed and heated at 140° for one hour. It was decomposed as usual. The pale green solid obtained was filtered, washed and crystallised from dilute ethanol, pale green needles, m.p. 135° (2.0 g.).

Analysis: 0.128 g. substance on Kjeldahl determination required 11.8 c.c. of 0.0504 N acid.

Found: N, 6.45 per cent.

\( C_{11}H_{19}NO_3 \) requires: N, 6.76 per cent.

It is soluble in the usual solvents. It dissolves in dilute alkali (5.0 %) with light green colour but is insoluble in dilute mineral acids. It gives deep blue colour with ethanolic ferric chloride.

II. At 160° for 1 hour. — The above migration when carried out at 160°, gave the ketone in slightly reduced yield (1.8 g.).

III. At 120-25° for 1 hour. — The migration was carried out at 120-25°, gave a mixture of the ketone (1.0 g.) and the unchanged \( p \)-acetaminophenyl propionate (0.4 g.).
FRIEDEL-CRAFTS PROPIONYLATION OF p-ACETAMINOPHENOL: FORMATION OF 2-HYDROXY-5-ACETAMINO PROPIOPHENONE:

p-Acetaminophenol (3.0 g.: 1 mol.), anhydrous aluminium chloride (6.0 g.: 2.2 mols.) and propionic anhydride (2.6 g.: 0.8 mol.) were heated on an oil bath at 140-45° for 3 hours. The mixture was then decomposed as usual when a pale green solid separated, which was crystallised from dilute ethanol, pale green needles, m.p. and mixed m.p. 135° (1.8 g.).

1) The benzoyl derivative was prepared by heating 2-hydroxy-5-acetamino propiophenone (0.5 g.), benzoyl chloride (0.5 c.c.) and pyridine (2 drops) on a boiling water bath for 3 hours. It crystallised from ethanol, colourless needles, m.p. 151-52°.

Analysis: 0.0986 g. substance on Kjeldahl determination required 5.9 c.c. of 0.0504 N acid.

Found: N, 4.22 per cent.
C₁₈H₁₇NO₄ requires: N, 4.50 per cent.

2) Oxime, prepared by the usual method, crystallised from dilute ethanol, colourless needles, m.p. 178° (decomp.).

Analysis: 0.081 g. substance on Kjeldahl determination required 14.2 c.c. of 0.0504 N acid.

Found: N, 12.34 per cent.
C₁₁H₁₄N₂O₃ requires: N, 12.61 per cent.

3) Semicarbazone, prepared as before, crystallised from dilute
ethanol, pale yellow needles, m.p. $280^\circ$ (decomp.).

Analysis: 0.0714 g. substance on Kjeldahl determination required 21.1 c.c. of 0.0504 N acid.

Found: N, 20.84 per cent.

$C_\text{12}H_\text{16}N_\text{4}O_\text{3}$ requires: N, 21.21 per cent.

4) 2:4-dinitrophenyl hydrazone. — A solution of 2-hydroxy-5-acetamino propiophenone (0.5 g.) and 2:4-dinitro phenyl hydrazine (0.5 g.) in acetic acid (15.0 c.c.) was heated under reflux on wire gauze for an hour and acidified with concentrated hydrochloric acid (1.0 c.c.). On keeping overnight, red needles were obtained, which crystallised from ethanol, red needles, m.p. $180^\circ$.

DEACETYLYATION OF 2-HYDROXY-5-ACETAMINO PROPIOPHENONE: FORMATION OF 2-HYDROXY-5-AMINO PROPIOPHENONE:

A mixture of 2-hydroxy-5-acetamino propiophenone (1.0 g.) and concentrated hydrochloric acid (1:1-50.0 c.c.) was heated on a sand bath under reflux for 6 hours, when the solid went into solution. The resultant solution was concentrated to a small bulk and allowed to cool, when lustrous plates began to separate. The hydrochloride was collected and crystallised from ethanol, colourless lustrous plates, m.p. and mixed m.p. $220^\circ$ (0.8 g.).

