THE SYNTHESIS AND RESOLUTION OF TRISUBSTITUTED METHYLAMINES OF THE TYPE $R_1R_2R_3\cdot\text{NH}_2$.
THE ATTEMPTED RESOLUTION AND SOME REACTIONS OF ACENAPHTHENOL.

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SECTION I.

INDEX. (Discussion)

I. Introduction.

II. The Preparation of Amines of the Structure $R_1R_2R_3C.NH_2$.

A. Direct amination: a) $-OH \rightarrow NH_2$ 8
b) $-X \rightarrow NH_2$ (where $X=halogen$). 8

B. From Grignard complexes: a) with chloramine 10
b) with $O$-alkylhydroxylamines. 11

C. Hydrolytic methods: a) from isocyanates and isothiocyanates 11
b) from isonitriles 12
c) from $N$-alkyl amides 12
d) from $N$-alkyl phthalimides 12
e) from salts of hexamethylene tetramine. 13

D. Reduction methods: a) from nitro-compounds 14
b) from amides and thioamides 14
c) from cyano-compounds 14
d) from aldehydic substances. 15

E. Rearrangement reactions:

a) The preparation of trisubstituted acetic acids: 16

1. from tertiary alcohols;
   (i) with Grignard reagents 17
   (ii) with ethers. 17
2. from trisubstituted acetophenones. 18
3. from nitriles. 20
4. from esters. 23

b) Rearrangement reactions of derivatives of $R_1R_2R_3C.\text{COOH}$
1. The Curtius reaction. 24
2. The Hofmann reaction. 28
3. The Schmidt reaction. 30
4. The mechanisms of the Curtius, Hofmann and Schmidt rearrangements. 37

III. The Preparation of Optically Active Trisubstituted Methylamines. 42
A. Introduction. 42
B. The resolution of phenyl-p-tolyl-$\alpha$-naphthyl methylamine. 44
C. The preparation of active $\alpha$-methyl-$\omega$-phenyl-$n$-amylamine. 44

IV. The Deamination of Aliphatic Primary Amines. 46

V. Summary of Schemes of Synthesis in Present Experiments. 49

VI. Graphs and Tables:
A. Dispersion curve of $(+)$-$\omega$-methyl-$\omega$-phenyl-$n$-caproic acid in ether. 58
B. Dispersion curve of $(-)$-$\omega$-methyl-$\omega$-phenyl-$n$-caproyl chloride in $\text{CS}_2$. 59
C. Dispersion curve of $(-)$-$\omega$-methyl-$\omega$-phenyl-$n$-amylamine. 60
SECTION II.

INDEX. (Discussion)

I. Introduction. ........................................... 61

II. Formation of Polyacenaphthylene during the attempted Acylation of Acenaphthenol. ....... 63
I. INTRODUCTION.

As is by now well known, racemic secondary alcohols of the general formula \( R_1R_2\text{CHOH} \) may be conveniently resolved into their optically active isomerides by converting them into acid esters of dibasic acids such as phthalic and succinic acids. Alkaloidal salts of these acid esters normally undergo separation into their stereoisomerides, e.g. \( \text{dA1B} \) and \( \text{1A1B} \), when submitted to fractional crystallization from a suitable solvent. In this way, one or both of the active isomerides may be obtained in an optically pure form.

The procedure seems to be of general application and by its means a large number of secondary alcohols have been resolved; these alcohols have been of widely varying types as indicated by the following classification:

1. Purely aliphatic, e.g. \( \text{MeEtCHOH} \) (1)
2. Purely aromatic, e.g. \( \text{Ph.CH(OH)C}_6\text{H}_4\text{Me} \) (2)
3. Mixed aliphatic-aromatic, e.g. \( \text{Me.CH(OH)C}_{10}\text{H}_7 \) (3)
4. Mixed alicyclic-aromatic, e.g. \( \text{Ph.CH(OH)C}_6\text{H}_{11} \) (4)
5. Mixed alicyclic-aliphatic, e.g. \( \text{Me.CH(OH)C}_6\text{H}_{11} \) (5)
6. Hydroaromatic, e.g. \( \text{CH}_2\text{CH} = \text{CH} \\text{CH(OH)} \) (6)
7. Unsaturated aliphatic, e.g. \( \text{Me.CH(OH)CH=CH}_2 \) (7)
8. Unsaturated aliphatic-aromatic, e.g. Ph.CH(OH)CH=CH\text{Me} (8)
9. Heterocyclic, e.g. \( \frac{\text{CH}_2\text{CH}_2}{\text{CH}_2\text{CH}\text{CH}_2\text{OH}} \) (9)
10. Heterocyclic, e.g. \( \frac{\text{CH}_2\text{CH}_2}{\text{CH}_2\text{CH}\text{CH}_2\text{OH}} \) (10)
In view of this successful application of the general method to a wide range of secondary alcohols it becomes somewhat surprising that when the same procedure is applied to tertiary alcohols it has always, except in one instance which will be discussed below, proved fruitless.

Tertiary alcohols, as a rule cannot be converted into their acid esters by the same convenient procedure which is applicable in the case of secondary alcohols, i.e. by heating equimolecular proportions of the alcohol and of acid anhydride, with or without the addition of a molecular proportion of a tertiary base, usually pyridine.

This failure to yield acid esters by direct combination is probably due to more than one cause: (a) the much more pronounced tendency of tertiary alcohols to undergo dehydration to form an unsaturated hydrocarbon, and (b) the much lower reactivity of the hydroxylic hydrogen atom of tertiary alcohols, e.g. methyl-ethyl-n-propyl carbinol at its boiling-point (140°C.) is devoid of action on metallic sodium.

This difficulty can, however, be surmounted by the application of the procedure devised by Tiemann and Kruger (11), in which the tertiary alcohol is first converted into its potassio-derivative before adding it to a solution of the acid anhydride. In the case of phthalic anhydride, this reaction may be represented by the equation:

\[
R_{\text{OK}} + \begin{array}{c}
\text{CO}_2 \text{O} \\
\text{CO} \text{O}
\end{array} \rightarrow \begin{array}{c}
\text{COOR} \\
\text{COOK}
\end{array}
\]
By means of this device, the hydrogen phthalic esters of a number of tertiary alcohols, including methyl-ethyl-n-propyl carbinol, have been prepared, usually in good yields and as readily crystallizable compounds.

Furthermore, these esters can be made to give salts with the commoner alkaloids such as brucine, strychnine and cinchonidine, which recrystallize well from suitable solvents.

Yet, whereas in the case of secondary alcohols a quite pronounced difference in solubility between the diastereoisomeric salts, of which the mixture is presumably composed, is observed, this was not found to be true when tertiary alcohols were investigated. Very recently, Doering and Zeiss (12) have claimed to have resolved methyl-ethyl-isobutyl carbinol through the fractional crystallization of the brucine salt of its hydrogen phthalic ester, and to have obtained the following specific rotations for the active alcohol: \([\alpha]_D^{27} -2.6\) and \([\alpha]_D^{28} +1.5^\circ\) (\(c = 5\%\); in 95\% ethanol).

But in the many other attempts at resolving tertiary alcohols by this method, the various fractions obtained in the recrystallizations of the alkaloidal salts have invariably yielded an optically inactive hydrogen phthalic ester after removal of the alkaloid by the usual method of decomposition.

This failure has been met with in numerous cases in which the acid, the alkaloid and the solvent had been varied.

This behaviour is so uniform that it is difficult to account for it on the assumption that all the various
diastereoisomeric salts form "mixed crystals" under the different experimental conditions employed.

There is one obvious difference between the structures of secondary alcohols (and their corresponding acid esters) which undergo optical resolution, and of tertiary alcohols, which do not: the former contain a hydrogen atom attached to the carbon atom which gives rise to the molecular dissymmetry, and the latter do not. This difference has been pointed out by Lowry (13), who suggested that the hydrogen of the =CHOH radical may play an essential part in the resolution, perhaps by checking "free rotation":

\[
\begin{align*}
\text{R}_1 & \quad \text{H} \quad \text{O} \\
\text{R}_2 & \quad \text{O} - \text{C} - \text{R}_3
\end{align*}
\]

However, the formation of a hydrogen bond to C-H is nowadays regarded as occurring in very few, if any, cases. On the other hand, some little support for the idea may be derived from a consideration of the behaviour of dl-α-terpineol (I): in this racemic tertiary alcohol the molecular dissymmetry is due to an asymmetric carbon atom other than that to which the hydroxyl group is attached. The hydrogen phthalic ester of this tertiary alcohol yields salts with brucine, strychnine, cinchonidine and morphine, each of which, by fractional crystallization has readily yielded either the d- or the l-α-terpinyl hydrogen phthalate in an optically pure condition (14).
A second possible explanation for the difficulties encountered in attempts to resolve tertiary alcohols through their hydrogen-phthalic esters has been put forward by Hewitt and Hughes (29). It is based on the assumption that the alkyl group R is transferred from the oxygen atom in one carboxyl group to the other oxygen atom:

\[
\begin{align*}
\text{R} & \quad \text{O} \\
\text{O} & \quad \text{C} - \text{O} \\
\text{O} & \quad \text{C} - \text{O} \\
\text{O} & \quad \text{C} - \text{O} \\
\end{align*}
\]

Unfortunately, this hypothesis does not explain why the alkyl group of secondary alcohols particularly those in which the substituents are strongly electron-releasing (e.g., p-methoxybenzhydrol) should not behave in this way as well.

There is another compound which contains a hydroxyl group attached to a tertiary carbon atom, and which has been resolved. It is 9-benzyl-oxanthrone-2-carboxylic acid (II); in this case, however, the resolution was not carried out via the -OH group. Instead, fractional crystallization of the brucine salt of the acid itself was found to give the optical isomers (15).

An argument against Lowry's theory may be found in the fact that when the hydroxyl group of tertiary alcohols is
replaced by -COOH, a compound is obtained which is readily resolvable. Conant and Carlson (16) succeeded in resolving an acid of the type R1R2R3C.COOH through the fractional crystallization of one of its alkaloidal salts.

There is a third type of compounds which contains a functional group attached to an asymmetric tertiary carbon atom, viz. trisubstituted methylamines of the structure R1R2R3C.NH2. By similarity with trisubstituted acetic acids they should be resolvable, and if this were the case, the deamination of such an optically active amine might conceivably give rise to the formation of an optically active tertiary alcohol.

A thorough search in the literature showed that no resolution of a compound of the type R1R2R3C.NH2 had ever been tried, although amines of the structure R1R2CHNH2 have been successfully resolved, e.g. n-C8H13.CHNH2.CH3 (17).

It was accordingly decided to attempt the preparation and optical resolution of trisubstituted methylamines with the object of deaminating the active amine. Unfortunately, the difficulties encountered were such that the investigation became mainly a search for methods of synthesising the required amines, and it was not possible to carry out a thorough study of the deamination reaction.
II. THE PREPARATION OF AMINES OF THE STRUCTURE $R_1R_2R_3C\cdot NH_2$.

Whereas numerous primary amines of the type $R_1R_2CH\cdot NH_2$ have been prepared and examined, a search in the chemical literature showed that not more than one or two representatives of the type $R_1R_2R_3C\cdot NH_2$ had actually been prepared, and then only in unsatisfactory yields.

There is an appreciable number of methods which might be expected to lead to the synthesis of such trisubstituted methylamines but, as will be shown, very few of them can be made to give good yields of the pure product. Many of the standard methods of preparation of primary amines cannot be applied as they automatically lead to amines containing a hydrogen atom attached to the alpha carbon atom. Thus the reduction of oximes can only yield disubstituted methyamines:

$$(R_1R_2)C=NH \rightarrow (R_1R_2)CH\cdot NH_2$$

In the survey of preparative methods given below, particular emphasis will be laid on their applications to the work described in this dissertation.

Possible Methods of Preparation

A. Direct Amination.

B. From Grignard Complexes.

C. Hydrolytic Methods.

D. Reduction Methods.

E. Rearrangement Reactions.
A. Direct Animation.

a) The replacement of hydroxyl groups by amino or alkyl-amino groups has attracted great technical interest since the discovery by Sabatier of a suitable catalyst for the reaction. The lower alcohols are converted to amines by reaction with ammonia or with primary or secondary amines in the vapour phase over dehydrating catalysts such as $\text{ThO}_2, \text{Al}_2\text{O}_3, \text{W}_2\text{O}_5$ etc.

In recent times, this method has been refined through the use of improved catalysts and conditions (56). Even the preparation of the higher primary, secondary and tertiary amines has succeeded. Thus the higher fatty alcohols yield the corresponding amines when heated in a sealed tube at 300-400°C, under 50 atmospheres pressure with aluminium oxide as catalyst. However, even under the best experimental conditions, a mixture of various amines is invariably obtained. Ethyl alcohol, for example, gives a mixture of mono-, di- and triethylamines when it is heated with ammonium halides at 350-360°C. (18). Since the reaction obviously could not be carried out easily except in industrial laboratories, it was not investigated any further.

b) If the alcohol is first converted into one of the corresponding halides, the amine formation takes place more readily.

The reaction $R.X + \text{NH}_3 \rightarrow R.\text{NH}_2.X$ is of general application in the aliphatic series, but many other reactions
occur subsequently to this primary reaction. Excess ammonia liberates primary amines from the addition product, which reacts anew with the alkyl halide to form a secondary amine. In the same manner, a tertiary amine is formed from the secondary, and from the tertiary, finally, a certain amount of quaternary ammonium halide. The components of the reaction mixture, which form under all conditions, are more easily separated and obtained pure the larger the radical \( R \) is, because the difference in the boiling-points of the free bases is then greater.

Either the alkyl chloride, bromide or iodide can be used, although the iodide usually reacts the most rapidly; a tertiary alkyl iodide, however, such as \( \text{Me}_3\text{C-}I \), gives no amine but merely loses hydrogen iodide to form the olefine, e.g. \( \text{Me}_2\text{C-}I \to \text{Me}_2\text{C} = \text{CH}_2 \).

The ease with which the reaction takes place depends on the nature of the groups present in the halide molecule. Thus, whereas triphenyl chloromethane yields triphenylmethyamine on merely passing ammonia gas through its solution in benzene, methyldiphenyl chloromethane must be allowed to stand in the presence of liquid ammonia in a closed vessel for over a week before giving rise to the amine (19).

In the present experiments it has been found that neither \( \alpha \)-methyl-\( \omega \)-ethyl-\( n \)-amyl chloride nor \( \alpha \)-methyl-\( \alpha \)-phenyl-\( n \)-amyl chloride reacts with concentrated aqueous ammonia or gaseous-
ammonia, whereas the conversion of phenyl-p-tolyl-α-naphthyl chloromethane into the corresponding amine proceeds quite readily.

The results of Lebeau (20) and Chablay (21) on the reaction of sodamide with alkyl halides indicate that saturated and unsaturated hydrocarbons are formed principally, and only small amounts of amines. Shreve and Rothenberger (22), on the other hand, using a different method of preparing their sodamide, have found that hexylamine may be obtained in 75% yield from hexyl bromide. The preparation of the sodamide followed the procedure of Vaughn, Vogt and Nieuwland (23) in which sodium is treated with liquid ammonia in the presence of iron nitrate as catalyst.

When the two substituted amyl chlorides mentioned above were heated in the presence of sodamide, the quality of which had appeared satisfactory in other experiments e.g. the cleavage of acetophenones, no formation of amine resulted.

---

B. From Grignard Complexes.

a) With chloramine:

Grignard complexes in solution can react with chloramine in two ways: (i) $\text{RMgX} + \text{NH}_2\text{Cl} \rightarrow \text{RNH}_2 + \text{MgCl}$

(ii) $\text{RMgX} + \text{NH}_2\text{Cl} \rightarrow \text{RCI} + \text{MgXNH}_2$

If $R$ represents one of the lower alkyl groups, it is
mainly reaction (ii) which takes place, and one only obtains the halide, but when \( R \) is a heavier group, there is increased tendency for reaction (i) to occur (24).

b) With O-alkylhydroxylamine:

Another use of the Grignard reagents in the preparation of primary amines lies in the interaction with O-alkylhydroxylamines to give good yields of primary amines according to the equation:

\[
RONH_2 + R'MgX \rightarrow R'NH_2 + ROMgX.
\]

The yields depend on the nature of \( X \), decreasing strongly from chlorine to iodine (25).

