POLARISATION AND CHEMICAL REACTIVITY IN AROMATIC SUBSTANCES.

The Influence of the Sulphonyl Dipole on the Course Followed by Substitution, Displacement and Migration Reactions with Amines, Phenols and Amino-phenols.

A thesis submitted to the University of London for the degree of Doctor of Science

by

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I wish to express my great indebtedness to
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Abstract.

POLARISATION AND CHEMICAL REACTIVITY IN AROMATIC SUBSTANCES.

The Properties of some Phenols, Amines and Aminophenols.

The electronic interpretation of organic chemical reactions is based on a consideration of the properties of compounds containing the real poles associated with salt formation and ionisation. Modern views of valency have indicated that finite charges are present on the nitrogen atom of a nitro-compound and on the sulphur atom in a sulphone. Moreover the charge present on the sulphur atom should be twice that present on the nitrogen atom. A study has been made of the sulphonyl deriv- atives of some amines, phenols and aminophenols in order to obtain evidence for and determine the special properties associated with a positively charged sulphur atom. The work is presented in four main sections, the first dealing with the preparation, the second the scission and the third the substitution of sulphonanilides and phenylsulphonates. The fourth section deals with the migration of acyl radicals in o-aminophenols.

It is found that amines may be divided into three groups according to the nature of their reaction with a molecular amount of p-toluene-sulphonyl chloride. Most give a quantitative yield of the sulphonanilide but some fail to react at all whilst others give the disul-
of chelate rings (J., 1924, 125, 533), emphasise a certain similarity between the nitro-group and halogen atoms in respect of inductive displacements and show that effects can be transmitted through the -SO₂- group. Further light is thrown on the mechanism of conversion of nitrophenols into nitrochlorobenzenes under the action of p-toluenesulphonyl chloride (Ullmann, inter alia, Ber., 1908, 41, 3932). The work with nitroaminophenols provides additional examples of the effects observed with phenols and amines alone, and discloses the existence of a new class of compound—the anhydro-p-toluenesulphonamidopyridinium hydroxides.

The section on the scission of sulphonanilides and phenylsulphonates deals in particular with the use of piperidine. The exceptional behaviour of 2:4-dinitrophenyl-p-toluenesulphonate, which undergoes scission in two distinct ways, is discussed in some detail.

Substitution experiments have been made in the benzene, diphenyl and naphthalene series and the orienting effects of the -NH₂SO₂, -NMₑ₂SO₂, -N(SO₂)₂ and -0₂SO₂ groups determined. The experiments on diphenyl have involved the development of improved methods of preparation of the initial materials (Ph.D. Thesis, 1926) and the description of over one hundred of the common compounds such as bromo-4-hydroxydiphenyls, nitro-4-methoxydiphenyls, and nitro-2 and 4-aminodiphenyls. With naphthalene sufficient experiments have been made to show that the fusion of two Kekule rings does not lead to a full interpretation of substitution
such as bromo-4-hydroxydiphenyls, nitro-4-methoxydiphenyls, and nitro-2 and 4-aminodiphenyls. With naphthalene sufficient experiments have been made to show that the fusion of two Kolbe rings does not lead to a full interpretation of substitution results with this hydrocarbon. The o/p ratio of these substitutions is discussed.

The experiments which Raiford has made on the migration of acyl radicals in o-aminophenols (J. Amer. Chem. Soc., 1919 to date) have thrown little light on the mechanism of these changes. Introduction of the use of sulphonyl derivatives has revealed (1) the tendency towards benzoxazole formation in o-aminophenols (2) the dependence of the migration on some property of the acyl group absent from the arylsulphonyl group. A theory of these changes is advanced which has led to the detection of acyl migrations in diacyl-o-aminophenols and the correction of several of Raiford's results.

Little doubt can be entertained that the sulphur semipolar double bond is a stable entity although the magnitude of the charge present on the sulphur atom is smaller than might be anticipated. Electronic principles provide a uniform basis for the interpretation of the diverse types of reaction recorded in this thesis.
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V. EXPERIMENTAL

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The Influence of the Sulphonyl Ring on the Course followed by Substitution, Displacement and Migration Reactions with Amines, Phenols and Amino-phenols.

So rapid has been the acceptance of the electronic interpretation of valency and so rapid the application of electronic concepts to chemical theory that it is difficult to realise that the ideas of electrovalency and covalency were not put forward by Kossel and Lewis until 1916. At his London lectures in 1923 Lewis tersely summed up their views by saying that chemical compounds are formed according to the rule of two and the rule of eight. A pair of electrons constitutes a normal chemical link, eight electrons a stable grouping in the outer shell of an atom. Consequently a sodium atom with one electron in its outer shell readily combines with a chlorine atom, which has seven, by passing over its electron; it thereby acquires a unit positive charge whilst the chlorine atom acquires a unit negative charge. After combination the two atoms are held together by electrostatic attraction only and the link is said to be an electrovalency. Similarly, calcium with two electrons in its outer shell gives the electrovalent, ionised compound Ca$^{++}$ Cl$^-$ and aluminium Al$^{+++}$ Cl$^-$. However in passing up this series the positive charge on the metal atom, which will be tending to abstract electrons from the chlorine ions, increases from one to three. Also the tendency of the metal atom to complete its octet by absorbing
additional electrons is increasing in the same order. Consequently
the degree of ionisation falls off (Fajans). Carbon with four
electrons in its outer shell combines with four chlorine atoms

\[
\text{NaCl} \rightarrow \text{Na} + \text{Cl}^{-} \quad \text{Cl}^{-} + \text{Cl}^{-} \rightarrow \text{Cl}^{-} \text{Cl}^{-} \quad \text{Cl}^{-} \text{Cl}^{-} \rightarrow \text{Cl}^{-} \text{Cl}^{-} \text{Cl}^{-} \text{Cl}^{-}
\]

but now the ionised form of the molecule is incomparably less
stable than the unionised or covalent form. With the four chlorine
atoms united to it by covalencies the carbon atom is uncharged and
surrounded by an octet of electrons. This is the normal type of
linkage found in carbon compounds. A double bond is interpreted
as a group of four electrons and since even sharing prevails through-
out the molecule no atom carries a charge. Lewis clearly envisaged
a further type of linkage. He suggested that the two electrons of a
link might be supplied by one atom, boron trifluoride, for example,
completing its octet by union with a molecule of ammonia. Lowry,
however, first called attention to the exceptional nature of this
link (Trans. Faraday Soc., 1925/26, 21, 235). Taking the previous

\[
\text{F}^{-} + \text{H} \quad \rightarrow \quad \text{F}^{-} \text{H} \\
\text{F}^{-} \text{B}^{-} + \text{H} \quad \rightarrow \quad \text{F}^{-} \text{B}^{-} \text{H} \text{H} \\
\text{F}^{-} + \text{H} \quad \rightarrow \quad \text{F}^{-} \text{H}
\]
example, since the nitrogen which was neutral in ammonia is now
sharing two of its electrons with the boron atom it must be
positively charged whilst the boron atom is negatively charged.
Ionisation cannot arise for this would lead to destruction of the
nitrogen or boron octets so this linkage, clearly different from
the electrovalent link, was given the name semipolar double bond.
The two charged neighbouring atoms are said to constitute a dipole.
It was the work of Sutcliff, Reed and Wilkins (J., 1925, 1523) and
Phillips (ibid., 2552) which focussed attention on this novel type
of linkage. Sutcliff, Reed and Wilkins showed that compounds which
might be expected to contain such linkages e.g. nitro compounds,
showed very abnormal parachors. Phillips succeeded in preparing
ethyl-p-toluenesulphinate in an optically active state, an
achievement with which the long accepted structure of this substance
is incompatible. To obtain a sulphur octet whilst uniting the

\[
\begin{align*}
\text{O} & \quad \text{CC}_2\text{H}_5 & \quad \text{CC}_2\text{H}_5 & \quad \text{CC}_2\text{H}_5
\end{align*}
\]

sulphur atom, possessing six external electrons, with two radicals
and an oxygen atom it is necessary to assume that the sulphur atom
provides both electrons required for the link with the oxygen atom
and thereby acquires a positive charge. Sulphinates are easily
converted into sulphonates and to maintain the sulphur octet in
these compounds it is necessary to assume that both oxygen atoms
are united to the sulphur atom by non-polar double bonds. Conse-
sequently the sulphur atom carries a positive charge of twice the
magnitude of the negative charge carried by each of the oxygen atoms. The actual size of the charge will depend on the evenness of sharing of the bonding pairs and the extent of deformation of the outer octet of the sulphur atom. It appeared of interest therefore to investigate the properties of the sulphonyl derivatives of some amines, phenols and aminophenols in order to obtain evidence for and determine the special properties associated with a sulphone dipole. The work is presented in four main sections, the first dealing with the preparation, the second, the scission and the third the substitution of sulphonamides and ary1 sulphonates. The fourth section deals with the migration of acyl radicals in \(\alpha\)-aminophenols.

It is found that amines may be divided into three groups according to the nature of their reaction with a molecular amount of sulphonyl \(\alpha\)-toluenesulphonyl chloride. Most give a quantitative yield of the sulphonamide but some fail to react at all whilst others give the disulphonamides. The results provide evidence in favour of Sidgwick and Gallow's theory of chelate rings (J., 1924, 125, 544), emphasise a certain similarity between the nitro-group and halogen atoms in respect of inductive displacements and show that effects can be transmitted through the \(-SO_2-\) group. Further light is thrown on the mechanism of conversion of nitrophenols into nitrochlorobenzenes under the action of \(\alpha\)-toluenesulphonyl chloride (Ullmann, inter alia, Pom., 1900, 41, 3932). The work with nitroaminophenols provides additional examples of the effects observed with phenols and amines alone, and discloses the existence of a new class of
compound—the arsano-d-p-toluenesulphonamidopyridinium hydroxides.

The section on the scission of sulphonamides and phenyl-sulphonates deals in particular with the use of piperidine. The exceptional behaviour of 2,4-dinitrophenyl-d-toluenesulphonate, which undergoes scission in two distinct ways, is discussed in some detail.

Substitution experiments have been made in the benzene, dipheny1 and naphthalene series and the orienting effects of the —NO₂, —SO₂, —N(OC)₂ and —O₂ groups determined. The experiments on dipheny1 have involved the development of improved methods of preparation of the initial materials (Ph.D. Thesis, 1930) and the description of over one hundred of the common compounds such as bromo-4-hydroxydiphenyle, nitro-4-methoxydiphenylels and nitro-2 and 4-aminodiphenylels. With naphthalene sufficient experiments have been done to show that the fusion of two Kobele rings does not lead to a full interpretation of substitution results with this hydrocarbon. The o/p ratio of these substitutions is discussed.

The experiments which Haiford has made on the migration of acyl radicals in o-aminophenols (J. Amer. Chem. Soc., 1919 to date) have thrown little light on the mechanism of these changes. Introduction of the use of sulphonyl derivatives has revealed (1) the tendency towards benzoxazolo formation in o-aminophenols (2) the dependence of the migration on some property of the acyl group absent from the arylsulphonyl group. A theory of these changes is advanced which has led to the detection of acyl migrations in diacyl-o-aminophenols and the correction of several of Haiford’s results.

Electronic principles provide a uniform basis for the interpretation of the diverse types of reaction recorded in this thesis.
Although it is impossible from these data alone to tell in which direction the charges are distributed as between the group and the nucleus, a consideration of disubstituted benzenes enables this to be achieved. Assuming that the benzene ring is a rigid hexagon and possesses no moment and that the groups act independently it is a simple matter to sum up the effects and compare with the calculated values. Taking as an example the particularly easy case of the p-substituted nitrobenzenes we have:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>( m )</th>
<th>Deduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO(_2)</td>
<td>0.3</td>
<td>Approx. zero from symmetry</td>
</tr>
<tr>
<td>Cl</td>
<td>2.62</td>
<td>Clearly ( 5.75 - 1.69 = 2.17 ) and not ( 5.75 + 1.58 = 5.33 )</td>
</tr>
<tr>
<td>CH(_3)</td>
<td>4.33</td>
<td>Clearly ( 5.75 + 0.45 = 4.12 ) and not ( 5.75 - 0.45 = 5.32 )</td>
</tr>
<tr>
<td>Br</td>
<td>2.60</td>
<td>Clearly ( 5.75 - 1.96 = 2.19 ) and not ( 5.75 + 1.58 = 5.32 )</td>
</tr>
</tbody>
</table>

It is immediately visible that the dipoles of NO\(_2\), Cl and Br are of the same sign, whilst that due to CH\(_3\) is of opposite sign.

Since the dipole due to the nitro group must be in the direction of its semipolar linking, these results indicate permanent electron shifts in the directions:

\[ \text{C}_6\text{H}_5\cdot\text{CH}_3 \quad \text{C}_6\text{H}_5\cdot\text{Hal} \quad \text{C}_6\text{H}_5\cdot\text{NO}_2 \]

More recently, Hjortdahl (Physical Rev. 169, 1929, 30, 301) has shown that the dipole moments of p-nitrocresol and p-nitroaniline are abnormally large, which must mean that the two groups exercise considerable mutual influence.

It is well known that the nitration of toluene proceeds with
higher velocity than that of benzene and gives almost exclusively the \( \alpha \) - and \( \pi \)-derivatives. This reaction will serve to introduce modern views on activation. It is universally agreed that the ordinary reagents of substitution are hartenoid in character and seek negative centres for attack. If substitution occurs in the \( \beta \)-position it is accepted that the \( \pi \)-carbon atom is in a more negative condition than either the \( \alpha \) or \( \beta \) carbon atoms. Two distinct theories have been advanced to account for the \( \alpha \)-\( \pi \) substitution of toluene. Ingold suggests that the forcing of electrons into the nucleus by the methyl group results in corresponding displacements of all the valency electrons. A simple displacement would steadily diminish in intensity along a chain of atoms so that the \( \alpha \) atom might be expected to be more negative than the \( \beta \) atom which in turn would be more negative than the \( \pi \) atom. Neglecting steric effects substitution should proceed \( \alpha \)-\( \pi \)-2. Ingold surmounts this difficulty by assuming that effects can be transmitted directly across the nucleus, an assumption justified by Pauling's electronic interpretation of the formula of benzene \((J. Am. Chem. Soc., 1936, 58, 1172)\). Fig. 1 is taken from a recent essay (Ingold, Rec. trav. chim., 1929, 48, 803); \( \overline{\sigma} \) signifies a small negative charge; \( \overline{\pi} \) a like charge of smaller magnitude. It will be seen that the \( \alpha \) and \( \beta \) carbon atoms are activated directly whilst the activation of the \( \pi \) carbon atom is a second order effect. Robinson \((inter \: alia, J., 1926, 401)\) takes a different view. He suggests that the electronic changes which
in conjugated aliphatic systems give rise to the phenomena of
tautomorism occur with equal ease in aromatic systems. Taking,
for example, the butadienoid system (Fig. 2) displacement of the
electrons of C\textsubscript{a} results in the acquirement of a negative charge
by C\textsubscript{p} or C\textsubscript{f}. Similarly when the butadienoid system forms a part of
\[
\begin{array}{c}
\text{C} & \text{C} & \text{C} & \text{C} \\
\text{C} & \text{C} & \text{C} & \text{C} \\
\end{array}
\rightarrow
\begin{array}{c}
\text{C} & \text{C} & \text{C} & \text{C} \\
\text{C} & \text{C} & \text{C} & \text{C} \\
\end{array}
\rightarrow
\begin{array}{c}
\text{C} & \text{C} & \text{C} & \text{C} \\
\text{C} & \text{C} & \text{C} & \text{C} \\
\end{array}
\text{Fig. 2.}
\]

a benzene nucleus (Fig. 3). Suppose the atom X allows its electrons
to come more under the influence of C\textsubscript{a}; this latter will to a
corresponding extent relinquish its control of electrons held in
common with C\textsubscript{p}. As a result C\textsubscript{p} acquires a small negative charge
or the effect is transmitted through a further double bond and
C\textsubscript{f} becomes negative in character. Dipole-moment measurements

\[
\begin{array}{c}
\text{C} & \text{C} & \text{C} & \text{C} \\
\text{C} & \text{C} & \text{C} & \text{C} \\
\end{array}
\]

are that have shown that methyl is a group of this kind and so the
preponderating \(\sigma\)-\(\pi\) substitution is explained.

Völlender (Bar., 1919, 22, 283 et seq.) observed that phenyl-
trimethylammonium bromide, diphenyldichromate, triphenyl-
hydroxyphosphonium nitrate, triphenyl-
-antimony dinitrate, triphenyl-
bismuth dinitrate and diphenyl-lead dinitrate all underwent substitu-
tion in the \(m\)-position. Consequently he inferred that a positive
pole attached to the nucleus is \(m\)-orienting irrespective of the
nature of the charged atom. Introduction of successive saturated
carbon atoms between a positive pole and the nucleus diminishes the \( m \)-orienting effect. This is readily seen from the data obtained by Coss, Hartley and Ingold (J., 1927, 250) for the nitration of a series of ammonium salts.

Approx. \( \% \) of \( m \)-nitro-derivative.

<table>
<thead>
<tr>
<th></th>
<th>( \text{H}_2\text{N} )</th>
<th>( \text{CH}_2\cdot\text{H}_2\text{N} )</th>
<th>( \text{CH}_2\cdot\text{CH}_2\cdot\text{H}_2\text{N} )</th>
<th>( \text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{H}_2\text{N} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{H}_2\text{N} )</td>
<td>100</td>
<td>88</td>
<td>19</td>
<td>5</td>
</tr>
</tbody>
</table>

It is now necessary to account for the \( m \) carbon atom being more negative than either the \( \alpha \) or \( \beta \) atoms. Ingold (loc. cit.) pictures the process in the following way (Fig. 4). Electrons are drawn towards the positive centre so that the \( \alpha \) and \( \beta \) carbon atoms are directly deactivated whilst the \( m \) carbon atoms suffer only a second order deactivation. Substitution—which in any case will proceed less readily than in the case of benzene (\( \delta^+ \) absent)—will occur chiefly in the \( m \) position. Robinson (loc. cit.) suggests that in

the case of a group \( B \), which has a strong attraction for electrons, all displacements will be towards \( B \) so that \( m \)-substitution is inhibited. Of all the remaining displacements (Fig. 5) that indicated by (a) is the more likely to lead to reaction, because reaction depends on the requirement of a negative charge and of all the carbon atoms which can be activated \( C \), has the smallest positive charge. Moreover the general effect of the group \( B \) is to inhibit the exhibition of
enionoid character and therefore substitution will take place less readily than in benzene itself. Later (J., 1926,1680) Robinson views with favour Lapworth's suggestion that $m$-substitution arises through $\omega$-$\pi$ inhibition (Fig.6). In this connection it is of interest that the influence of a positive pole is damped out more rapidly by a double bond than by a single link. $\omega$-Nitrostyrene gives only 2% of the $m$-nitro-derivative, whilst $\beta$-phenylnitroethane under similar

$$ (2\%) \quad \begin{array}{c}
\text{CH} = \text{CH}_2 \to \text{NO}_2 \\
\text{CH} = \text{CH}_2 \to \text{CH}_2 \to \text{CH}_3
\end{array} \quad (15\%) $$

conditions gives 15% (Baker and Wilson, J., 1927,342).

In spite of the dipole moment of chlorobenzene being in the same direction as that of nitrobenzene, chlorine is almost exclusively $\alpha$-$\pi$ directing. The chlorine atom possesses lone pairs of electrons and it must be assumed that these are capable of entering into covalency changes with the nuclear carbon atom as are the lone pairs of nitrogen (in amines) and of oxygen (in phenols). Ingold is in agreement with Robinson's mechanism for the propagation of electronic changes initiated by atoms possessing free valency electrons (see Fig.7). Clearly the tautomeric displacements in substances such as the halogenobenzenes, although so effective in leading to reaction, cannot be otherwise than momentary as the molecule shows a dipole of opposite sense. If the attraction of electrons towards and the repulsion of electrons from the halogen atom are both conjugative in character, it is remarkable that the two effects are not summed up and, since the predominating phase is electron-attraction from the nucleus, result in $m$-substitution. Considerations
of this type give point to Ingold's contention that the two effects are different in character, an inductive effect permanent in character and a tautomeric effect momentary in nature and probably excited by the electron seeking reagent.

Both Robinson and Ingold postulate a direct action of substituents through space so that a negative atom promotes and a positive atom hinders substitution in the order o > m > p. A consideration of the substitution of bromochlorobenzene is instructive from this point of view. The electron affinity of chlorine is higher than that of bromine so that the direct deactivating effect of this atom is greater and the tautomeric effect is smaller than that of bromine. If $x$ and $x'$ represent the intensities of the direct effects due to Cl and Br respectively ($x > x'$) and if $f, f'$ and $f''$ are the factors (assumed the same for Cl and Br) expressing the distribution of this effect as between the o, m and p positions ($f > f' > f''$) then the direct effects will be as shown.

In the case of the o compound, effect 1. = effect 2. = $x(f-f') - x'$ ($f-f' > 0$), so that the deactivation is greater in position 1. than in position 2. With the o compound, effect 2. = effect 3. = $x(f'-f'') - f'(f'-f'') > 0$. Consequently the direct and tautomeric effects combine in the p compound to promote substitution o to the bromine atom. On the other hand the direct effect runs counter to the tautomeric effect in the o compound and actually nitration to the extent of 55% occurs in position 3 (Holloman, Rec. trav. chim., 1915,
Not all substitution reactions fall into line with theory so well as this as the application of the same principles to 3-nitrotoluene will show. If \( A, A', A'' \) measure the inductive influence of the methyl group on \( \beta, \beta \) and \( \gamma \) positions respectively and \( a, a', a'' \) the direct influence on \( \beta, \beta \) and \( \gamma \) positions and \( D, D', D'' \) and \( d, d', d'' \) the corresponding deactivating influences of the nitro group, we have as the total activating influence in position 2, \( A + a - D - d \)

\[
\begin{align*}
4 & = A' + a'' - D' - d' \\
5 & = A'' + a' - D'' - d''
\end{align*}
\]

Now \(2+4 = (A + a') + (a-a'') > 0 \)

Now \(2+4 = (A + a') + (a-a'') > 0 \)

\[
\begin{align*}
6-2 & = (D + D') + (d - d'') > 0 \\
6-5 & = (A + a') + (a-a'') + (d' - d'') - (D + D'') \\
4-5 & = (A + a') + (a-a'') - (D + D'') - (d - d'')
\end{align*}
\]

Substitution should occur therefore \(6 > 2 > 4 \) and the amount of 5 substitution will depend on the relative magnitudes of \( A \) and \( D \).

Hoessermann (Ber., 1894, 27, 2203) and Sirk (Rec. trav. chim., 1907, 27, 266) have studied the nitration of 3-nitrotoluene and reach the conclusion that substitution occurs \( 4 > 2 > 6 \); on bromination the principal product is the 6 derivative with a smaller amount of the 4 compound (Scheufelen, Annalen, 1885, 231, 171). Although it would be foolish to stress an example of this type against modern views of substitution, the complicated nature of apparently simple reactions is made evident.

The process of substitution itself is pictured by Ingold and...
Ingold (J., 1928, 1910) in the following way:

There is a preliminary attachment of the katinoid part of the reagent to the carbon atom which has in some way acquired a small negative (indicated by $\delta$). The completion of the process is brought about by a more powerful factor, in this case the tendency of the hydron and hydroxide ion to form undisassociated water.

since the present object is merely to outline the methods of transmission of electrical effects in aromatic systems, the main conclusions will be summarised with omission of all controversial detail. Effects may be propagated in three distinct ways:

(1) inductively along saturated chains and possibly in aromatic nuclei. In the former case the intensity diminishes regularly in passing along the chain and may be neglected, say, after the fourth carbon atom.

$\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{H} \quad \text{CH}_2\text{CH}_2\text{NO}_2 \quad \text{(-I)}$

In the latter the effect centres on the $\alpha$ and $\beta$ carbon atoms.

$\text{R} \quad \text{R}$

$\text{(}\alpha-\beta\text{ deactivation)} \\ \text{(}\alpha-\beta\text{ activation)}$

(2) Directly through space (+D; -D). The genesis of this effect is the same as that of the inductive effect and necessarily they possess a common direction. In saturated chains the effects are inseparable but in aromatic nuclei, whereas the
inductive effect favours the $p$ position compared with the $m$
position, the direct effect falls off in the order $o > m > 2$.

