R-SUBSTITUTED AZETIDINES

and

OTHER ASPECTS OF AZETIDINE CHEMISTRY

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ABSTRACT

Azetidine has been prepared and its nucleophilicity towards bromoaromatic compounds has been investigated. In this way the synthesis of a number of new N-arylazetidines has been accomplished. The infra red spectra of these azetidines, together with those of a few N-alkylazetidines, prepared from the corresponding 3-aminopropanols, have been compared. Cleavage of the 4-membered ring in N-substituted azetidines, using hydrogen bromide, has been briefly examined.
1. **INTRODUCTION**

The present project is concerned with the preparation of the hitherto unreported $N$-aryl- and of certain $N$-alkylazetidines. The only detailed review of the chemistry of azetidine and its derivatives is some years out of date and, although there has been a revival of interest in the azetidines in the last few years, the amount of factual material is still fairly small. It was therefore thought both advisable and practicable to design the introduction to this thesis as a review of the known chemistry of azetidine itself, with particular attention to its $N$-alkyl derivatives.

a. **Methods of Preparation**

Azetidine (I) was the last of the lower alkyleneimines to be isolated in pure form. It is still the least accessible of the series and many of its simpler derivatives are unknown. Moreover, the known $N$-alkylazetidines have often been prepared in low yields, particularly when the alkyl groups are small. In general, there are three possible
synthetic routes to azetidines:
(a) through reduction of the readily obtainable
2-azetidinones (β-lactams);
(b) through cyclization of 3-substituted amines; and
(c) through the condensation of 1,3-dihalopropyl
derivatives with primary amines or amides.

The reduction of 2-azetidinones has been investi-
gated by a number of workers with little success,
3-aminooxazoles being reported the main products of
attempted reductions unless the ring nitrogen atom is
unsubstituted. This characteristic was also noted by
Testa and co-workers, but Testa further reported that
reduction of 3-substituted azetidinones in which the
nitrogen atom was unsubstituted gave good yields of
azetidines when lithium aluminium hydride was used as
the reducing agent. It is to be noted that N-substituted

\[
\begin{align*}
    \text{CH}_2 & \\
    \text{C} & \\
    \text{R}_z & \\
    \text{NH} & \\
\end{align*}
\]

\[
\rightarrow
\begin{align*}
    \text{LiAlH}_4 & \\
    \text{CH}_2 & \\
    \text{C} & \\
    \text{R}_z & \\
    \text{NH} & \\
\end{align*}
\]

azetidines have not been prepared in this manner.

The preparation of azetidines by cyclization from
3-substituted amines affords the method of widest
scope. 1,3-Diaminopropane derivatives, 3-halo-α-propylamine
derivatives, 3-amino-propan-1-ol derivatives and
3-aminopropyl-1-sulphuric acid derivatives have all been used with varying degrees of success.

The pyrolysis of 1,3-diaminopropane derivatives to give azetidines was one of the earliest methods of preparation. The synthesis of azetidine itself, impure and in low yield, by dry distillation of 1,3-diaminopropane dihydrochloride was described by Ladenburg and Sieber in 1890.  

\[
\begin{align*}
\text{CH}_2\text{NH}_2\cdot\text{HCl} + \text{CH}_2\text{NH}_2\cdot\text{HCl} & \xrightarrow{\text{Dry Distillation}} \text{CH}_2\text{NH}_2 \cdot \text{HCl} + \text{NH}_4\text{Cl} + \text{HCl} \\
\end{align*}
\]

Two years earlier Balbiani reported the preparation of \(N\)-phenyl-azetidine by heating \(N\)-(3-aminopropyl) aniline dihydrochloride. However the

\[
\begin{align*}
\text{CH}_2\text{NH}_2\cdot\text{HCl} + \text{CH}_2\text{NH}_2\cdot\text{HCl} & \xrightarrow{\text{Heat}} \text{CH}_2\text{N-CH}_5 \cdot \text{HCl} + \text{NH}_4\text{Cl} + \text{HCl} \\
\end{align*}
\]

free base was not isolated but obtained as the chloroplatinate. This remains the sole recorded synthesis of an \(N\)-arylazetidine, a further claim by Scholtz being shown, quite recently, to be unfounded. Moreover, since Balbiani obtained his \(N\)-phenylazetidine from an acid solution, it seems unlikely that his chloroplatinate was that of \(N\)-phenylazetidine. Other attempts to obtain
azetidines by the pyrolysis of diamines have also been reported, but there is no claim of an N-alkylazetidine being made in this way. It is of interest that 3,3-dimethylazetidine (prepared by the pyrolysis of 2,2-dimethyl-1,3-diaminopropane dihydrochloride and isolated as the picrate) has subsequently been obtained by Testa and co-workers by reduction of the corresponding 2-azetidinone with lithium aluminium hydride.

Base-induced dehydrohalogenation of 3-haloalkylamines has been a common method of preparation of azetidines and high yields have occasionally been reported. The first preparation of azetidine, in impure form, was by this method. Gabriel and Weiner obtained a small amount of azetidine when 3-bromo-\( \sigma \)-propylamine was treated with potassium hydroxide. Quaternary azetidinium salts have been prepared by cyclization of the corresponding \( N,N \)-dialkyl-3-bromo-\( \sigma \)-propylamines, the stable azetidinium compounds forming spontaneously at room temperature.

\[
\text{Br-CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_2 \xrightarrow{\text{KOH}} \text{CH}_2-\text{CH}_2-\text{NH}^+\text{CH}_3 \quad \text{(KOH) (-HBr)}
\]

\[
\text{Br-CH}_2-\text{CH}_2-\text{CH}_2-NR_2 \xrightarrow{\text{?}} \text{CH}_2-N^+R\text{CH}_3 \quad \text{(Br\textsuperscript{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{\textcircled{R}}}}}}}}}}}}}}
\]
A more recent example of cyclization of a 3-halopropylamine to a 4-membered ring is that given by Vaughan, Klonowski et al., who report a good yield when sodium ethoxide is used as base. They obtained methanesulphonazetidide in 66% yield from N-(3-chloropropyl)-

\[
\begin{align*}
\text{CH}_3\text{SO}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{Cl} & \xrightarrow{\text{NaOEt}} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NSO}_2\text{CH}_3
\end{align*}
\]

methanesulphonamide. In investigations concurrent with the present work, L.M. Deady, in this department, has prepared a number of N-aryiazetidines using ethanolic sodium hydroxide as base. In general, it is reported that the dehydrohalogenation of 3-haloalkylamines, when the amine is primary and the halogen secondary, gives poor yields of azetidines. However, if the halogen is primary and the amine is secondary, cyclization takes place readily.

Of the remaining two types of 3-substituted amines from which cyclization to the 4-membered ring has been attempted, the 3-aminopropan-1-ol derivatives are reported to be resistant to such ring closure. If, however, the 3-aminopropan-1-ol hydrochlorides are treated with sulphuric acid or chlorosulphonic acid, the 3-aminomethyl-1-sulphuric acids obtained give azetidines on distillation from alkaline solution. This method has been used particularly for the preparation of
N-alkylazetidines, the yield of azetidine obtained increasing with increase in size of the N-substituent.

The most frequently exploited preparation of azetidine itself, by reduction of N-\textsubscript{p}-toluenesulphonamidoazetidine, is dependent on the reaction of 1,3-dibromopropane with \textsubscript{p}-toluenesulphonamide for the formation of the 4-membered ring. Other preparations of highly substituted azetidines by reaction of a dihalide and a sulphonamide have also been reported. N-alkylazetidines have not been prepared by this method, and the only recorded instance of the preparation of an azetidine from a dihalide and an amine is that of Scholtz who reported to have obtained N-phenylazetidine by the reaction of 1,3-dibromopropane and aniline. More recent workers, however, have shown that the compound described by Scholtz as N-phenylazetidine was probably 1, 2, 3, 4-tetrahydroquinoline. N-Phenylazetidine has now been prepared in this department by L.W. Deady through dehydrohalogenation of N-(3-bromopropyl)aniline.

b. Theory of Cyclization

Cyclization of 3-aminopropyl derivatives to the azetidine ring is a slow process. Freundlich and
Co-workers have investigated the kinetics of formation of alkylenenimines by ring closure of haloalkylamines. The first-order rate constants for the cyclization of bromoalkylamines indicate that the reaction is slowest for 3-bromo-n-propylamine and that the order of decreasing cyclization rates is \( \text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \to \text{BrCH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \to \text{BrCH}_2\text{CH}_2\text{NH}_2 \to \text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \to \text{BrCH}_2\text{CH}_2\text{NH}_2 \). This order is in accord with the report that 1-benzenesulphonamide-2,3-dibromopropane cyclizes to the ethylenenimine derivative and not to the azetidine compound.

\[
\text{Br}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{SOCH}_2\text{CH}_2\text{H}_2 \overset{\text{OH}^-}{\longrightarrow} \text{Br}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{SOCH}_2\text{CH}_2\text{CH}_2\text{H}_2
\]