In view of the practical impossibility of preparing Grignard reagents from tertiary alkyl halides, neither of the above methods could be tried.

C. Hydrolytic Methods.

a) The alkaline hydrolysis of isocyanates, prepared by the action of potassium cyanate on alkyl sulphates (Wurtz's method) is merely of historical interest and no longer used for practical purposes.

Isothiocyanates can be hydrolysed with acids to yield primary amines (26); with hydrochloric acid at 100°C, the following reaction takes place:

\[
R-N=C=S + 2H_2O \rightarrow RNH_2 + CO_2 + H_2S
\]

whereas if the reaction is carried out in the cold with concentrated sulphuric acid, the hydrolysis stops at an intermediate stage with formation of COS.
b) Isonitriles too give pure primary amines when heated with hydrochloric acid, formic acid being split off:

\[ R_2NC + 2H_2O \rightarrow R.NH_2 + H2CO \]

c) Substances in which the nitrogen atom is directly linked to both an alkyl and an acyl group (either formed through alkylation of amides or through acylation of amines) may yield amines on hydrolysis:

\[ CH_3COOH + H_2N.C_3H_7 \rightarrow CH_3CONH.C_3H_7 \rightarrow CH_3COOH + C_3H_7.NH_2 \]

\[ CH_3CONH_2 + HO.C_3H_7 \]

d) Alkyl phthalimides can be hydrolysed by acids into phthalic anhydride or phthalic acid, and primary amines (27). They may be prepared by one of three methods:

(i) By the action of phthalic anhydride on amines (28); since one actually starts with the base obtained in the final hydrolysis the main advantage of this method is that it enables one to prepare alkyl phthalimides in which the alkyl radical contains groups which react readily, e.g., halogen, nitrile etc.; these groups can be submitted to any desired transformation while the amino-group remains protected (29).

(ii) In a few cases, by the action of phthalic anhydride on isothiocyanates. Thus allylamine can be obtained in very good yield from allyl isothiocyanate: (30)
(iii) By the action of potassium phthalimide on substances containing a mobile halogen atom (Gabriel's Method) (31):

$$(\text{C}_6\text{H}_4)(\text{CO})_2\text{NK} + \text{R.Hal} \rightarrow (\text{C}_6\text{H}_4)(\text{CO})_2\text{NR} + \text{K.Hal}$$

The reaction is similar to the alkylation of ammonia by halogenated substances, but has the advantage of giving only primary amines. It is not always necessary to isolate the potassium phthalimide; one can occasionally obtain the alkyl phthalimide by heating the halogeno-compound and phthalimide in the presence of sodium carbonate (32). As the reaction appeared quite promising, and the reagents could be prepared easily, it was attempted to react potassium phthalimide with either $\alpha$-methyl-$\alpha$-ethyl-$n$-amyl chloride or $\alpha$-methyl-$\alpha$-phenyl-$n$-amyl chloride, but no reaction was observed.

e) Hydrolysis of tertiary salts of hexamethylene tetramine (Dèlepine's Method): hexamethylene tetramine, a tertiary base, gives addition products with some derivatives from alcohols, such as alkyl iodides and sulphates. These complexes are converted into primary amines by hydrolysis with hydrochloric acid:

$$\text{C}_6\text{H}_{12}\text{N}_4\text{RI} + 3\text{HCl} + 6\text{H}_2\text{O} \rightarrow 6\text{HCHO} + 3\text{NH}_4\text{Cl} + \text{RNH}_2\cdot\text{HI}$$

If the reaction is carried out in alcoholic solution, the formaldehyde is eliminated through the formation of methylal and thus prevented from starting secondary reactions (33,34).
D. Reduction Methods.

Amines are the ultimate product of the reduction of all kinds of nitrogenous compounds.

a) Reduction of nitro-compounds: in the aliphatic series, the nitro-compounds are prepared only with difficulty and are not readily reduced; the method in this case has therefore only theoretical interest, as opposed to its application to aromatic substances, when it is widely used.

b) Reduction of amides and thioamides: this method has only limited applicability in view of the tendency of the amide group to react in a different direction, hydrolysing at the same time as becoming reduced, consequently giving aldehydes and even alcohols instead of amines:

\[
\text{R,CONH}_2 \xrightarrow{\text{NH}_3 + \text{R,CHO}} \text{NH}_3 + \text{R,CH}_2\text{OH} \quad (i)
\]

\[
\text{R,CONH}_2 \xrightarrow{\text{R,CH}_2\text{NH}_2} \quad (ii)
\]

When acetamide is treated with sodium and alcohol, an 80% yield of ethylamine is obtained, but on using higher homologues reaction (i) tends to overshadow the other mechanism, and above caproamide one obtains only the alcohol.

c) Hydrogenation of cyano-compounds: nitriles can be hydrogenated either by the use of nascent hydrogen or catalytically. Acid and alkaline reducing agents tend to give only the primary amine: \( \text{R,CN} + 4\text{H} \rightarrow \text{R,CH}_2\text{NH}_2 \)

On the other hand, reducing agents which are practically neutral, such as Devarda's alloy, in addition to producing
primary amines, also yield secondary amines. The tendency of the -CN group to break down and give rise to ammonia is a further difficulty often encountered. Isonitriles tend to give the same products as the nitriles themselves.

Isocyanates cannot be hydrogenated catalytically because of the ease with which they undergo hydrolysis.

d) Hydrogenation of aldehydic substances:

(1) Imines: since these are formed as intermediates in the reduction of nitriles, the products from their hydrogenation are the same as those obtained with nitriles.

(ii) Oximes: the hydrogenation of oximes in acid solution yields only primary amines, whereas in neutral solution one also obtains secondary and tertiary bases in varying amounts. These results are parallel to those obtained when starting with nitriles; the reaction depends on the same mechanism and goes through the same intermediate stage, viz. the imine.

(iii) Hydrazones and azines: their hydrogenation can give rise to either substituted hydrazines or to amines:

\[ \text{R.CH=N.NH Ph} \rightarrow \text{RCH}_2\text{NH.NH Ph} \rightarrow \text{RCH}_2\text{NH}_2 + \text{PhNH}_2 \]

In alkaline solutions, the reactions stops at the first stage, whilst in acid medium primary amines are formed. (35). As can be seen from the examples given above, the primary amines obtained through reduction methods nearly always contain the amino-group attached to a primary or secondary
carbon atom and consequently these methods were unsuitable for preparing trisubstituted methylamines.

E. Rearrangement Reactions.

There are three rearrangement reactions which can be used for the preparation of trisubstituted methylamines. Known as the Curtius, Hofmann and Schmidt reactions, they are carried out on acid azides, acid amides and on carboxylic acids themselves, respectively.

The first two have now been successfully applied in the degradation of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproic acid, but the Schmidt reaction unexpectedly led mainly to the formation of aniline.

In view of the major importance of these rearrangement reactions for the present work, separate sections will be devoted to each one of them (sect. "E" 1 to 4 incl.).

However, since these reactions require acids or acid derivatives as starting materials, various methods for the preparation of such compounds had to be investigated (sect. "a" 1 to 4 incl.).

a) The Preparation of Trisubstituted Acetic Acids.

Of the various methods available for the preparation of carboxylic acids, only four were considered worth being examined in detail for the preparation of trisubstituted acetic acids.
The starting substances for these were:

1. Tertiary alcohols
2. Trisubstituted acetophenones
3. Nitriles
4. Esters.

-------------

1. From tertiary alcohols.

(i) Certain Grignard reagents derived from alkyl halides are known to react with carbon dioxide to form a product which on hydrolysis yields a carboxylic acid:

\[ \text{RMgX + CO}_2 \rightarrow \text{RCOOMgX} \rightarrow \text{RCOOH}. \]

This method is successful for the preparation of trimethyl-acetic acid (36), but with slightly higher homologues the yields very rapidly decrease, mainly because of the difficulty in forming the Grignard reagent (37).

In the present investigations, various attempts were made to induce reaction between either \( \alpha \)-methyl-\( \alpha \)-ethyl-\( \alpha \)-amyl chloride or \( \alpha \)-methyl-\( \alpha \)-phenyl-\( \alpha \)-amyl chloride and magnesium, but all failed.

(ii) A rather more suitable procedure to convert a tertiary alcohol into the corresponding carboxylic acid consists in preparing first its potassic-derivative by the action of a sodium-potassium alloy in an atmosphere of nitrogen, and then treat it with carbon dioxide to give the alkali salt of the acid (38):
This method has now been tried on methyl-(α-methyl-α-phenyl-n-amyl) ether. It was found that the liquid sodium-potassium alloy was difficult to handle and that the final yield of the acid was too small to make the procedure worth applying.

2. From trisubstituted acetophenones.

This method is based on the preparation of trisubstituted acetamides by the cleavage of aryl-t-alkyl ketones through the action of sodamide.

Haller and Bauer (39, 40, 41) have shown that in some cases it is possible to decompose trisubstituted acetophenones by heating them with finely powdered sodamide in a dry inert solvent. The following reaction is supposed to take place:

\[
R_1R_2R_3\text{CO.C}_6\text{H}_5 + \text{NaNH}_2 \rightarrow R_1R_2R_3\text{CO.NHNa} + \text{C}_6\text{H}_6
\]

and, following addition of water:

\[
R_1R_2R_3\text{CO.NHNa} + \text{H}_2\text{O} \rightarrow R_1R_2R_3\text{CO.NH}_2 + \text{NaOH}.
\]

This view receives support from the isolation of benzene, when another solvent is used as reaction medium, and of the appropriate amide.

However, during the present study of the action of sodamide on α-methyl-α-ethyl-n-caprophenone, it has been found that although the main reaction seems to go along the lines indicated above, there was also some cleavage on the other side of the carbonyl group. This was indicated by the
isolation of a small amount of benzamide from the reaction product:

$$R_1R_2R_3CO.C_6H_5 + NaNH_2 \xrightarrow{\text{water}} C_6H_5CONH_2 + R_1R_2R_3CH,$$

where $R_1, R_2$ and $R_3$ are methyl, ethyl and n-butyl respectively.

In general, this splitting up to give substituted acetamides proceeds quite readily in benzene when the tertiary alkyl group is small, but when larger groups are introduced, higher boiling solvents such as toluene and xylene must be used, and even then the yields tend to become much lower.

The required ketone itself is prepared by systematically replacing the two activated hydrogen atoms adjacent to the carbonyl group in propiophenone (when one of the groups in the t-alkyl radical is to be methyl). This is best carried out by forming the sodio-derivative through the interaction of the original ketone with sodamide in an inert solvent, e.g., benzene, and then adding an alkyl halide. The main difficulty in this procedure lies in separating reaction product from unchanged reactant, as their physical constants are extremely near to one another and their chemical properties alike. To mention one instance, the boiling point of propiophenone is $115^\circ/20$ mm, and that of $\alpha$-butyl propiophenone $123^\circ/23$ mm. In order, therefore, to make sure that one is using pure reagents in the subsequent stages, only a relatively small fraction of the product can be used. One way to avoid this difficulty is, of course, to introduce large radicals, but when this was
tried out, it was found that the molecule thus obtained, viz., \( \alpha \)-methyl-\( \alpha \)-benzyl-n-caprophenone, do not react at all readily with sodamide.

3. From Nitriles.

The preparation of trisubstituted acetonitriles and their subsequent hydrolysis to carboxylic acids of the type \( R_1R_2R_3C\cdot COOH \) was found to be the most suitable method for obtaining the required acids in reasonable quantities. The general method of preparation of the nitrile, \( \alpha \)-methyl-\( \alpha \)-phenyl-n-capronitrile, was rather similar to that employed in the synthesis of trisubstituted acetophenones. Starting with benzyl cyanide, addition of one equivalent of sodamide followed by a solution of the calculated amount of dimethyl sulphate in benzene, yielded hydrafroponitrile. It was found impossible to separate these two nitriles by fractional distillation, as their boiling points lay within two degrees of each other at 13 mm. pressure. Use was therefore made of the property of benzyl cyanide to react with sodium ethoxide and benzaldehyde to give the crystalline benzalbenzylcyanide under conditions which leave hydrafroponitrile unaffected (42); this made it possible to separate the two homologous cyanides.

To a solution of the pure product in benzene were added simultaneously the calculated amounts of n-butyl bromide and sodamide, using Ziegler and Ohlinger's method (43), and this gave reasonably good yields of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-capronitrile.
The various attempts at hydrolysing this compound brought to light some interesting features. The hydrolysis of mono- or di-substituted acetonitriles usually proceeds quite readily in both acid and alkaline media. By varying the experimental conditions the hydrolysis can be arrested at the amide stage or be carried through to completion to give the acid. Thus benzyl cyanide can be converted to phenyl-acetamide by the action of concentrated sulphuric acid at room temperature, whereas refluxing it with 70% sulphuric acid yields phenylacetic acid (44). However, when the last hydrogen of substituted acetonitriles is replaced by an alkyl or aryl group, hydrolysis becomes much more difficult. With some of the lower members one can still separate appreciable amounts of the amide, as shown by Bodroux and Taboury (45), who, after having refluxed diethyl-phenyl-acetonitrile in amyl alcoholic potash for several hours, obtained 80% of the amide. On the other hand, dibutyl-phenyl-acetonitrile gave only an extremely small amount of amide when refluxed in the same alkaline medium, and was not affected by 85% sulphuric acid. In the case of triphenylacetonitrile, long boiling with alcoholic potash resulted in very limited hydrolysis; this takes place more readily on heating the nitrile for several hours with glacial acetic acid and fuming hydrochloric acid at 200-220°C (46).

The nitrile which was prepared in the series of
experiments now to be described, viz. \( \alpha \)-methyl-\( \alpha \)-phenyl-n-capronitrile, was found to be unaffected by the following reagents: concentrated hydrochloric acid and phosphoric acid (cold and hot), a mixture of glacial acetic and concentrated sulphuric acids, and cold concentrated sulphuric acid; hot concentrated sulphuric acid was found to decompose the acid. Only refluxing for many days with alcoholic KOH led to the formation of both the amide and the acid.

Although the reactions involving the substitution of the methylenic hydrogen atoms of benzyl cyanide were eventually found to be the most suitable for the preparation of the particular trisubstituted acetonitrile required, other preparative methods too were investigated. The reaction of an organic halide and a metallic cyanide was first carried out by Wohler and Liebig (47) who obtained benzoyl cyanide by distillation of benzoyl chloride over mercuric cyanide. Conversion of alkyl halides to the nitriles by the use of the cyanides of alkali metals was accomplished by Williamson in 1854 (48), and the action of the heavy metal cyanides was studied by Gautier (49).

The possible action of sodium cyanide on \( \alpha \)-methyl-\( \alpha \)-ethyl- and on \( \alpha \)-methyl-\( \alpha \)-phenyl-n-amyl chlorides was examined, but only either the unchanged chloride or the corresponding alcohol, according to the reaction medium, could be isolated from the product.
The simple metathetical reaction involving direct esterification of an alcohol with hydrocyanic acid has only recently been demonstrated with certainty. Such reactions had been reported to take place in the vapour phase over dehydration catalysts such as alumina or thoria at 300°C (50). However, the actual reagent in these cases may have been either the olefine or the ether derived from the alcohol. Both derivatives are known to react with hydrogen cyanide. In a more recent report, it is stated that 2-butene-1,4-diol will react with HCN in the liquid phase at 60–80°C; the catalyst in this case consists of ammoniacal cuprous chloride dissolved in dilute hydrochloric acid:

\[
\text{HO,CH}_2\text{CH = CH} \cdot \text{CH}_2\text{OH} + 2\text{HCN} \rightarrow \text{CNCH}_2\text{CH} = \text{CHCH}_2\text{CN} + 2\text{H}_2\text{O}
\]  
(70% yield)

Other reactive alcohols, such as allyl and benzyl alcohols, react similarly.

4. From Esters.

Polgar and Robinson (51) have prepared trisubstituted acetic acids by a method which bears a fundamental resemblance to the one on which is based the preparation of fully substituted acetonitriles. They synthesised methyl-n-decyl-n-dodecylacetate by reacting its sodium enolate with methyl iodide. It was found that the trisubstituted acetic acids obtained on hydrolysis of the esters contained unchanged disubstituted acetic acid and full purification was long and
tedious. Eventually the pure acids were obtained by fractional crystallization of their amides.

As this method did not appear more promising than the one described in section 3, no attempts were made to try it out in the preparation of the compounds aimed at in the present work.