On treatment with ammonium hydroxide, the hydrochloride (0.5 g.) gave 2-hydroxy-5-amino propiophenone, m.p. $106-08^\circ$.
(0.2 g.), mixed melting point with the product described before remaining undepressed.

(11) **Fries rearrangement of p-acetaminophenyl butyrate:**

**Preparation of p-acetaminophenyl butyrate.** — A mixture of p-acetamino phenol (10.0 g.), butyryl chloride (7.0 g.) and pyridine (3-4 drops) was heated on a boiling water-bath for 2 hours. After the usual treatment a colourless solid separated, which was crystallised from ethanol, colourless thin plates, m.p. 140° (12.0 g.).

**Analysis:** 0.139 g. substance on Kjeldahl determination required 12.0 c.c. of 0.0504 N acid.

**Found:** N, 6.09 per cent.

C₁₂H₁₅N₃O₃ requires N, 6.33 per cent.

**Fries Transformation of p-acetamino phenyl butyrate: formation of 2-hydroxy-5-acetamino butyrophe none:**

I. An intimate mixture of p-acetamino phenyl butyrate (3.0 g.: 1 mol.) and anhydrous aluminium chloride (6.0 g.: 3.3 mols.) was heated as before at 140° for an hour and then worked up as before. The yellowish green product obtained crystallised from ethanol, thick light green needles, m.p. 95° (1.6 g.).
Analysis: 0.1214 g. substance on Kjeldahl determination required
10.4 c.c. of 0.0504 N acid.

Found: N, 6.04 per cent.

C₁₂H₁₅NO₃ requires: N, 6.33 per cent.

It is soluble in the usual solvents. It gives deep blue
colouration with ethanolic ferric chloride.

II. At 160° for 1 hour. — The above rearrangement, when
carried out at 160° for an hour, the ketone was obtained in nearly
the same yield (1.5 g.).

III. At 120-25° for 1 hour. — The migration when carried
at 120-25° for an hour gave the alkali soluble ketone (0.8 g.)
and an insoluble paste which could not be crystallised or further
purified.

FRIEDEL-CRAFTS BUTYRYLATION OF p-ACETAMINO PHENOL: FORMATION OF
2-HYDROXY-5-ACETAMINO BUTYRO PHENONE:

To an intimate mixture of p-acetamino phenol (3.0 g.: 1 mol.)
and anhydrous aluminium chloride (5.9 g.: 2.2 mols.),
butyryl chloride (2.2 g.: 1 mol.) was added gradually. The
temperature of the reaction mixture was then slowly raised to 140°
and maintained at that temperature for 3 hours. The hard cake was
decomposed as usual when a pale green solid separated, which was
crystallised from ethanol, thick light green needles, m.p. and
mixed m.p. 95° (1.5 g.).

1) The benzoyl derivative, prepared by Schottan-Baumann method of benzoylation, crystallised from ethanol, colourless needles, m.p. 142-43°.

Analysis: 0.108 g. substance on Kjeldahl determination required 6.3 c.c. of 0.0504 N acid.

Found: N, 4.11 per cent.

C_{19}H_{19}NO_{4} requires: N, 4.31 per cent.

2) Oxime, prepared in the usual manner, crystallised from dilute ethanol, colourless plates, m.p. 185°.

Analysis: 0.0872 g. substance on Kjeldahl determination required 14.2 c.c. of 0.0504 N acid.

Found: N, 11.49 per cent.

C_{12}H_{16}N_{2}O_{3} requires: N, 11.87 per cent.

3) Semicarbazone, prepared as before crystallised from dilute ethanol, pale yellow needles, m.p. 230° (decomp.).

Analysis: 0.092 g. substance on Kjeldahl determination required 25.8 c.c. of 0.0504 N acid.

Found: N, 19.78 per cent.

C_{13}H_{18}N_{4}O_{3} requires: N, 20.14 per cent.