The low rate of cyclization to azetidine has been accounted for by Freundlich and Salomon, who considered the ease of cyclization to be the resultant of two competing factors. The statistical frequency of mutual approach of the reacting groups at the ends of the chain diminishes with increasing chain length. Hence ring closure will become less likely with increase in chain length. However, during cyclization the bond angle must decrease from the normal carbon tetrahedral value (109°) to the value of the angle in the ring.
Since the ring angle decreases with decrease in the size of the ring, the strain in the rings simultaneously increases, and this second factor alone would result in easier ring closure with greater chain length. It is assumed that with the cyclic imine the resultant of these two factors leads to a minimum in the rate of cyclization to the 4-membered ring. This has also been found with the cycloalkanes. However, the reported rate of cyclization of 3-bromo-n-propylamine is said to be too low to fit in with the simple two-factor argument of Freundlich and Salomon.\textsuperscript{10}

The rate of cyclization of a 3-aminopropyl chain to azetidine will inevitably be affected by substituents on the chain. The conformational aspects of chain substitution have been discussed in a recent paper.\textsuperscript{1}

The transition state for cyclization (II) is such that

substituents on carbons 2 and 3 are eclipsed. Thus large \textit{erythro} substituents on carbons 2 and 3 will reduce the rate of cyclization. In addition, \textit{erythro} substituents on carbons 2 and 3 will decrease the stability of the ring once it is formed. Large \textit{erythro}
substituents on carbons 1 and 2 will also reduce the rate of cyclization since they are similarly eclipsed in the transition state. However, the effect of erythro substituents, attached to carbons 1 and 2, on the rate of cyclization will be less serious than that of erythro substituents on carbons 2 and 3 since the latter must also be eclipsed in the conformation leading to the ground state and this will materially reduce the probability of cyclization. Three substituents, on the other hand, should not conformationally affect the rate of cyclization.

The low rate of cyclization to azetidine will affect the amount of cyclic product obtained, in that competing reactions are given more chance to occur. Thus azetidine is understandably the most difficult alkyleneimine to prepare and product yields are generally low by comparison with the other alkyleneimines, which are formed more rapidly from alkylamines. Grob has listed the competing processes to cyclization which are able to occur in a reaction involving 3-aminopropyl halides. Four reaction pathways, in opposition to cyclization,
are available but owing to different potential mechanisms of fragmentation etc. it is not generally possible to estimate the relative importance of any particular process. Tertiary halides would presumably favour carbonium ion formation and the resultant carbonium ion would then be involved in solvent capture (substitution), loss of a proton (elimination), or fragmentation. An alternative
mechanism for fragmentation in which electron release from the amino group assists the process, is also possible.

\[
\begin{align*}
\text{N-C-C-C-X} & \rightarrow \text{N=C-C-C-X} \\
\text{N=C} & + \text{C=H} + X
\end{align*}
\]

Of the remaining potential reaction paths, dimerization (or quaternization), which may be controlled by appropriate dilution of reactants, has long been recognised as a process competing with cyclization. Syntheses of the highly strained ethylenimine and azetidine ring systems are both prone to yield cyclic dimers, and ethylenimine derivatives are known to form piperazine derivatives under the action of halogen acids. Elimination has not been reported to occur to any great extent, although L.W. Deady has obtained \( N\)-allylaniline as well as \( N\)-phenylazetidine upon dehydrohalogenation of \( N\)-(3-bromopropyl)aniline.\)

Vaughan, Klonowski and co-workers have applied Gröb's stereoelectronic requirements for fragmentation to the problem of azetidine synthesis from 3-halo or 3-0-sulphonylpropylamines. By considering the relative effects of \( N\)-substitution upon fragmentation and cyclization, these workers have accounted for the low yields of azetidines obtained when the ring nitrogen is
unsubstituted, and for the improvement in yield when the nitrogen is substituted. When the nitrogen has a large substituent, cyclization is more favoured because in the transition state the electron pair is less suitably orientated for fragmentation and the possibility of bond formation with carbon I is thereby increased.

Although the rate of cyclization on N-substitution may be unfavourably affected by decreasing the probability of the transition state for cyclization, the rate of fragmentation will be more seriously depressed owing to its great sensitivity to stereo-electronic factors. Hence the ratio of cyclized product to fragmented product will increase with increase in the size of the
N-substituent.

c. The Chemistry of Azetidine

It is presumably because azetidine is difficult to prepare that the chemistry of this compound has not been extensively studied. The theoretical instability of the 4-membered ring, which must be considerably strained, is reflected in the cleavage reactions readily undergone by azetidine and its derivatives. Dilute and concentrated inorganic acids open the azetidine ring to yield 3-aminopropyl derivatives. In view of this, it is not surprising that few hydrohalides of azetidines have been reported, and that these few are usually found to be unstable.

The azetidine molecule should, on theoretical grounds, contain a flat ring because this arrangement is that of least strain and steric interaction. Consequently geometric and optical isomers would be expected when the ring is disubstituted, provided that the substituents do not occur on the same ring carbon atom. However, no report of the resolution of disubstituted azetidines is to be found in the literature.

Azetidine is a secondary amine and has basic properties. Three papers dealing with the basicity of azetidine and the other alkylene-imines have been published. Although the results in these three papers are not in complete agreement, it appears that
azetidine is the most basic, while ethyleneimine is the least basic of the series. Brown and Gerstein have reported the order of basicity of the alkyleneimines to be 4→5→6→3-membered imines. This order was concluded from a study of the electron-donor ability of alkyleneimines to trimethylboron. The low basicity of ethyleneimine was ascribed to an increase of the internal strain (I-strain) which might be expected to occur when the base coordinates with an acid; the decrease in basicity in going from the 5 to the 6-membered cyclic imine was ascribed to an increase in the steric effects of the α-methylene groups (F-strain). An explanation of the high basicity of the 4-membered trimethyleneimine ring was offered on the basis of a small I-strain compared with that associated with ethyleneimine, and a small F-strain compared with that in pyrrolidine.

On the other hand, a direct measurement of the thermodynamic basicity constants of the alkyleneimines in aqueous solutions indicates pyrrolidine to be the most basic of the series. Searles and colleagues reported the order of basicity with ring size to be 3 < 6 < 4 < 5 for both the unsubstituted cyclic imines and the N-methyl derivatives. This order was confirmed, in the same paper, by a spectroscopic determination of
the hydrogen-bonding ability of the unsubstituted imines and their N-methyl derivatives, with CH$_3$OD. In each ring size, the addition of a methyl group to the nitrogen atom was reported to cause a decrease in the basicity constant, but an increase in the hydrogen-bonding ability.

However, the work of Sheinker and Peresleni agrees with that of Brown and Gerstein. Both these groups report azetidine to be the most basic imine of the series and the order of basicity to be $4 \gtrsim 5 \gtrsim 6 \gtrsim 3$. The Russian workers obtained actual values for the basicity constants of the alkyleneimines and these are tabulated below. It is readily seen that ethyleneimine

<table>
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<th>$K_b$</th>
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<tr>
<td>Ethyleneimine</td>
<td>$1 \times 10^{-6}$</td>
</tr>
<tr>
<td>Azetidine</td>
<td>$2 \times 10^{-3}$</td>
</tr>
<tr>
<td>Pyrrolidine</td>
<td>$0.9 - 1.3 \times 10^{-3}$</td>
</tr>
<tr>
<td>Piperidine</td>
<td>$1.2 \times 10^{-3}$</td>
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</table>

is by far the weakest base of the series and on this point all the reports are in agreement.

Closely related to the basicity of the alkyleneimines, and of particular interest to the present work, is the relative nucleophilic strength within the series. Piperidine has been well studied and many N-alkyl derivatives have been prepared.
has also been found to be an especially good nucleophile for aromatic substitution, reacting smoothly with a wide range of halo-aromatics when the activity of the halogen has been enhanced by the presence of electron-withdrawing groups in the molecule. Little correlation between the basicity and nucleophilicity of a reagent is generally possible, otherwise the much less reactive diethylamine, which has a basic strength comparable with that of piperidine, would show similar nucleophilic activity. The observed difference in reactivity between diethylamine and piperidine is explicable on the basis of steric interference by the ethyl groups of diethylamine which are free to rotate and to hinder attack on the nitrogen atom. On the other hand, the α- methylene groups of piperidine are held rigidly in the 6-membered ring, thus leaving the nitrogen atom relatively unprotected from attack by other groups. However, within a closely related series like the alkyleneimines, the order of nucleophilicity would be expected to follow closely the order of basicities, both properties being related to the electron-donor ability of the molecule concerned. Thus, since azetidine is a stronger base than piperidine, its nucleophilicity should be higher and nucleophilic replacement of halogen from aromatic compounds should take place more readily.

Remarkably little attention has been paid to
the reaction of azetidine with alkyl halides. This again is probably attributable to the difficulty in obtaining workable quantities of azetidine. Consequently, those N-alkylazetidines that have been prepared have usually been obtained from N-substituted aminopropyl derivatives. Only three references to the N-alkylation of azetidine have been noted. Two of these papers deal with attempts to methylate azetidine in the 1-position. Yanbikov and Dem'yanov in 1936 reported that a compound having the correct analysis for N-methylazetidine hydriodide was formed by treatment of azetidine with methyl iodide in ether. More recently, Gibson et al. stated that they were unable to prepare the N-methyl product from azetidine and methyl iodide. When the reactants were mixed in cold ether, the product was azetidine hydriodide and no other products were identified. When the reaction was carried out in alcoholic potassium hydroxide, complete methylation to the quaternary iodide occurred. The only other attempt to prepare an N-alkylazetidine was a successful one. Testa and co-workers have reported the preparation of 1-benzyl-3-phenylazetidine by the reaction of benzyl bromide and 3-phenylazetidine, in the presence of triethylamine.
Because of the paucity of information concerning the alkylation of azetidine, no conclusions as to the reactivity of azetidine with alkyl halides can be drawn. However, from the work of Testa it seems that alkylation of azetidine, under suitable conditions, and particularly if the halogen is labile (as it is in benzyl bromide), can be performed readily. The use of a basic solvent to remove the hydrogen halide would appear to be advisable. This point affords an explanation of the results of Gibson who, with ether as solvent and without a large excess of azetidine, obtained the quaternary compounds on reaction of azetidine with methyl iodide. It would seem, in any case, that the alkylation of azetidines merits further investigation.

d. The Present Project.