---

b) Rearrangement Reaction of Derivatives of trisubstituted Acetic Acids.

(i) The Curtius Reaction.

The Curtius reaction, which consists mainly in the decomposition of acid azides to isocyanates and nitrogen, can be used for the conversion of a carboxyl group into an amino group:

\[ R\text{COOH} \rightarrow R\text{CON}_3 \rightarrow R\text{NCO} \rightarrow R\text{NH}_2 \]

The reaction is, in fact, a preparative method for isocyanates and for compounds derivable from isocyanates such as urethanes, ureas, amides and amines.

The rearrangement of acid azides into isocyanates was originally discovered by Curtius (52) while investigating the properties of some derivatives of hydrazoic acid, but he did not at that time realise its true nature.

Acid azides are commonly prepared by treating acid hydrazides in cold aqueous solution with nitrous acid. The required hydrazides are prepared from esters by reaction with
hydrazine. Acid azides can also be made by treating acid chlorides with sodium azide.

\[ R\text{-COOCH}_3 + \text{NH}_2\text{NH}_2 \rightarrow R\text{CONHNH}_2 + \text{CH}_3\text{OH} \]
\[ R\text{-CONHNH}_2 + \text{HNO}_2 \rightarrow R\text{CON}_3 + 2\text{H}_2\text{O} \]
\[ R\text{-COCl} + \text{NaN}_3 \rightarrow R\text{-CON}_3 + \text{NaCl} \]

Whereas the hydrazide method was the most widely used one in the original experiments, the acid chloride - sodium azide method too was known and used (53). The second procedure has become more widely applied since Naegeli and his fellow workers (54) have shown that not only can it be employed in most cases where the hydrazide method is suitable, but that it is often preferable.

The reaction between an acid chloride and sodium azide can be carried out under anhydrous conditions according to procedures described by Schroeder (55), Forster (56) and Naegeli (57), or with aqueous sodium azide according to Lindemann (58).

The dry method is the only practical one for highly reactive chlorides, such as acetyl chloride, or for the preparation and rearrangement of very unstable azides; it provides a means of carrying out the reaction sequence

\[ \text{RCOOH} \rightarrow \text{RCOCl} \rightarrow \text{RCON}_3 \rightarrow \text{RNCO} \rightarrow \text{RNH}_2 \]  in the same reaction vessel as one multiple step. On the other hand it is not a reliable method, for many acid chlorides are inert to dry sodium azide. The reaction is sometimes difficult to
control, since the heating required for the formation of the azide may also cause rearrangement; the two exothermic reactions occurring simultaneously sometimes get out of control. The use of aqueous sodium azide requires the isolation of the azide as an extra operation, but the reaction is more reliable, easier to control and usually much faster.

In the dry method, the acid chloride, dissolved in an inert solvent, is stirred and/or heated with powdered sodium azide, the quality of which has been known to affect the yields of azide very appreciably (57). Part or all of the azide may be converted to isocyanate at the same time, a step which is completed by refluxing. This product may then either be isolated or converted to the urea, urethane or amine, by an appropriate method.

Benzene (59), toluene (60), xylene (59) and many other solvents have been used in the dry method. Ethyl ether, although occasionally used (61), suffers from the disadvantage of having a boiling-point which is below the decomposition temperature of many azides.

In the wet method, a concentrated aqueous solution of sodium azide is stirred into a solution of the acid chloride in an organic solvent miscible with water, usually acetone, which appears to be the most generally satisfactory (62). The reaction mixture is normally kept at or below room temperature. The azide is precipitated completely by further dilution with water.
The readiness with which azides rearrange varies from rapid, spontaneous reaction at room temperature (63) to complete inertness (64). However, in the vast majority of cases the rearrangement can be brought about by refluxing in a solvent boiling at about 80°C.

The Curtius reaction has been successfully applied to carboxylic acids of most kinds, either starting with their hydrazides or with the acid chloride. The preparation of azides by the action of sodium azide on the acid chloride goes more readily than the alternative method in the case of very low-molecular-weight acids, whose hydrazides and azides are difficult to extract from water; by this method acetyl chloride is converted to methyl isocyanate through the azide in 60-72% yield (65).

Low-molecular-weight esters react quite readily with hydrazine, but heavier ones must be coerced. Branchings of the carbon chain alpha to the ester group retards hydrazide formation; in contrast with ethyl acetate, which reacts spontaneously with hydrazine at room temperature, ethyl pivalate requires a temperature of 140°C, and adamantane 1,3-dicarboxylic ester (I) failed to form a hydrazide under all conditions that were tried (66).

![Chemical structure](attachment:structure.png)
In view of this fact, no attempt was made to prepare the hydrazide of $\alpha$-methyl-$\alpha$-phenyl-$n$-caproic acid, especially as it was found that the Curtius reaction went quite smoothly via the acid chloride.

----------

(ii) The Hofmann Reaction.

In the Hofmann reaction an amide is converted to an amine with one less carbon atom by treatment with bromine (or chlorine) and alkali (67). The reaction

$$RCONH_2 + Br_2 + 4OH^- \rightarrow R.NH_2 + CO_2 + 2Br^- + 2H_2O$$

is applicable to the preparation of amines from amides of aliphatic, aromatic, arylaliphatic and heterocyclic acids.

The first product of the reaction was identified by Hofmann as being a N-haloamide, which was found to react with alkali to give unstable salts (68):

$$RCONH_2 + Hal_2 + OH^- \rightarrow RCONHHal + Hal^- + H_2O$$

$$RCONHHal + OH^- \rightarrow [R.CONHal]^- + H_2O$$

This unstable compound then rearranges in such a way that the organic residue migrates from the carbon to the nitrogen atom, to yield an isocyanate $(RCONHal)^- \rightarrow RN=CO + Hal^-$. In the presence of water and an excess of alkali, the isocyanates are hydrolyzed to amines:

$$[R.NHCOO]^- + OH^- \rightarrow R.NH_2 + CO_3^-$$

Isocyanates derived from some of the higher aliphatic amides react more rapidly with the haloamide salts than with
water and alkali, so that, when these amides are subjected to the Hofmann reaction in aqueous medium, only small amounts of amines are formed. Although amines arise from the hydrolysis of the alkyl acyl ureas formed, they are largely oxidised to nitriles by the excess of hypobromite present:

\[
R_NHCONHCO_R + H_2O \rightarrow R_NH_2 + R_CONH_2 + CO_2
\]

\[
RCH_2NH_2 + 2 OHal^- \rightarrow R_CN + 2 Hal^- + 2H_2O
\]

Such amides can, however, be readily converted into the required amine by using an alternative way of carrying out the Hofmann reaction (see further).

**Methods**

1. Hofmann carried out the degradation of acid amides by dissolving them in an equimolecular amount of bromine and then adding caustic potash. The lower aliphatic amides were converted into the amine in yields above 70%, but while hexylamine was obtained in 70% yield, heptylamine could only be prepared in 30% yield; the amide of d-phenyl propionic acid gave less than 30% of d-phenylethylamine (67).

2. Hoogewerf and Van Dorp (69, 70) improved the method by dissolving the amide in a very slight excess of cold aqueous hypohalite solution, followed by rapid warming.

3. Although the method of Hoogewerf and Van Dorp is generally used for the degradation of simple amides, it fails to give good yields when applied to the amides of the higher aliphatic acids. Such amides are, however, smoothly
converted to methyl carbamates if bromine (1 mole) is added with thorough mixing to a methanolic solution of the amide (1 mole) containing sodium methoxide (2 moles):

\[ \text{RCONH}_2 + \text{Br}_2 + 2\text{NaOCH}_3 \rightarrow \text{RNCOOCH}_3 + 2\text{NaBr} + \text{CH}_3\text{OH} \]

Warming the solution completes the reaction in a few minutes. The urethane is isolated easily from the reaction mixture, and the amine may be obtained in good yields by saponification with sodium, potassium or calcium hydroxide (71, 72).

In the present experiments, the amide of \( \alpha \)-methyl-\( \alpha \)-phenyl-\( n \)-caproic acid was reacted with sodium hypochlorite and gave a 10% yield of \( \alpha \)-methyl-\( \alpha \)-phenyl-\( n \)-amylamine.

(iii) The Schmidt Reaction.

The Schmidt reaction covers the interaction between carbonyl compounds and hydrazoic acid in the presence of strong mineral acid. It affords a convenient method for the preparation of primary amines from carboxylic acids, according to the scheme:

\[ \text{RCOOH} + \text{HN}_3 \xrightarrow{\text{H}_2\text{SO}_4} \text{R.NH}_2 + \text{CO}_2 + \text{N}_2 \]

Aldehydes yield nitriles and formyl derivatives of amines, and ketones yield amides:

\[ \text{RCHO} + \text{HN}_3 \xrightarrow{\text{H}_2\text{SO}_4} \text{R.CN} \text{ and } \text{R.NHCHO} \]

\[ \text{RCOR} + \text{HN}_3 \xrightarrow{\text{H}_2\text{SO}_4} \text{RCONHR} + \text{N}_2 \]
The mechanism of the Schmidt reaction has not been established with certainty. Schmidt (73) suggested that the hydrazoic acid is cleaved by the strong mineral acid to nitrogen, and the imide radical (NH). This radical is supposed to add to the carbonyl group, followed by a rearrangement either directly or by a Beckmann transformation of an intermediate oxime to the amide:

\[
\text{RCOR} + \text{HN}_3 \rightarrow \text{RCOR'OH} \rightarrow \text{RCOR'OH} \rightarrow \text{RCONHR}
\]

Oliveri-Mandala (74), on the other hand, suggested that the initial step is probably the addition of hydrazoic acid to the carbonyl group to form the corresponding azide, which would then undergo decomposition to give the products obtained by Schmidt.

\[
\text{RCOR'} + \text{HN}_3 \rightarrow \text{RCOR'(OH)N}_3 \rightarrow \text{RNHCOR'} \text{ or RCONHR'}
\]

There is strong evidence that the Schmidt mechanism is incorrect. If the imino-radical is concerned, the rate of reaction should be controlled by the rate of decomposition of the hydrazoic acid. Schmidt himself found, however, that decomposition does not occur below 30°, and even at 60°-70° it is not complete for five hours, whereas a number of ketones, e.g. cyclohexanone and benzylacetone, react vigorously at 0°C. That the oxime is also not an intermediate as postulated by Schmidt is proved by the fact that the oxime of
α-hydrindone is unchanged by heating with concentrated sulphuric acid at 100°C (75), whereas in the Schmidt reaction α-hydrindone is smoothly converted into hydrocaryl-bostyryl at 40°C (76).

Hurd (77), Briggs and Lyttleton (78) have advanced a mechanism for the Schmidt reaction based on the linear formulation of hydrazoic acid as a resonance hybrid (79), (I) being the stable, and (II) and (III) the reactive forms:

\[
\begin{align*}
\text{I} & : \quad H - N = N^+ = N^+ \\
\text{II} & : \quad H - N = N = N \\
\text{III} & : \quad H - N = N = N \\
\end{align*}
\]

If one considers formula II as being the one involved in the Schmidt reaction, the latter can then be formulated as follows:

\[
\begin{align*}
\text{(a)} & : \quad R - C - N - N = N \\
\text{(b)} & : \quad R - C - N - N = N \\
\text{(c)} & : \quad R - C - N^+ = H + N_2 \\
\text{(d)} & : \quad R - C - NH.R'
\end{align*}
\]

The first phase (a) is the activation of both the ketone or acid and the hydrazoic acid under the influence of the strongly polar sulphuric acid, followed by addition (b) of the active hydrazoic acid molecule to the positive carbon.
of the carbonyl group. The addition complex loses nitrogen (c) and the remaining structure undergoes a further transformation (d) analogous to that postulated for the pinacol-pinacolone and allied transformations. When R in the Schmidt reaction is OH (i.e., carboxylic acid) a carbamic acid is formed which loses carbon dioxide spontaneously and yields the corresponding amine.

The reaction, which is usually carried out in an inert solvent like chloroform and at a temperature of about 40°C, has been applied to many aliphatic and aromatic carboxylic acids, and in each case the corresponding amine was obtained. Although in the original experiments an aqueous solution of hydrazoic acid was used, Oesterlin (80) showed that the much less dangerous and far easier to handle sodium azide could be employed directly.

Using this improved technique, Briggs, DeAth and Ellis (81) showed that the action of hydrazoic acid on podocarpic acid (I), which contains a carboxyl group attached to a tertiary carbon atom (82), led to the formation of the corresponding amine in good yields, so there seems to be little steric effect in the Schmidt reaction.

Similarly, camphoric acid (II) (83) and the isobutyric acid derivative (III) are readily converted to the corresponding amine.
Cinnamic acid yields phenylacetaldehyde, probably through formation of styrylamine (I), rearrangement to the aldimine (II) and subsequent hydrolysis (80):

\[
\begin{align*}
C_6H_5CH=CHCOOH + HN_3 & \rightarrow [C_6H_5CH=CHNH_2] \rightarrow I \\
\left[ C_6H_5CH_2CH=NH \right] & \rightarrow C_6H_5CH_2CHO \\
\end{align*}
\]

Appreciable amounts of aniline are obtained in this reaction but Oesterlin does not put forward any explanation to account for its formation.

In the present experiments it was found that when \( \alpha \)-methyl-\( \alpha \)-phenyl-\( n \)-caproic acid was degraded by the Schmidt method, the only basic product obtained was aniline. This appears to be the only instance in which an aliphatic carboxylic acid does not yield the corresponding amine.

Although the mechanism put forward by Briggs and Littleton (78) may be of general application in those reactions where the degradation proceeds to give the expected product, it does not account for the behaviour of
\( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproic acid when reacted with hydrazoic acid in the presence of concentrated sulphuric acid.

There is insufficient experimental evidence on which to base a possible mechanism for this reaction, but it does appear quite conceivable that there is first formation of the acid azide which then proceeds to lose a nitrogen molecule, as is the case in the Curtius reaction, to form the unstable \((R,\text{CON})\) (I). Normally, this would rearrange to \(R,\text{NCO}\) (II) by migration of the radical \(R\) from carbon to nitrogen. However, in the case under consideration one would have to assume that instead of a link being formed between the tertiary carbon atom and the nitrogen atom, the latter preferentially attaches itself to the phenyl group while at the same time the phenyl-carbon bond breaks down.

The resulting phenyl isocyanate, the smell of which can be recognised during the reaction, would then yield aniline after hydrolysis.

Strong confirmatory evidence for the above hypothetical mechanism was obtained by the isolation of hexene, which would account for the residual part of the molecule.
In connection with this reaction, there are a few points which must be borne in mind. Firstly, there is the fact that when the azide of o-methyl-o-phenyl-n-caproic acid is submitted to the Curtius degradation the expected substituted amylamine is formed. The mechanism in this case is known with certainty and includes the conversion of the unstable compound (I) into the isocyanate (II). Therefore the formation of the new linkage has taken place between the nitrogen and the tertiary carbon atom. Since in the Curtius rearrangement the reaction taken place in a neutral medium, viz. benzene, it would seem that it is the concentrated sulphuric acid which activated the phenyl radical in such a way that it attracts the unshared electrons on the nitrogen atom.

Secondly, the Schmidt reaction has been successfully carried out on methyl-phenyl acetic acid to yield o-phenyl-ethylamine (64). The only difference between this acid and the substituted caproic acid lies in the fact that the alpha hydrogen atom in the former acid has been replaced by an n-butyl group. Since this is usually a rather inert group, it is not easy to see why its presence should exert any great influence on the reactivity of the phenyl radical. It is possible that the butyl group exerts a steric effect.
4. The Mechanism of the Curtius, Hofmann and Schmidt Rearrangements.

When some of the mechanisms put forward to explain the Curtius, Hofmann and Schmidt reactions are examined, the most important step in each case consists in the rearrangement of the unstable \((R,\text{CON})\) residue into an isocyanate \(R,N\text{CO}\), after the group \(R\) has migrated from the carbon to the nitrogen atom:

\[
\begin{array}{c}
\text{R} \cdot \text{C}_\text{O}^0 \\
\text{N}
\end{array} \rightarrow \text{C}_\text{N}^0 \cdot \text{R}
\]

There is considerable evidence of a stereochemical character that this is an intramolecular change, i.e., one in which the fragments of the molecule do not have a separate existence, and that the breaking of the R-C bond and the formation of the N-R bond are simultaneous.