4) 2:4-dinitrophenyl hydrazone, prepared as usual, crystallised from ethanol, dark red needles, m.p. 220-22°.
(iii) Fries rearrangement of \( p \)-acetaminophenyl benzoate:

Preparation of \( p \)-acetaminophenyl benzoate. — It was prepared by heating a mixture of \( p \)-acetamino phenol (10.0 g.), benzoyl chloride (9.4 g.) and pyridine (4 drops) on a boiling water bath for 2 hours. On working it up as before a colourless solid separated, which was crystallised from acetic acid, colourless thin plates, m.p. 230° (12.5 g.).

Analysis: 0.1482 g. substance on Kjeldahl determination required 11.0 c.c. of 0.0504 N acid.

\[ \text{Found: N, 5.23 per cent.} \]
\[ \text{C}_{16}\text{H}_{13}\text{NO}_3 \text{ requires: N, 5.49 per cent.} \]

FRIES TRANSFORMATION OF \( p \)-ACETAMINOPHENYL BENZOATE: FORMATION OF 2-HYDROXY-5-ACETAMINO BENZOPHENONE:

I. \( p \)-Acetaminophenyl benzoate (3.0 : 1 mol.) and anhydrous aluminium chloride (5.2 g. : 3.3 mols.) were heated together at 155-60° for 1½ hours, and the solid cake formed was worked up as before. The yellow solid was collected and crystallised from ethanol, light yellow needles, m.p. 151-52° (1.2 g.).

Analysis: 0.123 g. substance on Kjeldahl determination required 9.2 c.c. of 0.0504 N acid.

\[ \text{Found: N, 5.27 per cent.} \]
\[ \text{C}_{16}\text{H}_{13}\text{NO}_3 \text{ requires: N, 5.49 per cent.} \]
It is soluble in the common organic solvents and gives dirty blue colouration with ethanolic ferric chloride.

II. At 180° for 1 hour. — The same migration when carried out at 180° for 1 hour gave a pasty mass which could not be crystallised from any solvent.

III. At 140° for 1½ hours. — The migration when carried out at 140° for 1½ hours, gave the hydroxy ketone (0.7 g.) and an alkali-insoluble paste which could not be crystallised.

**FRIEDEL-CRAFTS BENZYLATION OF p-ACETAMINO PHENOL: FORMATION OF 2-HYDROXY-5-ACETAMINO BENZOPHENONE:**

p-Acetaminophenol (3.0 g. : 1 mol.), anhydrous aluminium chloride (5.9 g. : 2.2 mols.) and benzoyl chloride (2.8 g.) were mixed and the temperature of the mixture was raised slowly to 160° during 45 minutes and then maintained at that temperature for 2½ hours. The solid cake was then decomposed as usual, when a yellow solid separated. It was collected, washed and crystallised from ethanol, light yellow needles, m.p. and mixed m.p. 151-52° (1.3 g.).

1) The benzoyloxy derivative was prepared by Schotten-Baumann method and crystallised from acetic acid, pale yellow needles, m.p. 215°.
Analysis: 0.1012 g. substance on Kjeldahl determination required 5.3 c.c. of 0.0504 N acid.

Found: N, 3.69 per cent.

C_{22}H_{17}NO_4 requires: N, 3.90 per cent.

2) Oxime, prepared by the usual method, crystallised from ethanol, colourless plates, m.p. 194-95° (decomp.).

Analysis: 0.0792 g. substance on Kjeldahl determination required 11.4 c.c. of 0.0504 N acid.

Found: N, 10.15 per cent.

C_{15}H_{14}N_2O_3 requires: N, 10.37 per cent.

3) Semicarbazone, prepared as before crystallised from ethanol, light yellow needles, m.p. 295° (decomp.).

Analysis: 0.087 g. substance on Kjeldahl determination required 21.8 c.c. of 0.0504 N acid.

Found: N, 17.68 per cent.

C_{16}H_{16}N_4O_3 requires: N, 17.95 per cent.