The effectiveness of piperidine as a nucleophilic agent for aromatic substitution has already been mentioned. The expected increased nucleophilicity of azetidine compared with piperidine has also been discussed. Since N-arylazetidines were unknown, the preparation of N-arylazetidines from azetidine by reaction with aryl-halides was of twofold interest, and an investigation into this problem promised to be doubly fruitful. The range of N-arylazetidines amenable to direct preparation from azetidine, was expected to be dependent upon the
nucleophilic strength of azetidine, but it was realised that such N-arylazetidines would all contain electron-attracting substituents in the aryl ring.

The success of the investigation depended largely upon a good source of azetidine and this had been reported to be available by the reduction of p-toluene-sulphon-azetidide, using a modification of the original method of Howard and Marshwald. Attention was therefore turned to the choice of aromatic compounds from which N-arylazetidines might be obtained. Halogen substituents, which are commonly ejected in such nucleophilic displacements, had been reported to show the order of mobility $F > Cl > Br > I$ unless the fission of the ring carbon-halogen bond is rate determining. This order is in accord with steric considerations, the small fluorine atom offering less steric hindrance to an approaching nucleophile, than the larger halogen atoms. However, the rate of fission of the carbon-halogen bond could be expected to affect the rate to some extent, and since it was known that piperidine undergoes nucleophilic substitution smoothly with a number of bromo-aromatic compounds, it was decided to use bromoaromatic compounds whenever possible.

Irrespective of whether the rate of rupture of the carbon-halogen bond is rate-determining, the rate of nucleophilic substitution in aromatic compounds is always dependent on the rate of attack of the nucleophile at the
reaction centre. Thus the rate of reaction is always affected by the electron density at the reaction centre, being accelerated in this reaction by a low electron density at that centre. In the current work, the choice of bromoaromatic compounds was limited by this consideration.

Before the preparation of N-arylanilazetidines from azetidine could be satisfactorily investigated it was considered necessary to prepare a few N-alkylazetidines. A minor reason prompting such work was the very limited data available on such compounds, particularly data on their stability to acids. The major purpose in preparing some N-alkylazetidines, however, was to record their infra red spectra, which had hitherto not been reported. Not only would these spectra be of interest in themselves, but it was hoped that they would be of use in confirming the nature of the N-arylanilazetidines it was anticipated would be prepared. To assist the assignation of absorption bands in the infra red spectra of N-alkylazetidines it was decided to examine the spectra of other alkyleneimines, and a discussion of the spectra that were measured may be found on p. 70.
2. EXPERIMENTAL OUTLINE AND DISCUSSION OF RESULTS.

a. Synthesis of Azetidine

Azetidine was required in large quantities and particular attention was paid to reported methods by which it could be synthesized in high yield from readily available compounds. In the light of a recent paper, an attractive method was that first described by Howard and Marekmauld and since repeated by many workers. It involves cleavage-reduction of $p$-toluenesulphonazetidide by sodium in amyl alcohol:

![Chemical structure of azetidine synthesis]

This method seemed to provide by far the highest reported yield of azetidine, provided that some constraint was applied to the free flow of hydrogen gas from the hot solution. The required $p$-toluenesulphonazetidide has commonly been prepared by the reaction of 1,3-dibromo-propane with $p$-toluenesulphonamide in the presence of alkali, the highest reported yield being 55%.
An alternative synthesis of p-toluenesulphonazetidide, in 88% yield from 3-aminopropan-1-ol, has also been described. This method involves the reduction of 3-(p-toluenesulphonamido)propyl-p-toluenesulphonate (from 3-aminopropanol and p-toluenesulphonylchloride). The highest yield was given when potassium-t-butoxide was used as the reducing agent, but the use of sodium ethoxide was also described.
Both methods of preparation of \( p \)-toluenesulphonazetidide were investigated. The first method, starting with dibromopropane, was found to be the more straightforward of the two. This method was also found to be adaptable to an increase in concentration of reactants and alkali (over those given in the literature) without the yield being much affected. This was particularly advantageous since a large quantity of \( p \)-toluenesulphonazetidide was required.

The second method, from 3-aminopropanol, although described as giving higher yields than the first, was found in practice to be less suitable than the first method. This was because the high yields reported involved a second step using very high dilution of reactant (0.0055M 3-(\( p \)-toluenesulphonamido)propyl-\( p \)-toluenesulphonate in \( \beta \) - butyl alcohol). The low concentrations were chosen in order to minimise dimerisation and when, in the present work, the concentration of 3-(\( p \)-toluenesulphonamido)propyl-\( p \)-toluenesulphonate was increased (0.036M) the yield was only 65%. The formation of 3-(\( p \)-toluenesulphonamido)propyl-\( p \)-toluenesulphonate from 3-aminopropanol also gave a lower yield (41%) than that reported in the literature. This was largely because it was found difficult to remove, by recrystallization, all the traces of pyridine from the 3-(\( p \)-toluenesulphonamido)propyl-\( p \)-toluenesulphate.
\(N, N'-\text{bis-}\text{p-toluene sulphonyl-}1,5\text{-diazocyclooctane}

(III) was formed as a by-product of the preparation of

\[
\begin{array}{c}
\text{CH}_3 \\
\text{O} \quad \text{N} \\
\text{CH}_2 - \text{CH}_2 - \text{CH}_2 \\
\text{CH}_2 - \text{CH}_2 - \text{CH}_2 \\
\text{SO}_2 \\
\text{H}_2 \text{C} \\
\end{array}
\]

\(p\)-\text{toluene sulphonazetidide} from 1,3-\text{dibromopropane}. This
compound has been obtained in the same manner by a number of workers
and its formation is illustrative of the tendency of 3-\text{aminopropyl}
derivatives to dimerize under the conditions used for cyclization. The
cleavage-reduction of \(p\)-\text{toluene sulphonazetidide} was carried out
on the same scale as that described by Vaughan and Klonowski (75g. \(p\)-\text{toluene sulphonazetidide}; 21.\text{amyl alcohol}).
Moreover, since small amounts of azetidine (ca. 2g.) are not easily isolable
from the steam-distillate, small quantities of reactants were not practicable. Sodium
in \text{amyl alcohol} was used as the reducing agent, and the
temperature of the refluxing \text{amyl alcohol} (128-132\degree) was
well above the boiling point (61\degree) of azetidine. Considerable loss of
azetidine with the escaping hydrogen gas was therefore to be expected unless a dry ice condenser,
or some other suitable trap for the azetidine was used. In the present work, a sulphuric acid trap, similar to that described by Vaughan et al., was used. However, it is of interest that these workers state that the yield of azetidine was not decreased when the acid from the trap was discarded instead of being incorporated with the reaction mixture. In other words, the nature of the trap contents would seem to be of no significance, the function of the trap being largely mechanical, effecting almost complete retention of the azetidine within the reaction vessel.

The use of sulphuric acid to extract azetidine raises an interesting point. It is well known that both dilute and concentrated inorganic acids readily open the azetidine ring by direct addition, forming substituted \( \text{n} \)-propylamines in which the acidic group is in the 3 position. This reaction is said to be reversible in alkaline solution, particularly if the 3-substituted amine is subjected to steam distillation, and the ring compound is thus regenerated. Dilute sulphuric acid (2N) would be expected to open the azetidine ring with the formation of 3-aminopropyl-1-sulphuric acid.

\[
\begin{align*}
\text{CH}_2 & \quad \text{CH}_2 \\
\text{CH}_2 & \quad \text{NH} \\
\text{CH}_2 & \quad \text{CH}_2 \\
\end{align*}
\]

\[\xrightarrow{2\text{H}_2\text{SO}_4} \]

\[
\begin{align*}
\text{NH}_3 & \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2\text{OSO}_3\text{H} \quad \text{HSO}_4^+ \\
\end{align*}
\]
This, in acidic solution, might be expected to hydrolyse with the formation of 3-aminopropan-1-ol, a compound which does not undergo ring closure so readily. Moreover,

\[
\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-OSO}_3\text{H} \xrightarrow{\text{dilute acid}} \text{NH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{OH}
\]

it has been found recently that 3-aminopropyl-1-sulphuric acid, when treated with excess base and distilled, gives only a low yield (1.7%) of azetidine. Thus it would appear that any azetidine, opened by the action of sulphuric acid under the conditions used in the present experiment, is unlikely to be regenerated, irrespective of whether the 3-aminopropyl-1-sulphuric acid is further hydrolysed or not.

The use of sulphuric acid to extract azetidine from the amyl alcohol layer does not seem, therefore, to be at all desirable. This is especially so because at the time of the extraction most of the azetidine should be in the amyl alcohol layer, and hence a large percentage of the total azetidine formed must be treated with sulphuric acid. Howard and Marckwald themselves followed this procedure of extraction with sulphuric acid, and it is possible that the low yields of azetidine obtained by later workers using their method may be partly explicable
on this basis.