If \(R\) is an optically active group, linked to the remainder of the molecule by the asymmetric carbon atom, asymmetry will be lost, largely or completely, if \(R\) becomes free at any stage. An almost quantitative retention of optical activity has been found by Arcus and Kenyon (85) however, when hydatropamide \((\text{C}_6\text{H}_5)(\text{CH}_3)\text{CHCONH}_2\) undergoes the Hofmann degradation; it was also found (86) that from the analogous Curtius rearrangement of the azide of \((+)-\text{hydantropic acid}\) is obtained \((-)-\alpha\)-phenyl-ethylamine of no less than 99.3% optical purity. Using the Schmidt method of
converting optically active hydrotropic acid into the corresponding amine, Campbell (84) obtained a retention of activity of 99.6%.

Similarly, Wallis and his co-workers have observed absence of racemization during the Curtius, Hofmann and Lossen degradations of optically active derivatives of benzylmethyl-acetic acid, the rotations of the amines obtained from azide, bromoamide and hydroxamate being identical (87,88,89).

A complete preservation of optical activity is also found during the Hofmann degradation of (+)-3,5-dinitro-2-α-naphthylbenzamide (I), where optical activity is due to restriction of rotation about the bond between the benzene and naphthalene nuclei. If at any time during the rearrangement the migrating group had been free, the restriction would have been removed, and at least partial racemization would have occurred (90).

Similar results have been obtained in the Curtius reaction; thus, in the rearrangement of o-(2-methyl-6-nitrophenyl)-benzazide (II), the amine obtained is optically pure (91).

Further, a quantitative yield of tert.-butylmethylamine is obtained from tert.-butylacetamide (92), whereas
reactions in which dissociation occurs invariably lead to tert.-amyl derivatives by rearrangement of the group (92,93), and only one isocyanate is produced when benzylmethylacetazide is degraded in presence of triphenylmethyl radicals (94).

In fact, experimental evidence indicates that the Curtius rearrangement is also unimolecular (95,87,96). Unfortunately, no quantitative studies have been made, as of the Hofmann reaction, to determine the rate-controlling step in the process. In the latter case, it is the release of the halide ion from the haloamide anion which determines the rate of reaction (97,98).

From the examples given above, it is obvious that there can be no doubt regarding the intramolecular character of the migration of the group R from carbon to nitrogen; the group is not free at any stage. Whitmore (99) suggests that this group migrates with its electron pair, but such a process is difficult to visualize without postulating its freedom for a momentary period, and it seems more probable that the binding of R by the unshared electrons of the nitrogen atom and the release of a pair by R to the carbon atom occur simultaneously. These electronic movements may be written:

\[ \text{R} - \text{N}^{\text{\equiv}} - \text{A} \rightarrow \text{R} - \text{N}^{\text{\equiv}} - \text{N} \rightarrow \text{R} - \text{N}^{\text{\equiv}} - \text{C} \]
This is similar to the mechanism suggested for the Beckmann rearrangement where, however, the group A does not leave the molecule. These rearrangements have one feature in common: the group R migrates to an atom which has unshared electrons, and it is easy to envisage its attachment by these electrons as occurring simultaneously with the release of the pair by which it was linked originally.

It has been shown by Wallis and Nagel (88), and by Jones and Wallis (87) that (+)-benzylmethylacetic acid is converted by the Hofmann and Curtius rearrangements into (-)-benzylethylamine. It has also been shown by Kenyon, Phillips and Pittman (100) that (-)-benzylmethylacetic acid has the same configuration as (+)-benzylethylamine. Thus it appears highly probable that in these rearrangements and consequently also in the Schmidt reaction there is not only retention of asymmetry, but also of configuration i.e. no Walden inversion takes place. Although the difficulty of relating rotation to configuration has as yet prevented extensive confirmation of the absence of Walden inversion in the Hofmann rearrangement of aliphatic amides, the point in question has been studied in the Curtius rearrangement of optically active azides of the type \( \text{R}_1 \text{R}_2 \text{C} \equiv \text{ON}_3 \) (86) and has been conclusively proved for the closely analogous Wolff reaction. Thus (+)-1-diazo-3-phenyl-3-methyl-heptan-2-one rearranges to the configurationally identical (optically
pure) (-)-\beta-\text{phenyl}-\beta-\text{methylenanthonic acid (101)}:

\[
\text{Me} \quad \begin{array}{c}
\text{OH} \\
\text{H}
\end{array} \quad \begin{array}{c}
\text{OH} \\
\text{H}
\end{array} \quad \begin{array}{c}
\text{H}_2\text{O}
\end{array} \
(+\text{R} \cdot \text{C} \cdot \text{N}_2 \rightarrow \text{R} \cdot \text{C} \cdot \text{O} \text{H} \rightarrow (-) \text{R} \cdot \text{CH}_2\text{COOH where R is n-Bu-C-}
\text{Ph})
\]

This fact, in conjunction with the results obtained in cyclic systems, leaves no doubt that the Hofmann reaction also always involves retention of configuration.

It is of interest to note that the closely related Hofmann reaction does not yield results identical with the Schmidt and Curtius changes, since in the former rearrangement slight racemization is found (85). Kenyon and Young (86) suggested that this is due to racemization of the amide and this probable explanation has been reinforced by the work of Delepine and Badoch (102). These authors found that (+)-hydratropamide by acid hydrolysis yields (+)-hydratropic acid, but by alkaline hydrolysis yields dl-acid together with highly racemized amide, and they suggested that this was due to enolization of the amide under alkaline conditions. Such conditions are also present in the Hofmann rearrangement.
III. PREPARATION OF OPTICALLY ACTIVE TRISUBSTITUTED METHYLAMINES.

A. Introduction.

After Pasteur had made the first and fundamental observations of the optical activity of organic compounds in 1859 and Le Bel and Van 't Hoff had introduced the conception of the tetrahedral symmetry of the carbon atom (1874), the road was open for the investigation of all kinds of compounds which contain an asymmetric carbon atom.

In 1886, Ladenburg (103) carried out the first resolution of a racemic base when he combined synthetic coniine with d-tartaric acid, and separated the stereo-isomeric salts by fractional crystallization. Since then, bases of very many kinds and structures have been resolved.

In general, camphorsulphonic acid, as well as brom- and chlor-camphorsulphonic acids, are more suitable as resolving agents than tartaric acid, partly because these acids are very highly dissociated in aqueous solution, and therefore are comparable with mineral acids in their acidity, and partly because, unlike tartaric acid, they are monobasic and therefore do not form two series of salts. Amongst the other acids which have been used at one time or another to resolve bases may be mentioned malic and 6,6'-dinitrodiphenic acids (104).

Many primary amines of the type $R_1R_2CHNH_2$ have been
successfully resolved by the method indicated above. The optical properties of these substances have been thoroughly investigated, and Levene and Marker (105) have compared the rotations in homologous series of aliphatic amines with those of the corresponding alcohols. A definite connection was found to exist between the two types of compounds. This fact, together with the peculiar behaviour of tertiary alcohols when their resolution is attempted, brought up the question whether it was possible to resolve the amine analogue of tertiary alcohols, viz., primary amines of the structure $R_1R_2R_3C\cdot NH_2$.

Such amines have not previously been obtained in an optically active form, and it was decided to try both direct and indirect methods of resolution:

1. Using d-camphorsulphonic acid as the resolving agent, both stereoisomeric forms of phenyl-p-tolyl-$\alpha$-naphthyl-methylamine were obtained in an apparently optically pure condition.

2. The indirect method consisted in converting optically active $\alpha$-methyl-$\alpha$-phenyl-n-caproic acid into $\alpha$-methyl-$\alpha$-phenyl-n-amyl-amine through the Curtius reaction. The amine was obtained in an active form.
B. The Resolution of phenyl-p-tolyl-α-naphthyl-methylamine.

The optical resolution of phenyl-p-tolyl-α-naphthyl-methylamine was carried out by the repeated fractional crystallisation of its salt with α-camphorsulphonic acid from an aqueous alcoholic solution.

The decomposition of the salt with decinormal aqueous sodium carbonate solution yielded fully optically active phenyl-p-tolyl-α-naphthyl-methylamine which had a molecular rotatory power \([M]_D^{18} = -4.2^\circ\) in carbon disulphide solution. Similarly, the \(l\)-camphorsulphonic acid led to the isolation of the (+)-amine with the same magnitude of rotatory power.

The recrystallisations of the various crops of salt could not be carried out in boiling aqueous alcohol as under these conditions the amine was found to react in the presence of the acid and give rise to the corresponding alcohol. It was already known that triphenylmethylamine on boiling with dilute acids gave triphenylcarbinol (106).

---------------

C. The Preparation of Active \(α\)-methyl-\(α\)-phenyl-n-amylamine.

Since only small amounts of \(α\)-methyl-\(α\)-phenyl-n-amylamine were available, it was not attempted to resolve this amine by direct methods. Instead, optically active \(α\)-methyl-\(α\)-phenyl-n-caproyl chloride was submitted to the Curtius rearrangement and as expected (see chapter II, section E4) this resulted in the formation of optically —
active $\alpha$-methyl-$\alpha$-phenyl-$n$-amylamine. It was found that the reaction took place with change of sign.

This phenomenon was also observed when optically active amine was converted into its benzoate by the Schotten-Baumann procedure, and when it was dissolved in 0.5N HCl, all readings being taken in sodium light.

Optical data for the active $\alpha$-methyl-$\alpha$-phenyl-$n$-amylamine and for active $\alpha$-methyl-$\alpha$-phenyl-$n$-caproic acid are given in table II.

The resolution of the $\alpha$-methyl-$\alpha$-phenyl-$n$-caproic acid was carried out by fractional crystallization of its quinine salt in aqueous alcohol. This yielded fully active acid with a specific rotatory power $[\alpha]_D^{15} = +17.3^\circ$ (homogeneous).
IV. THE DEAMINATION OF ALIPHATIC PRIMARY AMINES.

It has been known for many years that primary aliphatic amines are converted by nitrous acid into alcohols, nitrogen being evolved, but the exact mechanism of the reaction has not so far been fully elucidated.

The deamination can be represented by the following equation, although the actual mechanism is undoubtedly more complex:

\[ R,\text{NH}_2 + \text{O}_2\text{N.OH} \rightarrow R,\text{OH} + \text{N}_2 + \text{H}_2\text{O} \]

The alcohol is not always the main product of the reaction; a certain amount of olefin is very often formed, and profound changes in the structure of the molecule may take place. Thus, Henry (107) found that n-propylamine \( \text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2 \) gives 42\% of n-propyl alcohol \( \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} \) and 58\% of isopropyl alcohol \( \text{CH}_3\text{CHOH}.\text{CH}_3 \).

The outstanding feature in the published experimental details is that the reaction between primary aliphatic amines and nitrous acid is very slow at ordinary temperatures and requires heat. Further, excess nitrous acid and no excess mineral acid should be present. This is in direct contrast with the diazotisation of primary aromatic amines. It has also been shown that the reaction between aliphatic amines and nitrous acid is of the third order (108); it is not a simple decomposition, but the velocity varies as the product \( (RNH_3^+)(NO_2^-)(\text{HNO}_2) \).
Huckel and Wilip (109) suggest that when an aliphatic primary amine is treated with nitrous acid, a diazonium compound is first formed, as in the aromatic series, but which in this case is very labile. Its cation loses nitrogen and the residual cation (with the positive charge on the carbon atom) reacts either with water leading to the formation of an alcohol and a hydrogen ion, or it loses, spontaneously or by collision with a water molecule, a proton at the adjacent carbon atom, in which case an olefin is formed. Finally, the cation can attach itself to the anion of an organic acid which may be present (e.g., acetic acid), to yield an ester.

All the results published so far in connection with the deamination of primary aliphatic amines refer only to mono- and disubstituted methylamines. There is no direct information on how amines of the type prepared in the present experiments \((R_1R_2R_3C,NH_2)\) would react with nitrous acid.

Of the two optically active amines which have now been prepared, \(\alpha\)-methyl-\(\alpha\)-phenyl-\(n\)-amylamine was not obtained in sufficient quantity for deamination. Phenyl-\(p\)-tolyl-\(\alpha\)-naphthyl-methylamine, which is comparatively readily prepared, also has the advantage of having three aryl groups directly attached to the asymmetric carbon atom which makes it less likely to give rise to by-products of the types indicated above.
The experimental procedure used consisted in refluxing a known amount of amine hydrochloride with three equivalents of sodium nitrite in either water or a mixture of water and an organic solvent as reaction medium. Care was taken not to heat the solution of the amine hydrochloride until the sodium nitrite had been added in view of the property of triarylmethylamines to react on boiling with dilute solutions of strong acids to give the corresponding alcohol (106). The crude product, obtained in approximately 70% yield was found to be extremely difficult to purify, despite the application of most of the usual physical and chemical methods of purification. The phenyl-p-tolyl-α-naphthyl carbinol was, however, obtained in an analytically pure form.

When the reaction was carried out on optically active phenyl-p-tolyl-α-naphthyl-methylamine, the resulting alcohol showed no sign of optical activity.
V. **SUMMARY OF SCHEMES OF SYNTHESIS IN PRESENT EXPERIMENTS**.

After elimination of methods which had appeared unpromising, either by reference to the literature or as the result of preliminary experiments, a number of preparative routes were investigated in detail and these are summarised below (Table I). Two of them yielded trisubstituted methylamines, viz. phenyl-p-tolyl-α-naphthyl methylamine and α-methyl-α-phenyl-n-amylamine, and both these amines were obtained in an optically active form.

A third amine of the same general type, but with two of the alpha substituents identical (α-phenyl-isopropylamine) was also prepared.

Optical data for the two active amines and some of their derivatives was collected and is given in Table II.

In addition the action of nitrous acid on optically active phenyl-p-tolyl-α-naphthyl methylamine was investigated.
TABLE I.

Notes: Compounds marked with * have not been recorded previously.

y = yield.

I. 1. Preparation of α-methyl-α-phenyl-n-caproic acid.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Analysis</th>
<th>Found</th>
<th>Calcd.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhCH₂CN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>b.p.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NaNH₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me⁻/CHCN</td>
<td>y=59%</td>
<td>114°C/16mm.</td>
<td></td>
</tr>
<tr>
<td>n-BuBr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me⁻/n-Bu-CCN</td>
<td>y=71%</td>
<td>147°C/16mm.</td>
<td></td>
</tr>
<tr>
<td>NaNH₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n-Bu-KOH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me⁻/n-Bu-CCOOH</td>
<td>y=65%</td>
<td>157°C/14mm.</td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph⁻/NaN₃</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph⁻/H₂SO₄</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PhNH₂ + C₆H₁₂</td>
<td>y=55%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Schmidt reaction.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Analysis</th>
<th>Found</th>
<th>Calcd.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me⁻/n-Bu-CCOOH</td>
<td>b.p.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph⁻/NaN₃</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph⁻/H₂SO₄</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PhNH₂ + C₆H₁₂</td>
<td>y=55%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3. Curtius reaction.

Me
\(\rightarrow\) n-Bu-COOH
Ph
\(\downarrow\) SO\(_2\)Cl\(_2\)
Me
\(\rightarrow\) n-Bu-(COCl)
Ph
\(\downarrow\) via
azide
Me
\(\rightarrow\) n-Bu-CNH\(_2\) \(\cdot\) HCl
Ph
\(\downarrow\) +
Me
\(\rightarrow\) n-Bu-CNH\(_2\)
Ph
\(\downarrow\) PhCOCl
\(\downarrow\) NaOH
Me
\(\rightarrow\) n-Bu-CNH\(_2\) \(\cdot\) COPh
Ph
Analysis

<table>
<thead>
<tr>
<th>Found</th>
<th>Calcd.</th>
</tr>
</thead>
<tbody>
<tr>
<td>b.p.</td>
<td>157°/14 mm.</td>
</tr>
<tr>
<td>Cl 16.5</td>
<td>Cl 16.1%</td>
</tr>
<tr>
<td>m.p.</td>
<td>144-147°</td>
</tr>
<tr>
<td>C 80.9</td>
<td>C 81.0</td>
</tr>
<tr>
<td>H 8.5</td>
<td>H 8.2</td>
</tr>
<tr>
<td>N 4.9</td>
<td>N 4.9%</td>
</tr>
</tbody>
</table>

Me
\(\rightarrow\) COO\(_2\)H
Ph
\(\downarrow\) via chloride
\(\downarrow\) and azide
Me
\(\rightarrow\) CNH\(_2\)
Ph
| b.p.  | 95°/18 mm. | m.p.  |
| C 79.8 | C 79.9 |
| H 9.5 | H 9.7 |
| N 10.8 | N 10.3% |
| m.p.  | 158° | m.p.  |
| C 74.1 | C 73.6 |
| H 7.8 | H 8.0 |
| N 8.7 | N 8.6% |
4. Hofmann reaction.