(3) By tautomeric displacements ($T$). The group $R$ increases its
covalency with the nucleus and the resulting electron dis-
placements lead to the development of negative charges on the
$2$ $R$ carbon atoms. These displacements are
temporary in nature but exceed in magnitude
those produced by methods (1) and (2).

B. The Influence of Substituents on the Velocity of Conversion of
Amines into Sulphonanilides and the Special Factors Determining
the Ease of Formation of Disulphonanilides.

Although sulphonanilides have been known for a very long time
(Biffi, Annalen, 1854, 91, 107) no peculiarities attending their
preparation have been recorded. The usual way of obtaining these
compounds is to treat the amine with the theoretical amount of the
sulphonyl chloride in the presence of a tertiary base, such as
pyridine or diethylaniline, which will absorb the hydrogen chloride
set free in the reaction. This method as a rule furnishes the pure
sulphonanilide in almost quantitative yield but two types of divergence
from this general behaviour have been noticed. First, certain compounds
can be recovered unchanged from this treatment. 2,4-Dinitroaniline
and 3,5-dinitro-2-aminodiphenyl belong to this group, since they have
not as yet been converted directly into their $p$-toluenesulphonyl
derivatives. In a second class are those amines which with one
molecule of the chloride give either a mixture of sulphonanilide and
disulphonanilide or disulphonanilide alone. Both $p$-nitroaniline with
$3$-nitrobenzenesulphonyl chloride and 1:8-dinitro-2-naphthylamine with
p-toluenesulphonyl chloride yields a mixture of mono- and di-sulphonanilides, whilst 3:5-dibromo- and 3:5:4'-tribromo-4-aminodiphenyle with p-toluenesulphonyl chloride and 2-nitro-p-toluidine and 6-nitro-2-toluidine with p-nitrobenzenesulphonyl chloride gave only the disulphonanilides. The yield of disulphonanilide was not quantitative even when two molecules of the sulphonyl chloride were employed, and therefore the velocity of disulphonanilide formation must be high compared with that of monosulphonanilide formation. It is therefore necessary first to account for the sluggish formation of p-nitrosulphonanilides and the ready conversion of these compounds into disulphonanilides. Sidgwick and Calow (J., 1924, 125, 533) in reviewing the abnormal properties of ortho compounds reach the conclusion that such compounds contain five or six membered rings, one member of which is a co-ordinated hydrogen atom. The formula for an p-nitrosamine on this view is (I), and if the chelate ring is stable under alkaline and neutral conditions the failure to react with sulphonyl chlorides in pyridine solution or with boiling acetic anhydride is readily understood. Rings of this high stability appear to be present in compounds II-VIII, but can be immediately broken by addition of a little sulphuric acid when acetylation proceeds with normal ease. It would appear that the velocity of disulphonanilide formation is determined by the tendency of the
sulphononilide hydrogen atom to undergo ionisation. For instance, the \( \mu \)-nitro-benzensulphonyl derivatives of the nitroanilines (X) react readily with a molecule of a sulphonyl chloride, whereas that of aniline (IX) reacts very slowly. This accords with the electron absorbing character of the nitro group which is most easily satisfied if the hydrogen of the amino- group separates with a positive charge (gives up its electron and separates as a hydrogen ion). This increase in acidic strength is shown by the fact that even organic bases yield stable salts with nitrated \( \mu \)-toluenesulphonanilides, \( \mu \)-toluenesulphon-\( \mu \)-nitro-anilide,
for example, giving the piperidine salt, \( \text{C}_9\text{H}_{10}^+\text{NO}_2^\cdot\text{C}_6\text{H}_4^\cdot\text{NH}_3\text{SO}_2\cdot\text{C}_7\text{H}_7^- \). Again, \( m\)-nitrobenzenesulphon-\( p\)'-nitro-\( q\)'-toluidide (XI) is readily prepared but \( m\)-nitrobenzenesulphon-\( q\)'-nitro-\( p\)'-toluidide (XII) and \( m\)-nitrobenzenesulphon-\( q\)'-nitro-\( q\)'-toluidide (XIII), in which the amino hydrogen atom will be more highly ionised, react immediately to give the corresponding disulphonanilides.

Rather surprisingly the mobility of this hydrogen

![Chemical structures](structures.png)

appears to be considerably influenced by the substituents present in the benzenesulphonyl group. For example, \( m\)-nitrobenzenesulphon-\( m\)'-nitroanilide (XIV) reacts quantitatively with \( p\)-toluenesulphonyl chloride, whereas under the same experimental conditions \( p\)-toluenesulphon-\( m\)'-nitroanilide (XVI) gives only a 50\% yield of the same compound (XV) when treated with \( m\)-nitrobenzenesulphonyl chloride.

![Chemical structures](structures.png)

This result might be attributed to a smaller reactivity
of the chlorine atom in m-nitrobenzenesulphonyl chloride compared with p-toluenesulphonyl chloride, but the following experiment minimizes the importance of this factor. Although p-toluenesulphonyl chloride reacts normally with o-nitroaniline, indicating that p-toluenesulphon-o'-nitroaniline (XVII) has not exceptional reactivity, m-nitrobenzenesulphonyl chloride gives largely the disulphonylanilide, owing to the high reactivity of the intermediate m-nitrobenzenesulphon-o'-nitroanilide (XVIII) towards, in this case, m-nitrobenzenesulphonyl chloride. A similar effect is made evident when

![Chemical structures](XVII) and (XVIII)

the nitration of benzylmethyisulphone is compared with that of toluene-o'-sulphonyl chloride (p. 40).

The same considerations apply to brominated amines. Co-ordination diminishes the reactivity of the free amino (XIX) but the inductive effect of the halogen atoms leads to special reactivity of the amino-hydrogen of the intermediate sulphonanilides (XX). Consequently 3:5-dibromo- and 3:5:4'-tribromo-4-aminodiphenyls give only disulphonanilides (XXI).

![Chemical structures](XIX), (XX), and (XXI)
C. The Influence of Nitro Groups on the Stability of Arylsulphonates and the Mechanism of Conversion of Nitrophenols into Nitrochlorobenzenes under the Action of Sulphonyl Chlorides.

Interaction of a phenol with a molecular quantity of a sulphonyl chloride in pyridine solution usually results in the production of a quantitative yield of the corresponding sulphonate. Ullmann and Nadai, however, observed that nitrophenyl sulphonates were extremely reactive and could be isolated only when sodium carbonate was used as the condensing agent (Bez., 1908, 41, 1879). Substances such as 2,4-dinitrophenyl-\( \rho \)-toluenesulphonate and 2,4-dinitro-\( \rho \)-naphthyl-\( \rho \)-toluenesulphonate reacted instantly with pyridine to give pyridinium salts (XXII and XXIII). Later, Ullmann and Bruck (ibid., 3952) showed that nitrophenols could be converted into the corresponding chlorobenzenes by the action of \( \rho \)-toluenesulphonyl chloride.

As a typical example, picryl chloride was obtained from picric acid and similar results have been obtained by later workers (Sane and Joshi, J., 1924, 125, 2481; Borsche and Peake,
Since the chelate ring present in an o-nitroamine is broken by sulphuric acid, the chelate ring of an o-nitrophenol (Sidgwick and Callow, loc. cit.) would not be expected to persist in the presence of basic media. Consequently all nitrophenols would be expected to react easily with sulphonyl chlorides in pyridine solution. To establish this point beyond question the interaction of picric acid with p-toluenesulphonyl chloride in the presence of cold pyridine was examined. No difficulty was experienced in isolating picrylpyridinium-p-toluenesulphonate (XXIV) in almost quantitative yield and therefore it appears that all nitrophenols do react easily with p-toluenesulphonyl chloride. Picrylpyridinium-p-toluenesulphonate was a rather unstable compound which readily gave rise to the already known picrylpyridinium picrate (XXV) (Busch and Kogel, J. pr.
either by repeated crystallisation or by solution in cold acetic acid. With alcoholic hydrogen chloride it gave an easily separable mixture of picryl chloride (XXVI) and picrylpyridinium chloride (XXVII), and the latter was easily decomposed by warm water to give picrylpyridinium picrate.

It appears probable therefore that the conversion of a phenol into the corresponding chlorobenzene by the action of p-toluenesulphonyl chloride involves always the following changes:

\[ \text{Phenol} \rightarrow \text{Phenyl-p-toluenesulphonate} \rightarrow \text{Phenylpyridinium-p-toluenesulphonate} \]

The mechanism of severance of the p-toluenesulphonate ion from the nucleus is discussed later (p. 30).
D. The Varied Behaviour of Aminophenols with
Sulphonyl Chlorides and the Isolation of a
New Class of Substances containing ortho,
meta and para Dipoles.

Employing the pyridine method it was found that
\( p \)-aminophenol reacted cleanly with \( p \)-toluenesulphonyl
chloride to give first the \( N-p \)-toluenesulphonyl derivative
and then the \( N:O-di-p \)-toluenesulphonyl derivative. As
would be anticipated from the previous sections marked
divergence from this simple reaction was observed when
nitro- groups were present in the molecule.

Picric acid was first studied. In this compound
the nitro-groups are so situated as to activate the hyd-
roxyl group. With one molecule of \( p \)-toluenesulphonyl
chloride it gave the pyridine salt of 4\(:6 \)-dinitro-\( 2-p \)-toluenesulphonamidophenol (XXIX) stable to acetic acid
but giving the free phenol (XXVII) after precipitation
from aqueous ammonia. This pyridine salt could be acety-
lated to give the pyridine salt of 4\(:6 \)-dinitro-\( 2-p \)-toluenesulphonacetamidophenol (XXXI), alternatively prepared by
addition of pyridine to an acetic anhydride solution of
4\(:6 \)-dinitro-\( 2-p \)-toluenesulphonacetamidophenyl acetate
(XXX). This interesting reaction has a parallel in the
immediate precipitation of pyridine picrate on addition
of pyridine to picryl acetate dissolved in acetic anhydride.
\( x = \text{SO}_2\cdot\text{C}_7\text{H}_7 \)

With two molecules of p-toluenesulphonyl chloride in pyridine solution picric acid gave a bright orange compound insoluble in the usual solvents but easily soluble in dilute acids with formation of colourless salts. These salts were decomposed by boiling aqueous sodium acetate to regenerate the original compound, which consequently appears to have the constitution anhydro-2:4-dinitro-6-p-toluenesulphonamidophenyl pyridinium hydroxide (XXXIII).

A compound containing a similar type of ortho dipole (XXXIV) has been described by Pries and Schimmelchmidt (Annalen, 1930, 424, 245). The possibility of obtaining related compounds with meta and para dipoles was then examined.
The directions given by Reverdin and Widmer (Ber., 1913, 46, 4068) for the nitration of the di-p-toluene sulphonamido derivative of p-aminophenol were found to be incorrect. However, under new conditions, 2:4-dinitro-5-p-toluene sulphonamidophenyl-p-toluene sulphonate (XXXV) was obtained and this reacted readily with pyridine to give anhydro-2:4-dinitro-5-p-toluene sulphonamidophenyl pyridinium hydroxide (XXXVI). This compound was alternatively prepared by solution of 1-chloro-2:4-dinitro-5-p-toluene sulphonamidobenzene (XXXVII) in pyridine. Rowe and his co-workers (J., 1931, 1068) have recently described a number of compounds (e.g., XXXVIII) containing a somewhat different type of meta dipole.

Isopicroanic acid with two molecules of p-toluene sulphonyl chloride in pyridine solution gave anhydro-2:6-dinitro-4-p-toluene sulphonamidophenyl pyridinium hydroxide (XXXIX), which was much less stable than the corresponding
The compound (XXXVIII) was the only product obtained from interaction of 4-nitro-4'-aminophenol and potassium acetate. A derivative of picramic acid. It was easily soluble in acetic acid and consequently the salts were not completely decomposed by sodium acetate as in the previous cases.

Next were examined compounds in which the nitro-groups were in α-β-positions to the amino-group. 5-Nitro-2-aminophenol readily gave 5-nitro-2-p-toluene sulphonic acidophenyl-p-toluene sulphonate (XL) but 5-nitro-2-aminophenol would...
give only 3-nitro-2-aminophenyl-$p$-toluenesulphonate (XLI). The amino-group is here so well protected that the compound can be directly nitrated to give 3:5-dinitro-2-aminophenyl-$p$-toluenesulphonate (XLIV), which was the only product obtained by interaction of 3:5-dinitro-2-aminophenol (XLIII) with $p$-toluenesulphonyl chloride.
II. THE SCission OF SULPHONANILIDES AND ARYLSULphonATES

BY MEANS OF PIPERIDINE.

A. The Exceptional Behaviour of Dinitrophenyl-p-toluencesulphonate.

Although sulphonanilides are hydrolysed under conditions comparable with those required in the case of acetanilide, phenylsulphonates differ markedly from the corresponding acetates in their resistance to hydrolytic agents. This is readily accounted for by their difference in structure. In the case of acyl derivatives the presence of the carbonyl group renders the molecule singularly prone to the attack of negative ions:

\[
\begin{align*}
\text{R.O.C.R'} & \quad \rightarrow \quad \text{R.O.C.R'} & \quad \rightarrow \quad \text{R.O} + \quad \text{C.R'}
\end{align*}
\]

On the other hand arylsulphonates are more resistant to hydrolytic agents in general and are usually unattacked by cold concentrated sulphuric acid or hot hydrochloric acid. For example, 5-nitro-2-p-toluencesulphonamide (acetamide, \( \beta \)-naphthamido-) phenyl-p-toluencesulphonates are all cleanly hydrolysed by acid to 5-nitro-2-amino-
phenyl-\(\text{p}\)-toluenesulphonate (XLIV) and also 3-nitro-2-acetamido-\(\text{p}\)-toluenesulphonate is hydrolysed to 3-nitro-2-amino-phenyl-\(\text{p}\)-toluenesulphonate (XLVI). Hydrolysis may be affected by means of alkalis and Forna and Lepworth (J., 1912, 161, 273) have made some interesting observations on this subject. Although alkyl-\(\text{p}\)-toluenesulphonates are readily severed at the alkyl-oxygen linkage, arylsulphonates show no tendency to break in this position. The anomalous reaction between phenyl-\(\text{p}\)-toluenesulphonate and sodium ethoxide is explained as occurring in two stages:

\[
\text{C}_6\text{H}_5\text{O} \cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7 + \text{Na} \cdot \text{OC}_2\text{H}_5 = \text{C}_6\text{H}_5\text{O} \cdot \text{Na} + \text{C}_2\text{H}_5\cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7
\]

\[
\text{C}_6\text{H}_5\cdot \text{Na} + \text{C}_2\text{H}_5\cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7 = \text{C}_6\text{H}_5\cdot \text{C}_2\text{H}_5 + \text{Na} \cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7
\]

The use of hydrazine as a fission agent is described by Freudenberg and Hess (Annalen, 1920, 429, 121). With alkyl-\(\text{p}\)-toluenesulphonates the reaction proceeds according to equation (a) and with aryl-\(\text{p}\)-toluenesulphonates according to equation (b).

\[
\text{Alk}\cdot \text{O} \cdot \text{SO}_2 \cdot \text{R} + \text{NI}_2 \cdot \text{NH}_2 = \text{Alk} \cdot \text{NI} \cdot \text{NH}_2 + \text{H} \cdot \text{O} \cdot \text{SO}_2 \cdot \text{R} \quad (a)
\]

\[
\text{Ar} \cdot \text{O} \cdot \text{SO}_2 \cdot \text{R} + \text{NI}_2 \cdot \text{NH}_2 = \text{Ar} \cdot \text{C} \cdot \text{H} + \text{NI}_2 \cdot \text{NI} \cdot \text{SO}_2 \cdot \text{R} \quad (b)
\]

More recently, Turner and his co-workers (J., 1933, 512; 1936, 962, 1953) have shown that phenylsulphonates can be very neatly severed by piperidine according to the general equation (A). It is now found that although this type of

\[
\text{R} \cdot \text{O} \cdot \text{SO}_2 \cdot \text{R} \cdot + \text{NI}_2 \cdot \text{NH}_2 \cdot \text{H} \cdot \text{O} = \text{R} \cdot \text{CH} + \text{C}_6\text{H}_{10} \cdot \text{N} \cdot \text{SO}_2 \cdot \text{R} \quad (A)
\]

reaction occurs with the mononitrophenylsulphonates, e.g.
2-nitrophenyl \( p \)-toluenesulphonate, with 2:4-dinitrophenyl \( p \)-toluenesulphonate the reaction may follow a second course. In this case the nuclear link is severed and 2:4'-dinitro-\( 1 \)-phenylpiperidine results. The possibility that 2:4-dinitrophenol is an intermediate product is ruled out by the fact that this phenol forms a stable piperidine salt which shows no tendency to undergo change under the conditions of the experiment.

Ullmann (P.R.P.194941) has described other reactions in which dinitrophenyl-\( p \)-toluenesulphonates undergo severance at the nuclear bond. To give only one example, 2:4-dinitro-\( \alpha \)-naphthyl-\( p \)-toluenesulphonate is easily converted into 2:4-dinitro-\( \alpha \)-naphthylphenylamine (XLVII) when heated with

\[
\begin{align*}
\text{2:4-Dinitro-} \alpha \text{-naphthylphenylsulphonate} & \quad \xrightarrow{\text{heat}} \quad \text{2:4-Dinitro-} \alpha \text{-naphthylphenylamine (XLVII)}
\end{align*}
\]

aniline. Moreover the previous sections record many examples of the product of pyridinium salts when nitrophenylsulphonates are treated with pyridine. In these reactions the sulphonate group can hardly separate as other than a negative ion, leaving the nucleus with a positive charge, and yet this type of reaction occurs only when the nucleus is already overburdened with positively charged groups. It
might be suggested that the nitro- groups are so combined with the base that their normal electrical character is lost, as is that of the amino- group on solution in sulphuric acid. Bennett and Willie (J., 1929, 283) have suggested that bases can add on to the nitro- group by the conversion of the nitrogen-oxygen double bond into a semipolar double bond; the additive compounds involving pyridine might therefore be written as (XLVIII). Although it is difficult to conceive of such a complex acting as an electron source, the nitro- group can no longer absorb electrons by a covalency change. Attempts were made to isolate such additive compounds, but the following substances were recovered in a pure condition after solution in boiling pyridine: 4'-nitro-4-p-toluenesulphonylxydiphenyl, 3:4'-dinitro-4-p-toluenesulphonyldiphenyl, di-p-toluenesulpho-p'nitroanilide, p-toluenesulpho-p'-nitroanilide, and di-p-toluenesulpho-p'-nitroanilide. The only indication of compound formation was obtained with picric acid which combined with two molecules of piperidine, one being very loosely attached. It is possible that additive compounds are formed only when the nitro group tends to be specially positive owing to the presence of many other electron-absorbing groups in the same molecule, and that when formed lead to immediate reaction. With tertiary bases the primary result may be slight ionisation of the sulphonate group, followed by immediate introduction of a further molecule.
of the tertiary base to give the salt, and with secondary bases the mechanism may be the same or may involve a migration of the secondary radical as suggested by Brewin and Turner (J., 1929, 338). Since the base-catalysis still applies to the fixation of ordinary substitutions, but there is an added complication of the positive character of the radical atom in sufficient to cause a negative character of the molecule atom in sufficient to cause a negative character.

These reactions can be viewed from a somewhat different standpoint. Robinson (Chem. and Ind., 1925, 49, 117) pointed out that although the positive ions of ordinary substitutions seek negative centres, negative ions would seek positive centres. As an example he gives the reaction of nitrobenzene potassiumcarbazole to form \( p \)-nitrophenylcarbazole. More recently Ingold (Rec. trav. chim., 1930, 49, 803) has discussed the elimination of halogen by negative groups, and the process of elimination of chlorine from \( p \)-nitrochlorobenzene is stated in the following terms. The nitro group by its combined tautomeric, inductive and direct effects tends to make the

\[
\begin{align*}
\text{O} & \rightarrow N \\
\text{O} & \rightarrow N \\
\end{align*}
\]

para carbon atom positive in character. The halogen atom assists in the capture of the attacking negative ion by the influence of its own attraction for the electrons of the
carbon atom to which it is attached. The process culminates in the transfer of the negative charge of the reagent ion across the carbon atom to the chlorine which is being ejected as an ion. Clearly the same mechanism will apply to the fission of arylsulphonates, but there is the added complication of two competing positive centres. Normally the affinity of the phenoxyl group for a negative charge combined with the positive character of the sulphur atom is sufficient to cause severance to occur at the oxygen-sulphur linkage. However, when the nuclear carbon atom is made sufficiently positive (at least two nitro groups are required), fission can occur there with the assisting affinity of the sulphonate group for a negative charge.

Frauenberg and Hess (loc. cit.) state that hydrazine severs 2:4-dinitrophenyl-p-toluenesulphonate to give only 2:4-dinitrophenol, whilst ammonia gives dinitrophenol or dinitroaniline according to the condition of the experiment. This difference in the action of bases awaits exploitation; it may be connected with the relative anionoid activity of the reagent as o/p ratio is in part determined by the kationoid activity of the substituent (p. 61).
B. The Scission of Diaryl sulphphonanilides.

The hydrolysis of a sulphonanilide can be brought about by solution in cold concentrated sulphuric acid but it was found that many disulphonanilides are resistant to this treatment. However such compounds could be readily converted into the sulphonanilides by means of piperidine (equation A). In view of the previous work with nitroaryl-sulphonanilates it appeared possible that dinitrosulphonanilides might react according to equation (B).

\[ R,N(\text{SO}_2\text{R}')_2 + H,\text{NC}_6\text{H}_5 = R,N,\text{SO}_2\text{R}' + C_6\text{H}_5\text{NC}_6\text{H}_5,\text{SO}_2\text{R}' \]  
\[ (A) \]

\[ R,N(\text{SO}_2\text{R}')_2 + H,\text{NC}_6\text{H}_5 = R,N,\text{NC}_6\text{H}_5 + R,N(\text{SO}_2\text{R}')_2 \]  
\[ (B) \]

Actually all the disulphonanilides investigated passed smoothly into monosulphonanilides.

Since disulphonanilides are so very stable towards acids it appears probable that the facile piperidine scission is brought about by the ability of piperidine to act as an electron donor. Equation (C) shows that the fission will be

\[ \begin{align*}
\text{Ar.} N - N & \quad \rightarrow \quad \text{Ar.} N + X \\
\text{H} & \quad \text{H} \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad 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\quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad '\]
gave \( \text{m-nitrobenzenesulphon-} \text{m'-nitroanilide (L)} \).

Moreover \( \text{m-nitrobenzenesulphon-} \text{p'-nitroacetanilide (LI)} \)

\[
\text{(LI)} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{NO}_2 \\
\end{array} \quad \xrightarrow{H \text{NCO}_3 \text{H}_2 \text{O}} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{N} \text{H} \\
\end{array} \\
+ \text{C}_5 \text{H}_{10} \text{N} \text{SO}_2 \text{C}_7 \text{H}_7
\]

\[
\text{(LII)} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{NO}_2 \\
\end{array} \quad \xrightarrow{\text{N'}Ac} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{NO}_2 \\
\end{array} \\
+ \text{C}_5 \text{H}_{10} \text{N} \text{Ac}
\]

\[
\text{(LIII)} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{N} \text{Ac} \\
\end{array} \quad \xrightarrow{\text{N'}Ac} \quad \begin{array}{c}
\text{NO}_2 \\
\text{SO}_2 \text{C}_6 \text{H}_4 \text{N} \text{Ac} \\
\end{array} \\
+ \text{C}_5 \text{H}_{10} \text{N} \text{Ac}
\]

gave \( \text{m'-nitrobenzenesulphon-} \text{p'-nitroanilide (LII) and} \)

\( \text{p'-toluenesulphon-} \text{m'-nitroacetanilide (LIII) gave} \)

\( \text{p'-toluenesulphon-} \text{m'-nitroanilide (LIV).} \)
III THE ORIENTING POWERS OF THE ARYLSULPHON-
AMINO AND ARYLSULPHONAMINO GROUPS IN AROMATIC
SUBSTITUTION AS SHOWN BY EXPERIMENTS IN THE
BENZEN, DIPHENYL AND NAPHTHALENE SERIES.