Vaughan and Klonowski, following the method of Howard and Marcikwald, also extracted the amyl alcohol layer with sulphuric acid. These workers, however, took the precaution of chilling the amyl alcohol before extraction, possibly in the hope of minimising the amount of 3-amino-propanol formed by hydrolysis of 3-aminopropan-1-sulphuric acid. But they did not, apparently, purify their azetidine, but simply collected and dried the amine layer obtained by saturating the watery distillate with potassium hydroxide. The refractive index \( n_\text{D}^{22} = 1.4110 \) of their azetidine is much less than other recorded values, and, in particular, below the value of 1.4278 \( n_\text{D}^{25} \) given by Ruzicka, Salomon and Meyer for carefully purified azetidine.

In the present work, after Vaughan's preparative procedure had been followed, the dried amine layer was fractionally distilled. Less than 50% (by weight) of this material proved to be azetidine, and a high boiling residue was obtained. In order to determine the nature of this high boiling fraction, the amine layers (65g.) from five reduction-cleavages on the scale described were combined and fractionally distilled. The azetidine \( (b.p. 61-71^\circ; 27g.) \) amounted to 41.5% of the amine layer, and 53.7% \( (35g.) \) of the layer came over at 140\(^\circ\) and above. The yield of azetidine was thus 26.6%, a figure comparable with the best reported yield previous to the work of
Vaughan, that attained by Yanbikov and Dem'yanov (36\%) using the same method. Had the whole of the amine layer been taken as azetidine the apparent yield would have been 64.3\%.

The higher boiling fraction was further fractionated, to give 21g. of colourless liquid (b.p. 186 - 190°) which was finally identified as octahydro-1,5-diazo-cine (IV). This may well have been

![Diagram]

the compound described by Heine et al, who, on attempted synthesis of azetidine from 3-aminopropyl-1-sulphuric acid, obtained a high boiling fraction (b.p. 110 - 190°) in unspecified yield which was not characterised.

The formation of octahydro-1,5-diazo-cine in this experiment is interesting. At some stage dimerization of the trimethyleneimine ring must occur, via ring cleavage. Since steam-distillation is generally reported to aid cyclization, the 8-membered cyclic dimer may be formed during steam distillation of the aqueous azetidine. This would require cleavage of the azetidine ring to occur either during the reduction with sodium or during the extraction of the azetidine with sulphuric acid.
Cleavage during the sodium-reduction cannot be precluded, but it does at least seem unlikely, because the azetidine ring, once formed, has considerable stability in the absence of acids. Because acids open the azetidine ring, it seems much more reasonable to assume that cleavage occurs during extraction with acid. Two reaction paths are then possible, with dimerization and cyclization occurring either in a one-stage, or a two-stage process:

A further possibility that octahydro-1,5-diazocine is not formed until the final distillation of the amine mixture cannot be overruled. The mono-amine compounds most likely to be present at this stage are azetidine and 3-aminopropanol, but individually, each of these could be
shown to distil quantitatively without change of refractive index. If, then, the cyclic dimer is formed at the final distillation stage, it must be the product of reaction between azetidine and the aminopropanol. This is clearly possible, and it is not irrelevant to note that N-(hydroxymethyl)-azetidine reacts with azetidine to form bisazetidinomethane:

\[
\begin{align*}
\text{CH}_2\text{N-CH}_2\text{OH} + \text{CH}_3\text{NH} & \rightarrow \text{CH}_2\text{N-CH}_2\text{N-CH}_2\text{CH}_2 + \text{H}_2\text{O}
\end{align*}
\]

Thus 3-azetidino-1-aminopropane (V) could similarly be formed and could rearrange to octahydro-1,5-diazocine:

\[
\begin{align*}
\text{CH}_3\text{NH} + \text{OHCH}_2\text{CH}_2\text{CH}_2\text{NH}_2 & \rightarrow \text{CH}_2\text{N-CH}_2\text{CH}_2\text{CH}_2\text{NH}_2
\end{align*}
\]

\[\text{Heat} \rightarrow \text{N-CH}_2\text{OH (oon OF neuse)}\]

much greater than normal alcohol on
Unfortunately, the cyclic dimer was only identified conclusively some time after the preparative work on azetidine had been completed. It was found impracticable in the time available to return to the preparation for an obvious test of this hypothesis. The necessary test is to analyse the amine layer, before distillation, in a gas chromatograph.

Clearly, although this preparative method for azetidine has now been shown to be less successful than was claimed by earlier workers, the present identification of octahydro-1,5-diazocine as a hitherto unreported reaction product is of help in any further refinement of the method. Thus, if the stage at which this compound is formed could be located, it is highly likely that the technique could be modified to avoid losses of azetidine in this way.

b. N-Alkylazetidines

N-Alkylazetidines were prepared by the well-established method involving reaction of the corresponding N-alkyl-3-aminopropan-1-ol hydrochlorides with chlor-sulphonic acid; the reaction mixture is made strongly alkaline and steam-distilled. The procedure is probably equivalent to steam-distilling an alkaline solution of the corresponding N-alkyl-3-aminopropyl-1-sulphuric acid. The N-alkyl-3-aminopropan-1-ols were readily obtained by
reaction of 3-chloro-, or 3-bromopropan-1-ol with an excess of the N-alkylamine. The hydrochlorides of the N-alkylaminopropanols were prepared in the usual manner.

The known syntheses of N-n-butylazetidine and N-ethylazetidine were repeated, and N-iso-propylazetidine, previously unreported, was also prepared. The yields of these compounds confirmed the trend to be expected with increase in size of the alkyl group (see p.6). This trend is illustrated by the figures given in Table I (p.31a). The yield of N-benzylazetidine appears to be out of line, and indeed, it has been suggested by Vaughan, Klonowski et al. that the 26% yield of N-benzylazetidine,
<table>
<thead>
<tr>
<th>N-Alkyl-3-propylsulphonate</th>
<th>Azetidine % yield</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ions</td>
<td>Literature</td>
<td>Present Work</td>
</tr>
<tr>
<td>$\left[ -\text{OSO}_3(\text{CH}_2)_3\text{NH}_2 \right]$</td>
<td>[1.7]</td>
<td></td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NHCH}_3$</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NHCH}_2\text{H}_5$</td>
<td>13</td>
<td>13.6</td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NHCH}_2\text{C}_6\text{H}_5$</td>
<td>5.9</td>
<td>1</td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NHCH(CH}_3)_2$</td>
<td>29.4</td>
<td></td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NH}-\text{t-C}_4\text{H}_9$</td>
<td>24.30</td>
<td>28</td>
</tr>
<tr>
<td>$-\text{OSO}_3(\text{CH}_2)_3\text{NH}-\text{t-C}_4\text{H}_9$</td>
<td>47</td>
<td>20</td>
</tr>
</tbody>
</table>
obtained by them from 3-N-benzylpropyl-\(p\)-toluenesulphonate hydrochloride, is a more reliable value.

The preparation of an \(N\)-arylazetidine from \(N\)-(3-hydroxypropyl)-\(p\)-toluidine was attempted, but no \(N\)-\(p\)-tolylazetidine was obtained. Only a high boiling, reddish oil was obtained, from which some colourless crystals, possibly formed by breakdown of the red compound, were isolated. The alkaline reaction mixture was ether-extracted instead of being steam-distilled, however no trace of \(N\)-\(p\)-tolylazetidine could be isolated. The bulk of the \(p\)-tolyl group is a factor expected to lead to a good yield of \(N\)-\(p\)-tolylazetidine, but it is possible that this factor was outweighed by the susceptibility of the activated aromatic ring to nuclear sulphonation by the chlorosulphonic acid. Moreover, the activated ortho position might be more favoured for ring closure than the nitrogen atom. Thus 6-methyl-1, 2, 3, 4-tetrahydroquinoline and derivatives could be formed.
Electron-withdrawing substituents in the aromatic ring of N-(3-hydroxypropyl)aniline would reduce the changes both of nuclear sulphonation and of cyclization to 1, 2, 3, 4-tetrahydroquinolines. However, the nucleophilicity of the nitrogen atom would be similarly decreased, and it is unlikely that N-arylazetidines would be obtained from such compounds. The concurrent work of Deady adds support to this, since he was only able to prepare N-arylazetidines from N-(3-bromopropyl)anilines which contained electron-donating substituents in the aromatic ring. Thus the preparation of N-substituted azetidines from N-substituted aminopropanols in the manner described does not seem to be applicable to the synthesis of N-arylazetidines.

c. **N-Arylazetidines**

A selection of bromoaromatic compounds of varying susceptibility to nucleophilic replacement of the bromine atom were allowed to react with azetidine. A large excess of azetidine was used to absorb the hydrogen bromide formed, and thereby to protect the N-arylazetidine from possible attack. Most of the bromoaromatic compounds, particularly those having nitro substituents, gave coloured solutions, often very intense, instantaneously on addition to azetidine. This occurred even in reactions from which no recognisable product was isolated
after some weeks. Thus the onset of colour in the reaction mixture was not indicative of the success of the reaction.

Those bromoaromatic compounds from which azetidyl derivatives were isolated, all contained ortho or para substituted nitro groups, although groups other than bromine were sometimes displaced. Two chloroaromatic compounds also gave azetidyl derivatives by displacement of the chlorine atom. Table II lists the bromo- and chloro-aromatic compounds from which N-arylanolides were obtained. This table also includes the times noted for first appearance of precipitated product and these, together with full reaction times and percentage yields, may tentatively be used for an approximate estimate of relative reactivities. (see p 36).