Analysis

<table>
<thead>
<tr>
<th>Found</th>
<th>Calcd.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>b.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

Me
n-Bu-CCOOH
Ph
↓ SO₂Cl₂,
↓ NH₄OH
Me
n-Bu-CCONH₂
Ph
↓ NaOCl
Me
n-Bu-CNHz
Ph

II. 1. Preparation of phenyl-p-tolyl-x-naphthyl methylamine.

\[ \text{p-CH₃C₆H₄COC₆H₅} + \]
\[ \text{α-C₆H₅CH₃Br} \]
\[ \ ↑ \text{Grignard} \]
\[ \text{C₆H₅} \]
\[ \text{p-C₆H₄-COH} \]
\[ \text{γ-C₆H₅CH₃} \]
\[ \ ↑ \text{HCl gas} \]
\[ \text{C₆H₅} \]
\[ \text{p-C₆H₄-CCl} \]
\[ \text{γ-C₆H₅CH₃} \]
\[ \ ↑ \text{NH₃ gas} \]
\[ \text{C₆H₅} \]
\[ \text{p-C₆H₄-CNHz} \]
\[ \text{γ-C₆H₅CH₃} \]

157°/14mm.
187°/15mm.

<table>
<thead>
<tr>
<th>b.p.</th>
<th>C 75.6</th>
<th>C 76.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H 8.8</td>
<td>H 9.3</td>
</tr>
<tr>
<td></td>
<td>N 6.5</td>
<td>N 6.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>m.p.</th>
<th>C 89.1</th>
<th>C 89.1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H 6.51</td>
<td>H 6.55</td>
</tr>
<tr>
<td></td>
<td>N 4.17</td>
<td>N 4.33%</td>
</tr>
</tbody>
</table>

y=10%
y=33%(fr. 142° ketone)
y=81%
2. Preparation of $\alpha$-methyl-$\alpha$-ethyl-n-amyI chloride.

\begin{align*}
\text{Me.CO.Et} & \quad + \\
n-BuBr & \\
\downarrow \text{Grignard} & \\
\text{Me} & \quad \text{Et} \rightarrow C.OH \\
\downarrow \text{HCl gas} & \quad y=62\% \\
n-Bu & \quad \text{Et} \rightarrow C.Cl \\
\downarrow \text{aq. NaCN or} & \\
o.880 \text{ NH}_4\text{OH} & \\
\text{Me} & \quad \text{Et} \rightarrow C.OH \\
n-Bu & \\
\text{NaNH}_2, & \\
dry \text{NH}_3, & \\
\text{Mg or} & \\
\text{K-phthalimide} & \\
\downarrow & \\
\text{no reaction} & \\
\end{align*}

b.p 160-162$^\circ$

3. Preparation of $\alpha$-methyl-$\alpha$-phenyl-n-amyI chloride.

\begin{align*}
\text{Me.CO.Ph} & \quad + \\
n-BuBr & \\
\downarrow \text{Grignard} & \\
\text{Me} & \quad \text{n-Bu-C.OH} \\
\downarrow \text{HCl gas} & \quad y=55\% \\
n-Bu & \quad \text{n-Bu-C.Cl} \\
\downarrow \text{aq. NaCN or} & \\
o.880 \text{ NH}_4\text{OH} & \\
\text{Me} & \quad \text{n-Bu-C.OH} \\
\text{Ph} & \\
\text{NaNH}_2, & \\
dry \text{NH}_3, & \\
\text{Mg or} & \\
\text{K-phthalimide} & \\
\downarrow & \\
\text{no reaction} & \\
\end{align*}

b.p 164-7$^\circ$/27mm.
Analysis

Found  Calcd.

Me
n-Bu-C.OMe  y=65%
Ph

\[ \text{Me} \xrightarrow{\text{MeOH}} \xrightarrow{\text{H}_2\text{SO}_4} \xrightarrow{\text{Na-K}} \xrightarrow{\text{CO}_2} \xrightarrow{\text{Me}} \text{n-Bu-C.OMe} \]

130°/27mm.

Me
n-Bu-C,COO H  y=25%
Ph

III. 1. Preparation of \( \alpha \)-methyl-\( \alpha \)-benzyl-n-caprophenone.

\[ \text{CH}_3\text{CH}_2\text{COOC}_6\text{H}_5 \]

\[ \xrightarrow{\text{NaNH}_2} \text{PhCH}_2\text{Cl} \]

\[ \text{CH}_3 \xrightarrow{\text{NaNH}_2} \xrightarrow{\text{n-BuBr}} \text{C}_6\text{H}_5\text{CH}_2 \]

y=56%  181°/10mm.

b.p.

C 85.7  C 85.7
H 7.4  H 7.2%

C\_6\_H\_5\_C\_2\_O\_C\_6\_H\_5 \text{y=30%}  192.6°/13mm

b.p.

C 85.2  C 85.6
H 8.1  H 8.6%

\[ \text{no reaction.} \]
2. Preparation of \( \delta \)-methyl-\( \gamma \)-ethyl-\( n \)-caprophenone.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{COC}_6\text{H}_5 & \quad \text{NaNH}_2 \\
\text{CH}_3 & \quad \text{n-BuI} \\
\text{CH}_3 & \quad \text{CHOC}_6\text{H}_5 & \quad y=58\% & \quad \text{b.p.} 123^\circ/23\text{mm}.
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{CHCOC}_6\text{H}_5 & \quad y=59\% & \quad \text{b.p.} 140^\circ/13\text{mm}. \\
\text{NaNH}_2 & \quad \text{EtI} \\
\text{C}_2\text{H}_5& \quad \text{COC}_6\text{H}_5 & \quad y=59\% & \quad \text{b.p.} 145^\circ/16\text{mm}. \\
\text{NaNH}_2 & \quad \text{water} \\
\text{C}_6\text{H}_5& \quad \text{CONH}_2 & \quad y=58\% & \quad \text{b.p.} 145^\circ/16\text{mm}. \\
\text{C}_6\text{H}_5,\text{CONH}_2 & \quad \text{trace}
\end{align*}
\]

Deamination of phenyl-p-tolyl-\( \psi \)-naphthyl-methylamine.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{p-C}_7\text{H}_7-\text{C.NH}_2 & \quad \text{m.p.} 127-128^\circ \\
\text{C}_6\text{H}_5 & \quad \text{p-C}_7\text{H}_7-\text{C.OH} & \quad \text{m.p.} 109^\circ
\end{align*}
\]

---

**Analysis**

**Found**

**Calcd.**

\[
\begin{align*}
\text{C} & \quad 82.9 & \quad 82.5 \\
\text{H} & \quad 10.0 & \quad 10.1 \\
\text{N} & \quad 6.76 & \quad 6.83
\end{align*}
\]
### Optical Data

<table>
<thead>
<tr>
<th>Compound</th>
<th>Optical Activity</th>
<th>Solvent</th>
<th>Concentration</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me\n-Bu-(\text{C},\text{COOH}) Ph</td>
<td>Homog. (\left[\alpha\right]_{D}^{15} = +17.3)</td>
<td>(1= 0.5 dm.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in ether (\left[\alpha\right]_{D}^{15} = +11.6)</td>
<td>(c=1%; l=2 dm.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot; (\left[\alpha\right]_{5461} = +13.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in (\text{CS}<em>2) (\left[\alpha\right]</em>{D}^{17} = +21.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot; (\left[\alpha\right]_{5461} = +26.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in (\text{CS}<em>2) (\left[\alpha\right]</em>{D}^{18} = +6.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me\n-Bu-(\text{C},\text{NH}_2) Ph</td>
<td>Homog. (\left[\alpha\right]_{D}^{16} = -1.32)</td>
<td>(1=0.5 dm.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot; (\left[\alpha\right]_{5461} = -1.66)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in ether (\left[\alpha\right]_{D}^{17} = -1.2)</td>
<td>(c=1%; l=2 dm.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot; (\left[\alpha\right]_{5461} = -1.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in (\text{CS}<em>2) (\left[\alpha\right]</em>{D}^{17} = -2.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in (\text{N}/2 \text{HCl}) (\left[\alpha\right]_{D}^{16} = +0.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me\n-Bu-(\text{C},\text{NHCOPh}) Ph in (\text{C}_6\text{H}<em>6) (\left[\alpha\right]</em>{D}^{18} = +3.5)</td>
<td>(c=1%; l=2 dm.)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
\[
\text{p-CH}_3\cdot\text{C}_6\text{H}_4\cdot-\text{C},\text{NH}_2 \\
\alpha-\text{C}_{10}\text{H}_7
\]

in CS\(_2\) \(\frac{[\alpha]}{D}^\text{17} = (+)\) and \((-)1.3\) fully active \((c=3.7\%; l=2 \text{ dm})\)

\[
\text{in CS}_2 \quad \frac{[\alpha]}{D}^\text{17} = +1.0
\]

\[
\text{p-CH}_3\cdot\text{C}_6\text{H}_4\cdot-\text{C},\text{NH}_2\text{HCl}\text{(in water)} \quad \frac{[\alpha]}{D}^\text{17} = +1.5
\]

\[
\text{(in N/10 HCl)} \quad \frac{[\alpha]}{D}^\text{17} = +1.3
\]

---

**Dispersion Ratios.**

\[
\begin{align*}
\text{Me} & \backslash \text{n-Bu-} - \text{C},\text{COOH} & \text{in ether} & 1.68 \\
\text{Ph} &          &          &          \\
\text{Me} & \backslash \text{n-Bu-} - \text{C},\text{COCl} & \text{in CS}_2 & 2.0 \\
\text{Ph} &          &          &          \\
\text{Me} & \backslash \text{n-Bu-} - \text{C},\text{NH}_2 & \text{homog.} & 2.0 \\
\text{Ph} &          &          &          
\end{align*}
\]
A. DISPERSION CURVE OF (\(\dagger\))\(\text{MMETHYL-}\alpha\text{-PHENYL-}\(\eta\)-CAPROIC ACID IN ETHER.}

\((c = 6.41\% \quad \text{temp. 15}^\circ\text{C.})\)

\[
\begin{array}{|c|c|}
\hline
\lambda (\AA) & \text{read.} \\
& (1=2 \text{ dm.}) \\
\hline
4358 & 2.99 \\
4678 & 2.48 \\
4800 & 2.47 \\
5086 & 2.10 \\
5461 & 1.77 \\
5893 & 1.49 \\
6438 & 1.20 \\
\hline
\end{array}
\]
B. DISPERSION CURVE OF (-)\textalpha-METHYL-\textalpha-PHENYL-n-CAPROYL CHLORIDE IN CS\textsubscript{2}.

(c = 18.8\% - temp. 18\textdegree C.)

<table>
<thead>
<tr>
<th>(\lambda(A))</th>
<th>read. (I=2 dm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4358</td>
<td>-1.41\textdegree</td>
</tr>
<tr>
<td>4678</td>
<td>-1.14\textdegree</td>
</tr>
<tr>
<td>4800</td>
<td>-1.08\textdegree</td>
</tr>
<tr>
<td>5086</td>
<td>-0.94\textdegree</td>
</tr>
<tr>
<td>5461</td>
<td>-0.70\textdegree</td>
</tr>
<tr>
<td>6438</td>
<td>-0.52\textdegree</td>
</tr>
</tbody>
</table>
C. DISPERISON CURVE OF (-)-METHYL-α-PHENYL-α-AMYLAMINE.

(homogeneous - at 16° C.)

\[
\begin{array}{cc}
\lambda(A) & \text{read} \\
\hline
4358 & -1.70^\circ \\
4678 & -1.32^\circ \\
4800 & -1.25^\circ \\
5086 & -1.03^\circ \\
5461 & -0.83^\circ \\
5893 & -0.66^\circ \\
6438 & -0.56^\circ \\
\end{array}
\]
1. Introduction.

From two points of view, (a) the relation between chemical constitution and rotatory power, and (b) to ascertain whether its carboxylic esters undergo hydrolysis by acyl- or alkyl-oxygen fission, an attempt was made to resolve acenaphthenol into its optically active forms.

Although this secondary alcohol yielded a crystalline acid phthalic ester and also a hydrogen succinic ester, the attempt failed because neither of these esters could be induced to give a crystalline salt with any of the more usually employed alkaloids.

A number of new derivatives of acenaphthenol are described, but it was found that certain reactions which the alcohol itself and some of its simpler derivatives might be expected to undergo did not in fact take place because of the great tendency of these compounds to polymerise in the presence of acidic reagents. The formation of polyacenaphthylene under these conditions is discussed in chapter II.

The fact that the hydrogen phthalic ester of acenaphthenol does not appear to react with sodium p-toluene sulphinate seems to indicate that in the hydrolysis of the ester alkyl-oxygen fission does not take place readily, if at all; otherwise, the sulphone would have formed, according to the following reaction:
\[
\text{COO-R} + \text{p-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{Na} \rightarrow \text{COONa} + \text{p-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{R}
\]
II. Formation of Polyacenaphthylene during the attempted Acylation of Acenaphthenol.

Under the conditions indicated in the following scheme, in all of which acenaphthenol was reacted with reagents expected to effect acylation, polyacenaphthylene was formed:

In reactions 3, 4, 7 and 8, HCl or HBr was originally present and in so far as the corresponding ester was initially formed, HCl was generated in reactions 1 and 6. In reactions 2 and 5, benzoic acid was generated and formic acid was present, respectively.

Dolinski and Dziewanski (65) obtained a polymer of (number-average) M.W. 760 from acenaphthylene by heating
the latter with acetic acid-concentrated hydrochloric acid mixture, thus establishing the acid-catalysed polymerisation of acenaphthylene.

The mechanism of this polymerisation is considered to be that generally accepted for acid-catalyzed polymerisation of olefins:

\[
\text{CH} = \text{CH} + \text{H} \xrightarrow{[\text{CH} = \text{CH}]^{+}} \text{CH} = \text{CH} + \text{H}^{+}
\]

\[
\text{CH}_{2}-\text{CH}^{+} + \text{CH} = \text{CH} \xrightarrow{[\text{CH} = \text{CH}]^{+}} \text{CH}_{2}-\text{CH} - \text{CH} - \text{CH}^{+}
\]

The end of the chain may occur through ejection of a proton, reaction with H\textsubscript{2}O or with an anion X\textsuperscript{-}, giving respectively

\[
\begin{align*}
\text{CH} = \text{CH} + \text{H}^{+} & \rightarrow \text{CH} = \text{CH(OH)} + \text{H}^{+} \\
\text{CH} = \text{CH} + \text{H} & \rightarrow \text{CH} = \text{CHX} + \text{H}^{+}
\end{align*}
\]

Reverting to the results which have now been obtained, the reaction of acenaphthenol with HCl is considered to take the following course (Mechanism A):

\[
\text{CH} = \text{CH} + \text{H}^{+} \rightarrow \text{CH} = \text{CH(OH)} + \text{H}^{+}
\]
Reaction between acenaphthylene (II) and its protonated derivative (I) yielding polyacenaphthylene by the mechanism above can then proceed.

The formation of the polymer appears to be irreversible and the above equilibria will be progressively displaced in the required directions.

The same arguments in all probability apply to the reaction of acenaphthenol with hydrobromic acid.

For the reaction of the acetate and hydrogen phthalate with HCl the following mechanism (B) is proposed:
followed by (irreversible) polymerisation between (I) and (II), with corresponding displacement of equilibria.

In reactions 1 and 6 above, esterification with formation of HCl having proceeded to some extent, mechanisms A and B may both operate. The same applies to 2, with benzoic acid as the catalyst hitherto supplied by HCl.

Finally, with anhydrous formic acid, mechanism A is applicable with HCl and Cl\textsuperscript{-} replaced by HCOOH and HCOO\textsuperscript{-}.