A. The Structure of the Arylsulphonamido and
Arylsulphonamino Groups.

Ingold and Shaw (J., 1927, 2913) have classified
orienting groups into four categories represented by
the following combinations of inductively propagated
electronic strain (I →) and tautomeric transforma-
tions, (T, ν) (p. 14):

\[
\begin{align*}
\text{Type } 1 & : & \tau^R \\
\text{Type } 2 & : & -\tau^R \\
\text{Type } 3 & : & -\tau^R + T \\
\text{Type } 4 & : & +\tau^R + T
\end{align*}
\]

Type 1 is exemplified by toluene, and measurements of
the velocity of nitration have shown that the methyl
group greatly activates the \( \sigma \) and \( \sigma^* \) positions and
to a much less extent the \( \pi \) position. The propon-
derating \( \sigma-\pi \)-substitution is the result of this prefer-
tential activation. Phenylammonium and benzenesulphonyl
compounds exemplify type 2. Here velocity measurements
show that all the positions are deactivated but the \( \pi \)-
position to a less extent than the \( \sigma-\pi \)-positions.

\( \pi \)-Substitution arises through \( \sigma-\pi \) inhibition. Type 3 is
more complicated owing to the combination of two conflict-
ing effects. A series can be constructed such as \( \text{HNR'} \), \( \text{OR, I, Br, Cl, F} \) representing progressively increasing \(-\text{I}\) and diminishing \(+\text{T}\) effects. At a certain point in the series the velocity of reaction becomes less than unity compared with benzene, but \( \text{o-} \) substitution occurs almost exclusively. Type 4 is instanced by the phenoxide ion; great activation of all positions occurs and \( \text{o-} \)-substitution is favoured by the preferential inductive and tautomeric effects.

Clearly most substituents belong to type 3, which includes in addition to the groups already mentioned, the acyloxy, alkoxyloxy, acylamido, acylalkylamido and diacyl-

amido groups.

Lapworth and Robinson (Chem. Manchester Phil. Soc., 1927, 72, 43) suggest that as a result of the presence in the benzene nucleus of a group A having a smaller attraction for electrons than has the hydrogen atom, electron availability and therefore reactivity should tend to be greater in the \( \text{p} \) than in the \( \text{p} \)-position. With a substituent \( \text{B} \) which attracts electrons the effect is reversed and consequently reaction should occur \( \text{p'} > \text{o'} \). This leads
to the expectation of a high \( \text{o/p} \) ratio for groups of types 1 and 4 (above) and a low one for \( \text{m} \)-directive groups (type
2) and also for \( \sigma \)-p-directive groups having a natural 
electron attraction (type 3). Anomalous orientation 
may supervene if the initial attachment of the reagent 
is to the side chain; in this case the \( \sigma \) position is 
unduly favoured. The following results support their 
deductions:

The high \( \sigma/p \) ratio for nitration of toluene is progressively 
diminished in passing through the series benzyl-
chloride, benzylidene chloride and benzoctrichloride. On 
the other hand the \( \sigma/p \) ratio for nitration of fluorobenzene 
is low but rises in the series chlorobenzene, bromobenzene, 
iodobenzene owing to the diminishing inductive \( \{F > Cl > Br > I\} \)
and increasing tautomeric \( \{I > Br > Cl > F\} \) effects of the 
halogen atoms. In substances of type \( \text{Ph}_2\text{Cl}_2\text{Br}_3\text{X} \) the 
B effect is very strong and it is an experimental fact 
that the percentage of \( \sigma \)-isomeride is very low.

In the following substitution experiments the orient-
ing groups \( -a, b, c, d \) belong clearly to the \(-\text{I}+\text{F} \) type 
(3, above). The nitrogen atom has a lone pair of electrons

\[
\begin{align*}
\text{(a)} & \quad \text{H} \swarrow \searrow \quad \text{Me} \swarrow \searrow \quad \text{SO}_2^- \swarrow \searrow \\
\text{(b)} & \quad \text{N} \swarrow \searrow \quad \text{N} \swarrow \searrow \quad \text{O} \swarrow \searrow \\
\text{(c)} & \quad \text{N} \swarrow \searrow \quad \text{N} \swarrow \searrow \quad \text{O} \swarrow \searrow \\
\text{(d)} & \quad \text{N} \swarrow \searrow \quad \text{N} \swarrow \searrow \quad \text{O} \swarrow \searrow 
\end{align*}
\]
which can enter into tautomeric displacements with the nucleus, but the sulphur dipole must exert an attraction on electrons since the positive pole is nearer the nucleus than the negative pole. Predominating o-p substitution associated with a low e/p ratio would be anticipated.

A number of papers throw light on the magnitude of the effects associated with dipoles. Baker and Ingold (J., 1928,2462) have compared the nitrations of nitrobenzene, phenylnitromethane and \( \beta \)-phenylnitroethane with those of the corresponding ammonium salts, with the following results:

<table>
<thead>
<tr>
<th>Approx. % of ( m )-nitro derivative</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>( MN_3 )</td>
<td>( \text{CH}_2^+ \text{NM}_3 )</td>
<td>( \text{CH}_2\text{CH}_2^+ \text{NM}_3 )</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>88</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>( K_2 )</td>
<td>( \text{CH}_2^+ K_2 )</td>
<td>( \text{CH}_2\text{CH}_2^+ K_2 )</td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>48</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

It will be seen that in each case the proportion of \( m \)-isomeride is less than that for the free positive ion. However if the electrostriction of the ammonium ions is increased by the presence of common ions the proportion of \( m \)-derivative is very considerably diminished. Flürschein and Holmes (J., 1928,1682) by addition of ammonium sulphate to the acid used in the nitration of diethylbenzylamine lowered the percentage of \( m \)-isomeride from ca. 41\% to ca. 34\% whilst Pollard and Robinson (J., 1927,5770) obtained even greater effects by addition of rubidinium nitrate and trimethylammonium nitrate to benzylpiperidine (see however,
Robinson and Watt, J., 1931, 920). The partial compensation of neighbouring charges is clearly proved.

With sulphonates a similar effect is evident (Ingold and Shaw, J., 1927, 815; Chatterjee and Robinson, ibid., 2790; Bottomley and Robinson, ibid., 2795). Benzylmethylsulphone on nitration gives only 30% of the p-isomeride, toluene-ω-sulphonic acid 14%, and toluene-ω-sulphonyl chloride 51%.

\[
\begin{align*}
C_6H_5\rightarrow CH_2 \stackrel{\text{S}}{\rightarrow} CH_3 & \quad C_6H_5\rightarrow CH_2 \stackrel{+}{\rightarrow} S \cdot Cl & \quad C_6H_5\rightarrow CH_2 \stackrel{-}{\rightarrow} S \cdot Cl
\end{align*}
\]

(30%)

(14%)

(51%)

In the acid there are three negatively charged oxygen atoms compensating the charge on the sulphur atom, but in the chloride the electron demand of the sulphur is coupled with the inductive demand of the chlorine atom (compare p.19).

Of greater interest is the fact that the two semipolar double bonds of the sulphone group cause the sulphur atom

\[
\begin{align*}
\text{CH}_2 \cdot H \stackrel{\text{S}}{\rightarrow} \text{CH}_2 \cdot S \cdot \text{H} & \quad \text{CH}_2 \cdot H \stackrel{\text{S}}{\rightarrow} \text{CH}_2 \cdot S \cdot \text{H}
\end{align*}
\]

(43% m-)

(50% m-)

to bear a smaller positive charge (as measured by \( \eta \) directing action) than that on the nitrogen atom in a nitro group. Ingold and Shaw (loc. cit., p.618) attribute this to absorption of the effect of the ionic charge of the sulphur nucleus in passing through the outer electron shells of the atom. The effect is similar to that which occurs in passing up a family in the
periodic table (Ingold, Shaw and Wilson, J., 1928, 1930; Ingold and Ingold, ibid., 1930; Flörnheim and Holmes, ibid., 1907).

Approx. % of m-nitro derivative.

<table>
<thead>
<tr>
<th></th>
<th>HNO₃</th>
<th>FNO₃</th>
<th>AsNO₃</th>
<th>SbNO₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td></td>
<td></td>
<td>98</td>
<td>86</td>
</tr>
<tr>
<td>CH₂⁺HNO₃</td>
<td>CH₂⁺FNO₃</td>
<td>CH₂⁺AsNO₃</td>
<td>CH₂⁺SbNO₃</td>
<td></td>
</tr>
<tr>
<td>88</td>
<td>10</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₂F</td>
<td>CH₂Cl</td>
<td>CH₂Br</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>17.5</td>
<td>13.0</td>
<td>2.0</td>
<td>6.9</td>
</tr>
</tbody>
</table>

Chatterjee and Robinson take a different view. According to these authors the higher nuclear charge and smaller electron density of the outer shell of sulphur allow greater distortion, with corresponding greater reduction of the effective ionic charge, than is possible in the case of nitrogen. Recently Pollard and Robinson (J., 1930, 1935) have found that benzyl-diethylsulphonium picrate on nitration gives only 29% of the m-derivative, a striking confirmation of the easy deformation of the sulphur atom compared with that of the nitrogen atom.

Also Baker and Moffitt (ibid., 1933) have obtained the following results on the nitration of various sulphonium and selenonium nitrates given above. The nitro-derivatives (28% m-)

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Also Baker and Moffitt (ibid., 1933) have obtained the following results on the nitration of various sulphonium and selenonium nitrates given above. The nitro-derivatives (28% m- and 85% m-).
tocates:

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Total yield</th>
<th>( % )-Isomorxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \mathrm{Ph}_2\mathrm{SMe}_2 )</td>
<td>04</td>
<td>100</td>
</tr>
<tr>
<td>( \mathrm{Ph}_2\mathrm{CH}_2 \cdot \mathrm{SMe}_2 )</td>
<td>85</td>
<td>52</td>
</tr>
<tr>
<td>( \mathrm{Ph}_2\mathrm{SeMe}_2 )</td>
<td>09</td>
<td>100</td>
</tr>
<tr>
<td>( \mathrm{Ph}_2\mathrm{CH}_2 \cdot \mathrm{SeMe}_2 )</td>
<td>09</td>
<td>16</td>
</tr>
</tbody>
</table>

No doubt can remain that the charge developed by a sulphur atom as a result of sulphonium salt or sulphone formation is appreciably less than that developed by the nitrogen atom in ammonium salts or nitro-compounds. This gradual diminution in the effective charge and increasing possibility of ionic distortion may account for the failure to resolve salenoxides and telluroxides analogous to the optically active sulfoxides (Phillips, J., 1925, 2555; Gaylwaite, Kenyon and Phillips, J., 1928, 2200).

B. Experiments in the Benzene Series.

Section 1. The Directing Influence of the Aryl-
sulphonoxy Group.

The first example of the use of the \( p \)-toluenesulphonyl group for the protection of hydroxyl in substitution experiments occurs in a patent of the firm Momet, Gilliard and Cartier (D.R.P. 91314). Phenyl-\( p \)-toluenesulphonate with fuming nitric acid was found to yield \( p' \)-nitrophosphyl-\( p \)-nitro-\( p \)-tolyene-
sulphonate (IV). Less vigorous nitration with concentrated nitric acid gives almost pure \( p' \)-nitrophosphyl-\( p \)-tolyene-sulphonate.
(LVI) Reverdin and Cépèaux, Ber., 1909, 45, 1459. Consequently the orienting power of the \( p \)-toluenesulphonyloxy group appears to be small. Further evidence on this point was sought.

Phenyl-\( p \)-nitrobenzenesulphonate with fuming nitric acid gave \( p' \)-nitrophenyl-\( p \)-nitrobenzenesulphonate (LVI) without any by-products being isolated. Mononitration under these conditions clearly shows the small orienting influence of the group, the approximation of the o/p ratio to zero, its \(-I\) character, whilst the absence of any \( m \)-nitro-derivative is somewhat surprising if the sulphur atom carries a large positive charge. Next, \( p \)-toly1-\( p' \)-nitrobenzenesulphonate underwent nitration in the 2-position (LVI), the methyl group overcoming the influence of the \( p \)-nitrobenzenesulphonate group. This result may in part

be attributed to the low o/p ratio of the \( p \)-nitrophenylsulphonyloxy group, combined with the high o/p influence of the

(set) taken by entering nitro group.)
methyl group, since the only compound isolated from the product of nitration of o-tolyl-p′-toluenesulphonate was (IXI) (Reverdin, Ber., 1912, 1450). A paper by Brady, Quick and Welling (J., 1925, 127, 2264) contains some related results. These authors find that the amino-group is predominantly p-directive after introduction of a bivalent acyl group. For example, phthalanil on nitration gives the 4-nitro-derivative (IXI). On the other hand 4-methylphthalanil gives 76% of the 3-derivative (IX) and 2-methylphthalanil gives the 5- and 6-mononitro-derivatives as the only isolable products (Staedel, Annalen, 1884, 235, 885) (IXII and IXIII). An interesting series is obtained: Cl > O,SO₂, C₇H₇ > N;Phth... A methyl group can only partially compete

(Position taken by entering nitro group.)
with a chlorine atom in the \( \beta \)-position (Goldschmidt and Nenig, *Ber.*, 1927, 30, 300) and is overcome by an \( \beta \)-chlorine atom (Idem, *Ber.*, 1926, 49, 8440). However, when \( \beta \) to the \( \beta \)-toluencesulphonamoyl group it dominates substitution and with the phthalimide group it governs substitution even when in \( \beta \)-position to that group.

**Section II. The Directing Influence of the Aryl-sulphonamido Group.**

It has been previously shown that sulphonanilides undergo easy nitration in the \( \beta \)-position (A. G. P. A., *D. R. P.* 157859; 163519), or when this position is blocked, as in \( \beta \)-phenetidines, in the \( \beta \)-position (*D. R. P.* 164130).

![Chemical Structures](image)

Moreover, Everest (*B. P.* 261499; 261322) and Flürscheim (*D. R. P.* 245079) have shown that more than one nitro group can be easily introduced into a sulphonanilide. Thus \( \beta \)-toluidine yields compound (LXIV), \( \beta \)-chloroaniline compound (LXV) and \( \beta \)-nitroaniline compound (LXVI). These results show that the \( \beta \)-toluencesulphonamido group is a powerful directing group and additional evidence on this point was soon obtained. \( \beta \)-Nitrobenzenesulphon-\( \beta \)-tolylenamide readily gave the 3:5-dinitro derivative (LXVII).
contrast LIVIII) and 3-p-toluosesulphonamido-p-toluene-sulphonate gave first the 5-nitro (LXVIII) and then the 3,5-dinitro (LXIX) derivatives in almost quantitative yield. The low o/p ratio indicated by formation of (LXVIII) is in accord with anticipation but the formation involves a ten electron shift round the sulphur atom. On the other hand, the o/p ratio is 100% of (a) in which the negative charge on the nitrogen is only very partially neutralised by the charge on the sulphur atom. Interesting evidence in favour of such a form is
provided by von Braun and Weissbach (Ber. 1930, 63, 2836),
who find that some sulphonamides e.g. \( \text{p}-\text{butylsulphon-}
\text{ethylanide} \), react with phosphorus pentachloride to give
stable chloro derivatives, to which they assign formulae
of type (a) or (b). It will be seen that these formulae
involve a ten electron shell round the sulphur atom,

\[
\begin{align*}
\text{(a)} & \quad \begin{array}{c}
\text{Cl} \\
\text{Du-S-NEt} \\
\text{0}
\end{array} \\
\text{(b)} & \quad \begin{array}{c}
\text{Cl} \\
\text{Du-S-NEt} \\
\text{0}
\end{array} \\
\text{(c)} & \quad \begin{array}{c}
\text{0} \\
\text{Du-S-NEt} \\
\text{0}
\end{array} \\
\text{(d)} & \quad \begin{array}{c}
\text{Cl} \\
\text{Du-S-NEt} \\
\text{0}
\end{array}
\end{align*}
\]

which seems intrinsically improbable. On the other hand
formula (c) is in keeping with the octet rule and provides
a satisfactory representation of the properties of the
compound.

The similarity between the reactions of sulphonamides
and phenols is further shown by the fact that \( \alpha- \) and \( \beta-\text{p-}
\text{naphtoluenesulphonicamides} \) couple with diazotised aniline
(Witt, Ber. 1904, 37, 2370) and \( \text{p}-\text{nitroaniline} \) (König and
Köhler, Ber. 1921, 54, 931) as readily as do the correspond-
ing naphthols. Just one type of reaction appears to be
specific to the phenols. It is well known that nitrous
acid will displace bromine from most bromophenols. In
the present work it was found that 3:5-dibromo-4-hydroxy-
diphenyl (LXX) was readily converted into a mixture of
3-bromo-5-nitro- and 3:5-dinitro-4-hydroxydiphenyls and
3:5:4'-tribromo-4-hydroxydiphenyl (LXXI) gave 3-nitro-5:
4'-dibromo-4-hydroxydiphenyl. Analogous changes do not...
Section III. The Directing Influence of the Arylsulphonamido and Diarylsulphonamido Groups.

The exceptionally high orienting power of the arylsulphonamido group has been attributed to the existence of a reactive phase in which the nitrogen atom was left with a negative charge by removal of a hydrogen atom. When this hydrogen atom is replaced by a methyl group or by a further arylsulphonyl residue this phase is suppressed and it would be predicted that the orienting power would fall off as does that of the hydroxyl group on conversion to methoxyl. Moreover the orienting power of the diarylsulphonamido group should be less than that of the sulphonamethylamido group because the inductive effect of the methyl group is such as to activate the nucleus whilst the
inductive effect of the arylsulphonyl residue will lead
to deactivation. This was found to be the case. \( p \)-
Toluenesulphonmethylamylanilide underwent nitration much
less readily than \( p \)-toluenesulphonanilide. 10 g.
gave \( p \)-toluenesulphonmethyl-4-nitroanilide (8g.) and
\( p \)-toluenesulphonmethyl-2-nitroanilide (1.5g.) and the
general conclusion was reached that the orienting power
of the \( p \)-toluenesulphonmethylamido group is very similar
to that of the acetamido- group.

Di-\( m \)-nitrobenzenesulphonanilide was remarkably
resistant to substitution. It was recovered unchanged
after heating with concentrated nitric acid, a condition
sufficiently powerful to di-nitrate the sulphonanilide
and mononitrate the methylsulphonanilide. With fuming
nitric acid it gave a product containing a considerable
proportion of the \( m \)-nitro derivative. Di-\( m \)-nitrobenzene-
sulphon-\( p' \)-toluidide (LXXII) with fuming nitric acid gave
di-\( m \)-nitrobenzenesulphon-\( o' \)-nitro-\( p' \)-toluidide (LXXIII)
and di-\( m \)-nitrobenzene-\( o' \)-toluidide (LXXIV) a mixture of
the \( o' \) and \( p' \) nitro compounds. Again, di-\( m \)-nitrobenzene-
sulphon-\( o' \)-nitroanilide (LXXV) could be recovered un-
changed after solution in fuming nitric acid, whereas
\( m \)-nitrobenzenesulphon-\( o' \)-nitroanilide was immediately
converted into the \( o' \): \( p' \)-dinitro derivative (LXXVI)
under the same conditions.
Section IV. The Further Substitution of

\[ \text{o-Disubstituted Benzenes} \]

The subject of substitution of o-disubstituted benzenes has been discussed by Ingold and Ingold (J., 1926, 1310), Holmes, Ingold and Ingold (J., 1926,
1884) and Ingold and Smith (J., 1927, 1690) and the hypothesis advanced that, in general, the proportion of y-substitution is a function of the disparity between the polar activities of the groups. The following results are used to exemplify this hypothesis:

![Chemical structures](image)

It will be seen that as the groups approach one another in p-p-directive power the amount of vicinal substitution steadily diminishes. During the course of the experiments herein described, four derivatives of 2-aminophenol were mononitratored with the results indicated below.

2-Acetamidophenyl-p-toluenesulphonate gave only a poor yield, a result attributed to the marked deactivating influence of the p-toluenesulphonyl group on the nucleus. The remaining results are sufficient to show that the above-mentioned hypothesis can be of only limited application. 2-Acetamidophenyl acetate gives about 50% of the y-derivative so that on replacement of the acetyl by the more powerfully directing p-toluenesulphonyl radical.
almost exclusive \( \gamma \)-substitution might be expected. Actually the amount falls to a very low value. With 2-\( \gamma \)-toluenesulphonamido-\( \gamma \)-toluenesulphonate, in which the disparity between the groups is very high, \( \gamma \)-substitution appears to be absent. It is probable that the directive power of the \( \gamma \)-toluenesulphonate group is so small that it is unable to interfere in any way with the electron displacements leading to substitution para to the sulphonamido group. Consequently \( \gamma \)-substitution occurs owing to the extremely low \( o/p \) ratio of that group. The acetoxy group shows more successful competition and when pitted against the acetonido group produces substitution mainly ortho to that group.
Section 1. Rules Governing the Entry of Substituents into the Diphenyl Nucleus.

Although little was known on the subject of substitution in the diphenyl series prior to 1925, since that date there has been a rapid succession of papers on this topic. A synopsis of the principal results is given below.

The qualitative results of Bell, Kenyon and F.H. Robinson (J., 1926, 1239) and Bell and Kenyon (ibid., 2705) on the nitration of diphenyl have been supplemented by the quantitative observations of Gull and Turner (J., 1939, 491) with the following results:

![Chemical Structures]

The data for the nitration of 3- and 4-nitrodiphenyls are in accord with expectation (p. 57), since the introduction of a nitro group in the one nucleus is bound to diminish the electron availability in the ortho position of the other. However, the results with 2- and 2,4-dinitrodiphenyls can only be interpreted as indicating intermediate compound formation.

More important from a theoretical point of view is the absence of the 3 derivative in the nitration of...
diphenyl itself. It seems necessary to postulate some such phase as (a), which at the demand of the reagent
gives rise to displacements resulting in activation of positions 2 and 4 only. The failure of the two nuclei
to form a single conjugated system is rather perplexing in view of the results obtained with the phenylpyridines
(p. 64). Other substitution results remain of a qualitative character but the general conclusions are not
likely to be altered. Scarborough and Waters (J., 1926, 5:8) put forward three orientation rules which, in the
main, have been upheld by subsequent experiments.
(1) The usual directive influence is to be ascribed to all the simple groups.
(2) The phenyl group and the group C₆H₅X (where X may be an ortho-para or meta-directing group) have a strong
o-p-directing influence.
(3) The amino-, hydroxy and derived groups promote substitution in the same nucleus.

A few illustrations of the application of these rules will be given. 4-Hydroxydiphenyl on nitration (García
Banks and Guiteras, Anal. Fís. Quím., 1923, 21, 126; Rainford and Colbert, J. Amer. Chem. Soc., 1925, 47, 1456) and bromin-
ation (Bell and F. H. Robinson, J., 1927, 1128) gives successively the 3-, 3:5- and 3:5:4'- derivatives. 4-Aminodiphenyl on bromination gives the 3:5-dibromo derivative (Bell, J., 1926, 2705). Again, 4-acetamidodiphenyl on nitration (Bell, J., 1926, 2705) and bromination (Scarborough and Waters, loc. cit.) and chlorination (Scarborough and Waters, loc. cit.) and 4-dimethylaminodiphenyl on nitration (García Borrás and Ferrer Tomás, Anal. Fís. Quím., 1921, 18, 293) and bromination (Konyon and F. H. Robinson, J., 1926, 3050) give the 3- derivatives.