(C) FRIES MIGRATION OF p-BENZAMINOPHENOL ESTERS:

p-Benzaminophenol (m.p. 212°) required for this work was prepared according to the method of Smith (Ber., 1891, 24, 4042).
(1) Fries rearrangement of p-benzaminophenyl acetate:

Preparation of p-benzaminophenyl acetate. — A mixture of p-benzaminophenol (10.0 g.), acetic anhydride (5.0 c.c.) and pyridine (4 drops) was heated on a boiling water-bath for 2 hours. On working up as before, a colourless solid separated, which was crystallised from acetic acid, colourless needles, m.p. 170-71° (10.0 g.).

Analysis: 0.1434 g. substance on Kjeldahl determination required 10.6 c.c. of 0.0504 N acid.

Found: N, 5.21 per cent.

C_{15}H_{13}NO_{3} requires: N, 5.49 per cent.

FRIES TRANSFORMATION OF p-BENZAMINOPHENYL ACETATE: FORMATION OF 2-HYDROXY-5-BENZAMINOACETOPHENONE:

I. p-Benzaminophenyl acetate (3.0 g.: 1 mol.) and anhydrous aluminium chloride (5.2 g.: 3.3 mols.) were intimately mixed and heated on an oil bath at 140-45° for an hour. On working up the mixture as before, a pale yellow solid was obtained, which crystallised from ethanol, golden yellow plates, m.p. 149-50° (1.7 g.).

Analysis: 0.1318 g. substance on Kjeldahl determination required 9.8 c.c. of 0.0504 N acid.

Found: N, 5.24 per cent.

C_{15}H_{13}NO_{3} requires: N, 5.49 per cent.
It is soluble in the usual solvents and in dilute alkali (5.0 %). It gives dark blue colour with ethanolic ferric chloride.

II. At 160° for 1 hour. — The same migration, when carried out at 160° for an hour, gave the hydroxy ketone in nearly the same yield (1.6 g.).

III. At 180° for 1 hour. — The migration at 180° for 1 hour diminished the yield of the ketone (1.4 g.).

IV. At 120-25° for 1 hour. — The migration when carried out at 120-25° for 1 hour gave the desired hydroxy ketone (0.8 g.), and the unchanged p-benzaminophenyl acetate (1.0 g.).

FRIEDEL-CRAFTS ACETYLATION OF p-BENZAMINOPHENOL : FORMATION OF 2-HYDROXY-5-BENZAMINO ACETOPHENONE :

A mixture of p-benzamino phenol (3.0 g. : 1 mol.), anhydrous aluminium chloride (3.9 g. : 2.2 mols.) and acetic anhydride (2.0 c.c.) was slowly heated to 145° within half an hour and then maintained at that temperature for 2½ hours. On working it up as usual, a yellow solid obtained, which crystallised from ethanol, golden yellow plates, m.p. and mixed m.p. 149-50° (1.5 g.).

1) The acetoxy derivative was prepared by heating the hydroxy ketone (0.5 g.), acetic anhydride (1.0 c.c.) and pyridine (1 drop) on a boiling water-bath for 3 hours. It crystallised
from ethanol, colourless needles, m.p. 135°.

Analysis: 0.116 g. substance on Kjeldahl determination required 7.3 c.c. of 0.0504 N acid.

Found: N, 4.43 per cent.

C\textsubscript{17}H\textsubscript{15}N\textsubscript{4} requires: N, 4.71 per cent.

2) Oxime, prepared by the usual method, crystallised from dilute ethanol, tiny pink coloured needles, m.p. 196-97°.

Analysis: 0.0786 g. substance on Kjeldahl determination required 11.2 c.c. of 0.0504 N acid.

Found: N, 10.06 per cent.

C\textsubscript{15}H\textsubscript{14}N\textsubscript{2}O\textsubscript{3} requires: N, 10.37 per cent.

3) Semicarbazone, prepared as before, crystallised from dilute ethanol, small grey needles, m.p. 304°.

Analysis: 0.0682 g. substance on Kjeldahl determination required 10.8 c.c. of 0.0504 N acid.

Found: N, 17.71 per cent.