Points arising are:
a) The formula \( \text{HO-} \left[ \begin{array}{c} \text{CH - CH} \\ n \end{array} \right] \text{-OH} \) is unlikely for the polymér, and hence the excellent fit of the molecular weight and analysis (see experimental section) may be fortuitous. Alternately, there may be two oxygen atoms per polymer molecule, but how is not clear.
b) The fact that the polymer was not given by acetic, phthalic and succinic anhydrides may be due to either the weakness of the corresponding acids or the stability of the esters against mechanism B.
EXPERIMENTAL

SECTION.
SECTION I.
INDEX. (Experimental)

Preparation of trisubstituted methylamines. 68

I. From trisubstituted acetic acid. 68
1. Preparation of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-capronitride. 68
2. Preparation of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproic acid. 69
3. Schmidt reaction on \( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproic acid. 71
4. Curtius reaction on \( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproyl chloride. 73
5. Hofmann reaction on \( \alpha \)-methyl-\( \alpha \)-phenyl-n-caproamide. 76

II. From tertiary alcohols. 78
A1. Preparation of phenyl-p-tolyl-\( \alpha \)-naphthyl carbinol. 78
2. Preparation of phenyl-p-tolyl-\( \alpha \)-naphthyl chloromethane. 79
3. Preparation of phenyl-p-tolyl-\( \alpha \)-naphthyl methylamine. 79

B1. Preparation of \( \alpha \)-methyl-\( \alpha \)-ethyl-n-amyl alcohol. 80
2. Preparation of \( \alpha \)-methyl-\( \alpha \)-ethyl-n-amyl chloride. 80
3. Some chemical properties of \( \alpha \)-methyl-\( \alpha \)-ethyl-n-amyl chloride. 81

C1. Preparation of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-amyl alcohol. 82
2. Preparation of \( \alpha \)-methyl-\( \alpha \)-phenyl-\( \alpha \)-amyl chloride. 83
3. Some chemical properties of \( \alpha \)-methyl-\( \alpha \)-phenyl-n-amyl chloride. 83
4. Preparation of methyl (\( \alpha \)-methyl-\( \alpha \)-phenyl-n-amyl) ether and its reaction with potassium and carbon dioxide. 84
III. From trisubstituted acetophenones.

A1. Preparation of \( \alpha \)-methyl-\( \alpha \)-benzyl-\( \alpha \)-caprophenone. 86
2. Reaction of \( \alpha \)-methyl-\( \alpha \)-benzyl-\( \alpha \)-caprophenone with sodamide. 87

B1. Preparation of \( \alpha \)-methyl-\( \alpha \)-ethyl-\( \alpha \)-caprophenone. 88
2. Preparation of \( \alpha \)-methyl-\( \alpha \)-ethyl-\( \alpha \)-caproamide. 89

Deamination of phenyl-p-tolyl-\( \alpha \)-naphthyl-methylamine. 91


<table>
<thead>
<tr>
<th>SECTION II.</th>
<th>INDEX. (Experimental)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I.</strong> Preparation of Acenaphthenol.</td>
<td>93</td>
</tr>
<tr>
<td><strong>II.</strong> Reactions of Acenaphthenol with Acid Anhydrides.</td>
<td>95</td>
</tr>
<tr>
<td>1. With phthalic anhydride.</td>
<td>95</td>
</tr>
<tr>
<td>2. With succinic anhydride.</td>
<td>96</td>
</tr>
<tr>
<td>3. With benzoic anhydride.</td>
<td>96</td>
</tr>
<tr>
<td>4. With acetic anhydride.</td>
<td>97</td>
</tr>
<tr>
<td>5. With nitrophthalic anhydride.</td>
<td>98</td>
</tr>
<tr>
<td><strong>III.</strong> Reactions of Acenaphthenol with Acid Chlorides.</td>
<td>99</td>
</tr>
<tr>
<td>1. With benzoyl chloride.</td>
<td>99</td>
</tr>
<tr>
<td>2. With acetyl chloride.</td>
<td>100</td>
</tr>
<tr>
<td>3. With p-toluene sulphonyl chloride.</td>
<td>101</td>
</tr>
<tr>
<td><strong>IV.</strong> Reactions of Acenaphthenol with Acids.</td>
<td>102</td>
</tr>
<tr>
<td><strong>V.</strong> Preparation of Acenaphthenyl Urethanes.</td>
<td>104</td>
</tr>
<tr>
<td>1. Phenyl urethane.</td>
<td>104</td>
</tr>
<tr>
<td>2. α-Naphthyl urethane.</td>
<td>104</td>
</tr>
<tr>
<td>3. p-Xenyl urethane.</td>
<td>104</td>
</tr>
<tr>
<td><strong>VI.</strong> Attempted Reaction of Acenaphthenyl Hydrogen Phthalate with sodium p-toluene sulphinate.</td>
<td>105</td>
</tr>
<tr>
<td><strong>VII.</strong> Constitution of Polyacenaphthylene.</td>
<td>106</td>
</tr>
</tbody>
</table>
I. From Trisubstituted acetic acid.

1. Preparation of \( \alpha \)-methyl-\( \gamma \)-phenyl-\( n \)-capronitrile.

(i) A suspension of sodamide (47 g.) in dry ether was gradually added to a solution of redistilled benzyl cyanide (140 g.) in ether (100 c.c.) and the mixture heated under reflux for three hours.

A dark red heterogeneous mixture was obtained. It was cooled in ice, and dimethyl sulphate (170 g.) added gradually. After the mixture had been stirred for several hours, water was added and the ethereal layer separated and dried over sodium sulphate.

The solvent was evaporated and the residue distilled under reduced pressure. The hydrotroponitrile distilled at \( 114^\circ/16 \text{ mm.} \)

Yield : 92 g. (59% theor.).

(ii) To a mixture of hydrotroponitrile (79 g.) and \( n \)-butyl bromide (85 g.) in dry benzene (100 c.c.) was added a suspension of sodamide (24.5 g.) in the same solvent. A strongly exothermic reaction immediately started, with evolution of ammonia. The reaction mixture was heated on a steam-bath and simultaneously stirred for several hours. When no further evolution of ammonia could be observed, water was added. The benzene layer was repeatedly washed-
with water, then dried, and finally the solvent was removed by evaporation. The \( \omega \)-methyl-\( \omega \)-phenyl-n-capronitrile distilled at 147°/16mm.

Yield: 80 g. (71% theor.). Found: C, 83.2; H, 9.19; N, 7.64; \( \text{C}_{13} \text{H}_{17} \text{N} \) requires C, 83.3; H, 9.15; N, 7.48%.

------------------------

2. Preparation of \( \omega \)-methyl-\( \omega \)-phenyl-n-caproic acid.

a) The nitrile (5 g.) was added to a mixture of water (3.1 c.c.), glacial acetic acid (3.7 c.c.) and conc. sulphuric acid (4.1 c.c.). No reaction took place in the cold; on warming the solution, darkening rapidly took place and profound decomposition appeared to occur.

b) A small amount of the nitrile was kept on a steam-bath for several days in presence on excess concentrated hydrochloric acid, but no hydrolysis occurred. Nor was the substance hydrolysed when the hydrochloric acid was replaced by phosphoric acid.

c) 17 g. of the substituted capronitrile were dissolved in a hot solution of potassium hydroxide (16 g.) in alcohol (90 c.c.) and water (25 c.c.). The clear solution was refluxed for ten days, after which the alcohol was distilled off. Addition of a small amount of water gave a clear solution, but further dilution caused the formation of an emulsion. Extraction with either benzene or ether.
was unsatisfactory because of the very appreciable solubility of the sodium salt of the carboxylic acid in these solvents.

Acidification of the reaction product followed by extraction with benzene gave a mixture of acid, amide and some unchanged nitrile. It was found that the first two could not be wholly separated from each other, but purification was completed by addition of excess alkali and repeated extraction with chloroform.

A third method tried for the separation of amide from acid consisted in dissolving a small amount of the mixture in alcohol, accurately neutralizing the acid with caustic soda solution and removing all traces of solvent by distillation in vacuo. However, instead of obtaining two layers as expected, a perfectly homogeneous solution of the sodium salt in the amide was obtained. The amide was found to be readily extractable with petroleum ether (60-80°), and to distil at 187°/15mm. \( \text{(Found: C, } 75.6; \text{ H, } 8.8; \text{ N, } 6.5; \text{ C}_{13}\text{H}_{19}\text{ON requires: C, } 76.0; \text{ H, } 9.3; \text{ N, } 6.8\% ) \).

The \( \alpha\)-methyl-\( \alpha\)-phenyl-n-caproic acid obtained by any of the methods indicated above was collected at 173°/16mm. On titrating the acid with 0.1N. alcoholic potash solution, its equivalent was found to be 208.0 \( \text{(C}_{12}\text{H}_{17}\text{.COOH requires equivalent 206.3) } \).

The yields under the conditions given above were
approximately 65% acid, 25% amide and a trace of tarry material; the remainder consisted of unchanged nitrile.

In a further experiment, using less carefully fractionated trisubstituted acetonitrile, a small amount of α-phenyl-isobutyric acid was isolated. This acid distilled at 157°/14 mm. Titration with 0.1N alcoholic potash gave it an equivalent of 165.6 (C₉H₁₁COOH requires equivalent 164.2). The amide of α-phenyl-isobutyric acid was also isolated. It was distilled at a slightly higher temperature than the corresponding acid, and readily crystallised out. It was obtained as small needles, m.p. 158°C, from aqueous alcohol. (Found: C, 74.0; H, 7.8; N, 8.7; calcd. for C₁₀H₁₃ON: C, 73.6; H, 8.0; N, 8.6%).

3. Schmidt Reaction on α-methyl-α-phenyl n-caproic acid.

To a solution of α-methyl-α-phenyl n-caproic acid (5.5 g.) in dry chloroform (45 c.c.), was added concentrated sulphuric acid (13 c.c.). The mixture acquired a greenish-brown colouration which disappeared as sodium azide (2.1 g.) was added under vigorous stirring.

Through carefully controlling the rate of addition of the azide, the reaction temperature could be kept at 40-45° without the application of external heat for most of the time.

When nearly all the sodium azide appeared to have gone
into solution, stirring was continued for another hour, after which the mixture was poured into cold water.

The aqueous layer was separated, washed repeatedly with small amounts of chloroform and then made alkaline with caustic soda. An emulsion formed, and the oil was extracted with benzene and dried over anhydrous potassium carbonate. After removal of both drying agent and solvent, the residue was distilled under reduced pressure and yielded 1.2 g. of a clear liquid, b.p. approx. 60°/18 mm., which was identified as aniline through two of its derivatives, p-toluenesulphonanilide, m.p. 103°, and acetanilide, m.p. 113°; an analysis of the oil confirmed its identity (Found: C, 77.4; H, 7.7; N, 14.7; calc. for C₆H₇N; C, 77.3; H, 7.5; N, 15.0%).

From the chloroform layer, 0.6 g. of unchanged acid was recovered, so that the yield of aniline, calculated on the amount of acid which had reacted, was 55%.

After the unchanged acid had been extracted, the chloroform layer was carefully dried, and bromine added very gradually until the brown colouration just persisted. The excess bromine was removed by washing with sodium thiosulphate solution.

The solvent was evaporated and the residue distilled; dibromohexane was collected at approx. 95°/15 mm. (Found: Br, 64.3; calc. for C₆H₁₂Br₂:Br, 65.4%).

The reaction was repeated using different temperatures and employing activated sodium azide, but these variations affected neither the nature nor the yield of the product.
4. Curtius Reaction on $\alpha$-methyl-$\alpha$-phenyl-$n$-caproyl chloride.

**Preparation of $\alpha$-methyl-$\alpha$-phenyl-$n$-caproyl chloride:**

A mixture of $\alpha$-methyl-$\alpha$-phenyl-$n$-caproic acid (11.5 g.) and thionyl chloride (50 c.c.) was refluxed on a steam-bath in the absence of moisture. When no more hydrogen chloride appeared to be evolved, the excess thionyl chloride was distilled at ordinary pressure and the residue under reduced pressure.

The $\alpha$-methyl-$\alpha$-phenyl-$n$-caproyl chloride was collected at 123°/18 mm.

**Yield:** 11.1 g. (89% theor.).

On titration of a measured excess of standard alcoholic potash in which a known amount of acid chloride had been dissolved, with acid, the equivalent of the chloride was found to be 228; $C_{12}H_{17}COCl$ requires an equivalent of 225.

**Curtius Reaction (Wet method).**

A solution of sodium azide (5 g.) in water (20 c.c.) was added under vigorous stirring to a solution of $\alpha$-methyl-$\alpha$-phenyl-$n$-caproyl chloride (15.4 g.) in acetone (150 c.c.). The mixture was kept in an ice-bath, and after 30 minutes water was added very gradually until a homogeneous solution was obtained. Stirring of the cold reaction mixture was continued for one hour. More water (200 c.c.) was then added, and the precipitated oil extracted with ether and dried over anhydrous calcium sulphate. Slight evolution
of gas-bubbles seemed to indicate that decomposition of the acid azide had already started in the cold.

After the drying agent had been filtered off, dry toluene was added and the ether evaporated. The remaining solution was refluxed for several hours to complete the decomposition and rearrangement of the azide. Concentrated hydrochloric acid (150 c.c.) was added and the mixture stirred for six hours on a steam-bath.

The aqueous layer was separated, washed with benzene and evaporated to small bulk. Addition of caustic soda solution in excess precipitated an oil which was extracted with ether. Evaporation of the solvent and distillation of the residue yielded 2.7 g. of α-methyl-α-phenyl-n-amylamine, b.p.127°/18 mm. and identified through its benzoyl derivative, obtained by the Schotten-Baumann reaction, M.p. of benzoate 146-147°C. (Small, silky needles from benzene-ligroin).

(Found: C,80.9; H,8.5; N,4.9; C₁₉H₂₃ON requires C,81.0; H,8.2; N,4.9%).

The toluene layer was dried and the solvent removed by distillation. Addition of ether converted the residual viscous material into a crystalline mass. The latter was filtered and repeatedly recrystallised from benzene-petroleum ether (60-80°). The small crystals (0.6 g.) which had a melting-point of 144-147°C., could not be purified any further and were found to be quite soluble
in water. Analysis showed them to be the hydrochloride of \( \alpha \)-methyl-\( \alpha \)-phenyl-\( \eta \)-amylamine (Found: Cl, 16.5; \( \text{C}_{16}\text{H}_{20}\text{NCl} \) requires Cl, 16.1%). This was confirmed by converting the hydrochloride into the benzoyl derivative and identifying the latter by a mixed melting-point determination with an authentic sample of \( \alpha \)-methyl-\( \alpha \)-phenyl-\( \eta \)-amylamine benzoate, Curtius Reaction (Dry method).

To a solution of \( \alpha \)-methyl-\( \alpha \)-phenyl \( \eta \)-caproyl chloride (8.8 g.) in dry toluene (40 c.c.) was added sodium azide (2.9 g.), previously activated with hydrazine hydrate, according to Nelles' method.

The mixture was stirred and refluxed for eight hours, after which no more gas appeared to be evolved. The unchanged sodium azide was filtered off from the cooled solution, and most of the solvent removed by distillation. Excess concentrated hydrochloric acid was added, and the hydrolysis of the isocyanate allowed to proceed on a steam-bath for a few hours.

The aqueous layer was then separated and made alkaline with caustic soda solution. The oily suspension thus formed was extracted with ether, dried and distilled under reduced pressure. The \( \alpha \)-methyl-\( \alpha \)-phenyl \( \eta \)-amylamine, b.p. 127\(^\circ\)/18 mm., was converted through a Schotten-Baumann reaction into its benzoate.

Yield: 1.7 g. (25% theor.)
The experiment was repeated using dry benzene instead of toluene, but the yield remained approximately the same. In a third experiment, the acid chloride and sodium azide were stirred together in cold, dry ether for 10 hours before refluxing, and here again a yield of slightly over 20% of amine was obtained.

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5. Hofmann Reaction on α-methyl-α-phenyl-n-caproamide

Preparation of α-methyl-α-phenyl-n-caproamide.

To a large excess of 0.880 aqueous ammonia (200 c.c.) was added very gradually α-methyl-α-phenyl-n-caproyl chloride (12 g.), and the mixture evaporated on a steam-bath until most of the water had been removed.