A few exceptions have been encountered, certain derivatives of 2- and 4-aminodiphenyl undergoing heteronuclear substitution. 4-Diphenyltrimethyl ammonium nitrate (Vöhringer, Ber., 1925, 58, 1683) and 4-benzylideneamino-phenyl (in sulphuric acid) (LXXVIII) (Bell and Kenyon, J., 1926, 2705) both undergo nitration in the 4'-
position. This is not surprising for the nitrogen atoms in these two compounds are positive in character (Baker and Ingold, J., 1930, 431). Again, 4-acetamidodiphenyl on treatment with bromine leads to the bromo-derivatives (LXXVII) and (LXXVIII) (see through the notes, 2771)

![Chemical Structures](image)

bromination gives about 30% of the 4'-bromo-derivative (LXXIX) (Kenyon and P. H. Robinson, loc. cit.) and 2-acetamidodiphenyl, in the presence of some sulphuric acid, yields the 4'-nitro derivative (LXXX). It was found (Bell, J., 1926, 2770) that 2-acetamidodiphenyl on nitration in acetic acid gave the 5-nitro derivative (LXXXI) so that the previous result is attributed to salt formation

![Chemical Structures](image)

between the acetamide group and the strong acid (see inter alia, Dadswell and Kenner, J., 1927, 1102). The bromination of 4-acetamidodiphenyl is discussed at a later
Higher substitutions are not so uniform in character. Thus 3-chloro- and 3-nitro-4-aminodiphenyls on treatment with bromine readily yield the 5-bromo- derivatives (LXXXII and LXXXIII) (Scarborough and Waters, J., 1937, 1133) but substitution of the corresponding acetyl derivatives proceeds with much greater difficulty. However, 3-chloro-4-acetamidodiphenyl and 3-nitro-acetamidodiphenyl can be brominated and nitrated to give in each case the 4'- derivative (e.g. LXXXIV and LXXXV). The acetamido- group cannot override the deactivating influence of a nitro- group or halogen atom, assisted in the latter case by opposing tautomeric displacements, and further substitution, controlled by the substituted phenyl group acting as a whole, takes place in the other nucleus. Similar considerations apply to the bromination and nitrination of 4-methoxydiphenyl for the products obtained are 3:4'-dibromo-4-methoxydiphenyl (LXXXVI) and 3:4'-dinitro-4- methoxydiphenyl (LXXXVII) respectively (Bell, J., 1930, 1078).
Section II. The Substitution of Arylsulphonamides and the Bearing of the o/p Ratio of the Directing Group on Heteronuclear Substitution.

In accordance with expectation 4-<sub>p</sub>-toluenesulphonamidodiphenyl underwent nitration much more easily than 4-acetamidodiphenyl. It gave first the 3-derivative and then the 3:5-dinitro derivative. When 4-<sub>m</sub>-nitrobenzene-sulphonamidodiphenyl was used the process was carried a stage further to give 3:5:4'-trinitro-4-<sub>m</sub>-nitrobenzenesulphonamidodiphenyl (LXXXVIII). Again, 2-<sub>p</sub>-toluenesulphonamidodiphenyl underwent nitration first in the 5-

\[
\begin{align*}
\text{Ph} & \quad \text{NO}_2 \\
\text{NH}_2 & \quad \text{NO}_2 \\
\text{NO}_2 & \quad \text{Ph}
\end{align*}
\]

(LXXXVIII)

and then in the 3-position; when 2-<sub>m</sub>-nitrobenzene-sulphonamidodiphenyl was used the 3:5:4'-trinitro derivative (LXXXIX) was obtained. It is evident that the sulphonamide group does overcome the deactivating influence of the nitro group.

In view of this result some quantitative measurements of Orton and Bradfield (J., 1927, 986) and of Bradfield and
Jones (J., 1928, 3073) occasion surprise. These authors have determined the velocity coefficient of chlorination of certain anilides in acetic acid solution under standard conditions and the comparative numbers are: - acetic acid, 66.5; p-toluenesulphonilide, 65.11; benzene sulphonilide, 41.2. Instead of the values for the sulphonilides being very considerably higher than that for acetic acid they are actually less. This result can only be interpreted as indicating a difference in the mechanisms of nitration and halogenation or that the normal character of the acetamide- group is modified by salt formation in the presence of mineral acid, with consequent lowering of its orienting power relative to that of the sulphonamide- group. It is significant that "the amount of hydrochloric acid employed produces an appreciable effect on the velocity of chlorination, the effect on acetic acid being a decrease in speed as the hydrochloric acid is increased, although with benzene sulphonilide this effect is reversed" (Orton and Bradfield, loc. cit.). The difference which exists between the nitration and bromination of 4-acetamidodiphenyl (p. 56) cannot be overcome in this way. Substitution in the 3- position (nitration) is directly controlled by the group in position 4-, whilst entry in position 4' (bromination) is controlled by the substituted phenyl group, conjugative effects between the nuclei being discredited (Le Fèvre and Turner, J., 1928, 245). If the possibility of indirect sub-
Substitution via the acetylamido- group can be left out of account (Korsten, Kopor and Williams, J., 1928, 986) it appears that the acetylamido- group is more effective in nitrations than in brominations.

It appeared of interest to see whether a similar difference between nitrations and bromination was shown by p-toluene sulphonamides. 4-p-Toluenesulphonamido- diphenyl underwent nitration quantitatively in the 3-position but bromination of the compound led to so many products that great stress could not be laid on the absence of the 4'-derivative. 3-Nitro-4-p-toluenesulphonamidodiphenyl proved unsuitable for use because although nitration proceeded cleanly to the 3:5-dinitro- derivative, bromination in acetic acid was accompanied by much hydrolysis and formation of 5:4'- dibromo-5-nitro-4-amidodiphenyl. However, 4-bromo-3-p-toluenesulphonamidodiphenyl on bromination gave quite a good yield of the 3:4'- dibromo- compound (XC), whilst on nitration 3-bromo-5- nitro-4-p-toluenesulphonamidodiphenyl (XCI) was obtained.

![Diagram](image.png)

(XC)

(XCI)

It appears therefore that the nature of the entering group must be taken into account as a factor not entirely overruled by conditions of substitution and strength of orienting group.
Lewworth and Robinson (Mem. Manchester Phil. Soc., 1927, 72, 43) have emphasised the distinction between degree and frequency of activation of a nuclear carbon atom. Reference is given to the work of Gattermann and Lüblemann (Annalen, 1912, 393, 118) on the formation of azo compounds from 1-naphthol and 1-naphthyl-amine 3- and 5-sulphonic acids, e.g. (XCII).

Employing diazonium compounds derived from sulphanilic acid, p-chloroaniline, 2:5-dichloroaniline, 2:4:5-trichloroaniline, o-, m- and p-nitroanilines, 4-chloro-3-nitroaniline, 2:4-dinitroaniline and 2-nitroaniline-p-sulphonic acid there was found to be a gradation in this order. The earlier members attacked the 2- positions but the more negative diazonium salts attacked the 4- position to a predominating extent. Since the kations of these salts constitute a series of increasingly energetic kationoid reagents it is suggested that the degree of activation in position 4- is smaller than in position 2-, but that the frequency of activation in position 4- is greater than in position 2-.

The more energetic agents can take advantage of the higher frequency of activation. Experimentally and theoretically therefore the ortho-para ratio is greatly influenced by the

![Diagram](Image)
nature of the reagent and the conditions of the reaction. Applying this hypothesis to the substitution of 4-acetamidodiphenyl (XIII) it might be suggested that position 4' has a lower degree but a higher frequency of activation than position 3, and bromine, a more energetic kationic reagent, enters position 4'. Evidence in favour of this view is obtained from the results of substitution experiments with 2-chlorotoluene. The methyl group is of the +I type, the chlorine of the -I, +T type and the normal condition of the molecule must be somewhat as represented in (a). Positions 3 and 5 suffer primary deactivation and only secondary activation; positions 4 and 6 primary activation and only secondary deactivation. Clearly positions 4 and 6 will show a slight permanent negative character and substitution should occur there with a sufficiently energetic kationic reagent. On the other hand, a less energetic reagent will only be capable of reaction in those phases of the molecule in which the slight activation of positions 3 and 5 is coupled with the large tautomeric displacements initiated at the chlorine atom (b). Experimentally it is found that 2-chloro-
whereas nitration (Goldschmidt and König, Ber., 1886, 19, 466) occurs principally in position 5.

Since 4-hydroxymetaphenyl brominates in positions 3, 5 without formation of the 3, 4'-derivative (p. 55), it appears that when the activation in positions 3 and 5 is sufficiently high, so that every tentative union proceeds to completion, the higher frequency of activation of position 4' is more than counterbalanced. The activating power of a p-toluenesulphonamido-group can be increased by removal of its incipiently ionized hydrogen atoms by salt formation, and therefore the bromination of 4-p-toluenesulphonamidodiphenyl in pyridine solution was examined. It was found to give the 3, 5-derivative (XCIII; contrast XC) in good yield. Similarly 4'-bromo-4-p-toluenesulphonamidodiphenyl gave the 3, 5, 4'-tribromo-derivative, 4'-nitro-4-p-toluenesulphonamidodiphenyl the 3, 5-dibromo-derivative (XCIV), 3-nitro-4-p-toluenesulphonamidodiphenyl the 5-bromo-derivative

\[
\text{[XCIII]} \quad \text{[XCIV]} \quad \text{[XCV]}
\]

and 5-bromo-2-p-toluenesulphonamidodiphenyl the 3-bromo-
derivative (XCV). Without an exceptionally reactive compound bromine in cold pyridine is of no value as a brominating agent. 5- (and 4')-Bromo-4-methoxydiphenyls, 4'-bromo-4-acetamidodiphenyl and even 4-acetamidodiphenyl were recovered in quite good amount after treatment with 1-2 molecules of bromine in this way. Moreover a negative pole present in one nucleus has little effect on the reactivity of the other nucleus for 3,5-dibromo- (and dinitro-) 4-p-toluenesulphonamidodiphenyls and 3,5-dibromo-2-p-toluenesulphonamidodiphenyl were unchanged by bromine in pyridine solution. It is remarkable that the influence of even a positive pole can be transmitted from nucleus to nucleus in other ring systems. For example 4-phenylpyridinium sulphate undergoes nitration to the extent of 29% in the p-position of the benzene nucleus (Forsyth and Ryman, J., 1926, 2012; contrast p. 54).
Section III. The Substitution of Arylsulphonates, 
Arylsulphonmethylanilides and 
Diarylsulphonanilides.

4-<b>o</b>-Toluene sulphonphonoxydiphenyl (XCVI) underwent 
nitrátion in the 4'-position (XCVII) and was then re- 
sistant to hot concentrated nitric acid. This is a 
striking confirmation of the marked deactivating 
influence of a positive substituent on the neighbouring 
positions because 4-methoxydiphenyl very readily gives 
3:4'-dinitro-4-methoxydiphenyl and the primary point of 
attack is the 3'-position.

Further examples of the fall in orienting power of 
the NH₂SO₂ group on conversion into the NH₂SO₂ and 
H(SO₂)₂ were obtained in this series. 2- and 4-<b>o</b>- 
Toluene sulphonmethylanilidodiphenyls and 5-nitro-2-di-<b>m</b> 
nitrobenzenesulphonanilido phenyl gave mononitro-derivatives 
(XCVIII, XCIX and C) under conditions which led to dinitra- 
tion of the corresponding sulphonanilides.
D. EXPERIMENTS IN THE NAPHTHALENE SERIES.

Owing to the complicated character of the results obtained substitution in the naphthalene series has been the subject of little theoretical speculation. Moreover the basic experimental work is far from being complete outside the limits of compounds of immediate industrial application. To give only two examples, the nitration of \( \beta \)-naphthol has been worked out only as far as the 1:6-dinitro-derivative (Wallach and Michelau, \textit{Ber.}, 1870, 3, 840; Schmidt, \textit{Ber.}, 1900, 33, 3216), whilst the bromination, leading to the production of the antiseptic providone which was stated to be the 1:3:6-derivative has been recently shown to give 1:4:6-tribromo-\( \beta \)-naphthol (Fries and Schirmelschmidt, \textit{Annalen}, 1930, 484, 245).

Nitration of aceto-\( \beta \)-naphthalide (CI) gives first a mixture of 1-, 6- and 8-mononitro derivatives and then a mixture of 1:5- and 1:6-dinitro derivatives (Jacobson, \textit{Ber.}, 1931, 14, 905; Vosek and Jakos, \textit{Bull. Soc. chim.}, 1923, 23, 842). On repetition of this work little difficulty was experienced in isolating some of the 1:6-dinitro-derivative, but no indication of nitration in the 5-position was obtained. This appeared remarkable if conjugative displacements of a type similar to those in the benzenoids series occur in naphthalene derivatives (CII). Polarisation in position 3- seems at least as probable
as that in position 1-, and an even simpler process than that leading to substitution in positions 6- and 8-.

A solution of the difficulty might be sought in the $\pi$-directing character of the acetamido-group, coupled with the deactivating effect of the nitro-group in position 1-.

Many examples have already been given of the introduction of two nitro-groups in $\sigma$-positions to a sulphonamido-group and therefore the nitration of $\mu$-nitrobenzenesulphon-\(\beta\)-naphthalide was investigated. It was found that it could be almost quantitatively converted into $\mu$-nitro-
benzenesulphon-1:6-dinitro-β-naphthalide (CIII), and that this on solution in cold fuming nitric acid gave the 1:6:8-trinitro-derivative (CIV). Moreover p-toluenesulphon-6- (and 8-) nitro-β-naphthalides were easily converted into the 1:5- and 1:8- dinitro derivatives (CV and CVI) respectively, without indication of by-products. Therefore even the benzenesulphonamide- group is unable to direct a group into the 3-position of β-naphthylamine.

This small reactivity of the 3-position is confirmed by some experiments of Groeneveld (Thesis, Leiden 1930). Refinds that β-naphthyl urethane undergoes nitration first to give the 1:6- and 1:8-dinitro- derivatives and then the
1:6:8-trinitro- derivative (CVII). Also N-β-naphthyl-
N'-ethylurea was converted into N-1:6:8-trinitro-β-
naphthyl-N'-nitro-N'-ethylurea (CVIII). These results
are to be contrasted with those of Worringer (Thesis,
Leiden 1931), who finds that N-4-diphenyl-N'-ethylurea
readily gives N-3:5:4'-trinitro-4-diphenyl-N'-nitro-
N'-ethylurea (CIX), whilst 4-diphenyl urethane gives

\[ \text{(CIX)} \]

\[ \text{(CX)} \]

the 3:5:2:4'-tetranitro- derivative (CX).

It appears that substitution experiments may throw
some light on the long debated topic of the constitution
of naphthalene.
IV. THE MIGRATION OF ACYL GROUPS IN o-AMINOPHENOLS.

A. Possible Intermediates formed during the Migration of an Acyl Group in an o-Aminophenol. The Interaction of 2-Benzylideneaminophenol with p-Toluenesulphonyl chloride.

Many examples are known of the migration of an acyl group during the preparation and also the hydrolysis of diacyl-o-aminophenols. Thus Nelson and Rothrock have shown (J. Amer. Chem. Soc., 1929, 51, 2761) that 2-valeramidophenyl benzoate (CXI) on hydrolysis gives 2-benzamidophenol (CXII), whilst Rainford and Lankelma (Ibid., 1925, 47, 1111) have shown that 4-methyl-6-chloro-2-acetamidophenol (CXIII) with α-naphthoyl chloride gives 4-methyl-6-chloro-2-α-naphthamidophenyl acetate (CXIV). Complete failure had attended efforts to find a simple generalisation underlying these changes, and it appeared that further work on the hydrolysis of diacylated-o-aminophenol was unlikely to add materially to our knowledge. It was decided to have a different and easily removable type of group present on the nitrogen atom and for this purpose the benzylidene group

\[
\begin{align*}
\text{CXI} & \quad \text{CXII} \\
\text{CXIII} & \quad \text{CXIV}
\end{align*}
\]
seemed specially suitable.

An attempt was made to prepare suitable acyl derivatives by interaction of 2-benzylideneamidophenol with acid chlorides in pyridine solution, but the only isolable product with acetyl, benzoyl, α-naphthoyl or β-naphthoyl chloride was the corresponding N-acyl-2-aminophenol. When, however, p-toluenesulphonyl chloride was used there was produced a mixture of two isomeric substances. One of these was readily hydrolysed to 2-aminophenyl-p-toluene-sulphonate from which it could be regained by interaction of this amine with benzaldehyde in alcoholic solution; it must therefore possess the constitution (CXV). The other, less soluble, higher melting isomeride on hydrolysis gave 2-p-toluenesulphonamidophenol, which indicates that the p-toluenesulphonyl residue is already present on the nitrogen atom. Kelsey and his co-workers (ibid., 1912, 34, 361; 1913, 35, 282; 1914, 36, 603; 1915, 37, 502; 1922, 44, 2655) have shown that benzylideneanthranilic acids on treatment with acetic anhydride yield dihydrobenzoxazones of the general formula (CXVI). By analogy, the N-p-toluenesulphonyl derivative obtained above is probably 2-p-toluenesulphonyl-1-phenyl-dihydrobenzoxazole (CXVII), in which case it contains an
asymmetric carbon atom. Consequently the corresponding
camphorsulphonyl derivative (CXVIII) should be separable
into diastereoisomers, whilst the \( \text{p-dimethylamino-}
\text{bengylidene} \) analogue (CXIX) should be capable of resolution
by combination with optically active acids. Attempts to
prepare compound (CXVIII) resulted in the production of
viscous gums, whilst compound (CXIX) in contact with acid
underwent addition of water to give (CXX) (compare Dimroth
and Zeppritz, Ber., 1902, 35, 988). Consequently, conclusive
proof of the correctness of the benzosasole structure is
lacking, but it is regarded as more probable than the
possible alternative of imino ammonium salt formation
(CXXI), analogous to that in the anhydride of 2-hydroxy-
phenyltrimethylammonium hydroxide (CXXII) described by
Gries (Ber., 1880, 13, 249). The only compound which could
be isolated from a pyridine solution of molecular quantities
of \( p \)-benzylideneaminophenol and \( p \)-toluenesulphonyl chloride was the \( O \)-\( p \)-toluenesulphonyl derivative. Unfortunately, it was not found possible to prepare \( p \)-benzylideneaminophenol because \( p \)-aminophenol reacted very readily with benzaldehyde to give complex products.

Since these experiments make it almost certain that dihydrobenzoxazines readily arise from \( \beta \)-aminophenols, the possibility at once suggests itself that the migration of acyl during hydrolysis of a diacylated-\( \beta \)-aminophenol involves the intermediate formation of a compound of type (A). Evidence on this point was sought.

![Diagram](image)

(A)

B. The Hydrolysis of Sulphonyl Derivatives of 2-Aminophenol; Indirect Evidence on the Mechanism of Migration of Acyl Radicals.

If the migration of an acyl radical during hydrolysis of a substituted \( \beta \)-aminophenol involves the intermediate production of a compound of type (A), then clearly such migrations should be inhibited if one of the acyl radicals
is replaced by an arylsulphonyl group (B). This was

![Chemical structure](B)

found to be the case. 2-β-Toluenesulphonamidophenyl acetate (CXXII) was distinct from 2-acetamidophenyl-β-toluenesulphonate (CXXXIII) and the first on hydrolysis gave pure 2-β-toluenesulphonamidophenol and the second pure 2-acetamidophenol. This normal hydrolysis (inhibition of migration) was obtained with the corresponding α- and β-naphthoyl derivatives (CXXIV) and, again, 2-acetamidophenyl-β-naphthoylsulphonate (CXXV) was easily hydrolysed to give pure 2-acetamidophenol. More recently Rainford and Grosz (J. Amer. Chem. Soc., 1931, 53, 3420) have provided a large amount of confirmatory evidence on this point. They have studied the benzenesulphonyl, β-naphthalenesulphonyl, 2-chloro-5-nitrobenzenesulphonyl, 3-nitro-4-methylbenzenesulphonyl, 4-bromobenzenesulphonyl and 3:4-dichlororbenzenesulphonyl derivatives of 2-amino-4-methyl-8-bromophenol and summarise their results in the following
concluded that one isomer was obtained and as a result there was a change in the reaction conditions.

C. The Interconversion of Isomeric Diacyl-3-aminophenols. Theoretical aspects of the Alkaline Hydrolysis of these Substances.

The views expressed in the above sections lead to the conclusion that three forms of a diacyl-3-aminophenol, $a$, $b$, $c$, might be capable of isolation.

The statement of Bailey (J. Amer. Chem. Soc., 1920, 42, 3038) that acylation of 3-benzenecarboxylic acid with the sulphonyl group and the other the carbonyl or carboxyl group, isomeric diacyl derivatives will be obtained, depending on the order in which the radicals are introduced. The isomers give normal results on hydrolysis. These statements hold, also, when both radicals contain the sulphonyl group (loc. cit., p. 348).

Contrary to the statement of Ralford (J. Amer. Chem. Soc., 1920, 42, 3038), acylation of 3-benzenecarboxylic acid with the sulphonyl group and the other the carbonyl or carboxyl group, isomeric diacyl derivatives will be obtained, depending on the order in which the radicals are introduced. The isomers give normal results on hydrolysis. These statements hold, also, when both radicals contain the sulphonyl group (loc. cit., p. 348).
acetylation of 2-benzamidophenol was found to give a compound different from that obtained by the benzoxylation of 2-acetamidophenol. Both compounds had ill defined melting points which varied according to method of crystallisation and rate of heating from 133°-140°, but mixtures of the two always gave clear melts below 120°. The liquids obtained on melting were singularly reluctant to crystallise on cooling and these observations suggested that some change was taking place. Both substances were therefore maintained in the molten state for some time and the viscous masses so obtained crystallised from alcohol. Only the original material

![Structure (CXXVI)](image) ![Structure (CXXVII)](image) ![Structure (CXXVIII)](image)

was isolated from 2-acetamidophenyl benzoate but 2-benzamidophenyl acetate (CXXVI) was largely converted into the former substance.

Treatment of 2-acetamidophenol with α-naphthoyl chloride gave a compound different from that obtained by the acetylation of 2-α-naphthamidophenol (contrast, Ralford and Greider, *ibid.*, 1923, 36, 430) and with this pair of substances a different type of behaviour was observed. On maintaining 2-acetamido-α-naphthoate (CXXVIII) above its melting point for an hour it was largely transformed
into 2-α-naphthamidophenyl acetate (CXXVII), but this in turn could be partly converted into 2-acetamido-α-naphthoate (compare Nelson and Davis, ibid., 1926, 42, 1877, for an apparent equilibrium between 2-propionamidophenyl acetate and 2-acetamidophenyl propionate).

2-α-Naphthamidophenyl benzoate (CXXIX) was quite different from 2-benzenamidophenyl-α-naphthoate (CXXXI) (contrast, Raiford and Greider, loc. cit.) and both were recovered unchanged after remaining in the molten condition for one hour. On the other hand both gave 2-α-naphthamidophenol (CXXX) on hydrolysis, which suggests that alkaline conditions are very favourable for isomeric change.

Attempts to correlate migration of acyl with negative character or molecular weight of the group have failed. Certainly, migration is not so much determined by the ortho position of the amino- and hydroxyl- groups as by their arrangement in space. Raiford and Clarke (ibid., 1926, 42, 403) have established that migration of acyl can take place in 8-amin-1-naphthol but it has now been shown that migration is inhibited in normal meta compounds. This is in favour of ring formation as previously suggested (p. 73).
and if it is tentatively granted that the interchange of 2-acetamidophenyl benzoate and 2-benzamidophenyl acetate involves the intermediates (CXXXII, CXXXIII, CXXXIV), the failure to obtain any simple generalisation is readily understood.

\[ \text{(CXXXII)} \quad \text{(CXXXIII)} \quad \text{(CXXXIV)} \]

Formation of the benzoxazoles (CXXXII and CXXXIV) will be partly determined by the positive character of the amine-hydrogen atom and partly by the tendency of the \( \text{\text{a}} \)-carbonyl group to undergo polarisation in the way required, for easy interchange of the isomeric pair the radical of the \( \text{\text{a}} \)-acyl group should be an electron sink, whilst that of the \( \text{\text{a}} \)-acyl group should be an electron source. Clearly the changes will be promoted by alkaline conditions. If (CXXXIII) is the formula of the diacyl compound at the moment of hydrolysis, it appears that this process may involve the following stages: addition of hydroxyl ion, attraction of hydrogen ion to the nitrogen and severance.
Each of the initial processes is favoured by an electron-donating R, so that of the two acyl groups attached to the nitrogen that derived from the acid of lower dissociation constant should sever first. In other words, the acyl group derived from the acid of high dissociation constant should be found attached to the nitrogen. To summarise, if the two acyl groups are of comparable character, ready interchange of the isomeric pair would be anticipated and on hydrolysis the more acidic should be found attached to the nitrogen. On the other hand, if the groups are of very different electrical character, the isomeride in which the electron sink is attached to the oxygen will tend to exist to the exclusion of that in which it is attached to the nitrogen, and consequently on hydrolysis the less acidic group will be found attached to the nitrogen atom. This appears to agree with experimental facts, as the following table compiled from the results of Raiford and Couture (ibid., 1924, 46, 2305) and Raiford and Lankelma (loc. cit.) shows. In the first column are the pairs of radicals introduced into the o-aminophenol, in the second the dissociation constants of the acids corresponding to the acyl radicals and in the third the acyl group attached to the nitrogen atom after hydrolysis with dilute alkali.
<table>
<thead>
<tr>
<th>Radicals R.CO</th>
<th>Diss. const. R.COON</th>
<th>Radical on N after hydrolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-Chlorobenzoyle</td>
<td>9.9</td>
<td>p-Chlorobenzoyle&lt;sup&gt;X&lt;/sup&gt;</td>
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<tr>
<td>p-Nitrobenzoyle</td>
<td>40</td>
<td>p-Chlorobenzoyle&lt;sup&gt;X&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acetyl</td>
<td>1.8</td>
<td>Acetyl&lt;sup&gt;X&lt;/sup&gt;</td>
</tr>
<tr>
<td>p-Nitrobenzoyle</td>
<td>40</td>
<td>p-Chlorobenzoyle&lt;sup&gt;X&lt;/sup&gt;</td>
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<td>7.2</td>
<td>Benzoyle&lt;sup&gt;X&lt;/sup&gt;</td>
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<tr>
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<td>40</td>
<td>p-Chlorobenzoyle&lt;sup&gt;X&lt;/sup&gt;</td>
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<tr>
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<tr>
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</tr>
<tr>
<td>o-Chlorobenzoyle</td>
<td>135</td>
<td>o-Chlorobenzoyle</td>
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<sup>X</sup> Using 4:6-dibromo-2-aminophenol; the other results were obtained with 6-chloro-4-methyl-2-aminophenol.