1-Chloro-2,4-dinitronaphthalene reacted extremely readily with azetidine, at room temperature, to give a compound which analysed satisfactorily for the expected 1-(N-azetidine)-2,4-dinitronaphthalene (VI). It should be pointed out that these assigned positions of
<table>
<thead>
<tr>
<th>Haloaromatic</th>
<th>Time before deposition of product</th>
<th>Reaction Time</th>
<th>% Yield (recrystallized)</th>
<th>Product</th>
</tr>
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<tbody>
<tr>
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<td>-</td>
<td>240 hr.</td>
<td>40</td>
<td><img src="image2" alt="Image" /></td>
</tr>
<tr>
<td><img src="image3" alt="Image" /></td>
<td>15 mins.</td>
<td>50 hr.</td>
<td>96</td>
<td><img src="image4" alt="Image" /></td>
</tr>
<tr>
<td><img src="image5" alt="Image" /></td>
<td>40 hr.</td>
<td>30 hr.</td>
<td>80</td>
<td><img src="image6" alt="Image" /></td>
</tr>
<tr>
<td><img src="image7" alt="Image" /></td>
<td>170 hr.</td>
<td>50°C</td>
<td>67</td>
<td><img src="image8" alt="Image" /></td>
</tr>
<tr>
<td><img src="image9" alt="Image" /></td>
<td>60 hr.</td>
<td>110 hr.</td>
<td>57</td>
<td><img src="image10" alt="Image" /></td>
</tr>
<tr>
<td><img src="image11" alt="Image" /></td>
<td>30 hr.</td>
<td>50 hr.</td>
<td>53</td>
<td><img src="image12" alt="Image" /></td>
</tr>
<tr>
<td><img src="image13" alt="Image" /></td>
<td>Immediate</td>
<td>15 hr.</td>
<td>41</td>
<td><img src="image14" alt="Image" /></td>
</tr>
</tbody>
</table>

* Reactant insoluble in azetidine.
substituents in the product are not fully proven. Indeed, unambiguous labelling of positions was not generally easy, except for the 1,4- and 1,2- disubstituted aromatic compounds obtained, in which the positions of substituents could be confidently assigned by a study of the relevant infra red spectra. In other cases, the position of substituents was inferred by analogy with 1,4- and 1,2- substituted N-arylasetidines.

Azetidine was observed to react with p-chloronitrobenzene at an appreciably slower rate than with p-bromonitrobenzene and in both cases the same product was obtained. This would indicate that the strength of the carbon-halogen bond was of major influence on reaction rate. 0-Bromonitrobenzene reacted with azetidine less readily than p-chloronitrobenzene and far less readily than p-bromonitrobenzene. It is possible that this
effect is a result of steric interaction between bromo- and nitro- substituents in \( \alpha \)-bromonitrobenzene. This interference would prevent the nitro group from lying in the plane of the benzene ring, and would therefore lead to a marked reduction in the ability of the nitro group to withdraw electrons by a conjugative mechanism. Activation to nucleophilic attack would therefore be reduced.

A further steric factor, adversely affecting the reaction rate with \( \alpha \)-bromonitrobenzene (VII), could be direct shielding of the reaction site by the ortho nitro group, although the attack by azetidine must take place laterally and the effect may not therefore be a major one. However it may be relevant to note that 4-bromo-2-methylnitrobenzene (VII\( ^a \)) appears to react more readily than \( \alpha \)-bromonitrobenzene. (VII)

When 3,4-dinitro bromobenzene was reacted with azetidine, both the 3 nitro group and the bromine atom were displaced, and a diazetidyl derivative was obtained.
The same diazetidyl derivative was given when 3-methoxy-4 nitro bromobenzene was reacted with azetidine, the methoxy and bromine groups being displaced.

The relative orders of mobility of aromatic leaving groups are reported to be \( F > NO_2 > CI, Br, I > NR_3 \)

OR \( \geq NR_2 \), the nitro group being more readily replaced than the bromine atom. This is, of course, provided that the effect of substituents upon the electrondensity at the position of attachment of the leaving group to the aromatic ring is identical in the molecules being considered. For example, when azetidine is reacted with p-bromonitrobenzene, the bromine group is displaced in preference to the more mobile nitro group. This is because the position para to the nitro group is much more activated to nucleophilic attack than that para to the bromine atom. If, however, p-bromonitrobenzene and p-dinitrobenzene were compared it would be expected that the order of mobilities of leaving groups would prevail and that the p-dinitrobenzene would be substituted faster by an attacking nucleophile than p-bromonitrobenzene.

In 3,4-dinitro bromobenzene (VIII) it is not easy
to predict whether N-(3,4-dinitrophenyl)azetidine or N-(5-bromo-2-nitrophenyl)-azetidine would be the initial product because of the uncertainty in weighing the two factors (a) mobility of departing group, and (b) activation at reaction site. However, Mann has shown that for reaction of piperidine with 3,4-dinitro- bromobenzene the two compounds N-(5-bromo-2-nitrophenyl)-piperidine and 2,4-bis(piperidinonitrobenzene) can be successively isolated from the reaction mixture. Of the possible interpretations, it seems to the writer to be most reasonable to assume that in the azetidine reaction, nitro replacement takes place before displacement of bromine.

Other results of Mann are relevant to the formation of 2,4-bis(N,N'-azetidino)nitrobenzene (IX) from 3-methoxy-4-nitro bromobenzene. When this substrate

![structure](image)

was attacked by piperidine, he isolated only N-(3-methoxy-4-nitrophenyl)piperidine. Since the bromine atom is more
mobile than the methoxy group; this would be expected to
be the first displacement in the azetidine reaction, and
the subsequent formation of 2,4-bis(N,N'-azetidino)nitrobenzene in good yield seems indicative of the
greater nucleophilicity of azetidine over piperidine.

Further evidence for the strong nucleophilic
character of azetidine was sought through a study of the
reactions of azetidine with bromoaromatics of weak
activation to nucleophilic substitution. Unfortunately
the conditions found to be so favourable for the prepara-
tion of ortho and para nitrophenylazetidines were not
found to be suitable for the preparation of other aryl-
azetidines. In the time available other reaction
conditions were not investigated and the present work was
restricted to a survey of the reaction of bromoaromatics
with azetidine, using excess azetidine as solvent. Under
these conditions it appears that when nucleophilic
replacement is slow, reactions competing with simple
nucleophilic substitution by azetidine may dominate
the reaction.

ortho and para Nitrobromobenzenes reacted so
cleanly and readily in excess azetidine that the same
conditions could well be favourable to N-arylazetidine
production from bromobenzenes containing less activating
substituents. Therefore, bromobenzene, 2-bromonaphthalene
and p-chlorobromobenzene were all separately dissolved in
excess azetidine and left in sealed tubes at 50° for as long as was practicable. However, after several weeks, all three bromo compounds could be recovered unchanged from the reaction mixtures.

Of the other bromoaromatic compounds examined, all except one contained meta nitro substituents. The exception was p-bromobenzonitrile, a compound in which the activating substituent is a cyano group, and which was known to react with piperidine to yield N-(p-cyanophenyl)-piperidine. However, after 28 days at 50°, no crystalline product had deposited from the solution of p-bromobenzonitrile and azetidine. A white sticky solid was precipitated when dilute alkali was added to the solution but the material could not be purified. Of the reactions which could compete with simple nucleophilic substitution there is one possibility that arises from the difference in stability between the azetidine and the piperidine ring systems. If initially some bromine from p-bromobenzonitrile was displaced by azetidine, the formation of hydrogen bromide should result in ring-fission in some of the excess azetidine, to give 3-aminopropylbromide. This compound, despite its low concentration, has a primary amine group, and might well be the cause of products other than the expected one. It is to be noted, in particular, that amidines are known to be formed by the addition of primary amines to the unsaturated nitrile bond.

Being chemically analogous to ortho and para...
nitrobromobenzenes, though less reactive, meta nitro-
bromobenzenes could still react favourably with azetidine
under the chosen conditions, despite previous reports of
problems encountered in the synthesis of similar piperidyl
compounds. Consequently $\omega$-nitrobromobenzene and
3,5-dinitro bromobenzene were dissolved in azetidine under
the conditions already described. Each of these compounds
gave an immediate very intense colour. That this colour
did not indicate that an extensive reaction had taken
place was shown by the fact that after a short time both
the aromatic starting materials could be recovered from
their respective reaction mixtures in high yield. When
a longer reaction time was allowed, dark, fairly brittle
material was isolated in each case. The material obtained
was of a different nature from that given by the reaction
of azetidine and $p$-bromobenzonitrile, but was equally
intractable.