The residual oil was extracted with benzene and the solution dried. After removal of the solvent, the amide was distilled and collected at 187°/15 mm. (Found: C, 75.6; H, 8.8; N, 6.5; C₁₅H₂₂O₇N requires C, 76.0; H, 9.3; N, 6.8%).

Yield: 7.7 g. (74% theor.).

Preparation of α-methyl-α-phenyl-n-amylamine.

1.96 g. of acid amide was vigorously shaken with 60 c.c. of aqueous sodium hypochlorite solution*, kept at 40°C., until nearly all the amide had gone into solution. The

* A 0.25N solution of NaOCl prepared by allowing 105 g. of conc. HCl (s.g. 1.17) to flow through a dropping funnel on to 16.2 g. of KMnO₄, and collecting the chlorine in 500 c.c. of cold 10% NaOH solution.
mixture was then gradually heated to 80°C., and at this stage a yellow oil separated. It was extracted with benzene and the solution mixed with concentrated hydrochloric acid in excess. The benzene was removed by evaporation and the residue heated for several hours. The very small amount of oil which remained on the surface of the acid solution was extracted with ether, leaving a clear aqueous layer which was then evaporated to a small volume. This solution was mixed with benzoyl chloride, using the Schotten-Baumann procedure, and the product was found to be identical in its physical properties with an authentic specimen of the benzoate of α-methyl-α-phenyl n-amylamine (m.p. 146-147°).

Yield of amine benzoate: 0.27 g. (10% theor.).
II. From Tertiary Alcohols.


(i) Preparation of phenyl-p-tolyl ketone.

To a mixture of benzoyl chloride (35 g.) and dry toluene (138 g.) was added aluminium chloride (30 g.), previously ground under toluene. The addition was made gradually over a period of 45 minutes. The dark solution was then refluxed until hydrogen chloride had practically ceased to be evolved and, after slight cooling, was poured into a mixture of ice and hydrochloric acid. After thorough shaking, the toluene layer was separated, washed with water, dried, and the solvent evaporated. The residue was distilled and the fraction collected at 173-176°C/10mm, was allowed to crystallize. It was then recrystallized from alcohol. M.p. 59°C.

Yield 35 g. (72% theor.).

(ii) Preparation of phenyl-p-tolyl-o-naphthyl carbinol.

A Grignard reagent was prepared by the interaction of o-bromo-naphthalene (45.5 g.) and magnesium (5.4 g.) in ether (135 c.c.). The reagent did not form readily but after three hours' refluxing most of the magnesium had gone into solution.

A solution of phenyl-p-tolyl ketone (43.5 g.) in ether (200 c.c.) was added very gradually under vigorous stirring, while keeping the mixture on a steam-bath. After four hours
the mixture was cooled and decomposed with ice and ammonium chloride (25 g.). The ethereal layer was separated, washed, and dried. After most of the solvent had evaporated and the residue crystallised out, the alcohol was recrystallized from ligroin (m.p. 109°C).

2. Preparation of phenyl-p-tolyl-α-naphthyl chloromethane.

The alcohol thus obtained was dissolved in ether, and dry hydrogen chloride passed through the solution. A small amount of chloride soon crystallised out, and a few c.c.s of acetyl chloride were added to remove the water formed during the reaction. After the gas had been passed through the mixture for several hours, the solvent and excess acetyl chloride were evaporated and the residual carbinyl chloride recrystallised from 40-60°C petroleum ether.

Yield: 25 g. (33% calcd. on ketone).
M.p. 142°C.


Dry ammonia gas was passed through a solution of phenyl-p-tolyl-α-naphthyl chloromethane (25 g.) in benzene (500 c.c.) until no more ammonium chloride separated. The latter was filtered, and the solvent evaporated. Addition of petroleum ether (40-60°C) to the residual gum yielded a light-brown powder which on recrystallisation from alcohol gave small white needles, m.p. 127-128°C.
Yield: 19 g. (81% theor.).

(Found: C, 89.1; H, 6.51; N, 4.17; C₂₄H₂₁N requires C, 89.1; H, 6.55; N, 4.33%).

Bl. Preparation of α-methyl-α-ethyl-n-amyl alcohol.

A Grignard reagent was prepared in the standard way by the interaction of n-butyl bromide (262 c.c.), previously dried over calcium chloride and dissolved in dry ether (750 c.c.), with magnesium (60.8 g.).

This reagent was cooled in an ice-salt mixture, and a solution of methyl ethyl ketone (223 c.c.) in ether (250 c.c.) slowly run in, under constant stirring.

The addition product was hydrolysed by pouring it into ice and ammonium chloride (250 g.). The ethereal layer was separated, washed several times with water, and dried over anhydrous potassium carbonate.

The solvent was evaporated and the residue distilled under reduced pressure. The fraction collected at 78-80°/35 mm. was redistilled at normal pressure, the alcohol coming over at 160-2°.

Yield: 203 g. (62% theor.).

2. Preparation of α-methyl-α-ethyl-n-amyl chloride.

A sample of α-methyl-α-ethyl-n-amyl alcohol was cooled to -5°C in a freezing mixture, and dry hydrogen chloride passed through it for several hours.
When the liquid appeared to be saturated with hydrogen chloride the halide layer was separated and freed from excess HCl by standing it in an evacuated desiccator over sodium hydroxide. It was then washed with a 5% sodium carbonate solution, and dried.

The substituted amyl chloride was finally distilled under reduced pressure, giving a colourless liquid, b.p. 55°/15 mm.

3. Some Chemical properties of \( \alpha - \text{methyl-\( \alpha - \text{ethyl-n-amyl} \) chlorine.} \\

a) With aqueous sodium cyanide solution;

5 g. of sodium cyanide were nearly completely dissolved in 6 c.c. of hot water, and 6 c.c. of the chloride slowly run into the solution.

After the solution had been kept on a steam-bath for several hours, excess of water was added and the non-aqueous layer separated, washed and dried. On distillation, it yielded only \( \alpha - \text{methyl-\( \gamma - \text{ethyl-n-amyl} \) alcohol.}

b) With 0.880 ammonia solution;

5 c.c. of chloride were shaken for three days with 20 c.c. of ammonia solution (s.g. 0.880). Oily globules on the surface of the aqueous layer were extracted with ether and identified as the alcohol corresponding to the chloride.

c) With dry gaseous ammonia;

Dry ammonia gas was passed for several hours through
the chloride kept first at \(-5^\circ C\), and then at room
temperature, but no reaction took place.
d) With sodamide:

A suspension of sodamide in benzene was added to a
sample of the chloride and the mixture refluxed for several
hours. No reaction appeared to take place, and after
filtering off the sodamide, the chloride was recovered
nearly quantitatively.
e) With magnesium:

An attempt was made to prepare a Grignard reagent by
allowing a dry ethereal solution of the chloride to react
with magnesium, but it was found impossible to get any
appreciable amount of interaction to take place.
f) With phthalimide:

A mixture of potassium phthalimide and \(-\)-methyl-\(-\)-
ethyl-\(-\)-amyl chloride was heated for several hours in an
oil-bath at 100-120\(^\circ C\), but no substituted phthalimide was
found in the reaction product. The addition of toluene to
the mixture had no effect.

--------------
Cl. Preparation of \(-\)-methyl-\(-\)-phenyl-\(-\)-amyl alcohol.

A Grignard reagent, prepared from n-butyl bromide
(274 g.), dissolved in ether (625 c.c.), and magnesium
(48.6 g.), was treated at 0\(^\circ C\) with an ethereal solution
of acetophenone (240 g.).
The reaction product was hydrolyzed with ice and ammonium chloride (150 g.) and the alcohol, after the ethereal layer had been washed and dried, distilled.

The \(-\text{methyl-\(-\text{phenyl-n-amy1 alcohol had a boiling-point of 164-167}^\circ\text{C}/27 \text{mm.}

Yield: 195 g. (55\% theor.).

2. Preparation of \(-\text{methyl-\(-\text{phenyl-n-amy1 chloride.

Through a sample of the amyl alcohol containing a trace of zinc chloride, was passed a slow stream of dry hydrogen chloride. The liquid was kept at \(-5^\circ\text{C. until it appeared to be saturated with hydrogen chloride and separation into two layers had taken place.

The excess HCl was removed in a vacuum desiccator and the non-aqueous layer shaken with anhydrous potassium carbonate and filtered.

The chloride was distilled in vacuo and the pure substance collected at 115^\circ\text{C}/13\text{mm. as a colourless liquid with pungent odour.}

3. Some Chemical properties of \(-\text{methyl-\(-\text{phenyl-n-amy1 chloride.

A series of tests, identical to those carried out on \(-\text{methyl-\(-\text{ethyl-n-amy1 chloride (see above), was carried out on \(-\text{methyl-\(-\text{phenyl-n-amy1 chloride. Under these conditions there appeared to be no difference in reactivity between the two carbinyl chlorides and no suitable method}
was found of converting either of them into the corresponding amine.

4. Preparation of $\alpha$-methyl-$\alpha$-phenyl-$n$-caproic acid.

(i) A solution of $\alpha$-methyl-$\alpha$-phenyl-$n$-amyI alcohol (30 g.) in methyl alcohol (50 c.c.) was allowed to stand overnight in the presence of concentrated sulphuric acid (2 c.c.). Two layers formed and the product of the reaction was dissolved in ether. It was then washed with water and with a sodium carbonate solution, dried and the solvent evaporated.

The residue was distilled and methyl ($\alpha$-methyl-$\alpha$-phenyl-$n$-amyI) ether collected at 130°/27 mm.

Yield: 21 g. (65% theor.).

(ii) To a solution of the methyl ether (8.9 g.) in dry benzene (200 c.c.) was added a liquid sodium-potassium alloy (8 c.c.) in an atmosphere of nitrogen. The alloy had been prepared by melting together under paraffin sodium and potassium in the ratio of 23 to 77 w./w.

No reaction was at first observed, but after some time the solution became increasingly cloudy and dark. It was then heated to 60-70°C. and soon a dark-red solution was obtained. The mixture was allowed to cool down and dry carbon dioxide was passed through it for about one hour, by which time the colour had entirely disappeared. Excess alloy was decomposed by adding moist ether and alcohol.
The solution was extracted several times with water. The alkaline solution was acidified and the liberated acid extracted with ether and dried.

The residue was distilled and \(\alpha\)-methyl-\(\gamma\)-phenyl-n-caproic acid collected at 157°/15 mm.

Yield: 1.9 g. (25% theor.).

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III. From Trisubstituted Acetophenones.

Al. Preparation of α-methyl-α-benzyl-n-caprophenone.

(1) To a solution of propiophenone (170 g.) in dry benzene (650 c.c.) was gradually added a suspension of sodamide (51 g.) in the same solvent. The mixture, which rapidly acquired a reddish-brown colouration due to the formation of the soda-derivative, was refluxed for several hours until no further evolution of ammonia could be observed.

Redistilled benzyl chloride (160 g.) was then added and the refluxing continued, together with vigorous stirring, until the colour of the reaction mixture had changed to pinkish-yellow.

The mixture was cooled and water added to dissolve the precipitated sodium chloride. The benzene layer was washed with water, dried over sodium sulphate and the solvent evaporated. The residual oil was distilled under reduced pressure and the α-benzyl-propiophenone collected at 181°/10 mm. (Found: C, 85.7; H, 7.4; C₁₆H₁₆O requires C, 85.7; H, 7.2%).

Yield: 159 g. (56% theor.).

Throughout the experiments involving the use of sodamide as condensing agent, the conditions were kept anhydrous, by fitting a calcium chloride drying tube to the condenser and a mercury seal to the stirrer.

(ii) The reaction of α-benzyl-propiophenone, first with sodamide (27 g.), then with n-butyl bromide (95 g.) was
carried out as described above, using the same solvent (650 c.c.) and identical experimental conditions.

The ω-methyl-ω-benzyl n-caprophenone was found to distil at 192-196°/13 mm. (Found: C, 85.2; H, 8.1; C₂₀H₂₄O requires C, 85.6; H, 8.6%).

Yield: 58 g. (17% theor. calcd. on original propriophenone).

2. Reaction of ω-methyl-ω-benzyl n-caprophenone with sodamide.

a) In benzene: to a solution of ω-methyl-ω-benzyl n-caprophenone (58 g.) in dry benzene (250 c.c.) was added a suspension of finely-ground sodamide (12 g.). The mixture was refluxed for five hours and water then added to decompose the excess sodamide and any sodio-derivative of the substituted caproamide which might have been formed.

The benzene layer was washed with dilute acid, and dried. The solvent was evaporated, but the residue, on distillation yielded only unchanged ketone together with a tar.

b) In toluene: the recovered trisubstituted acetophenone (44 g.) was dissolved in dry toluene (200 c.c.) and refluxed for several hours in the presence of sodamide (10 g.). As in the first experiment, no trace of amide could be found in the product.
c) In xylene: the recovered ketone was heated in the presence of excess (1.2 equiv.) sodamide, using dry xylene as solvent. After the mixture had been refluxed for a few hours, it was cooled and decomposed as described above. The distilled reaction product was found to contain nitrogen, but all attempts at separating any product from the unchanged ketone failed.

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Bl. Preparation of \(\alpha\)-methyl-\(\delta\)-ethyl-n-caprophenone.

(1) To a solution of propiophenone (182 g.) in dry benzene (650 c.c.) was added a suspension of sodamide (53 g.) in the same solvent. The mixture was stirred and refluxed; after about one hour, a bulky precipitate of the sodium derivative suddenly formed. Refluxing was continued for another three hours, after which no more ammonia appeared to be evolved.

A solution of \(n\)-butyl bromide (186 g.) in benzene (100 c.c.) was gradually added to the boiling mixture, and stirring was continued for several hours. Water was then added, and the benzene layer separated, washed and dried. After removal of the solvent, the residue was distilled and the \(\alpha\)-methyl-n-caprophenone collected at 123\(^\circ\)/23 mm.

Yield: 148 g. (58\% theor.).

(11) \(\alpha\)-Methyl-\(\delta\)-ethyl-n-caprophenone was prepared in the same way as \(\alpha\)-methyl-n-caprophenone, using 148 g. of the latter ketone, dissolved in 650 c.c. of benzene, 38 g. of
sodamide and 122 g. of ethyl iodide. Care was taken to
immerse the lower end of the dropping funnel, containing the
alkyl halide, in the reaction mixture in order to avoid
reaction between ethyl iodide and the ammonia evolved.

B. p. of $\alpha$-methyl-$\alpha$-ethyl-$n$-caprophenone: 140°/13 mm.
(Found: C, 82.2; H, 9.98; Cl₅H₂₂O requires C, 82.5; H, 10.16%).
Yield: 100 g. (59% theor.).

2. Preparation of $\alpha$-methyl-$\alpha$-ethyl-$n$-caproamide.

20 g. of $\alpha$-methyl-$\alpha$-ethyl-$n$-caprophenone were dissolved
in 100 c.c. of dry benzene and a suspension of 5 g. of
finely-ground sodamide in the same solvent was added to the
solution. The mixture was refluxed for four hours under
anhydrous conditions, and water then added very slowly.

The benzene layer was separated and, repeatedly washed
with dilute acid. The solvent was evaporated, leaving an
oil which distilled at 125-140°/16 mm. An attempt at
fractionally distilling this liquid was unsuccessful;
analysis showed it to contain approximately 4% of nitrogen.
If the liquid consisted only of unchanged ketone and of the
corresponding trisubstituted acetamide this would indicate
that about one half of the mixture consisted of amide.

To 12.6 g. of this liquid mixture dissolved in 60 c.c.
of dry toluene were added 3 g. (30% excess) of sodamide.
On heating the mixture, strong evolution of ammonia was
observed, probably indicating the formation of the sodio-
derivative of the amide. After the mixture had refluxed for seven hours, it was cooled and water slowly added. The organic layer was treated as before, but the product, isolated at approx. 140°/13 mm, was still not pure amide.

Finally, the process was repeated using xylene as solvent and refluxing the mixture for four hours; pure \(\gamma\)-methyl-\(\gamma\)-ethyl-n-caproamide was isolated - B.p. 145°/16 mm.

(Found: N, 6.76; C\(_{13}\)H\(_{19}\)ON requires N, 6.83%).

In addition, a small amount of benzamide was isolated which on hydrolysis readily yielded benzoic acid. The latter was identified by a mixed melting-point determination with an authentic sample of benzoic acid and by an analysis.