It will be noticed that in the first five pairs one member contains a nitro group whilst the other contains no electron sink comparable with this. Hydrolysis, therefore, leaves the less acidic group attached to nitrogen. In the second five pairs the groupings are of comparable type (in spite of being derived from acids of widely different dissociation constants in three cases) and con-
Sequentially, hydrolysis results in the production of an H-acylaminophenol corresponding to the stronger acid.

Nuclear substituents would be expected to have a modifying influence on the course of these acyl migrations but up to the present no evidence has been obtained on this point. Rainford and his co-workers have employed the aminophenols (CXXXV) to (CXLIV) without recording any difference in their behaviour. In the present work it was found that 5-nitro-2-acetamidophenol reacted with β-naphthonyl chloride to give a diacyl derivative which on hydrolysis gave 5-nitro-2-β-naphthamidophenol with compounds such as diacylaminophenols the (CXLV) and 3-nitro-2-acetamido-phenol showed an identical difficulties of interpretation are enhanced, from the behaviour (CXLVI).
Recent work has made clear the varied nature of hydrolytic changes. Thus, Tasman (Rec. trav. chim., 1927, 46, 655) studied the opening of the phthalide ring in alkaline solution and found that the order of facilitation by substitution was $\text{NO}_2 > \text{CN} > \text{I} > \text{Br} > \text{Cl} > \text{NHAc} > \text{NH}_2$. Kindler, on the other hand, from a study of the alkaline hydrolysis of ethyl benzoates obtained the sequence $\text{NH}_2 > \text{OMe} > \text{Me} > \text{Cl} > \text{Br} > \text{I} > \text{NO}_2$ (Annalen, 1926, 450, 1). In the first case it is necessary to assume that the velocity determining factor is electrostriction of the hydroxide ion at the carbonyl carbon atom (a), whilst in the second it is the tendency towards polarisation of the carbonyl group (b). With compounds such as diacylated-$a$-aminophenols the difficulties of interpretation are enhanced. First the
two groups are differently affected by conditions of acidity and alkalinity. An acyloxy group is very readily hydrolysed by alkali but an acylamido group much less so. With acid conditions affairs are reversed. Acylenilides are open to attack at two points (c and d) but owing to the higher electron affinity of the oxygen atom compared with nitrogen neither of these mechanisms can occur with alkaline under the present time. Production with the aid of electronic principles in a manner unconnected process, there can be little doubt that the intervention of the same case in phenylacetates. Acid hydrolysis of a substance such as 2-acetimidophenyl-α-naphthoate (CXLVII) results in the loss of the acetyl group, and, although owing to the added complication of acyl migration, it is not possible to compare this satisfactorily with the alkaline hydrolysis, this comparison can be made with the analogous sulphobenzoate (CXLVIII). Under alkaline conditions
the arylsulphonate group is split off, under acid it is the
acetamido-group which undergoes severance. In view of
the possible reactions involved and of the many ways in
which a single reaction can be viewed it is little to be
wondered that a completely adequate explanation of the
migration of acyl radicals in p-aminophenols is lacking.

Although, at the present time, prediction with the
aid of electronic principles is a somewhat unsafe process,
there can be little doubt that the interpretation of
chemical reactions in terms of electrons marks a big
step forward. No previous theory has possessed a flex-
ibility at all commensurate with the variety of chemical
reaction. A too simple and too rigid theory is soon
broken and it is far too early for the electronic theory
of organic reactions to adopt a system of cast-iron rules.
It is in process of development and a great systemisation
of organic chemical knowledge will be the inevitable
outcome.
V. EXPERIMENTAL.

The experimental work on which this thesis is based is contained in the following papers:

Investigations in the Diphenyl Series.

Part VIII. Derivatives of 2-Amino- and 4-Aminodiphenyl, J., 1930, 2770.

Part IX. Further Experiments with Sulphonamides, J., 1930, 1071.

Part X. The Eromination of 4-\(p\)-Toluenosulphonyl; diphenyl, J., 1931, 2338.

The Migration of Acyl Groups in \(\sigma\)-Aminophenols.


Part II. J., 1931, 2962.

The Nitration of \(\beta\)-Naphthylanine, J., 1930, 2764.

The Interaction of Nitroamines with Sulphonyl Chlorides, J., 1930, 2767.

The Interaction of Sulphonates and Sulphonamides with Piperidine, J., 1931, 609.

The Interaction of Nitroaminophenols with Sulphonyl Chlorides, J., 1931, 2543.
APPENDIX.

1. Four papers dealing with the preparation and substitution on diphenyl derivatives.

Investigations in the Diphenyl Series.

Part I. Migration Reactions. J.C.S., 1933, 1239
Part II. Substitution Reactions. ibid., 2705
Part III. Derivatives of 4-Hydroxydiphenyl. ibid., 3044
Part IV. Derivatives of 4-Amino- and 4-Hydroxydiphenyl.

(with Dr. J. Kenyon and Dr. P. H. Robinson)


The Space Formula of Diphenyl. J.Soc.Chem.Ind., 1926, 45, 564
(with Dr. J. Kenyon)

and experiments devised to test this theory.

Investigations in the Diphenyl Series.

Part VI. The Configuration of Diphenyl Derivatives. J.C.S., 1927, 1695
Part VII. The Relative Stability of Optically Active Diphenic Acids. ibid., 2234

(with assistance from Dr. P. H. Robinson)

3. Various notes dealing with topics out of the above work.

a. 3,4,7-Trinitrofluorobenzene. J.C.S., 1920, 1906
b. Preparation of Diethylaminoethanol Ethers of Diphenyl-2-carboxylic Acid and Derivatives. ibid., 3247
c. The Hydrolysis of Acetyl-o-benzylideneamino-phenol. J.C.S., 1933, 1393
d. Acetyl-o-phenylenediamine and Acetyl-1:2:3-benzenitrile. ibid., 954

(c. and d. published with Dr. J. Kenyon)

4. Dy-products of the Catterson Aldol Reaction.
(with Dr. T. A. Henry) J.C.S., 1928, 2215
SOME PREVIOUS PUBLICATIONS

(COMPLETE LIST: THESIS p.86)
The Hydrolysis of Acetyl-o-benzylideneaminophenol. By Frank Bell and Joseph Kenyon.

o-Benzylideneaminophenol (12 g.) was dissolved in acetic anhydride (12 c.c.), and the excess of the latter removed by distillation. The residual acetyl-o-benzylideneaminophenol separated from benzene-light petroleum as a white, microcrystalline powder, m. p. 93-96° (Found: C, 75-2; H, 5-5; N, 6-2. \( \text{C}_{12}\text{H}_{19}\text{O}_{2}\text{N} \) requires C, 75-3; H, 5-4; N, 5-9%). It suffered loss of both acetic acid and benzaldehyde on being warmed with dilute acid; but when it was boiled with water, benzaldehyde alone was evolved and \( N \)-acetyl-o-aminophenol, m. p. 202°, was obtained—an interesting illustration of the ease with which an acyl group migrates from oxygen to nitrogen.—Battersea Polytechnic, S.W.11.

[Received, February 23rd, 1926.]
INVESTIGATIONS IN THE DIPHENYL SERIES. PART I. MIGRATION REACTIONS.

BY
FRANK BELL,
JOSEPH KENYON,
AND
PERCY HARRY ROBINSON.

Reprinted from the Journal of the Chemical Society,
June, 1928.

By Frank Bell, Joseph Kenyon, and Percy Harry Robinson.

In view of the appearance of a paper by Vorländer (Ber., 1925, 58, 1913), in which 4-hydroxylaminodiphenyl is described, and of another by Scarborough and Waters on the chlorination and bromination of 4-aminodiphenyl (this vol., p. 557), it has been thought advisable to communicate some of the results already obtained by the authors in the same field.

The literature shows that numerous attempts have been made to elucidate the spatial relations of the two nuclei in diphenyl compounds, and there is considerable evidence in favour of the view of the closeness of the 4, 4'-positions in some derivatives. If the 4, 4'-positions in diphenyl are close together, there is a reasonable probability that those types of reactions which involve the para-migration of certain groups in simple benzene compounds might also be exhibited, under appropriate conditions, by certain derivatives of diphenyl, the migrating group passing from position 4 to position 4'. Migration reactions in the diphenyl series analogous to the following have been looked for, but have not been found:

\[
\begin{align*}
\text{(I)} & \xrightarrow{\text{H}_2\text{SO}_4, (\text{HCl})} \text{(II)} \xrightarrow{\text{OH(Cl)}} \text{(III)} \xrightarrow{\text{Cl}} \\
\text{H-N-OH} & \quad \text{NH}_2 \quad \text{Me-N-NO} \quad \text{Me-N-H} \quad \text{Ac-N-Cl} \quad \text{Ac-N-H}
\end{align*}
\]

In the corresponding diphenyl compounds decomposition occurs in case (II), whilst in cases (I) and (III) migration does take place, not, however, to the 4'-position but most probably to the adjacent 3-position.
There is an extensive literature on the preparation of diphenyl by the thermal decomposition of benzene, the most recent account being that of Lowe and James (J. Amer. Chem. Soc., 1923, 45, 2666), who, however, used an apparatus which is outside the resources of an ordinary laboratory. A simpler device is described in the experimental part; chlorobenzene, under similar treatment in the apparatus described, underwent extensive carbonisation, and no 4:4'-dichlorodiphenyl was obtained. The nitration of diphenyl was carried out by a modification of the methods due to Hübner (Annalen, 1881, 209, 339) and Van Hove (Bull. Soc. chim. Belg., 1923, 32, 52).

By the reduction of 4-nitrodiphenyl with aluminium amalgam and moist ether, there is obtained a complex mixture of 4-azo-diphenyl, 4-azoxydiphenyl, 4-aminodiphenyl, and 4-hydroxylaminodiphenyl, together with unchanged nitrodiphenyl. By crystallisation of this mixture from benzene, a 30% yield of 4-hydroxylaminodiphenyl is obtained. Vorländer (loc. cit.), who gives no experimental details whatever, states that the compound was prepared "nach bekanntem Verfahren" and melted at 132—134°.

The insolubility of 4-hydroxylaminodiphenyl militates seriously against migration experiments under favourable conditions. Sulphuric acid of various concentrations was employed at first, but as the minimum concentration of this acid necessary for solution of the hydroxylamino-compound at the ordinary temperature is above 50%, deep-seated decomposition occurs, and no crystalline material other than 4-azoxydiphenyl can be isolated from the products of the reaction. By the action of 10% sulphuric acid at 100°, a very small proportion of a new compound was formed. This substance has not yet been thoroughly investigated, but it is believed to be 4-diphenyl(4-amino-3-diphenylyl)amine.

\[ C_6H_4Ph\cdot NH\cdot C_6H_4Ph \cdot NH_2 \]

When hydrogen chloride is passed into a dry ethereal solution of 4-hydroxylaminodiphenyl, or when this compound is left for some time in contact with strong hydrochloric acid, 4-hydroxylaminodiphenyl hydrochloride is formed, which, on heating, decomposes to give principally 4-azoxydiphenyl.

An alcoholic solution of hydrogen chloride converts 4-hydroxylaminodiphenyl almost completely into 4-azoxydiphenyl, but at the same time there is produced a very small proportion of a compound which melts at 69° and contains chlorine.

Acetyl chloride reacts readily with 4-hydroxylaminodiphenyl to yield a diacetyl derivative believed to be diacetyl-4-hydroxylaminodiphenyl. This compound can be prepared in almost theoretical yield by dissolving 4-hydroxylaminodiphenyl in warm acetic
anhydride, and when warmed with strong hydrochloric acid it undergoes hydrolysis and simultaneous conversion into a chloro-base (m. p. 69°), the hydrochloride of which hydrolyses very readily, and in consequence has not been prepared in a sufficiently pure state for analysis. The chloro-base yields a monoaetyl derivative of m. p. 146° which is identical with that obtained by the action of acetic acid on diphenyl-4-acetylchloroamine (vide below), so that the course of this reaction is probably expressed by the following scheme:

\[
\begin{align*}
\text{Ph} & \underset{\text{N} \underset{\text{OH}}{\text{H}}} \rightarrow \text{Ph} \underset{\text{N} \underset{\text{Ac}}{\text{OAc}}} \rightarrow \\
\quad & \left[ \text{Ph} \underset{\text{N} \underset{\text{Cl}}{\text{H}}} \rightarrow \text{Ph} \underset{\text{NH}_2}{\text{Cl}} \right]
\end{align*}
\]

4-Methylaminodiphenyl was prepared by treating 4-acetylamino-diphenyl with sodium and methyl iodide with subsequent elimination of the acetyl group, and was purified by conversion into its nitroso-derivative.

4-Nitrosomethylaminodiphenyl, both alone and when suspended in ether (in which it is only sparingly soluble), was mixed with an alcoholic solution of hydrogen chloride, when slow reaction ensued with evolution of gas. No nitroso-4-methylaminodiphenyl was found in the reaction mixture, which consisted mainly of 4-methylaminodiphenyl together with a little of the unchanged substance.

4-Diazoaminodiphenyl is a by-product in the preparation of 4-nitrosomethylaminodiphenyl from the crude secondary amine, which probably contains a little 4-aminodiphenyl.

Diphenyl-4-acetylchloroamine. It is clear from the literature that the preparation of aryl acyl chloroamines is susceptible to slight variations in experimental conditions (compare Armstrong, J., 1900, 77, 1047; Chattaway and Orton, J., 1901, 79, 275).

A similar susceptibility has been found in the case of 4-acetylaminodiphenyl, which, however, reacts rapidly and quantitatively at 70–80°. One sample yielded 67% of diphenyl-4-acetylchloroamine after only 10 minutes' heating. Further, the state of subdivision is very important, and may account for the difficulties met with by Armstrong and his students in the case of acetanilide (loc. cit.). When the 4-acetylaminodiphenyl was powdered mechanically, the yields were poor.

When diphenyl-4-acetylchloroamine is warmed with glacial acetic acid it is transformed into a chloro-4-acetylaminodiphenyl believed to be 3-chloro-4-acetylaminodiphenyl (compare above).
No trace of 4'-chloro-4-acetylaminodiphenyl was detected, although its presence was specially sought.

3-Chloro-4-acetylaminodiphenyl results directly if the sodium hypochlorite solution used is above normal in strength. A quantitative yield of 3-chloro-4-acetylaminodiphenyl results also from the direct chlorination of 4-acetylaminodiphenyl in acetic acid. Again no trace of 4'-chloro-4-acetylaminodiphenyl was detected. This is in marked contrast with the bromination of 4-acetylaminodiphenyl in acetic acid, which yields 30% of the theoretical quantity of 4'-bromo-4-acetylaminodiphenyl together with 65% of a bromo-base (m. p. 65°) not yet fully examined.

**Experimental.**

**Diphenyl.**—The heating coil, which consists of about 1 yard of 32 gauge nichrome wire, is loosely threaded through a strip of mica 5" x 1½" and suspended in the neck and body of a 5-litre flask fitted with an upright condenser. Benzene (1½ litres) is placed in the flask and boiled. When benzene is dripping freely from the condenser, the current is switched on, and by means of a sliding resistance is gradually raised to the value (about 3 amps.) at which the flask begins to fill with fumes. Little attention is required, and at the end of about 30 hours the liquid is transferred to a flask and distilled. Benzene comes over first, and then the temperature rises rapidly. The fraction b. p. 245—260° is collected and crystallised from alcohol. The yield of pure diphenyl averages 9 g. per hour.

**Nitration of Diphenyl.**—To a solution of diphenyl in acetic acid (2 parts) at 70—90°, nitric acid (d 1·51; 2½—3 mols.) is added in small quantities. The solution darkens, and when about one-third of the acid has been added a visible and steady reaction sets in. The remaining acid is added more carefully, the experiment taking 1½ to 1½ hours from the first addition of acid. After cooling, the crystalline crop of 4-nitrodiphenyl is filtered off, and the filtrate diluted with water. The oily layer thus precipitated is separated roughly from the aqueous layer and filtered from a further amount of 4-nitrodiphenyl. The oil is heated in a current of steam to free it from residual acid and unchanged diphenyl, and then distilled in a vacuum. Moisture and a trace of diphenyl come over first, and the main bulk distils at 188—193°/20 mm. The distillate is dissolved in alcohol at 40° and the crystals of 4-nitrodiphenyl which separate on cooling are filtered off. After evaporation of the alcohol, 2-nitrodiphenyl crystallises in characteristic large plates or prisms. 100 G. of diphenyl give 60—70 g. of 4-nitrodiphenyl, m. p. 114°, and 35—39 g. of 2-nitrodiphenyl, m. p. 35—37°.
4-Hydroxylaminodiphenyl.—A solution of 4-nitrodiphenyl (50 g.) in ether (1300 c.c., previously distilled from sodium hydroxide) is cooled in a freezing mixture and to it is added aluminium amalgam (10 g.), in very thin sheets, at such a rate that the reaction does not become too vigorous; the reaction vessel is shaken from time to time. Very little hydrogen is evolved if the mixture is kept cold, and the amalgam takes about 2 hours for complete reaction. The mixture is then filtered, the bulky aluminium hydroxide washed several times with dry ether, and the filtrate and washings are evaporated to dryness. The residue is dissolved in the minimum amount (about 250 c.c.) of boiling benzene, and the yellow solution allowed to cool. 4-Hydroxylaminodiphenyl separates in almost colourless, glistening leaflets which appear to fill the whole bulk of the liquid. These are filtered off and dried (yield, 10—14 g.). The compound melts at 152—154° to a red liquid which sets, and in turn melts at 188—190° (Found: C, 77.8; H, 6.0; N, 7.7. C₁₂H₉ON requires C, 77.8; H, 6.0; N, 7.6%).

The formation of a deep damson colour with concentrated sulphuric acid is a sensitive reaction for this compound.

4-Hydroxylaminodiphenyl (2 g.) was maintained in the molten state for 30 minutes, and the cooled residue (1.86 g.) dissolved in boiling benzene. The solution on cooling deposited crystals of 4-azodiphenyl, and after evaporation of the benzene, the residue consisted of a mixture of 4-azoxydiphenyl (m. p. 211—212°) and 4-aminodiphenyl (m. p. 52°).

On treatment of an ethereal solution of 4-hydroxylaminodiphenyl with hydrogen chloride or by leaving a suspension in concentrated hydrochloric acid for some time, the hydrochloride is obtained as a white powder (Found: HCl, 16.6. C₁₂H₁₁ON.HCl requires HCl, 16.5%). The principal product obtained on heating the hydrochloride is 4-azoxydiphenyl.

Action of 10% sulphuric acid. 4-Hydroxylaminodiphenyl (5 g.) is triturated with sulphuric acid (600 c.c. of 10%), and the mixture heated on a steam-bath until the whole assumes a deep chocolate colour. It is then filtered hot, and the insoluble residue extracted with 2 litres of boiling water. The filtrates deposit amine sulphates, which are filtered off and suspended in sodium carbonate solution. The mixture is boiled and, after addition of some alcohol, filtered from a trace of impurity. On cooling, the liquid fills with fine, silky crystals, which are filtered off and crystallised from aqueous alcohol; m. p. 156°. It is difficult to make certain that the product is quite free from 4-aminodiphenyl, since the sulphate of this compound must be present in the filtrate. As the compound is insoluble in sodium hydroxide, it is tentatively suggested that it
may be produced by the o-semidine change of an intermediate reactive 4-hydrazodiphenyl (Found: C, 85.0; H, 6.1. \( \text{C}_{24}\text{H}_{20}\text{N}_2 \) requires C, 85.6; H, 6.0%).

By the action of an alcoholic solution of hydrogen chloride on the hydroxylamine there was obtained a small quantity of a chloro-base, m. p. 69° (see below).

**Diacetyl-4-hydroxylaminodiphenyl** was prepared by dissolving 4-hydroxylaminodiphenyl in acetic anhydride and pouring the solution, filtered from a little 4-azoxydiphenyl, into excess of water. The well-washed precipitate crystallised from alcohol in clusters of short, thick needles, m. p. 119° (Found: C, 71.2; H, 5.8; N, 5.2. \( \text{C}_{16}\text{H}_{15}\text{O}_3\text{N} \) requires C, 71.4; H, 5.6; N, 5.2%).

This compound gives a deep damson colour with concentrated sulphuric acid. This diacetyl derivative (24 g.) was dissolved in 90 c.c. of concentrated hydrochloric acid by warming on a water-bath, 500 c.c. of water were added, and the whole was filtered while boiling. The hydrochloride which separated on cooling was difficult to purify by crystallisation, as it was so readily hydrolysed. It was decomposed by sodium carbonate, and the oil obtained was filtered off after solidification. By repeated crystallisation from aqueous alcohol, it was obtained as a constant-melting chloro-base, m. p. 69° (Found: N, 6.9. \( \text{C}_{12}\text{H}_{10}\text{NC}_{1} \) requires N, 6.9%).

It gives an acetyl derivative which crystallises from alcohol in glistening needles, m. p. 146° (Found: C, 68.4; H, 5.0; N, 6.0. \( \text{C}_{12}\text{H}_{10}\text{ON}_{2} \) requires C, 68.4; H, 4.9; N, 5.7%).

**4-Aminodiphenyl.**—This compound is formed during the preparation of 4-hydroxylaminodiphenyl, but its separation from the accompanying azoxy-, azo-, and nitro-compounds is difficult. The benzene filtrate from 4-hydroxylaminodiphenyl was therefore evaporated to dryness, the residue finely powdered and suspended in ether, aluminium amalgam added until the ethereal solution became colourless, the filtered solution evaporated to dryness, and the residue dissolved in boiling alcohol; on cooling, 4-hydrazodiphenyl separated in colourless, glistening needles, m. p. 167—169°. This was filtered off, and by dilution of the mother-liquor 4-aminodiphenyl (m. p. 52—53°) was obtained.

4-Nitrodiphenyl is converted directly into 4-aminodiphenyl by the same process when excess of aluminium amalgam is added. This appears to be the cleanest method of preparation, and the yield is good.

**4-Hydrazodiphenyl** was heated with hydrochloric acid and sulphuric acid of various strengths, but only 4-azodiphenyl and 4-aminodiphenyl could be isolated from the products, thus confirming the observation of Rassow (*J. pr. Chem.*, 1901, **63**, 449).
4-Azodydiphenyl was isolated from the product obtained by partial reduction of 4-nitrodiphenyl, by means of its ready solubility in benzene and insolubility in alcohol. It melts at 212° whether prepared by this method or by Zimmermann's (Ber., 1880, 13, 1960), who, however, gives the m. p. as 206° (Found: C, 81·8; H, 5·2; N, 8·1. Calc. : C, 82·3; H, 5·1; N, 8·0%).

4-Azodiophenyl (m. p. 249°) was obtained by distilling a mixture of 4-azodydiphenyl and iron filings under reduced pressure.