Thus when bromoaromatic compounds were dissolved
in azetidine, no other compound being initially present,
only the ortho and para nitro substituted compounds were
observed to undergo nucleophilic aromatic substitution to
give $N$-arylazetidines.

d. The Action of HBr on Azetidines

The action of hydrogen bromide on $N$-substituted
azetidines was of interest. $N$-iso- Propylazetidine with
dry hydrogen bromide yielded N-iso-propylazetidine hydrobromide, a compound unstable in moist air, presumably opening to N-iso-propyl-3-aminopropylbromide:

\[
\begin{array}{c}
\text{CH}_2 \text{N}^+ \text{CH}_3 \\
\text{CH}_2 \text{H} \\
\text{CH}_3
\end{array} \quad \xrightarrow{2\text{HBr}} \quad \begin{array}{c}
\text{CH}_3 \\
\text{CH} \text{NH} \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_3 \text{Br} \\
\text{CH}_3
\end{array}
\]

N-iso-Butylazetidine hydrobromide has earlier been isolated but has also been reported as unstable.\(^{21}\)

N-Arylazetidine hydrobromides, on the other hand, seem to be too unstable to have any finite existence. Despite extreme precautions to exclude moisture, hydrogen bromide was found to yield only the open chain hydrobromide when reacted with N-(\(p\)-nitrophenyl)azetidine. This was so even when excess of the azetidine was used,

\[
\begin{array}{c}
\text{CH}_2 \text{CH}_2 \text{N} \text{NO}_2 \\
\text{CH}_2 \text{CH}_2
\end{array} \quad \xrightarrow{2\text{HBr}} \quad \begin{array}{c}
\text{B}^\text{+} \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{N}^\text{+} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{NO}_2 \\
\text{B}^\text{+}
\end{array}
\]

a small amount of the open chain hydrobromide being the only product isolated.
It would appear, therefore, that in \( N-(p\text{-nitroaryl}) \)
azetidines the hetero ring is much less stable to acids than
the corresponding ring in \( N \)-alkylazetidines. If this
instability is characteristic of \( N \)-arylazetidines in
general, it might account, in part at least, for the
complete absence in the literature, of authentic reports
of the isolation of \( N \)-arylazetidines. It may be noted
that, in the absence of acids, the \( N \)-arylazetidines
prepared during the current work are completely stable at
room temperature, and were stored without difficulty.
3. EXPERIMENTAL PROCEDURE

1. All melting points are corrected.

2. Microanalyses were carried out at Otago University (N.Z.).

AZETIDINE

p-Toluene sulphonazetidide.

Procedure A:

1. Sodium hydroxide (1 mole; 15% solution) was added over 6 hours to a stirred, refluxing solution of p-toluene sulphonamide (0.5 mole) and 1,3-dibromopropane (0.5 mole) in 95% ethanol (200 ml.). The alcohol was distilled off and the hard, yellow wax left on cooling was twice recrystallised from 96% hot ethanol. The yield of white, crystalline p-toluene sulphonazetidide was 46g. (44% yield); m.p. 112-116° (literature m.p. 112-115°, 120° pure).

11. The concentrations of reagents and reactants were increased from those given above and a further 3 hours were allowed for the reaction to reach completion. Quantities used were: sodium hydroxide (7 mole; 22.5% solution), p-toluene sulphonamide (3.5 mole), 1,3-dibromopropane (3.5 mole), 96% ethanol (11.). The yield of p-toluene sulphonazetidide was 319g. (51.5% yield); m.p. 114-116°.
N, N'-p-toluenesulphonyl-1,5-diazacyclooctane (X)

was also isolated as a secondary product of the reaction of 1,3-dibromopropane and p-toluenesulphonamide, the compound (X) being only sparingly soluble in ethanol and thus separable from the main product, p-toluenesulphonazetidide. The compound (X) was twice recrystallized from 95% hot ethanol to give white needles; m.p. 209-211° (literature m.p. 215°).

The infra red absorption spectrum of the compound showed no H-H absorption band. Molecular weight determination by depression of the freezing point of benzene was carried out, but was limited in accuracy by the sparing solubility of the compound (X) in benzene. Three determinations gave values of 456, 407 and 398; which support a molecular weight of 422.6 calculated for C_{20}H_{26}N_{2}O_{4}S_{2}.

**Analysis**

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C_{20}H_{26}N_{2}O_{4}S_{2}</td>
<td>56.84%</td>
<td>6.20%</td>
<td>6.63%</td>
</tr>
<tr>
<td>Found</td>
<td>56.64%</td>
<td>5.74%</td>
<td>6.01%</td>
</tr>
</tbody>
</table>
Procedure B:

3-(p-Toluene-sulphonamido)propyl-p-toluene-sulphonate.

A solution of 3-aminopropan-1-ol (50g.) in freshly distilled pyridine (1800 ml.) was cooled to -5° in an ice-salt bath. p-Toluene-sulphonylchloride (295g., 98.5% pure) was added in portions, with stirring, the temperature being kept below 5°. The initially colourless solution turned green and then orange during the addition of p-toluene-sulphonylchloride, which took 1.5 hours. The solution was stirred for 4 hours, the temperature being maintained between 0° and 5°. The precipitated pyridine hydrochloride was filtered off and the filtrate was poured into a mixture of ice and water (4l.). A red oil collected at the bottom of the container while the water held a yellow precipitate in suspension. The red oil set to a cake of orange crystals. Both solids were filtered off and the mixture of crystals was recrystallized from ethanol/water (4:1) to yield a yellow solid (105g., 41% yield). Further recrystallization from hot methanol gave almost white 3-(p-toluene-sulphonamido)-propyl-p-toluene-sulphonate; m.p. 116-118° (literature m.p. 120-121°).

Cyclization to p-toluene-sulphonazetidide.

Potassium metal (8.4g.) was added to a solution of 3-(p-toluene-sulphonamido)propyl-p-toluene-sulphonate
(51g.) in t-butyl alcohol (900 ml., sodium-dried). The solution was refluxed for 10.5 hours, with stirring. The fine precipitate of potassium p-toluenesulphonate (49.2g.) was filtered off from the hot solution and the solvent was removed by flash distillation from the filtrate. The residue, still containing some t-butyl alcohol, was taken up in hot methanol, filtered, and poured into water (1l.) whereupon p-toluenesulphonazetidide (27g. dry, 65.2% yield) precipitated.

Reduction-cleavage of p-toluenesulphonazetidide.

Amyl alcohol (21°, b.p. 128-132°) was placed in a 2-necked flask fitted with two reflux condensers, one of which led to a sulphuric acid (2N.) trap while the other was stoppered, except when sodium was being added down its central tube. The amyl alcohol was heated to boiling, p-toluenesulphonazetidide (75g.) was dissolved in it, and sodium metal (150g.) was added over 3 hours. The sodium took a further 3 hours to dissolve completely in the refluxing solution. The mixture was allowed to cool overnight and water (900ml.) added. The lower aqueous, alkaline layer was separated and distilled (about 150ml.) until no more amyl alcohol came over. The distillate was then added to the alcohol layer remaining in the separatory funnel. This was chilled, and enough dilute sulphuric acid was added, including that from the trap, to ensure acidity. The resulting acidic extract was itself ether-
Scheme for isolation of azetidine after reduction-cleavage of p-toluenesulphonazetidide

Reaction in AMYL ALCOHOL

**Add** H₂O

AMYL ALCOHOL Layer

**Add** H₂SO₄

AMYL ALCOHOL Layer

**Add** Ether

ETHER Layer

**Add** Ether

ACID Layer

AQUEOUS SOLUTION (ALKALINE)

**Distl**

200 ml.

AQUEOUS AZETIDINE

Saturate with KOH

AZETIDINE Layer

**Water**

Residue
extracted to remove any amyl alcohol present, and then freed of ether by an air stream, after which it was added to the original, strongly alkaline solution. Aqueous azetidine was distilled off and the distillate (about 200 ml.) was saturated with potassium hydroxide. The amine layer (13 g.) which separated was dried over potassium hydroxide.

The amine layers (65 g.) from five such reductions were combined and fractionally distilled to give azetidine (27 g., 26.6% yield); b.p. 61-70°. A pure sample of azetidine (for an infra red analysis) was obtained by fractional distillation of the impure azetidine; b.p. 61.0°, n°D$^20 1.4220$, (literature b.p. 59.5-70°, pure b.p. 60.5-62.5°; n°D$^20 1.4273$). The remainder of the amine layer (38 g.) distilled between 140 and 162°, and a large part of it (21 g.), a colourless liquid of ammoniacal odour, was collected at 186-190° (n°D$^25 1.4485$). This fraction contained only one component since the vapour phase chromatogram (Pye Argon) showed only one peak. The fraction was identified as octahydro-1,5-diazocine (XI) (literature b.p. 186°). Two picrates could be prepared.

\[
\begin{align*}
\begin{array}{c}
\text{H} & \text{N} & \text{H} \\
\bigg) & \bigg( & \bigg)
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2-\text{CH}_2-\text{CH}_2 \quad \text{CH}_2-\text{CH}_2-\text{CH}_2
\end{align*}
\]

(\text{XI})
The yellow di-picrate was obtained by mixing an excess of hot ethanolic picric acid with a hot ethanol solution of octahydro-1,5-diazocine (\(\text{III}\)). This di-picrate melted with decomposition at 224\(^\circ\) (literature m.p. 228\(^\circ\)). The yellow mono-picrate, which does not appear to have been previously known, was prepared by mixing equimolar hot ethanolic solutions of the compound (\(\text{III}\)) and picric acid. It darkened on heating and melted sharply (168-169\(^\circ\)).