(Found: C, 68.6; H, 5.0; calcd. for C\(_7\)H\(_6\)O\(_2\): C, 68.8; H, 4.9%).
Desamination of phenyl-p-tolyl-α-naphthyl-methylamine.

To a solution of phenyl-p-tolyl-α-naphthyl-methylamine hydrochloride (4.2 g.), prepared by passing hydrogen chloride through an ethereal solution of the amine, in water (75 c.c.), was added an aqueous solution of sodium nitrite (2.4 g. in 25 c.c.). This led to the formation of a white crystalline mass which did not dissolve on addition of a further amount of water (50 c.c.) to the mixture. The latter was boiled and the precipitate coagulated to a gummy mass floating on top of a clear solution.

Benzene was added to dissolve the supernatant solid and the two clear layers were stirred together and heated on a steam-bath for 24 hours.

The benzene layer was then separated, washed repeatedly with cold 3N. hydrochloric acid and then with warm water. After careful drying, the solution was treated with charcoal and finally purified by passing it through a column of activated alumina. The solvent was distilled under reduced pressure, leaving a residue which appeared to contain no nitrogen and which weighed 2.9 g. It was found extremely difficult to crystallize this product but after several weeks this was achieved. Small crystals were obtained from ligroin, and these were identified as phenyl-p-tolyl-α-naphthyl carbinol by a mixed melting-point determination with an authentic sample of the alcohol and by an analysis.
Yield: 1.2 g. (31% theor.).

The reaction was repeated using different media and keeping the proportions of amine hydrochloride and sodium nitrite as in the above experiment, but the product appeared to be the same in each case, without appreciable difference in yield. The solvents used were: a mixture of water and dioxan to give a perfectly homogeneous reaction mixture, and water only.

In a final experiment, optically active phenyl-p-tolyl-phenyl-methylamine hydrochloride (spec. rot. = 1.0 in water) was reacted with sodium nitrite under the conditions indicated above, but the resulting alcohol showed no sign of being optically active.
I. Preparation of Acenaphthenol.

(1) Acenaphthenyl acetate.

In a 1,000 c.c. round-bottomed flask were placed acenaphthene (77 g.) and glacial acetic acid (550 c.c.), previously distilled from 20 g. of potassium permanganate.

The solution was stirred and heated to 60°C, at which point the source of heat was removed and red lead (410 g.) added in portions of 25 g., each portion being added as soon as the colour due to the previous amount had been discharged. During this operation, which required 30 to 40 minutes, the temperature was maintained at 60-70°C, by external cooling.

The reaction was considered to have gone to completion when a portion of the solution gave no test for lead tetracetate (a drop of the reaction mixture was placed on a moist piece of starch-potassium iodide paper; the development of a blue colour showed the presence of lead tetracetate).

The dark-red syrupy solution, containing a few suspended particles of red lead and lead dioxide, was poured into 1,000 c.c. of water, and the acetate extracted with ether.

The extract was washed first with water and then with saturated sodium chloride solution, and was finally dried over sodium sulphate. After removal of the solvent, the acetate was distilled in vacuo. B.p. 177°C/14mm.

Yield: 80 g. (75% theor.).
Acenaphthenol.

To a solution of acenaphthenyl acetate (80 g.) in methanol (135 c.c.) was added a solution of sodium hydroxide (20 g.) in water (200 c.c.). The mixture was refluxed for several hours and then cooled to below 20°C.

The yellow crystalline acenaphthenol was filtered off and thoroughly washed with water. The product was air-dried and then dissolved in benzene (1,000 c.c.). The solution was treated with activated charcoal, filtered, and the filtrate concentrated to 500 c.c. On cooling, pale yellow crystals of acenaphthenol separated. After a further recrystallisation from benzene, their melting-point remained constant at 144°C.

Yield: 57 g. (66% theor. calcd. on acenaphthene).
II. Reactions of Acenaphthenol with Acid Anhydrides.

1. With phthalic anhydride.

To a warm solution of phthalic anhydride (7.4 g.) in pyridine (8.0 g.) was added finely-powdered acenaphthenol (8.5 g.). The reaction mixture was kept at 50-60°C, for two days and was then cooled and poured into a 5% sodium carbonate solution (100 c.c.), giving after a few minutes a clear brown solution.

This solution was acidified by pouring it into 3N hydrochloric acid (45 c.c.) to which had been added some ice. On stirring, a very viscous mass separated, which, after the aqueous layer had been decanted off, was dissolved in cold ether (100 c.c.). The ethereal solution was washed repeatedly with dilute hydrochloric acid to remove the last traces of pyridine. The solvent was then evaporated, and 5% sodium carbonate solution (100 c.c.) added. The solution thus obtained was allowed to stand for several hours and then treated with small portions of ether to remove unesterified alcohol and neutral phthalic ester.

The hydrogen phthalic ester was precipitated by pouring the solution into excess hydrochloric acid and ice, separating from solution as a viscous white mass. The latter was dissolved in chloroform, the solution dried and the solvent finally evaporated under reduced pressure. The residue was recrystallised several times from ether-petroleum ether (40-60°C), giving small, white crystals, m.p. 121°C.
Yield: 11.5 g. (72% theor.).

Found on titration with 0.1N NaOH solution: M, 317.5;
C₂₀H₁₄O₄ requires M, 318.2.

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2. With succinic anhydride.

The hydrogen succinic ester of acenaphthenol was prepared in the same way as the hydrogen phthalic ester, using similar conditions and amounts of reagents.

The acenaphthenyl hydrogen succinate was obtained as needles from benzene, m.p. 145°C.

Found on titration with 0.1N NaOH solution: M, 269.2;
C₁₆H₁₄O₄ requires M, 270.3.

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3. With benzoic anhydride.

(1) In pyridine: a clear solution obtained on warming together acenaphthenol (2.1 g.), benzoic anhydride (1.4 g.) and pyridine (10 c.c.) was allowed to stand for two days, most of the time on a steam-bath. The solution was then poured into excess hydrochloric acid and ice, and the precipitate thus obtained was extracted with benzene and washed with dilute hydrochloric acid. Most of the solvent was evaporated and on cooling a crystalline precipitate formed which was identified as acenaphthenol by its melting-point and by a mixed melting-point determination with an authentic sample of acenaphthenol.
(ii) In benzene; a solution ofacenaphthenol (1.78 g.) and benzoic anhydride (1.18 g.) in benzene (20 c.c.) was kept on a steam-bath for two hours. On evaporation of the solvent, a brown resin was obtained which was redissolved in the minimum amount of warm benzene. The addition of ether to this solution caused the precipitation of a yellow powdery substance which after having been filtered off and dried was found to weigh approximately 1.4 g., and to have a melting-point above 230°C. It was found to have the same properties as the polyacenaphthylene encountered in further experiments.

4. With acetic anhydride.

In a flask fitted with a reflux condenser and a calcium chloride tube, were placed acenaphthenol (4.3 g.), acetic anhydride (2.6 g., 100% excess) and a trace of zinc chloride.

The clear mixture obtained on heating the mixture, was refluxed for two hours. The reaction mixture was then distilled in vacuo; the product was collected at 190°C, 25mm., and its physical properties found to be identical with those of the acenaphthenyl acetate obtained during the preparation ofacenaphthenol.

Yield: 4 g. (74% theor.).
5. With 3-nitrophthalic anhydride.

The method used in the preparation of the hydrogen nitrophthalate ofacenaphthenol was the same as that used in the preparation of the unsubstituted hydrogen phthalate.

Using this procedure, a reaction mixture ofacenaphthenol (6.12 g.), nitrophthalic anhydride (6.95 g.) in dry pyridine (25 c.c.) yielded 5 g. (26% theor.) ofacenaphthenyl hydrogen 3-nitrophthalate. After recrystallisation from ether-petroleum ether (40-60°), the ester was found to have m.p. 152° C.

(Found: C, 65.8; H, 4.0; C₂₀H₁₃O₆N requires C, 66.1; H, 3.6%).

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III. Reactions of Acenaphthenol with Acid Chlorides.

1. With benzoyl chloride.

   a) 1 c.c. of benzoyl chloride was added to a well-cooled solution of 1.2 g. of acenaphthenol in 6 c.c. of dry pyridine. The solution was kept at room temperature overnight, and was then poured into dilute hydrochloric acid containing small pieces of ice. An oily substance was precipitated, and taken up in ether. The ethereal solution was washed and then dried over anhydrous sodium sulphate.

   After removal of the drying agent and of the solvent, the residue crystallised as needles, melting at 144°C, and was identified as unchanged acenaphthenol.

   b) 3.4 g. of acenaphthenol were dissolved in 17 c.c. of pyridine and the solution was cooled in a freezing-mixture. 2.9 c.c. of benzoyl chloride were added, and this resulted in the immediate precipitation of a crystalline mass. The mixture, however, became homogeneous on warming; after standing at about 90°C, for two hours and then at room-temperature for 48 hours, the mixture was acidified and treated as in (a). The product was again identified as acenaphthenol.

   c) A solution of acenaphthenol (5 g.) in dry pyridine (25 c.c.) was cooled, and a solution of benzoyl chloride (4.1 g.) in dry chloroform (15 c.c.) slowly run in. The clear mixture was allowed to stand on a water-bath for several
days, but only acenaphthenol could be recovered from the final reaction mixture.

d) 3 g. of acenaphthenol were dissolved in 30 c.c. of benzoyl chloride and the mixture was warmed on a steam-bath, giving after a few hours a dark greenish-brown homogeneous solution.

The mixture was cooled and poured into excess N/2 caustic soda solution. After standing for a few hours, a dark syrupy mass had separated, and was extracted with a small amount of benzene. Addition of ether to this extract produced a yellow powdery precipitate which, after drying, was found to have a melting-point above 250°C., and was assumed to be a polymer of the kind already encountered in previous experiments with acenaphthenol.

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2. With acetyl chloride.

A small amount of acenaphthenol was dissolved in a large excess of acetyl chloride, and the unreacted chloride was removed in a vacuum desiccator over caustic soda.

The residue consisted of a dark-brown viscous mass, which, on addition of ether, immediately changed into a yellow powder. The latter was filtered and identified as polyacenaphthylene by its very high melting-point and its giving a fluorescent solution in benzene.

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3. **With p-toluene sulphonyl chloride.**

To a solution of p-toluene sulphonyl chloride (2.5 g.) in cold, dry pyridine (10 c.c.) was added acenaphthenol (2.25 g.) dissolved in warm pyridine (10 c.c.). The clear solution thus obtained was kept on a steam-bath for several hours, and then poured into ice-cold dilute hydrochloric acid. The precipitate was extracted with ether, washed with dilute acid, and dried.

Removal of the solvent followed by cooling, yielded a crystalline residue which was identified as unchanged acenaphthenol.
IV. Reactions of Acenaphthenol and its Derivatives with Acids.

1. Acenaphthenol and Hydrochloric Acid.

2 g. of acenaphthenol were triturated in the cold with 10 c.c. of concentrated hydrochloric acid, but no reaction appeared to take place. The mixture was warmed to about 60°C., when the solid gradually changed into an oily substance. After cooling, the aqueous layer was decanted. The residue was dissolved in benzene, giving a solution which showed pronounced fluorescence. The addition of ether caused the precipitation of a yellow powdery mass, which could not be recrystallised from any of the usual solvents and could only be purified by dissolving it in the minimum amount of benzene and reprecipitating it with ether. The pale yellow powder finally obtained had a melting-point above 250°C., and its molecular weight was found to be roughly a multiple of that of acenaphthylene. The actual proportion between the molecular weights was not the same in different experiments, and appeared to vary with the length of treatment with acid.

2. Acenaphthenol and Hydrobromic Acid.

2 g. of acenaphthenol were triturated at 75-80°C. with 10 c.c. of hydrobromic acid solution, and after thorough shaking, the mixture was allowed to cool down. The solid mass which had formed was extracted with benzene, and treated as in (1), with identical results.
3. Acenaphthenol and anhydrous Formic Acid.

Using the same experimental conditions as in (1), it was found that acenaphthenol polymerises in the presence of formic acid in the same way as it does when treated with hydrochloric acid.

4. Acenaphthenyl Acetate and Hydrochloric Acid.

On warming acenaphthenyl acetate and hydrochloric acid together, polymerisation was found to take place in the same way as with the alcohol itself.

5. Acenaphthenyl Hydrogen Phthalate and Hydrochloric Acid.

The hydrogen phthalate was found to behave in the same way towards hydrochloric acid as the acetate, also yielding a polymer.

6. Acenaphthenyl Hydrogen Phthalate and 90% Formic Acid.

To 2.2 g. of hydrogen phthalate were added 5 c.c. of 90% formic acid. At room temperature, no reaction appeared to take place; on warming the mixture of a steam-bath, it remained heterogeneous, but turned yellow and then, after 10 hours, brown. The solid fraction was filtered off and dissolved in hot benzene, leaving however a residue which was identified as phthalic acid. To the benzene extract was added an excess of ether, and this resulted in the precipitation of the already previously encountered polymer.
V. Preparation of Acenaphthenyl Urethanes

1. Phenyl urethane.

3.42 g. of acenaphthenol were dissolved in 150 c.c. of warm, dry benzene, and an equimolecular amount of phenyl isocyanate (2.40 g.) in 10 c.c. of benzene added.

The mixture was refluxed for two hours, and most of the solvent then distilled off. On cooling, a bulky precipitate appeared which after drying, and recrystallising from alcohol, was found to melt at 137°C. (Found C, 78.9; H, 5.2; C_{19}H_{15}O_{2}N requires C, 78.9; H, 5.2%).

2. α-Naphthyl urethane.

To a warm solution of 3.45 g. of acenaphthenol in 150 c.c. of benzene were added 3.43 g. of α-naphthyl isocyanate. The clear solution was refluxed for a few hours, and most of the solvent was then distilled off. The residue was recrystallised from benzene.

M.p. of the naphthyl urethane which was obtained as small plates was 196°C. (Found C, 81.4; H, 5.18; C_{23}H_{17}O_{2}N requires C, 81.4; H, 5.07%).

3. p-Xenyl urethane.

A reaction mixture consisting of 3.08 g. of acenaphthenol and 3.52 g. of p-xenyl isocyanate dissolved in 150 c.c. of benzene, was refluxed for a few hours, and most of the solvent then evaporated. The p-xenyl urethane thus obtained was recrystallised from benzene yielding colourless needles melting at 177-178°C. (Found C, 82.7; H, 5.51; N, 4.10; C_{25}H_{19}O_{2}N requires C, 82.3; H, 5.24; N, 3.83%).
VI. Attempted Reaction of Acenaphthenyl Hydrogen Phthalate
with Sodium p-Toluene Sulphinate.

A solution of acenaphthenyl hydrogen phthalate (1.84 g.) in 0.25N. aqueous caustic soda (23.2 c.c.) containing a trace of ethyl alcohol, was filtered into a solution of sodium p-toluene sulphinate (1.03 g.) in water (25 c.c.).

The clear solution was then left in an ice-chest for several hours, but no precipitate appeared. The solution was allowed to stand at room temperature, but even after eight days no crystals had separated.
VII. Constitution of Polyacenaphthylene.

Three samples of polyacenaphthylene, obtained from different reactions, were analysed and the results are shown below:

<table>
<thead>
<tr>
<th>Reaction</th>
<th>% C</th>
<th>% H</th>
<th>M.W.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acenaphthenol + HCl</td>
<td>92.9</td>
<td>5.2</td>
<td>-</td>
</tr>
<tr>
<td>Acenaphthenol + PhCOCl</td>
<td>92.9</td>
<td>5.3</td>
<td>-</td>
</tr>
<tr>
<td>Acenaphthenol + (PhCO)₂O</td>
<td>92.9</td>
<td>5.3</td>
<td>1800</td>
</tr>
</tbody>
</table>

In all three cases, there appears to be an oxygen content of about 1.8%, which makes it most unlikely that the polymer merely consists of acenaphthene residues, viz.

\[
\left[\text{CH—CH—}\right]
\]

Such a compound would have contained 94.7% carbon and 5.3% hydrogen. On the other hand, if one assumes the polymer to consist of a straight chain of such residues, terminated at both ends with a hydroxyl group (see below), the above analyses would agree with the calculated values for such a polymer where \(n=11\) to 12 (M.W. 1744):

\[
\text{HO—}\left[\text{CH—CH—}\right]_n\text{—OH}
\]
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