4-Methylaminodiphenyl.— A mixture of 4-acetylaminodiphenyl (31·5 g., m. p. 171°), dry xylene (200 c.c.), and sodium (5 g.) was heated at 130° for 2—3 hours and cooled, methyl iodide (25 g.) was added, and the reaction completed by warming for a short period. The xylene was distilled off and the residue heated under reflux with alcoholic potash for 15 hours. Alcohol and xylene were removed in a current of steam, and the residue was extracted with ether. The ethereal extract was dried with sodium sulphate and after evaporation of the ether the residue distilled almost wholly at 198—203°/20 mm., the distillate setting to a semi-solid mass. This was best purified by conversion into the nitroso-derivative, and subsequent decomposition of this by boiling with concentrated hydrochloric acid according to the following procedure. The semi-solid mass was dissolved in glacial acetic acid, and the calculated amount of sodium nitrite added. The precipitate was filtered off, dried on porous plate, and boiled with alcohol, which extracted the nitrosoamine from an insoluble yellow product (A). On cooling the filtrate, the nitrosoamine crystallised, and was obtained as an almost colourless, microcrystalline powder, m. p. 116°, by recrystallisation from alcohol (Found : C, 73·6; H, 5·7. C_{12}H_{14}ON_{2} requires C, 73·6; H, 5·7%).

The nitrosoamine gave brilliant colours at the various stages of the Liebermann reaction. To obtain the secondary base, the nitroso-compound was boiled with concentrated hydrochloric acid. The hydrochloride thus obtained crystallised from dilute hydrochloric acid as a white powder (Found : HCl, 16·6. C_{12}H_{14}N.HCl requires HCl, 16-6%). On decomposition with sodium carbonate, 4-methylaminodiphenyl was obtained as an oil which rapidly solidified and had m. p. 38°. It was readily soluble in almost all organic solvents, gave an acetyl derivative, m. p. 118—119°, which was very soluble in alcohol and separated from aqueous alcohol in a gelatinous condition.

This base is much better characterised as its p-toluene sulphonyle derivative, which was readily prepared by the action of p-toluene-sulphonyl chloride in pyridine solution, and crystallised from alcohol in lustrous, white needles, m. p. 128° (Found : N, 4·2. C_{20}H_{14}O_{2}NS requires N, 4·2%).
Its constitution is easily checked, since it may also be prepared by shaking the p-toluenesulphonate of 4-aminodiphenyl with methyl sulphate and sodium hydroxide. The p-toluenesulphonate of 4-aminodiphenyl, prepared by the usual method, crystallises from alcohol in colourless needles, m. p. 160° (Found: N, 4-5. C_{13}H_{17}O_{2}NS requires N, 4-3%).

The yellow product (A) obtained in the preparation of 4-nitrosomethylaminodiphenyl crystallised readily from benzene in splendid, lustrous, yellow plates which decomposed violently at 187°. On boiling with dilute sulphuric acid, there was vigorous evolution of nitrogen. When this had ceased, water was added and the whole filtered boiling hot. 4-Methylaminodiphenyl sulphate crystallised from the filtrate; the residue, after solution in sodium hydroxide and precipitation, melted at 164° and was identical with 4-hydroxydiphenyl prepared directly from 4-aminodiphenyl. The compound (A) must therefore be 4-diazoethylaminodiphenyl (Found: C, 81-8; H, 5-7; N, 11-1. C_{23}H_{21}N_{2} requires C, 82-6; H, 5-8; N, 11-6%).

4-Diazoaminodiphenyl is formed by treating an acetic acid solution of 4-aminodiphenyl with sodium nitrite and forms yellow plates, m. p. 147° (Ber., 1925, 58, 1913).

4-Nitrosomethylaminodiphenyl both alone and when suspended in ether was treated with an alcoholic solution of hydrogen chloride. After 24 hours, the white solid was filtered off and decomposed with sodium hydroxide. The solid thus obtained was dissolved in alcohol, and on cooling, a small crop, m. p. 96°, was obtained. Although crystallisation does not alter this melting point, the product appears to be a mixture of unchanged 4-nitrosomethylaminodiphenyl and 4-methylaminodiphenyl, for, on treatment with acetic anhydride and subsequent crystallisation from alcohol, pure 4-nitrosomethylaminodiphenyl was obtained. After separation of the crop of m. p. 96°, the mother-liquor began to deposit an oil which, after purification, yielded 4-methylaminodiphenyl (m. p. 38°).

_Diphenyl-4-acetylchloroamine._—4-Acetylaminodiphenyl (31-5 g.) was dissolved in the minimum quantity of boiling alcohol, and the solution stirred rapidly into 3 litres of cold water, a paste of the consistency of whipped cream resulting. This paste was filtered off with the aid of the pump but not pressed out; it was washed with water to remove all alcohol, and then suspended in water (600 c.c.) containing potassium bicharbonate (60 g.). A considerable excess of sodium hypochlorite solution was added [equivalent to 11-6 g. of hypochlorous acid instead of 7-9 g. (calc.)], the strength of the whole mixture being 0-16N in respect of hypochlorous acid.
The mixture was maintained at about 70° with constant shaking for \(\frac{1}{2}\) hour, and then allowed to cool. The solid was filtered off and a sample extracted with chloroform. The solvent was removed by a current of air and finally by evacuation. A weighed quantity of this product was dissolved in chloroform and shaken with acetic acid and potassium iodide solution and the liberated iodine was estimated (Found: Cl, 13.9. \(\text{C}_4\text{H}_7\text{ONCl}\) requires Cl, 14.4%).

This compound crystallises from chloroform–light petroleum in square plates melting at 127° if heated rapidly, and at 160° undergoes a vigorous change, presumably to 3-chloro-4-acetylamidodiphenyl.

Transformation of Diphenyl-4-acetylchloroamine.—The main bulk of this substance was filtered off, well washed with water, dissolved in glacial acetic acid, and the solution kept at 80° for 10 minutes and cooled; the vessel then became filled with masses of colourless needles, m. p. 145°, and 147° after recrystallisation from aqueous alcohol. The final mother-liquors contained a little unchanged 4-acetylamidodiphenyl and a trace of a brown oil.

Fractional crystallisation of this substance and of the residues in the acetic acid mother-liquors failed to detect the presence of any trace of 4'-chloro-4-acetylamidodiphenyl. The compound, hydrolysed by boiling 50% sulphuric acid, gave a base which, after crystallisation from aqueous methyl alcohol, melted at 69°. 4'-Chloro-4-aminodiphenyl has m. p. 134°, so that it is highly probable that the above compound is 3-chloro-4-aminodiphenyl, and this view of its constitution is supported by its preparation by direct chlorination.

Chlorine (6.65 g.) (5% excess) was slowly bubbled through a solution of 4-acetylamidodiphenyl (21 g.) in glacial acetic acid (300 c.c.) in a tall vessel. A copious precipitate began to form at once, and after completion of the experiment 50 c.c. of water were added and the pale yellow product was filtered off. It melted at 144° and after recrystallisation from alcohol was obtained in fine, colourless needles, m. p. 146°. This substance on hydrolysis gave a base, m. p. 69°, identical with that obtained above. Exhaustive fractional crystallisation showed that the chlorination was practically quantitative, only 4% of unchanged 4-acetylamidodiphenyl being recovered and no trace of 4'-chloro-4-acetylamidodiphenyl was detected.

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BUNGAY, SUFFOLK.

By Frank Bell and Percy Harry Robinson.

The normal and the acid quinine salt of 4-nitrodiphenic acid can be crystallised without showing any sign of resolution. 6-Nitrodiphenic acid is readily resolvable, and the optical activity is apparently of a normal degree of permanence. This striking difference in behaviour of two such similarly constituted acids can be accounted for only by the assumption that the presence of the nitro-group in position 6 is essential to prevent the interchange of the enantiomorphs (I) and (II). The fact that it has so far proved impossible to prepare tetranitrofluorenone (III) or tetra-
nitrophenanthraquinone (IV), whilst diphenic acid and benzil readily yield tetranitro-derivatives (V and VI), could be anticipated

\[
\text{(III.) } \begin{array}{c}
\text{NO}_2 \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{CO} \\
\end{array} \\
\begin{array}{c}
\text{NO}_2 \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{CO} \\
\end{array}
\]

from this "obstacle" theory. Moreover, it would be expected that diphenic acids unsubstituted in the 6:6'-positions should

\[
\text{(V.) } \begin{array}{c}
\text{NO}_2 \\
\text{CO}_2\text{H} \\
\text{NO}_2 \\
\text{NO}_2 \\
\end{array} \\
\begin{array}{c}
\text{NO}_2 \\
\text{CO}_2\text{H} \\
\text{NO}_2 \\
\text{NO}_2 \\
\end{array}
\]

form anhydrides, in spite of many statements to the contrary (e.g., Adkins, Steinbring, and Pitcher, J. Amer. Chem. Soc., 1924, 46, 1918; Underwood and Kochmann, ibid., p. 2069). It is now found that 4-nitro- and 4:4'-dinitro-diphenic acids yield anhydrides under suitable conditions; an attempt to prepare the anhydride of 6-nitrodiphenic acid was, however, unsuccessful. According to the present hypothesis, a diphenyl derivative with two sufficiently large groups in the 2- and 2'-positions, that is, groups which, owing to size or electrical character, are unable to pass the 6'- and 6-positions, respectively, should be capable of resolution

\[
\text{(VII.) } \begin{array}{c}
\text{R} \\
\text{R'} \\
\text{R} \\
\text{R'} \\
\text{R} \\
\text{R'} \\
\end{array} \\
\begin{array}{c}
\text{R} \\
\text{R'} \\
\text{R} \\
\text{R'} \\
\text{R} \\
\text{R'} \\
\end{array}
\]

(VII and VIII). Suitable derivatives for testing this point have not yet been obtained. The dicamphorsulphonyl derivative of 2:2'-diaminodiphenyl was a viscous mass, and the camphor(and bromocamphor)-sulphonates of several 2:2'-derivatives of tetramethylbenzidine proved unsuitable for crystallisation. Menthyl hydrogen and di-\(\delta\)-octyl diphenates were not obtained in a solid condition, but dimethyl and \(\delta\)-octyl hydrogen diphenates were crystallised from several solvents without showing any indication of resolution. The resolvability of such compounds is therefore still an open question.

**Experimental.**

*Optically Active 6-Nitrodiphenic Acid.*—Morphine hydrate (7.7 g.) was added to a boiling solution of 6-nitrodiphenic acid (7.2 g.) in alcohol (500 c.c.). The precipitated salt (7.8 g.; m. p. 224°) (Found: C, 63.6, 63.7; H, 5.4, 5.3%). \([\alpha]_{D}^{641} -87.5^\circ\) in pyridine,
c = 4.99; l = 2.0) was extracted repeatedly with boiling alcohol, and the product ([\alpha]_D + 91.5° in pyridine; c = 4.81; l = 1.0) was dissolved in a large bulk of boiling water and decomposed with a slight excess of hydrochloric acid. The solution was extracted with ether, and the extract was repeatedly washed with dilute hydrochloric acid, dried with sodium sulphate, and then evaporated to dryness. The residue was further purified by reprecipitation from solution in ammonia by hydrochloric acid. The \( \delta + dl \)-nitrophenic acid melted indefinitely at 240—245°, and had 
\[ [\alpha]_{D} + 56.2^\circ \text{ (c = 5.91; l = 1.0) } \]
in absolute ethyl alcohol.

The alcoholic mother-liquor containing the more soluble salt 
\[ [\alpha]_{D} = 84.6^\circ \text{ in pyridine solution; c = 5.0; } l = 1.0 \]
was concentrated and poured into dilute hydrochloric acid, and the precipitated \( l + dl \)-acid recovered as described above. The \( l + dl \)-acid melted at 239—245° and had 
\[ [\alpha]_{D} = 66.7^\circ \text{ in ethyl alcohol (c = 5.07; } l = 1.0 \). Quinine hydrogen 6-nitrophenate was equally suitable and after one crystallisation gave on decomposition the \( \delta + dl \)-acid with 
\[ [\alpha]_{D} = 62^\circ \] .

The alcoholic mother-liquor containing the more soluble salt 
\[ [\alpha]_{D} = 57.6^\circ \text{ in pyridine solution; c = 5.0; } l = 1.0 \]
was concentrated and poured into dilute hydrochloric acid, and the precipitated \( l + dl \)-acid recovered as described above. The \( l + dl \)-acid melted at 239—245° and had 
\[ [\alpha]_{D} = 66.7^\circ \text{ in ethyl alcohol (c = 5.07; } l = 1.0 \). The acid 
\[[\alpha]_{D} = 66.7^\circ \text{ was dissolved in boiling acetic acid and allowed to crystallise slowly. The acid which crystallised had } [\alpha]_{D} = 57.6^\circ \text{, whilst the mother-liquor, on evaporation to dryness, gave an acid with } [\alpha]_{D} = 60.3^\circ \text{. Solutions of four different samples of acid having } [\alpha]_{D} = 1.12^\circ, -2.90^\circ, -3.38^\circ, \text{ and } +3.32^\circ \text{ respectively in absolute ethyl alcohol were left in corked flasks at laboratory temperature for 6 months; they then had the values } [\alpha]_{D} = 1.11^\circ, -2.92^\circ, -3.24^\circ, \text{ and } +3.24^\circ, \text{ respectively.}

**Dichloride of 4-Nitrophenic Acid.**—The acid was added slowly to warm thionyl chloride, and the resultant solution evaporated to dryness in a vacuum. The residual solid crystallised from benzene-light petroleum as a pale yellow powder, m. p. 90—92° (Found: C, 52.6; H, 2.1. \( C_{14}H_{10}Cl_2 \) requires C, 51.8; H, 2.8%).

**4-Nitrophenic Anhydride.**—Thionyl chloride was added drop by drop to 4-nitrophenic acid, and the resultant solution evaporated to dryness in a vacuum. The residual solid crystallised from acetic anhydride in small needles, m. p. 205—207° (Found: C, 62.8; H, 2.4. \( C_{14}H_{10}Cl_2 \) requires C, 62.4; H, 2.6%).

**4:4’-Dinitrophenic Anhydride.**—4:4’-Dinitrophenic acid (1.9 g.) and its acid chloride (2.1 g.) were heated under reflux with acetic anhydride for several hours. On cooling, the liquid filled with small prisms, which sintered at 125° and melted at 232—234° (Found: C, 51.9; H, 3.0; loss on drying to constant weight at 130°; 24.3. \( C_{14}H_{10}O_7N_2\) requires C, 51.9; H, 2.9; loss, 24.5%). After crystallisation from benzene, the anhydride formed.
a powder, m. p. 233—235° (Found: C, 54-1; H, 2-1. C_{14}H_{6}O_{7}N_{2} requires C, 53-5; H, 1-9%).

**Dichloride of 6-Nitrodiphenic Acid** (compare 4-nitrodiphenic acid).—This was a pale yellow powder, m. p. 87° (Found: C, 51-8; H, 2-2. C_{14}H_{7}O_{4}NCl_{2} requires C, 51-8; H, 2-2%). Attempts to prepare the anhydride of this acid resulted in viscous products only.

2:2'-Bibenzamidotetramethylbenzidine, prepared by interaction of the components in pyridine, separated from benzene as a crystalline powder, m. p. 201° (Found: C, 75-9; H, 6-1. C_{30}H_{30}O_{2}N_{4} requires C, 75-3; H, 6-3%), and 2 : 2'-di-p-toluenesulphonylamidotetramethylbenzidine, similarly prepared, crystallised from alcohol in leaflets, m. p. 203° (Found: C, 62-8; H, 5-8. C_{30}H_{34}O_{4}N_{4}S_{2} requires C, 62-3; H, 5-9%).

2-Aminotetramethylbenzidine, prepared by the same method as 2 : 2'-diaminotetramethylbenzidine, crystallised from alcohol in plates, m. p. 138° (Found: C, 74-8; H, 7-8. C_{16}H_{21}N_{3} requires C, 75-3; H, 8-2%).

d-β-Octyl hydrogen diphenate, prepared from diphenic anhydride and d-β-octanol in the usual way, formed large needles, m. p. 70—73°, when crystallised from light petroleum (Found: equiv., 349. C_{22}H_{26}O_{4} requires equiv., 354). It was unchanged in rotatory power ([\alpha]_{D} + 51°; c = 5-0; l = 1-0 in absolute ethyl alcohol) by recrystallisation from light petroleum or aqueous ethyl alcohol.

**Dichloride of Diphenic Acid.**—Diphenic acid (20 g.) was dissolved in warm thionyl chloride (100 c.c.), and the excess of thionyl chloride then removed in a vacuum. The residue was boiled with benzene, and the solution was filtered from diphenic anhydride (2—3 g.) and diluted with light petroleum. A yield of 80% of the dichloride, m. p. 97°, was obtained.

**Dimethyl Diphenate.**—(a) A solution of equivalent quantities of menthol and diphenic acid dichloride in ether was boiled for 15 hours in the presence of potassium carbonate. Water was then added and the ethereal layer was separated, dried, and evaporated. The oily residue was dissolved in light petroleum, from which it separated in plates (yield 30%), m. p. 123—126°, [\alpha]_{D}^{46} = -118-6°, which, after recrystallisation from light petroleum, had m. p. 126° and [\alpha]_{D}^{46} = -120-4° in chloroform solution (c = 4-88, l = 2-0) (Found: C, 78-3; H, 8-3. C_{36}H_{46}O_{4} requires C, 78-7; H, 8-9%). (b) A solution of equivalent quantities of menthol and diphenic acid dichloride in pyridine, after standing for 12 hours, was poured into water, and the resulting precipitate crystallised from light petroleum. Successive crops had [\alpha]_{D}^{46} = -119-6°, -119-2°, -119-0° (yield 60%).
and after recrystallisation from light petroleum or acetic acid the ester had $[\alpha]_{D}^{20} = -120.3^\circ (c = 4.94, l = 2.0)$.

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BATTERSEA POLYTECHNIC, S.W. 11.  
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CCXCIII.—Investigations in the Diphenyl Series.
Part VII. The Relative Stability of Optically Active Diphenic Acids.

By Frank Bell and Percy Harry Robinson.

The theory advanced to account for the asymmetry of certain diphenyl derivatives (Part VI, this vol., p. 1695; J. Soc. Chem. Ind., 1926, 45, 864) definitely indicates that the optical activity
of such compounds should gain in permanence with an increase in the number of groups in the central positions. Up to the present, it has not proved possible to prepare in an optically active condition a compound with only two central groups, although some of the alkaloidal salts of "non-resolvable" acids show marked heterogeneity (compare Christie and Kenner, J., 1923, 123, 779; 1926, 470).

It is now found that 6-nitro diphenic acid (I) is very much less optically stable than 4:4':6'-tetranitrodiphenic acid (II). Thus

an aqueous solution of the sodium salt of the former acid steadily falls in rotatory power, whilst no such change can be perceived in the case of the latter acid. Further, boiling acetic anhydride racemises 6-nitrodiphenic acid in a very short time, whilst 4:4':6'-tetranitrodiphenic acid loses only 25% of its activity after boiling with acetic anhydride for 10 hours. The failure which has attended attempts to resolve 5-nitrodiphenic acid (III) and 2:2'-dinitrodiphenyl-4:4'-dicarboxylic acid could have been anticipated from

the "obstacle" theory. It may be noted that 5-nitrodiphenic acid readily forms an anhydride, and with sulphuric acid easily undergoes condensation to form a fluorenone derivative, in marked contrast to 4:4':6'-trinitrodiphenic acid (V) which is unaffected by sulphuric acid at 160°. 4:4'-Dinitrodiphenic acid (VI) also does not undergo fluorenone formation (Underwood and Kochmann, J. Amer. Chem. Soc., 1924, 46, 2069).

Although the failure to resolve fluorenone-4-carboxylic acid has been already reported by Mills, Palmer, and Tomkinson (J., 1924, 125, 2365), it appeared possible that the introduction of a nitro-group in position 5 might stabilise the enantiomorphous forms which arise if the fluoren system is non-planar. However, 5-nitro-fluorenone-4-carboxylic acid (IV) was not resolved by crystallisation of its morphine or quinidine salts, and this result can be interpreted
as indicating that the 4 : 5 -positions of fluorene are farther apart than are the 6 : 6 '-positions in a diphenic acid. This conclusion agrees with the fact that, although such systems as (VII) are readily formed, attempts to prepare compounds of type (VIII) have repeatedly failed (see Meyer, Meyer, and Taeger, Ber., 1920, 53, 2034).

![Diagram](VII) ![Diagram](VIII)

**Experimental.**

**d- and 1-6-Nitrodiphenic Acids.**—The normal quinine salt of 6-nitrodiphenic acid was systematically crystallised from alcohol until it was separated into a slightly less soluble salt, \([\alpha]_{5461} + 286-6^\circ\) (c = 2-5 in chloroform), and a slightly more soluble salt, \([\alpha]_{5461} — 122-4^\circ\) (c = 2-5 in chloroform). The former on decomposition gave the \(d\)-acid with \([\alpha]_{5461} + 65-2^\circ\) (c = 3-01 in ethyl alcohol), whilst the latter gave the \(l\)-acid with \([\alpha]_{5461} — 66-4^\circ\) (c = 4-91 in ethyl alcohol). The \(l\)-acid had \([\alpha]_{5461} + 433^\circ\) (c = 4-69 in 0-261N-sodium hydroxide), whilst the \(d\)-acid, obtained from its morphine salt, had \([\alpha]_{5461} — 434^\circ\) (c = 4-73 in 0-426N-sodium hydroxide).

The solution of the sodium salt was kept at room temperature, and the following observations were made:

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>(\alpha_{5461})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-20-51°</td>
</tr>
<tr>
<td>2</td>
<td>-18-61°</td>
</tr>
<tr>
<td>9</td>
<td>-14-42°</td>
</tr>
<tr>
<td>23</td>
<td>-8-23°</td>
</tr>
<tr>
<td>36-5</td>
<td>-4-00°</td>
</tr>
<tr>
<td>51</td>
<td>-1-50°</td>
</tr>
</tbody>
</table>

Solutions of \(d\)-6-nitrodiphenic acid (1 g.) in 10 c.c. of acetic acid and in 10 c.c. of acetic anhydride were boiled under similar conditions for 1 hour, and they then had \(\alpha_{5461} + 11-55^\circ\) and 0-0° respectively (l = 2). After the acetic acid solution had been boiled for a further period of 5 hours, it had \(\alpha_{5461} + 0-94^\circ\).

**d-6-Nitrodiphenic acid** (1 g.) was converted into 5-nitrofluorenone-4-carboxylic acid (see below). The acid obtained was inactive (c = 2-4; l = 2).

\(l\)-6-Nitrodiphenic acid was dissolved in excess of thionyl chloride and the solution evaporated in a vacuum. The residue was crystallised from benzene–light petroleum and gave the \(l\) + \(dl\)-acid dichloride, m. p. 65–68°; \([\alpha]_{5461} — 209-5^\circ\) (c = 5-04; l = 2), whilst the mother-liquor on evaporation gave a further crop of the dichloride with \([\alpha]_{5461} — 220-6^\circ\) (c = 2-31; l = 2 in chloroform).

**d- and \(dl\)-4 : 4' : 6 : 6'-Tetranitrodiphenic Acids.**—Boiling alcoholic solutions of tetranitrodiphenic acid (35-7 g. in 1 l.) and
quinidine (30·5 g. in \( \frac{1}{3} \) l.) were mixed, and the precipitated salt was filtered off and boiled with alcohol until the residue attained constant rotatory power \( [\alpha]_{5461} = 243·5^\circ \) \((c = 2·15 \text{ in 14·7N-acetic acid})\); m. p. 252° (decomp.). The alcoholic filtrates were evaporated, the residue was dissolved in acetic acid, and the resultant solution poured into dilute hydrochloric acid. The liberated tetrainitrodiphenic acid was extracted with ether, and the well-washed extract dried with sodium sulphate and evaporated. The residue \( ([\alpha]_{4461} \text{ ca.} - 50^\circ) \) was boiled with benzene, and the more soluble material was repeatedly crystallised from benzene until it attained constant rotatory power. \( l + d\)-Tetrainitrodiphenic acid formed needles which, after being heated at 130° for \( \frac{1}{2} \) hour, melted at 224—226° and had \( [\alpha]_{5461} = -133·5^\circ \) \((c = 1·7 \text{ in ethyl alcohol})\). The less soluble quinidine salt was decomposed (a) by dissolving it in acetic acid and pouring the solution into dilute hydrochloric acid, (b) by dissolving in pyridine and pouring the solution into dilute ammonia, (c) by grinding with concentrated hydrochloric acid. The acids, recovered as described above and dried at 140°, had almost the same rotatory power, showing that racemisation does not occur during the recovery process.