**Analysis of mono-picrate.**

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>41.98%</td>
<td>4.99%</td>
<td>20.41%</td>
</tr>
<tr>
<td>Found</td>
<td>41.40%</td>
<td>5.18%</td>
<td>20.49%</td>
</tr>
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</table>

**N-Ethylazetidine**

**N-Ethyl-3-aminopropan-1-ol.**

Ethylamine (2 moles) was added to 3-chloropropan-1-ol (1 mole) in a 500 ml. flask fitted with an open-jacketed reflux condenser cooled with an acetone/solid CO\(_2\) mixture. The reaction mixture was shaken intermittently for 2 hours and left for a further 17 hours. Some heat was evolved by the initial reaction, and solid particles of amine hydrochloride were deposited on the sides of the flask and condenser. The excess ethylamine was distilled off and sodium hydroxide (125 ml.; 40% solution) was added to the reaction mixture. Further sodium hydroxide (flake) was added to make the solution strongly alkaline, and the solution was extracted with ether (2 x 50 ml). The ether extracts were dried over potassium carbonate, and fraction-
ally distilled to give colourless, liquid N-ethyl-3-
aminopropan-1-ol (76g., 74% yield); b.p. 183-192°,
ν₂⁰ 1.4521, (literature cf. ɳ₂ 1.4550 and ɳ₂⁰ 1.4463).

N-Ethyl-3-aminopropan-1-ol hydrochloride

Hydrogen chloride gas (dried over sulphuric
acid) was passed into a solution of N-ethyl-3-aminopropan-
1-ol (40g.) in ether (sodium-dried). N-Ethyl-3-
aminopropan-1-ol hydrochloride (56g.) was obtained as a
slightly sticky solid. A melting point determination was
unsatisfactory.

Cyclization of N-Ethyl-3-aminopropan-1-ol hydrochloride

N-Ethyl-3-aminopropan-1-ol hydrochloride (56g.)
was treated dropwise with freshly distilled chlorosulphonic
acid (90g.) in a 500 ml. flask fitted with a reflux
condenser. After the initial vigorous reaction had
subsided, the reaction mixture was heated on an oil bath
at 100° for 45 minutes, and then at 150° for 1.5 hours, and
left overnight. The dark gum which formed was dissolved
in water (140ml.) by long stirring to give a dark solution.
This solution was added, in portions, to an ice-cold
solution of potassium hydroxide (180g. in 200ml. water)
and the resulting alkaline solution was steam-distilled.
The aqueous distillate (about 300ml.) was made strongly
alkaline with potassium hydroxide, and twice extracted
with ether. The ether extracts were dried over potassium
hydroxide, the ether was removed by flash distillation, and
the remainder was fractionally distilled. Colourless, liquid N-ethylazetidine (4.5g., 13.6% yield based upon the weight of N-ethyl-3-aminopropan-1-ol taken) was obtained; b.p. 74°, n_D^{15.5} 1.4090, n_D^{25} 1.4020, (literature b.p. 74-75°, n_D^{25} 1.4090).

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
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<tbody>
<tr>
<td>Calculated for C_5H_{11}N:</td>
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<td>12.94%</td>
<td>16.47%</td>
</tr>
<tr>
<td>Found:</td>
<td>70.35%</td>
<td>12.81%</td>
<td>16.39%</td>
</tr>
</tbody>
</table>

**N-iso-Propylazetidine**

**N-iso-Propyl-3-aminopropan-1-ol.**

This was prepared in the same manner as N-ethyl-3-aminopropan-1-ol. Excess _iso_-propylamine (2 moles) was added to 3-bromopropan-1-ol (1 mole). The reaction mixture was stirred for 13 hours. Colourless, viscous, N-iso-propyl-3-aminopropan-1-ol (64g., 55% yield) was collected; b.p. 190-194°. The compound had a melting point of about 20° and was readily purified by fractional crystallization.

**N-iso-Propyl-3-aminopropan-1-ol hydrochloride**

Dry hydrogen chloride gas was passed into an ether (sodium-dried) solution of N-iso-propyl-3-aminopropan-1-ol (32g.). White, crystalline N-iso-propyl-3-aminopropan-1-ol hydrochloride (38g.) m.p. 83-84° was obtained.
Cyclization of \textit{N-iso-Propyl-3-aminopropan-1-ol}

\textit{N-iso-Propyl-3-aminopropan-1-ol} hydrochloride (35g.) was treated, as described for \textit{N-ethylazetidine}, with freshly distilled chlorosulphonic acid (43g.). Colourless liquid \textit{N-iso-propylazetidine} (7.7g., 29.4% yield); b.p. 94-96°C, \(n_\text{D}^25\) 1.4120 was obtained. Analysis of \textit{N-iso-propylazetidine} for carbon and hydrogen by combustion could not be carried out because of the explosive violence with which the compound oxidized, breaking the combustion tube on each attempt. A picrate m.p. 205-206° was therefore prepared.

\begin{center}
\textbf{Analysis of picrate}.
\end{center}

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for (\text{C}<em>{12}\text{H}</em>{16}\text{N}_4\text{O}_7)</td>
<td>43.90%</td>
<td>4.91%</td>
<td>17.07%</td>
</tr>
<tr>
<td>Found</td>
<td>44.23%</td>
<td>5.39%</td>
<td>16.70%</td>
</tr>
</tbody>
</table>

\textit{N-\textmu-Butylazetidine}

\textit{N-\textmu-Butyl-3-aminopropan-1-ol}.

This was prepared in a manner similar to that already described, \textit{\textmu-butylamine} (57.5g.) and 3-chloropropan-1-ol (37g.) being used. \textit{N-\textmu-butyl-3-aminopropan-1-ol} (16.5g., 31% yield) was obtained as a colourless oil b.p. 110-115°/18mm.; (literature b.p. 115-120°/20mm.).

\textit{N-\textmu-Butyl-3-aminopropan-1-ol} hydrochloride

\textit{N-\textmu-Butyl-3-aminopropan-1-ol} (16.5g.) in a solution of ether (sodium-dried) gave \textit{N-\textmu-butyl-3-
aminopropan-1-ol hydrochloride (21g.) upon treatment with dry hydrogen chloride. The hydrochloride was obtained as a gummy solid, the quality of which could not be improved. A melting point determination was unsatisfactory.

Cyclization of N-\(\eta\)-Butyl-3-aminopropan-1-ol hydrochloride.

Freshly distilled chlorosulphonic acid (24g.) was added dropwise to N-\(\eta\)-butyl-3-aminopropan-1-ol hydrochloride (21g.) and the subsequent procedure was as already described for N-ethylazetidine. N-\(\eta\)-Butylazetidine was obtained (0.4g., 28% yield); b.p. 124-130°, (literature b.p. 127-128°).

Attempted preparation of N-\(\pi\)-Tolylazetidine.

N-(3-Hydroxypropyl)-\(\pi\)-toluidine.

Reagent grade \(\pi\)-toluidine was distilled (b.p. 84°/10mm.) and heated on a water bath at 50-55°. 3-Bromopropan-1-ol (70g.) was added, with stirring. After being heated at 55-60° for 2 hours, the reaction mixture was cooled and made slightly alkaline with sodium hydroxide (10% solution). The solution was extracted with ether (700 ml.) and the separated ether layer was washed with water (3 x 100ml.), after which it was dried over potassium carbonate. The ether was removed by flash distillation and the remainder was fractionally distilled. N-(3-Hydroxypropyl)-\(\pi\)-toluidine (51g., 61%
yield) was obtained b.p. 189-190\(^\circ\)/22mm. The tail of the
distillate, although still distilling at 190\(^\circ\), was
coloured a pale orange.

**N-(3-Hydroxypropyl)-\( p \)-toluidine hydrochloride.**

N-(3-Hydroxypropyl)-\( p \)-toluidine hydrochloride
(61g.) was obtained from N-(3-hydroxypropyl)-\( p \)-toluidine
(51g.) (see p.53). The hydrochloride was obtained as
a gummy solid and a melting point determination was
unsatisfactory.

**Attempted cyclization of N-(3-Hydroxypropyl)-\( p \)-toluidine
hydrochloride.**

Freshly distilled chlorosulphonic acid (60g.)
was added dropwise to N-(3-hydroxypropyl)-\( p \)-toluidine
hydrochloride (61g.). The method described for N-
ethylazetidine was followed except that the final aqueous
alkaline solution was extracted with ether (3 x 100ml.)
instead of being steam-distilled. The yellow ether
extracts were dried over potassium hydroxide and the
ether was removed by flash distillation. The remainder
was fractionally distilled at reduced pressure. A red
oil, distilling steadily over a wide temperature range of
132-192/1mm., set in the receiver (N-\( p \)-tolylazetidine
b.p. 112-116\(^\circ\)/3mm.). The red solid was recrystallized
from 96\% ethanol to yield a red residue and colourless
crystals (0.2g.) m.p. 196-198\(^\circ\) (N-\( p \)-tolylazetidine m.p. 37\(^\circ\)).
yellow picrate m.p. 165°. Lassaigne's sodium fusion test indicated the presence of chlorine, but not of sulphur or nitrogen in the crystals. The red residue gave both a positive chlorine and a positive nitrogen test. A determination of the molecular weight of the crystals by depression of the freezing point of benzene was attempted, but a solution of the crystals in benzene slowly gave a brown precipitate in the benzene solution. Attempted recovery of the crystals by evaporation of the benzene led only to a brown residue. This residue defied all attempts at recrystallization.