C\textsubscript{16}H\textsubscript{16}N\textsubscript{4}O\textsubscript{3} requires: N, 17.95 per cent.

4) 2:4-Dinitrophenyl hydrazone, prepared as before, crystallised from ethanol, red needles, m.p. 265-66°.

(ii) Fries rearrangement of p-benzaminophenyl propionate:

p-Benzaminophenyl propionate was prepared by heating a mixture of p-benzaminophenol (10.0 g.), propionic anhydride (6.0 c.c.)
and pyridine (4-5 drops) on a boiling water bath for 2 hours. On working up the reaction mixture as before a colourless solid separated which was crystallised from acetic acid, colourless thin plates, m.p. 170° (11.0 g.).

**Analysis**: 0.145 g. substance on Kjeldahl determination required 10.2 c.c. of 0.0504 N acid.

**Found**: N, 4.96 per cent.

C_{16}H_{15}NO_{3} requires: N, 5.20 per cent.

**FRIES MIGRATION OF p-BENZALINOPHENYL PROPIONATE : FORMATION OF 2-HYDROXY-5-BENZAMINO PROPIONONE**:  

I. p-Benzaminophenyl propionate (3.0 g.: 1 mol.) and anhydrous aluminium chloride (4.9 g.: 3.3 mols.) were intimately mixed and heated at 140° for an hour. The cake formed was decomposed by the usual treatment when a dirty green solid separated, which crystallised from ethanol, pale green thin needles, m.p. 150-51 (1.5 g.).

**Analysis**: 0.125 g. substance on Kjeldahl determination required 8.7 c.c. of 0.0504 N acid.

**Found**: N, 4.91 per cent.

C_{16}H_{15}NO_{3} requires: N, 5.20 per cent.

It is soluble in the common solvents and gives deep blue colour with ethanolic ferric chloride.

II. **At 160° for 1 hour.** — The same migration when carried
out at $160^\circ$ for 1 hour gave the ketone in nearly the same yield (1.5 g.).

III. At $180^\circ$ for 1 hour. — At higher temperature like $180^\circ$ and the period of 1 hour, the yield of the ketone was reduced (1.2 g.).

IV. At $180^\circ$ for 1 hour. — When the migration was carried out at $120^\circ$, a mixture of the hydroxy ketone (0.7 g.) and the unchanged ester (1.2 g.) was obtained.

**FRIEDEL-CRAFTS PROPIONYLATION OF p-BENZALINOPHENOL : FORMATION OF 2-HYDROXY-5-BENZALINO PROPIOPHENONE**:

p-Benzaminophenol (3.0 g. : 1 mol.), anhydrous aluminium chloride (3.9 g. : 2.2 mols.) and propionic anhydride (2.0 c.c.) were mixed and the temperature was raised slowly to $140^\circ$ within half an hour and then maintained at that temperature for $2\frac{1}{2}$ hours. The reaction mixture was decomposed as usual, when a greenish solid was obtained, which crystallised from ethanol, thin pale green needles, m.p. and mixed m.p. $150-51^\circ$ (1.4 g.).

1) The acetoxy derivative, prepared by heating the hydroxy ketone (0.5 g.), acetic anhydride (1.0 c.c.) and pyridine (1-2 drops) on a boiling water-bath for 3 hours, crystallised from ethanol, colourless needles, m.p. $125^\circ$. 
Analysis: 0.110 g. substance on Kjeldahl determination required 6.6 c.c. of 0.0504 N acid.

Found: N, 4.23 per cent.

C₁₈H₁₇NO₄ requires: N, 4.50 per cent.

2) Oxime, prepared as before, crystallised from dilute ethanol, small colourless needles, m.p. 183° (decomp.).

Analysis: 0.0804 g. substance on Kjeldahl determination required 10.8 c.c. of 0.0504 N acid.

Found: N, 9.47 per cent.

C₁₆H₁₆N₂O₃ requires: N, 9.86 per cent.

3) Semicarbazone, prepared by the usual method, crystallised from dilute ethanol, pale yellow needles, m.p. 245-47° (decomp.).