\( d:4':4:6':6'-\text{Tetrainitrodiphenic acid, m. p. 226—227°} \) (Found : equiv., 211. Calo.: 211) (0·3696 g. in 20 c.c. of ethyl alcohol in a 2 dm. tube) gave:

\[
\begin{array}{cccccc}
\lambda & 4359 & 4602 & 5461 & 5790 & 6708 \\
a & +16·70^\circ & +11·64^\circ & +5·26^\circ & +4·12^\circ & +2·58^\circ \\
\end{array}
\]

whence \( [\alpha]_{5461} = +142·3^\circ \).

0·4209 G. in 20 c.c. of 1·033N/10-NaOH in a 2 dm. tube gave:

\[
\begin{array}{cccccc}
\lambda & 4359 & 4602 & 5106 & 5218 & 5461 \\
a & +29—31^\circ & +19—20·5^\circ & +10·84^\circ & +9·72^\circ & +8·00^\circ \\
\end{array}
\]

\[
\begin{array}{cccccc}
\lambda & 5790 & 5896 & 6104 & 6708 \\
a & +6·33^\circ & +5·86^\circ & +5·08^\circ & +3·78^\circ \\
\end{array}
\]

whence \( [\alpha]_{5461} = +190·5^\circ \).

After 39 days, this solution had \( [\alpha]_{5461} = +8·08^\circ \).

A solution of \( d\)-teainitrodiphenic acid in acetic anhydride (1 g. in 10 c.c.), with \( [\alpha]_{5461} = 23·15^\circ \), had after 2 hours' boiling \( [\alpha]_{5461} = +18·14^\circ \), and after 9 hours' boiling \( [\alpha]_{5461} = +17·12^\circ \).

\( l\)-Tetrainitrodiphenic acid was dissolved in thionyl chloride by boiling for 2 hours under reflux, and the solution was evaporated in a vacuum. The residue was difficultly soluble and melted indefinitely. Though no product was isolated in a pure condition, the optical activity was preserved, since \( [\alpha]_{5461} = -133^\circ \) \((c = 2 \text{ in pyridine})\).

5-Nitrodiphenic acid was prepared by the process described by
After 1 hour's boiling with acetic anhydride, the solution on cooling deposited crystals of 5-nitrodiyphenic anhydride, m. p. 193—195° (Found : C, 62-4; H, 2-9. \(\text{C}_{14}\text{H}_7\text{O}_5\text{N}\) requires C, 62-4; H, 2-6%). 5-Nitrodiyphenic acid (1-5 g.) in sulphuric acid (5 c.c.) was heated at 160° for \(\frac{1}{2}\) hour, and after cooling poured into water. The precipitated 6(?)-nitrofluorenone-4-carboxylic acid melted at 282° after crystallisation from acetic acid (Found : equiv., 270-5. \(\text{C}_{14}\text{H}_5\text{O}_4\text{N}\) requires equiv., 269).

5-Nitrodiyphenic acid gave non-crystallisable quinine, morphine, and quinidine salts. The brucine salt on crystallisation from water gave successive crops with \([\alpha]_\text{D}^\text{white} = -10-4°, -10-9°, -11-2°, -11-1° (c = 2-5; \; l = 2 \text{ in } 14-7\text{N-acetic acid})

5-Nitrofluorenone-4-carboxylic acid was prepared by the method of Moore and Huntress (J. Amer. Chem. Soc., 1927, 49, 1324). The quinidine salt showed slight irregularity in rotatory power (\([\alpha]_\text{D}\text{white} = -20-6°; \; c = 2-5 \text{ in chloroform}) but no resolution was effected. The morphine salt was crystallised from alcohol and showed a constant rotatory power of \([\alpha]_\text{D} = 73-5° (c = 2 \text{ in } 14-7\text{N-acetic acid}).

2 : 5 : 7(?)-Trinitrofluorenone-4-carboxylic acid, obtained by heating 5-nitrofluorenone-4-carboxylic acid (2-5 g.) with nitric acid (d 1-5; 50 c.c.) at 100° for 2 hours, pouring into water, and crystallising the resulting mass from aqueous alcohol, forms glistening, pale yellow plates, m. p. 254—255° (Found : C, 46-5; H, 1-7. \(\text{C}_{14}\text{H}_5\text{O}_5\text{N}_3\) requires C, 46-8; H, 1-4%).

2 : 2'-Dinitrodiyphenyl-4 : 4'-dicarboxylic acid was prepared from 4-bromo-3-nitrobenzoic acid. Its excessive insolubility militated against the production of uniform normal alkaloidal salts. The brucine salt on crystallisation from water varied in rotatory power between \([\alpha]_\text{D} = -40° and \([\alpha]_\text{D} = 56° (c = 2 \text{ in pyridine}), but the liberated acid was inactive when observed in 1-033\text{N/10-sodium hydroxide.}

Quinine salts of 4-nitrodiyphenic acid. An alcoholic solution of quinine (2 mols.) and 4-nitrodiyphenic acid (1 mol.) was allowed to crystallise slowly. Successive crops had \([\alpha]_\text{D} = 94-4°, + 84-0°, + 77-2° (c = 2-5 \text{ in chloroform}), and the mother-liquor on evaporation and desiccation gave a solid with \([\alpha]_\text{D} = 99-9°. Recrystallisation of the intermediate crops raised the rotatory power to \([\alpha]_\text{D} = 106-4°; \; m. p. 180° (indefinite) (Found : C, 68-3; H, 5-6%). The liberated 4-nitrodiyphenic acid was inactive in every case. The difference in rotatory power may be attributed to:

(a) resolution of the alkaloidal salt; (b) admixture of acid and normal quinine salts and quinine; (c) differences in the number of
molecules of solvent of crystallisation—none of the salts lost more than 0.5% by weight on drying for 1 hour at 120°, however; or
(d) possible presence of 6-nitro- and 4:4'-dinitro-diphenic acids as impurities.

In conclusion, the authors wish to express their thanks to the Department of Scientific and Industrial Research for a grant made to one of them.

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CCLXXXVIII.—By-products of the Gattermann Aldehyde Reaction.

By Frank Bell and Thomas Anderson Henry.

The Gattermann synthesis of p-hydroxybenzaldehydes, depending on the primary production of an aldimine by the action of hydrocyanic acid on a phenol, has been the subject of a considerable number of modifications, mainly designed to avoid the use of anhydrous hydrocyanic acid. That due to Adams and Montgomery (J. Amer. Chem. Soc., 1923, 45, 2373; 1924, 46, 1518) has been used in these laboratories (Henry and Sharp, J., 1926, 2432), and the present paper gives an account of certain by-products isolated during the preparation of p-hydroxybenzaldehydes by this method.

Thymol is stated to give a quantitative yield of the corresponding p-aldehyde (I), but a trace of the o-aldehyde (II) is invariably formed, together with a small amount of dithymylacetonitrile (III).

\[
\begin{align*}
\text{(I)} & : & \text{Me} & \text{CHO} \\
\text{(II)} & : & \text{OH} & \text{Pr}^3 & \text{CHO} \\
\text{(III)} & : & \text{OH} & \text{Pr}^3 & \text{Me} \\
\end{align*}
\]

Carvacrol gives analogous products. Kobek (Ber., 1883, 16, 2104) isolated a small amount of carvacrolaldehyde (IV) when preparing

\[
\begin{align*}
\text{(IV)} & : & \text{OHC} & \text{Pr}^3 & \text{CHO} \\
\text{(V)} & : & \text{OHC} & \text{Pr}^3 & \text{Pr}^3 & \text{OH} \\
\end{align*}
\]

carvacrolaldehyde by the Reimer-Tiemann process, and the formation of this dialdehyde in the Gattermann reaction is now
shown by the isolation of its condensation product (V) with carvacrol. In some experiments with thymol, isopropylbenzene and m-cresol-aldehyde (VI) (o-cresolaldehyde in the case of carvacrol) were isolated, the amounts of these compounds being greatest when the yield of aldehyde was least. This result was traced to the fact that under the conditions of aldehyde formation it is possible to convert thymol almost completely into m-cresol and isopropylbenzene when no hydrocyanic acid is present, thus providing a further example of the reversibility of the Friedel–Crafts synthesis (compare Jacobsen, Ber., 1885, 18, 339). The possibility of utilising this reaction to introduce the isopropyl group into compounds dissolved in non-reactive solvents, e.g., ether, xylene, or p-cymene, still awaits examination. A recent paper (Berry and Reid, J. Amer. Chem. Soc., 1927, 49, 3142) describes the transfer of an isopropyl group from diisopropylbenzene into naphthalene.

The conditions of the formation of substituted acetonitriles, such as dithymylacetonitrile (III), have been examined. It is well known that aromatic aldehydes show very varying behaviour on treatment with potassium cyanide in aqueous–alcoholic solution. One group, which includes benzaldehyde, p-chlorobenzaldehyde (Hantzsch and Glover, Ber., 1907, 40, 1519), and o-methoxybenzaldehyde (Irvine, J., 1901, 79, 670), readily yields the corresponding benzoins, whereas o- and p-hydroxybenzaldehydes undergo resinification, and in still other cases, e.g., o-nitrobenzaldehyde (Ekcrantz and Ahlqvist, Ber., 1908, 41, 878; 1910, 43, 2066), a variety of products other than the benzoin is obtained. There is little doubt of the correctness of Lapworth’s theory of the benzoin change (J., 1903, 83, 995; compare Greene and Robinson, J., 1922, 121, 2182), according to which the aldehyde, R-CHO, first adds on hydrogen cyanide, then combines with a further molecule of aldehyde, and finally eliminates hydrogen cyanide as in (A). It seemed possible that the cyanohydrin phase in the condensation might be detected in the case of

\[
\text{R-CHO} \xrightarrow{\text{CN}} \text{R-C-CN} \xrightarrow{\text{H}} \text{R-C-CH} \xrightarrow{\text{O}} \text{R-C-CHO} \xrightarrow{\text{H}} \text{R-C-CR} \xrightarrow{\text{CN}} \text{R-C-CN} \xrightarrow{\text{OH}} \text{R-C-CHO} \xrightarrow{\text{H}} \text{R-C-CR} \xrightarrow{\text{OH}} \text{R-C-CN} \xrightarrow{\text{OH}} \text{R-C-CHO} \xrightarrow{\text{H}} \text{(A)} \]

even the hydroxybenzaldehydes, if some substance were present in the solution with which the cyanohydrin might react to form a
stable product. Accordingly, mixtures of hydroxybenzaldehydes with the corresponding phenols were warmed with potassium cyanide. In one case only was crystalline material isolated, thymolaldehyde and thymol giving a 12% yield of dithymylacetanilide.

It might be anticipated that the yield of the nitrile would be considerably increased if the potassium cyanide were replaced by hydrogen cyanide. With this end in view hydrogen chloride was passed into a dry benzene solution of, e.g., thymolaldehyde and thymol containing zinc cyanide in suspension. Only derivatives of triphenylmethane were obtained, and this result is interpreted as indicating that cyanohydrins are not formed under these experimental conditions. The readiness of condensation suggests that the hydrogen chloride forms an intermediate addition product with the aldehyde as shown in (B). If, however, an alcoholic

solution of equimolecular quantities of the aldehyde and phenol is treated with hydrogen cyanide and the mixture is heated to the boiling point after the addition of zinc chloride, three types of behaviour are shown.

<table>
<thead>
<tr>
<th>Table I.</th>
</tr>
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<tbody>
<tr>
<td>(Behaviour of substituted benzaldehydes; CHO in position 1.)</td>
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<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>(produce nitriles).</td>
<td>(produce triphenylmethane derivatives).</td>
<td>(unreactive).</td>
</tr>
<tr>
<td>Me: PrH²: OH = 2:4:4</td>
<td>Cl = 2 or 4</td>
<td>NO₃ = 2</td>
</tr>
<tr>
<td>Me: PrH²: OH = 5:2:4</td>
<td>NO₂ = 3 or 4</td>
<td></td>
</tr>
<tr>
<td>Me: OH = 3:4</td>
<td>HO = 3</td>
<td></td>
</tr>
<tr>
<td>OH: OH = 3:4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OMe = 4</td>
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</tbody>
</table>

(1) The aldehydes in column A (Table I) give the corresponding diarylacetonitriles, in some cases in quantitative yields. That it is the nuclear hydrogen atom para to the hydroxyl group in the phenol, which is involved in this condensation is clear from the fact that o-cresolaldehyde and thymol give the same product (VII) as thymolaldehyde and o-cresol. Even when the o- and p-positions are both equally accessible, as in phenol, condensation takes place
almost exclusively in the $p$-position, the product then formed being (VIII), and the isomeride (IX) could not be detected.

\[
\begin{array}{c}
\text{HO} & \text{Me} & \text{CHO} \\
& \xrightarrow{\text{HON}} & \\
\text{Me} & \text{Pr}^\alpha & \text{HO} \\
\end{array}
\]

(VII.)

\[
\begin{array}{c}
\text{HO} & \text{Me} & \text{CHO} \\
& \xleftarrow{\text{HON}} & \\
\text{Me} & \text{Pr}^\alpha & \text{HO} \\
\end{array}
\]

(VIII.)

(IX.)

(2) On the other hand, benzaldehyde itself and its derivatives shown in column B (Table I) give triphenylmethane derivatives, and since the yield of these substances greatly exceeds that obtained when hydrogen cyanide is absent, it seems likely that reaction (II) is in operation in place of, or in addition to, reaction (I):

\[
\begin{align*}
(I) & \quad \text{R-CHO} + \text{HR'}\cdot\text{OH} \rightarrow \text{R-CH(OH)}\cdot\text{R'}\cdot\text{OH} \xrightarrow{\text{HON}} \text{R-CH(R'}\cdot\text{OH})_2 + \text{H}_2\text{O}. \\
(II) & \quad \text{R-CH(OH)}\cdot\text{CN} + \text{HR'}\cdot\text{OH} \xrightarrow{\text{HON}} \text{R-CH(R'}\cdot\text{OH})_2 + \text{H}_2\text{O}.
\end{align*}
\]

\(o\)-Nitrobenzaldehyde is unique in so far as it is isolated from the reaction mixture in the form of its cyanohydrin, which is apparently very unreactive.

This variety of results is all the more remarkable since mandelic acid and mandelonitrile condense normally with a whole series of phenols (Bistrzycki and Flatau, Ber., 1895, 28, 989; 1897, 30, 124; Bistrzycki and Simonis, Ber., 1898, 31, 2812; Cramer, ibid., p. 2813; Simonis, ibid., p. 2821). Considerable further investigation is required to determine the influence of (a) substituents and (b) physical conditions, \(e.g.,\) acidity of the solution, on the relative reactivity of the hydroxyl and cyano-groups of cyanohydrins. We have little doubt that the triphenylmethane formation indicates cyano-group reactivity, the intermediate diphenylmethanederivative undergoing further condensation under the experimental conditions, whereas nitrile formation indicates hydroxyl group reactivity (C).

\[
\begin{align*}
\text{R-C} & \xleftarrow{\text{HR'}} \text{H} \xrightarrow{\text{HON}} \text{R-C} & \text{H} & \xrightarrow{\text{HR'}} \text{H} \\
\text{R'} & \xleftarrow{\text{HON}} \text{CN} & \text{CN} & \text{CN}
\end{align*}
\]

(C)

The fact that the substituted nitriles do not undergo further con-
densation to triphenylmethane derivatives is only in line with the diminished reactivity of the cyano-group which is shown by its resistance to hydrolytic agents. It appears that the hydroxyl group by virtue of its lone pairs of electrons is a more ready electron source than the cyano-group and that when the nucleus of a cyano-hydrin has a positive character the hydroxyl group will tend to become, relative to the cyano-group, less negative, and at the same time less reactive.

**Experimental.**

*Thymoldehydes and By-products.*—Into an ice-cold, well-stirred mixture of thymol (50 g.), zinc cyanide (100 g.), and benzene (200 c.c.; distilled from phosphoric oxide), was passed a rapid stream of dry hydrogen chloride until it ceased to be absorbed. Aluminium chloride (75 g.) was then added and the stirring continued for 4 hours in a slow current of hydrogen chloride. Towards the end, the reaction bottle was kept immersed in water at about 50°. The semi-solid product was transferred into 10% hydrochloric acid and distilled in steam until thymoldehyde appeared in the condenser. The residue left on the removal of the solvent from the benzene layer of the steam distillate was distilled in three fractions; the residue in the flask then set solid and proved to be p-thymolaldehyde (I). The first fraction, b. p. 60—80°/15 mm., consists mainly of isopropylbenzene and is occasionally negligible in amount (see below). The second (b. p. 100—110°/15 mm.) and third (b. p. 110—120°/15 mm.) fractions were dissolved in alcohol and treated with aqueous-alcoholic semicarbazide solution. The precipitate immediately given with fraction 2, after repeated extraction with boiling alcohol, formed a white powder, m. p. 262° (decomp.), which was identified as m-cresolaldehyde semicarbazone (Found: C, 55-1; H, 5-6; N, 21-3. Calc.: C, 56-0; H, 5-7; N, 21-8%) by hydrolysis in the following manner: A mixture of the substance (3 g.), sulphuric acid (10 c.c.), and water (50 c.c.) was heated to boiling and the resultant m-cresolaldehyde (VI) removed in a current of steam. It crystallised from petroleum in long needles, m. p. 63° (Found: C, 70-4, 70-3; H, 5-8, 6-0. Calc.: C, 70-6; H, 5-9%).

In the case of fraction 3 acicular crystals gradually separated and after repeated crystallisation from alcohol had m. p. 198° (Found: C, 61-5; H, 7-2; Sem., 31-4%). The semicarbazide group (Sem. = N·NH·CO-NH₂) was estimated by the method of Veibel (*Bull. Soc. chim.*, 1927, 41, 1410). This compound can only be the semicarbazone of 2-aldehyde-3-methyl-6-isopropylphenol (o-thymolaldehyde) (II) (C₁₂H₁₇O₂N₂ requires C, 61-3; H, 7-2; Sem., 31-1%).

The residue left after steam distillation was extracted with ether, and the extract evaporated. Two methods of purifying the crude
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$p$-aldehyde (about 50 g.; identical with the yield obtained by Gattermann's original method, *Ber.*, 1898, **31**, 1765) were adopted: (1) extraction with 25% alcohol, a small crystalline residue, m. p. 205°, being finally obtained; (2) crystallisation from alcohol, the final low-melting crops being dissolved in chloroform and filtered from a small amount of the same substance, m. p. 205°, subsequently shown to be dithymylacetonitrile (see p. 2224). 4-Aldehyde-3-methyl-6-isopropylphenol (I) forms colourless needles, m. p. 135°; when aqueous-alcoholic semicarbazide solution is added to its alcoholic solution the slightly impure semicarbazone separates in deep yellow needles, m. p. 222° (Found: C, 60-6, 60.7; H, 7.3, 7.3%); which rapidly become colourless on recrystallisation from acetic acid or alcohol and melt at 226° (Found: C, 61-2; H, 7.3; Sem., 30.5. \( \text{C}_{12}\text{H}_{17}\text{O}_2\text{N}_2 \) requires C, 61.3; H, 7.2; Sem., 31.1%).

Attempts to convert \( p \)-thymolaldehyde into the corresponding dialdehyde by (a) the Adams and Montgomery method, (b) the Gattermann method were unsuccessful. This failure is not surprising in view of the highly substituted character of the ring, and also of the disinclination of hydrogen cyanide to attack the position ortho to a hydroxyl group. It may be mentioned that even \( p \)-cresol gives a very small yield of the aldehyde when submitted to the same treatment as produces a satisfactory yield from \( o \)-cresol (see below).

**Action of Aluminium Chloride on Thymol.**—As it was surmised that the formation of isopropylbenzene in the reaction just described was due to interaction of thymol and benzene in presence of aluminium chloride, a well-stirred mixture of thymol (25 g.), dry benzene (200 c.c.), and aluminium chloride (35 g.) was warmed at about 50° for 4 hours while a current of dry hydrogen chloride was passed in. The clear solution was poured into 10% hydrochloric acid and distilled in steam. The benzene layer of the steam distillate was separated and evaporated and the residue obtained was distilled in a vacuum, giving fractions b. p. 60°, 95—100°, 100—118°, and ca. 170°/15 mm. The low-boiling fraction (about 10 g.) was redistilled under ordinary pressure, and the fraction, b. p. 150—155°, redistilled from sodium. It then boiled constantly at 133° and agreed in properties with isopropylbenzene (Found: C, 90.3; H, 9-9. Calc.: C, 90.0; H, 10.0%). The fraction, b. p. 95—106°/15 mm., gave pure \( m \)-cresol, b. p. 200—202° (6 g.), which was identified as its \( p \)-nitrobenzoyl derivative. The higher-boiling fraction consisted of neutral substances, being apparently a mixture of \( m \)-tolyl ether and thymyl ether. When the above reaction was carried out in the presence of toluene a fraction, b. p. 65—75°/15 mm., was obtained which on redistillation had b. p. 175—180°, being slightly impure \( p \)-cymene.
Carvacrol aldehydes and By-products.—The preparation was effected as described for thymolaldehyde (see above). The steam distillate gave fractions, b. p. 60°, 100—110°, 110—120°, and 120—130°/15 mm., and a residue of the p-aldehyde, which could be sublimed at 150°/1 mm. The first fraction consisted of isopropylbenzene (see below). The remaining fractions were dissolved separately in alcohol and treated with aqueous-alcoholic semicarbazide solution. The fraction, b. p. 100—110°/15 mm., gave crude o-cresolaldehyde semicarbazone (compare thymol above), and from the fraction, b. p. 110—120°/15 mm., was isolated a trace of material which crystallised from pyridine or acetic acid in thick, pale yellow prisms, m. p. 275° (Found: C, 73-2; H, 7-9; N, 7-8%). It is suggested that this compound is the semicarbazone of 4-hydroxy-3-aldehydo-5-methyl-2-isopropylphenylcarvacyrmethane (V) (C_{13}H_{17}O_2N_3 requires C, 72-7; H, 7-9; N, 7-7%) formed by the interaction of carvacrol and carvacrolaldehyde during the distillation. The fourth fraction, b. p. 120—130°/15 mm., gave more soluble material, which crystallised from aqueous alcohol in long glistening needles, m. p. 180° (Found: C, 61-3; H, 7-3; Sem., 31-5%), and must be the semicarbazone of 2-aldehyde-6-methyl-3-isopropylphenol (o-carvacrolaldehyde semicarbazone) (C_{14}H_{17}O_2N_3 requires C, 61-3; H, 7-2; Sem., 31-1%).

The ether-soluble portion of the residue left after steam distillation was repeatedly extracted by decantation with petroleum (b. p. 90—120°), which slowly removed the p-carvacrolaldehyde (30—40 g.) as colourless plates, m. p. 102°. With aqueous-alcoholic semicarbazide solution this yielded a slightly impure, deep yellow semicarbazone, m. p. 222° (Found: C, 60-8; H, 7-3%), which on crystallisation from acetic acid gave colourless needles, m. p. 224° (Found: Sem., 31-1. C_{14}H_{17}O_2N_3 requires C, 61-3; H, 7-2; Sem., 31-1%). The tar which remained after the complete removal of this aldehyde was moistened with alcohol and kept for several weeks. Crystals slowly formed, which after recrystallisation from aqueous alcohol had m. p. 240° and were subsequently shown to consist of dicarvacrylacetonitrile (see p. 2223).