Analysis: 0.074 g. substance on Kjeldahl determination required 18.0 c.c. of 0.0504 N acid.

Found: N, 16.97 per cent.

C₁₇H₁₈N₄O₃ requires: N, 17.18 per cent.

(iii) Fries rearrangement of p-benzaminophenyl butyrate:

p-Benzaminophenyl butyrate was prepared by heating p-benzaminophenol (10.0 g.) with butyryl chloride (6.0 c.c.) and pyridine (3-4 drops) on a boiling water bath for 2 hours. On working up by the usual method, a colourless solid separated, which was crystallised from ethanol, colourless needles, m.p. 155° (12.0 g.).
Analysis: 0.149 g. substance on Kjeldahl determination required 9.8 c.c. of 0.0504 N acid.

Found: N, 4.63 per cent.

C₁₇H₁₇NΟ₃ requires: N, 4.95 per cent.

FRIE'S TRANSFORMATION OF p-BENZAMINOPHENYL BUTYRATE: FORMATION OF 2-HYDROXY-5-BENZAMINO-BUTYROPHENONE:

I. An intimate mixture of p-benzaminophenyl butyrate (3.0 g. : 1 mol. ) and anhydrous aluminium chloride (4.7 g. : 3.3 mols. ) was heated in an oil-bath at 140° for an hour. The reaction mixture was decomposed as usual, when a pale green solid separated, which crystallised from ethanol, pale green needles, m.p. 101-02° (1.3 g.).

Analysis: 0.132 g. substance on Kjeldahl determination required 8.8 c.c. of 0.0504 N acid.

Found: N, 4.70 per cent.

C₁₇H₁₇NΟ₃ requires: N, 4.95 per cent.

It is soluble in the usual solvents and gives a blue colour with ethanolic ferric chloride.

II. At 160° for 1 hour. — The migration at 160° for an hour was also successful without any appreciable change in the yield (1.2 g.).

III. At 120-25° for 1 hour. — When the migration was carried
out at 120-25° for 1 hour, a mixture of the ketone (1.0 g.) and the original ester (0.6 g.) was obtained.

**FRIEDEL-CRAFTS BUTYRYLATION OF p-BENZALMINOPHENOL: FORMATION OF 2-HYDROXY-5-BENZALINO BUTYROPHENONE:**

Butyryl chloride (2.0 c.c.), p-benzamino phenol (3.0 g.: 1 mol.), and anhydrous aluminium chloride (3.9 g.: 2.2 mols.) were mixed and heated in an oil-bath slowly up to 150° for 2½ hours. On working up in the usual manner, a greenish solid separated, which crystallised from ethanol, pale green needles, m.p. and mixed m.p. 101-02° (1.4 g.).

1) The acetoxy derivative, prepared by acetic anhydride-pyridine method, crystallised from ethanol, colourless needles, m.p. 126°.

**Analysis:** 0.0882 g. substance on Kjeldahl determination required 5.1 c.c. of 0.0504 N acid.

*Found:* N, 4.08 per cent.

\[ C_{19}H_{19}NO_4 \] requires: \( N \), 4.31 per cent.

2) Oxime, prepared by the usual method, crystallised from dilute ethanol, colourless needles, m.p. 135° (decomp.).

**Analysis:** 0.102 g. substance on Kjeldahl determination required 13.2 c.c. of 0.0504 N acid.

*Found:* N, 9.13 per cent.

\[ C_{17}H_{15}N_2O_3 \] requires: \( N \), 9.39 per cent.
3) Semicarbazone, prepared as before, crystallised from dilute ethanol, pale yellow needles, m.p. 297-98° (decomp.).

Analysis: 0.0884 g. substance on Kjeldahl determination required 20.3 c.c. of 0.0504 N acid.

Found: N, 16.20 per cent.

C₁₈H₂₀N₄O₃ requires: N, 16.47 per cent.

4) 2:4-Dinitrophenyl hydrazone, prepared as before, crystallised from ethanol, red shining needles plates, m.p. 218° (decomp.).