Action of Aluminium Chloride on Carvacrol (compare corresponding experiment with thymol, p. 2220).—Fractions, b. p. 60° (11 g.), 100° (11 g.), and 102—115°/15 mm. (5 g.) were obtained. The residue, after being heated to 150°/1 mm., crystallised from petroleum in long thick needles, m. p. 148—150° (0-3 g.) (Found: C, 83-3; H, 8-5; N, 8-8%). This substance was not obtained in sufficient quantity for identification. The low-boiling fraction was almost pure isopropylbenzene, and the intermediate fraction gave o-cresol, b. p. 188—190° (7 g.), identified as the p-nitrobenzoate.
Reimer-Tiemann Reaction with Carvacrol.—Carvacrol (20 g.), sodium hydroxide (40 g.), water (300 c.c.), and chloroform (25 g.) were used. The reaction mixture was acidified and distilled in steam. The distillate consisted of unchanged carvacrol and the o-aldehyde, isolated only as its semicarbazone (see above). The residue was purified as described above and gave a very small yield of the p-aldehyde, identical with that described above.

o-Cresolalddehydes.—Preparation as above, o-creosol (50 g.) being used in place of thymol. The steam distillate, freed from solvent, boiled at 85—90°/15 mm. (15 g.), leaving only a small residue of the p-aldehyde. To a solution of the fraction, b. p. 85—90°/15 mm., in alcohol (15 c.c.) was added aqueous-alcoholic semicarbazide solution. The resultant precipitate (3 g.) was repeatedly extracted with boiling alcohol; the residue then remained unchanged in m. p. (248°, decomp.) by crystallisation from pyridine, from which it separated in glistening needles. It was identified as the semicarbazone of 6-aldehyde-2-methylphenol (X) (Found: C, 55·5; H, 5·8; N, 21·6; Sem., 38·5. \( \text{C}_{10} \text{H}_{14} \text{O}_{2} \text{N}_3 \) requires C, 56·0; H, 5·7; N, 21·8; Sem., 37·8%). by hydrolysis to the corresponding aldehyde, which was then converted into the known phenylhydrazine.

The ether-soluble portion of the residue left after steam distillation was extracted with boiling water until all the p-aldehyde (XI) (about 20 g.) had been removed, leaving an uncryllallisable tar. The p-aldehyde gave a semicarbazone crystallising from acetic acid in needes, m. p. 216° (Found: N, 21·8; Sem., 37·2. \( \text{C}_{10} \text{H}_{16} \text{O}_2 \text{N}_2 \) requires N, 21·8; Sem., 37·8%).

Action of Potassium Cyanide on Hydroxybenzaldehydes.—(1) No crystalline material could be isolated from the gums obtained by the action of potassium cyanide on alcoholic solutions of salicylaldehyde, p-hydroxybenzaldehyde, or carvacraldehyde, either alone or when mixed with phenol or carvacrol respectively.

(2) Nine mixtures of thymolaldehyde, alone and with thymol, potassium cyanide and aqueous alcohol were heated under reflux for varying periods. In only one experiment (a) in which thymol was omitted was any yield of substance, m. p. 205°, obtained, and experiment (b) furnished the highest yield of the series.

(a) Thymolaldehyde (3·6 g.), alcohol (6 c.c.), potassium cyanide (1 g.), and water (2 c.c.) were mixed and heated at 100° for 1 hour. After 2 days the mixture was made acid and left for 10 days. The resultant tar was filtered off, and the residual solid crystallised from
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alcohol. Yield, 0.25 g.; m. p. 205°. As this experiment could not be repeated, it is assumed that the thymolaldehyde used in the first instance must have contained thymol.

(b) Thymolaldehyde (18 g.), alcohol (60 c.c.), thymol (12 g.), potassium cyanide (6 g.), and water (12 c.c.) were mixed and heated at 100° for 20 hours. After 2 days concentrated hydrochloric acid (10 c.c.) was added, and after 2 days more the mixture was poured into water and extracted with ether. The ethereal extract was evaporated, and the dried residue extracted with hot chloroform. The insoluble matter (4.0 g.) had m. p. 205° (see below).

Thymolaldehyde and benzonitrile underwent no interaction when a concentrated alcoholic solution was boiled under reflux or allowed to stand for some days. In the hope of obtaining the compounds in better yields, the following experiments were tried. (1) Thymolaldehyde (10 g.), thymol (20 g.), zinc cyanide (20 g.), and dry benzene (200 c.c.) were well stirred while a slow stream of dry hydrogen chloride was passed in. The mixture was maintained at 40—60° for the last 2 hours. The highly coloured, viscous mass was transferred into 10% hydrochloric acid by the aid of a small bulk of boiling alcohol, and then distilled in steam. The tarry residue was extracted with ether, the extract evaporated, and the dried mass boiled with chloroform. The colourless residue (15 g., m. p. 276°) after crystallisation from aqueous alcohol formed prisms, m. p. 280° (Found: C, 80.2; H, 8.6%). This substance must be trithymylmethane (C31H40O3 requires C, 80.8; H, 8.7%), a conclusion which was confirmed by the preparation of the acetyl derivative. The compound (2.5 g.) and acetic anhydride (15 c.c.) were heated under reflux for 2 hours. On cooling, the liquid filled with crystals of triacetylthymymethane, which after recrystallisation from benzene—petroleum formed glistening leaflets, m. p. 186° (Found: Ac, 22.0. C37H46O6 requires Ac, 22.0%).

(2) Carvacrolaldehyde (10 g.) and carvacrol (25 c.c.), treated as in (1), gave tricarvacrylmethane, m. p. 275° (Found: C, 80.8; H, 8.8%). The compound was acetylated as described above and yielded triacetylcarvacrylmethane, which after crystallisation from petroleum formed leaflets, m. p. 185° (Found: C, 76.1; H, 8.1. C37H46O6 requires C, 75.8; H, 7.9%). Both compounds gave the customary large depression in melting point when mixed with the corresponding derivatives of thymol.

Little condensation occurs if the zinc cyanide is omitted in these experiments. Moreover the yield of triphenylmethane derivatives is considerably greater than when the experiment is conducted in alcoholic solution with hydrogen chloride or zinc chloride as condensing agent.
Action of Hydrogen Cyanide on Substituted Benzaldehydes.—

General method. Dry hydrogen cyanide from potassium ferrocyanide (70 g.; method of Johnson and Lane, J. Amer. Chem. Soc., 1921, 43, 357) was passed into a solution of equimolecular proportions of the aldehyde (10 g.) and the phenol in absolute alcohol (50—100 c.c.). Zinc chloride (20—25 g.) was then added, the mixture boiled for 2 hours, and the solution poured into 10% hydrochloric acid. Excess of the reagents was removed in a current of steam, and the residual solid or plastic mass filtered off.

(1) Thymolaldehyde and thymol combined to give a quantitative yield of dithymylacetanitrile, which after recrystallisation from alcohol formed prismatic needles, m. p. 205° (Found : C, 78-4; 78-5; H, 8-2, 8-1; N, 4-3, 4-2. \( \text{C}_{22}\text{H}_{27}\text{O}_{2}\text{N} \) requires C, 78-3; H, 8-0; N, 4-1%). No combination occurred when the zinc chloride was omitted.

Dithymylacetanitrile was not attacked by boiling hydrochloric acid or by sulphuric acid (50—65%), and higher concentrations produced resinous masses (compare Michael and Jeanprêtre, Ber., 1892, 25, 1615). Hydrolytic experiments with 3% hydrogen peroxide (Radziszewski, Ber., 1885, 18, 353) or 100% phosphoric acid (Berger and Olivier, Rec. trav. chim., 1927, 46, 600) were also unsuccessful. The substance (5 g.) was heated at 100° with potassium hydroxide (20 g.) in 90% alcohol (100 c.c.) for 10 hours. After standing 2 days, the solution was poured into 10% hydrochloric acid and the precipitated dithymylacetamide crystallised from alcohol. It formed a colourless, heavy crystalline powder, m. p. 243° (decomp.) (Found : C, 73-8; H, 8-2. \( \text{C}_{22}\text{H}_{29}\text{O}_{3}\text{N} \) requires C, 74-4; H, 8-2%).

Diacyltethymylacetanitrile, formed by heating dithymylacetanitrile (3 g.) with acetic anhydride (15 c.c.) and recrystallising the product from chloroform—petroleum, formed needles, m. p. 174° (Found : C, 74-3, 74-1; H, 7-5, 7-5; Ac, 20-4. \( \text{C}_{26}\text{H}_{31}\text{O}_{4}\text{N} \) requires C, 74-1; H, 7-4; Ac, 20-4%). On hydrolysis with dilute alcoholic potassium hydroxide it regenerated dithymylacetanitrile, m. p. 205°.

(2) Carvacrolaldehyde and carvacrol, treated in like manner, gave a quantitative yield of dicarvacrylacetonitrile, which crystallised from aqueous alcohol in prisms, m. p. 240° (Found : C, 78-3; H, 8-2; N, 3-7. \( \text{C}_{22}\text{H}_{27}\text{O}_{3}\text{N} \) requires C, 78-3; H, 8-0; N, 3-1%). Diacylcarvacrylacetonitrile crystallised from alcohol in colourless needles, m. p. 196° (Found : C, 74-0; H, 7-6; N, 3-5. \( \text{C}_{26}\text{H}_{31}\text{O}_{4}\text{N} \) requires C, 74-1; H, 7-4; N, 3-3%).

(3) Thymolaldehyde and carvacrol, or carvacrolaldehyde and thymol, gave thymylcarvacrylacetonitrile, which formed prisms, m. p. 227°, from alcohol (Found : C, 78-1; H, 8-3. \( \text{C}_{22}\text{H}_{27}\text{O}_{3}\text{N} \) requires C, 78-3; H, 8-0%). It yielded a diacetyl derivative, m. p.
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145° (Found: C, 73-7; H, 7-4. C20H31O4N requires C, 74-1; H, 7-4%).

(4) o-Cresolaldehyde and thymol, or thymolaldehyde and o-cresol, gave tolylthymylacetetonitrile (VII), the first pair giving a quantitative and the second a 70% yield. It crystallised from aqueous alcohol in prisms, m. p. 153° (loss in weight on drying at 100° = 10-4%) (Found for dry substance: C, 77-1; H, 7-3). C19H21O2N requires C, 77-3, H, 7-1%). The substance (5 g.) was warmed with potassium hydroxide (20 g.) in 90% alcohol (100 c.c.) at 100° for 24 hours. The solution was poured into 10% hydrochloric acid and extracted with ether. The etheral extract was shaken with dilute sodium carbonate solution, and the aqueous and etheral layers were separated and well washed with ether and water respectively. The etheral layer was evaporated, and the dried residue extracted with hot benzene. The residual tolylthymylacetamide crystallised from alcohol in prisms, m. p. 211° (Found: C, 72-6; H, 7-4; N, 4-7). C19H21O2N requires C, 72-9; H, 7-3; N, 4-5%). The aqueous layer was poured into 10% hydrochloric acid, and the resulting gum dried in a vacuum desiccator. After boiling with benzene, it formed a pale brown powder, m. p. 188°. It was free from nitrogen and must be crude tolylthymylacet acid (Found: C, 71-2, 71-6, 71-2; H, 7-1, 7-2, 6-9). C19H21O4 requires C, 72-6; H, 7-0%). Acetyltoylthymylacetetonitrile forms prisms, m. p. 131° (Found: Ac, 23-3. C20H23O2N requires Ac, 22-7%).

(5) p-Hydroxybenzaldehyde and thymol gave a brown resinous mass, which crystallised from chloroform in needles, m. p. 142°. Recrystallised from benzene, p-hydroxyphenylthymylacetetonitrile (VIII) formed large prisms, which on drying at 110° lost 12-6% by weight and left a residue, m. p. 144° (Found: C, 76-3; H, 6-8. C18H19O2N requires C, 76-8; H, 6-8%). Phenol and thymolaldehyde gave an 80% yield of the same substance.

(6) Anisaldehyde (p-methoxybenzaldehyde) and thymol gave a thick oil, which was extracted with ether. The gum remaining after evaporation of the ether was dissolved in chloroform. After some days crystals separated, which were well washed with petroleum and repeatedly recrystallised from benzene, pure anisylthymylacetetonitrile being obtained in 10% yield. It formed large prisms, m. p. 106° (Found: C, 77-8; H, 7-2. C19H21O2N requires C, 77-3; H, 7-1%).

(7) Salicylaldehyde and thymol gave a resin, which crystallised from chloroform in prisms, m. p. 142°, and when dried at 110° lost 18-9% by weight (Found, for dry substance: C, 76-6; H, 6-9. C19H21O2N requires C, 76-8; H, 6-8%). The yield of purified o-hydroxyphenylthymylacetetonitrile (IX) was less than 50% of the theoretical.
(8) Protocatechuvaldehyde and thymol gave a gummy mass, which was extracted with benzene, and the product repeatedly crystallised from chloroform. Catechylthymylacetonitrile formed prisms, m. p. 147—149° (Found: N, 4.7. \( \text{C}_{15}\text{H}_{19}\text{O}_3\text{N} \) requires N, 4.7%).

(9) Benzaldehyde and thymol gave a quantitative yield of phenylthymylmethane, which crystallised in prisms, m. p. 167—168°, containing one molecule of alcohol (loss in weight at 110° = 10.5%; calc., 11%). This description agrees with that of Russanow (Ber., 1889, 22, 1947).

(10) \( m \)-Hydroxybenzaldehyde and thymol gave a poor yield of \( m \)-hydroxyphenylthymylmethane, which crystallised from chloroform in prisms, m. p. 165° (Found: C, 80.5; H, 8.1. \( \text{C}_{27}\text{H}_{32}\text{O}_3 \) requires C, 80.2; H, 7.9%).

(11) \( o \)-Nitrobenzaldehyde and thymol gave a product, which crystallised from chloroform in needles, m. p. 95—97°, and proved to be \( o \)-nitrobenzaldehydecyanohydrin (Found: C, 54.1; H, 3.5. Calc.: C, 53.9%; H, 3.4%). The fact that this cyanohydrin survives the general method of treatment (see above) is remarkable. No different result was obtained when phenol was used in place of thymol.

(12) \( m \)-Nitrobenzaldehyde and thymol gave an almost quantitative yield of \( m \)-nitrophenylthymylmethane, which crystallised readily from aqueous alcohol in prisms, m. p. 171° (Found: C, 74.7; H, 7.2. \( \text{C}_{27}\text{H}_{31}\text{O}_4\text{N} \) requires C, 74.8; H, 7.2%).

(13) \( p \)-Nitrobenzaldehyde and thymol gave a tarry mass; this after several recrystallisations from benzene formed colourless needles, which became pale yellow on drying and then melted at 145° (loss in weight on drying, 20.9. \( \text{C}_{27}\text{H}_{31}\text{O}_4\text{N}, \text{H}_4\text{C}_6\text{H}_5 \) requires loss, 21.2%) (Found for the residual \( p \)-nitrophenylthymylmethane: C, 75.0; H, 7.2. \( \text{C}_{27}\text{H}_{31}\text{O}_4\text{N} \) requires C, 74.8; H, 7.2%). The mother-liquor contained \( p \)-nitrobenzaldehydecyanohydrin.

(14) \( p \)-Chlorobenzaldehyde and thymol gave a quantitative yield of \( p \)-chlorophenylthymylmethane, which crystallised from alcohol in prisms; these, dried at 110°, lost 15.0% by weight, and the residue melted at 156° (Found: C, 76.4; H, 7.3. \( \text{C}_{27}\text{H}_{31}\text{O}_4\text{Cl} \) requires C, 76.7; H, 7.3%).

(15) \( o \)-Chlorobenzaldehyde and thymol gave a viscid mass, which, however, readily crystallised from aqueous alcohol to give an almost theoretical yield of \( o \)-chlorophenylthymylmethane. Dried at 110°, this lost 16.6% by weight, and the residue melted at 138° (Found: C, 76.4; H, 7.2. \( \text{C}_{27}\text{H}_{31}\text{O}_4\text{Cl} \) requires C, 76.7; H, 7.3%).

Since it might be suggested that when triphenylmethane formation occurs, combination takes place between the aldehyde and the...
phenol before the hydrogen cyanide is introduced, the experiments with m-nitro- and o- and p-chloro-benzaldehydes were repeated, the thymol not being added until after the passage of the hydrogen cyanide. The experimental results were unaltered, and this is not surprising in face of the results of the following experiments.

(a) The experiment with p-chlorobenzaldehyde (14 above) was repeated, this time without the addition of zinc chloride. No combination occurred.

(b) p-Chlorobenzaldehyde (5 g.), thymol (10-7 g.), and zinc chloride (20 g.) in absolute alcohol (40 c.c.) were heated under reflux for 4 hours and then poured into 10% hydrochloric acid and the excess of the reagents was removed in steam. The residual crude p-chlorophenylmethane weighed 4 g. (25% yield).

(c) m-Nitrobenzaldehyde and thymol treated as in (b) gave crude m-nitrodithymethane in only 20% yield.

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CCCXXXII.—Preparation of Diethylaminoethanol Esters of Diphenyl-2-carboxylic Acid and Derivatives.

By Frank Bell.

Roberts and Johnson (J. Amer. Chem. Soc., 1925, 47, 1399) have directed attention to the marked anesthetic action of diethylaminoethyl diphenate, and it was thought of interest to make the diethylaminoethyl esters of several related carboxylic acids.

Diphenyl-2-carboxylyl chloride reacted with diethylaminoethyl alcohol to give an ester hydrochloride with a well-marked anesthetic action. The chlorides of diphenyl-4-carboxylic, fluorenone-4-carboxylic, and 2'-cyanodiphenyl-2-carboxylic acids furnished esters of perceptible but smaller action. 2'-Cyanodiphenyl-2-carboxylyl chloride was obtained together with about 10% of diphenimide by the action of thionyl chloride on diphenamic acid (compare the action of thionyl chloride on diphenic acid; J., 1927, 1698).

\[
\text{C}_6\text{H}_4\text{CO}_2\text{H} \rightarrow \text{C}_6\text{H}_4\text{COCl} + \text{C}_6\text{H}_4\text{CO}\text{CN} + \text{C}_6\text{H}_4\text{CO}\text{NH}
\]

Diphenyl-2-carboxylyl chloride shows a great tendency to change into fluorenone during distillation. On the other hand, diphenoyl dichloride seems quite stable, although its boiling point is almost 50° higher. 2'-Cyanodiphenyl-2-carboxylyl chloride decomposed to only a slight extent; the 4-cyanofluorenone produced was found in the distillate. The considerable stability of this acid chloride is of interest, because the convenient process for obtaining 4-cyanofluorenone by the action of phosphorus pentachloride on phenanthraquinone monoxime (Borsche and Gander, Ber., 1914, 47, 2818) must depend on its intermediate formation.

Experimental.

Diphenyl-2-carboxylyl chloride was obtained as a pale yellow liquid, b. p. 163°/10 mm., when a solution of diphenyl-2-carboxylic acid in warm thionyl chloride was distilled in a vacuum (Found: C, 72.0; H, 4.1. Calc.: C, 72.1; H, 4.2%). (compare Schlenk and Bergmann, Annalen, 1928, 464, 33). In two subsequent experiments the chloride decomposed completely during distillation with the formation of pure fluorenone. Bretscher, Rule, and Spence (this vol., p. 1502) have apparently had the same experience and are investigating the reaction in detail.

Interaction of this chloride and 2-aminodiphenyl in pyridine solution gave the corresponding amide, which crystallised from acetic acid in needles, m. p. 194° (Found: C, 85.5; H, 5.5. \(\text{C}_{26}\text{H}_{19}\text{ON} \) requires C, 85.9; H, 5.4%).
Diethylaminoethyl Diphenyl-2-carboxylate. — Diethylaminoethyl alcohol (5 g.) was added to a solution of the acid chloride (9.2 g.) in benzene (20 c.c.). The semi-solid product was warmed on the water-bath for ½ hour and evaporated in a vacuum, and the residual gum dissolved in cold water. The base was liberated with ammonia, extracted with ether, and distilled in a vacuum, giving a colourless liquid, b. p. 183°/1 mm., which contained some impurity (Found: C, 75.9; H, 7.6. C_{19}H_{23}O_{2}N requires C, 76.8; H, 7.8%). It was treated in dry ether with hydrogen chloride (slightly less than the theoretical amount), the hydrochloride of diethylaminoethyl diphenyl-2-carboxylate being precipitated as a white powder, m. p. 109—110° (Found: HCl, 11.0. C_{19}H_{23}O_{2}N.HCl requires HCl, 10.9%). This hydrochloride is slightly hygroscopic, dissolves in a small amount of water to give a clear solution which becomes milky on dilution, and is markedly anesthetic to the tongue.

Diethylaminoethyl Diphenyl-4-carboxylate. — 4-Methyl diphenyl (Comberg and Perneit, J. Amer. Chem. Soc., 1926, 48, 1375) was converted by oxidation with 2% aqueous permanganate solution (Jacobson, Ber., 1895, 28, 2547) into the corresponding acid, and this into the acid chloride (m. p. 114°) by thionyl chloride. When the acid chloride (4.6 g.) in benzene was treated with diethylaminoethyl alcohol (2.5 g.), a crystalline deposit was immediately obtained; the reaction was completed by warming the mixture for ½ hour. The product was collected and dissolved in water, impurities were removed by extraction with ether, the base was liberated with dilute sodium carbonate solution and extracted with ether, and the extract was dried with sodium sulphate and treated with hydrogen chloride, the hydrochloride of diethylaminoethyl diphenyl-4-carboxylate being precipitated as a white powder, m. p. 183° (Found: HCl, 11.2. C_{19}H_{23}O_{2}N.HCl requires HCl, 10.9%). This hydrochloride is extremely soluble in water, but the solution becomes milky on dilution.

2'-Cyanodiphenyl-2-carboxyl chloride. — Diphenamic acid (16.7 g.) and thionyl chloride were warmed together for ½ hour and the resultant solution was evaporated in a vacuum. A solution of the residual paste in a little benzene was filtered from the needle crystals of diphenimide (1.5 g.), m. p. 217—219°, and diluted with light petroleum, 2'-cyanodiphenyl-2-carboxyl chloride being precipitated as a white powder, which crystallised from carbon tetrachloride in stout prisms (10.6 g.), m. p. 84° (Found: C, 69.8; H, 3.2. C_{14}H_{5}ONCl requires C, 69.6; H, 3.3%). On heating in a vacuum, it gave a pale yellow distillate, b. p. 222°/15 mm., containing about 3% of 4-cyanofluorenone, which remained undissolved by treatment with warm ether and then crystallised from alcohol in long, yellow needles, m. p. 243—244° (Borsche and Sander, loc. cit., give 240°).
Alternatively, the distillate was dissolved in warm sodium hydroxide solution; the 4-cyanofluorenone remained undissolved, and the filtered solution, when poured into dilute hydrochloric acid, gave 2'-cyanodiphenyl-2-carboxylic acid, which crystallised from alcohol in stout needles, m. p. 173° (Werner and Siguet, Ber., 1904, 37, 4311, give 170—172°).

Diethylaminoethyl 2'-cyanodiphenyl-2-carboxylate was prepared in a similar way to the diphenyl-4-carboxylate. The hydrochloride was obtained as white plates, m. p. 189° (Found: HCl, 10-3. C_{20}H_{22}O_{2}N_{2}HCl requires HCl, 10-2%), not hygroscopic though moderately easily soluble in water.

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2 : 4 : 7-Trinitrofluorenone. By FRANK BELL.

The interest attaching to heavily substituted fluorenones (Bell and Robinson, J., 1927, 1695) directed attention to the statement that fluorenone on nitration yields the 2 : 3 : 7-trinitro-derivative (I) (Schmidt and Bauer, Ber., 1905, 38, 3758). Apart from the exceptional orientation of this compound, its oxidation to yield 3 : 4-dinitrobenzoic acid called for further examination (for normal method of oxidation of fluorenone derivatives, see Moore and Huntress, J. Amer. Chem. Soc., 1927, 49, 1324).

4-Nitrofluorenone, prepared from 4-nitrophenanthraquinone (Schmidt and Bauer, ibid., p. 3741; Morgan and Thomason, J., 1926, 2695), was nitrated as follows: 1.25 g. in nitric acid (d 1.5; 25 c.c.) were warmed on a steam-bath for 2 hours, cooled, and poured into water. The precipitate after several crystallisations from benzene had m. p. 175° (Found: C, 49.5; H, 1.6. C13H5O7N3 requires C, 49.5; H, 1.6%). This trinitro-derivative must therefore be 2 : 4 : 7-trinitrofluorenone (II).

Fluorenone nitrated by the method of Schmidt and Bauer (loc. cit.) gave a product, m. p. 176° after repeated crystallisation from acetic acid or benzene (Found: C, 49.9; H, 1.8%). When mixed with the 2 : 4 : 7-trinitrofluorenone described above, it melted at the same temperature. Oxidation of this trinitro-derivative gave a very small amount of an impure acid, m. p. 165—170°. The m. p. of the purified acid would obviously exceed that of 3 : 4-dinitrobenzoic acid (164°).—BATTERSEA POLYTECHNIC, S.W.11. [Received, June 8th, 1928.]