**N-Arylazetidines**

**N-(p-Nitrophenyl)azetidine**

(i) \( p \)-Bromonitrobenzene (0.36g., 0.0018M) was dissolved in azetidine (1.07g., 0.019M) in a long tube, to give a yellow solution gradually deepening in colour. After 15 minutes yellow crystals were deposited from the solution and within 30 minutes crystals had spread throughout the solution. The tube was sealed and immersed in an oil bath maintained at 50°. After 50 hours, potassium hydroxide (0.4g. in 5ml. water) was added to the reaction mixture, which was shaken up and filtered. The yellow residue was twice recrystallized from hot ethanol to yield fine yellow needles of \( N-(p \)-nitrophenyl) azetidine (0.29g., 95.6% yield); m.p. 119°.
Analysis

<table>
<thead>
<tr>
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<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C₇H₁₀N₂O₂</td>
<td>60.65%</td>
<td>5.65%</td>
<td>15.74%</td>
</tr>
<tr>
<td>Found:</td>
<td>60.41%</td>
<td>5.78%</td>
<td>15.52%</td>
</tr>
</tbody>
</table>

N-(p-Nitrophenyl) azetidine gave an orange picrate which darkened on heating and finally decomposed at 212°.

(ii) p-Chloronitrobenzene (0.22g., 0.0014M) was dissolved in azetidine (0.52g., 0.009M) to give a yellow solution. After 40 hours at 50° yellow crystals were observed in the solution. A further 40 hours at 50° was allowed for the reaction, after which time the mixture was treated as in the preceding experiment. N-(p-Nitrophenyl) azetidine was isolated as yellow crystals (0.2g., 80% yield); m.p. 118.5°. A mixed melting point of the N-(p-nitrophenyl) azetidine with that already obtained showed no depression. The infra red absorption spectrum of the compound obtained from p-chloronitrobenzene was identical with that of the product from p-bromonitrobenzene.

The following compounds were all isolated from their respective reaction solutions in a manner analogous to that described for N-(p-nitrophenyl) azetidine. Except where stated, the reactions were carried out at 50°.
2,4-Bis(N,N'-azetidino) nitrobenzene

(1) 5-Bromo-2-nitroanisole (0.33g., 0.0014M) was dissolved in azetidine (0.91g., 0.016M) to give an immediate orange solution. Orange crystals were deposited from the solution after about 30 hours. A total of 50 hours was allowed for the reaction. The yellow, crystalline product was obtained as thin needles (0.16g., 53% yield) and was recrystallized from 96% ethanol. The melting point was 123° and the analytical figures indicated that the compound was 2,4-bis(N,N'-azetidino)-nitrobenzene (XII).

![Chemical Structure](attachment:image)

**Analysis**

<table>
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<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C(<em>{12}H</em>{15}N_3O_2)</td>
<td>61.76%</td>
<td>6.48%</td>
<td>18.01%</td>
</tr>
<tr>
<td>Found:</td>
<td>62.03%</td>
<td>6.65%</td>
<td>17.72%</td>
</tr>
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</table>

(ii) 3,4-Dinitro bromobenzene (0.25g., 0.001M) was dissolved in azetidine (0.6g., 0.01M) to give a red solution. The initial reaction was exothermic and took
place with effervescence. After 60 hours orange crystals were observed in the solution and after 110 hours golden yellow crystals (0.12g., 57% yield); m.p. 122-123° were obtained and recrystallized from 96% hot ethanol. A mixed melting point of this compound with that obtained from 5-bromo-2-nitroanisole showed no depression, indicating that the product in this case also was 2,4-bis(N,N'-azetidino)nitrobenzene (XII). The infra red spectra of the two samples of 2,4-bis(N,N'-azetidino)nitrobenzene were identical.

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C_{12}H_{15}N_{3}O_{2}</td>
<td>61.76%</td>
<td>6.48%</td>
<td>18.01%</td>
</tr>
<tr>
<td>Found:</td>
<td>61.07%</td>
<td>6.61%</td>
<td>17.53%</td>
</tr>
</tbody>
</table>

N-(O-Nitrophenyl)azetidine.

O-Bromo nitrobenzene (0.31g., 0.0015M) was dissolved in azetidine (0.84g., 0.015M) to give a yellow solution which slowly turned orange. The initial reaction was exothermic. No crystals were deposited in the solution, but after 10 days dilute potassium hydroxide (0.3g. in 5 ml. water) was added and the precipitated orange solid was recrystallized from petroleum ether (b.p. 50-70°). Orange crystals of N-(O-nitrophenyl) azetidine (0.1g., 49.0% yield) were obtained. m.p. 53.5°.
<table>
<thead>
<tr>
<th>Analysis</th>
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<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C$<em>9$H$</em>{10}$N$_2$O$_2$</td>
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<td>15.74%</td>
</tr>
<tr>
<td>Found:</td>
<td>61.2%</td>
<td>6.10%</td>
<td>15.41%</td>
</tr>
</tbody>
</table>

N-(3-Methyl-4-nitrophenyl)azetidine

3-Methyl-4-nitrobenzene (0.125g., 0.0005M) was dissolved in azetidine (0.45g., 0.008M) to give a pale yellow solution. After 20 hours a few small yellow crystals were deposited from the solution, but after 7 days the quantity of these crystals had not increased. Yellow, crystalline N-(3-methyl-4-nitrophenyl)-azetidine (0.008g., 67% yield) m.p. 67-68°C was precipitated from the solution on addition of potassium hydroxide (0.3g., in 5 ml. water) and recrystallized from hot 96% ethanol.

<table>
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<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for C$<em>{10}$H$</em>{12}$N$_2$O$_2$</td>
<td>62.48%</td>
<td>6.30%</td>
<td>14.29%</td>
</tr>
<tr>
<td>Found:</td>
<td>62.20%</td>
<td>6.63%</td>
<td>14.03%</td>
</tr>
</tbody>
</table>

1-(N-azetidino)-2,4-dinitronaphthalene

Azetidine (0.8g., 0.01M) was added to 1-chloro-2,4-dinitro-naphthalene (0.25g., 0.001M). The reaction was immediate, with effervescence and evolution of heat, to give a deep red solution and a yellow solid. After 15 hours at room temperature orange crystals of 1-(N-azetidino)-2,4-dinitronaphthalene (XIII) (0.11g.,
41% yield) were obtained and recrystallized from hot benzene. The crystals turned slowly black on heating but melted sharply 209-210°.

![Chemical structure image]

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
</tr>
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<tbody>
<tr>
<td>Calculated for C₁₃H₁₁N₅O₄</td>
<td>57.12%</td>
<td>4.03%</td>
<td>15.38%</td>
</tr>
<tr>
<td>Found</td>
<td>56.97%</td>
<td>4.39%</td>
<td>15.10%</td>
</tr>
</tbody>
</table>

Attempted syntheses of N-Arylazetidines from azetidine

N-Phenylazetidine

Azetidine (0.43g., 0.0075M) and bromobenzene (0.48g., 0.003M) were mixed together in a long tube. The tube was sealed and placed in an oil bath at 50° for 120 days. Potassium hydroxide (0.1g. in 6 drops of water) was added and the reaction mixture was shaken thoroughly. Three layers separated out: a surface azetidine layer, followed in succession by a water layer, and a bottom layer of unreacted bromobenzene. The
bromobenzene and the azetidine layers were separately
dried over potassium hydroxide, and a sample of each was
passed through the vapour phase chromatograph (Pye
Argon). The bromobenzene layer appeared to contain
no other compound. The azetidine layer was found to
contain a component other than azetidine but in very
small quantities. The presence of this component was
indicated by a very small peak and the retention time
proved to be similar to that of a sample of N-phenyl-
pyrrolidine (b.p. 110°/9mm.); (N-phenylazetidine b.p.
ca. 100°/9mm.). However the amount of compound, as
indicated by the peak area, was too small to be isolated.
It was evident, therefore, that under the experimental
conditions very little reaction had taken place between
the bromobenzene and the azetidine.

N-(p-Chlorophenyl)azetidine

p-Bromochlorobenzene (0.67g., 0.0035M) was added
to azetidine (0.5g., 0.009M) to give a colourless
solution. After 98 days at 50° p-bromochlorobenzene
(0.6g.) was recovered from the solution.

N-(2-Naphthyl)azetidine

2-Bromonaphthalene (0.72g., 0.0035M) was added
to azetidine (0.5g., 0.009M) to give a brown solution.
After 99 days at 50° 2-Bromo-naphthalene was isolated
from the solution.
N-(3,5-Dinitrophenyl)azetidine

(1) 3,5-Dinitrobenzobenzene (0.2g., 0.002M) was added to azetidine (0.8g., 0.014M) to give immediately a very intense, dark red solution. Because of this rapid coloration, the reaction was quenched after 30 minutes by addition of water (10ml.). However, only relatively pure 3,5-dinitrobenzobenzene (ca. 0.2g.) was precipitated.

(11) 3,5-Dinitrobenzobenzene (0.67g., 0.0026M) was added to azetidine (0.5g., 0.009M). After 21 days at 50° only black solid intractable material could be isolated. This material appeared to be of high molecular weight, being insoluble in a wide range of solvents, and it could not be purified further.

N-(m-Nitrophenyl)azetidine

(1) m-Bromonitrobenzene (0.8g., 0.004M) was added to azetidine (0.5g., 0.009M). The colourless azetidine immediately turned pink and then red. However after 50-60 hours at room temperature, only m-bromonitrobenzene could be recovered from the reaction mixture.

(11) m-Bromonitrobenzene (0.6g., 0.003M) was added to azetidine (0.5g., 0.009M). After 38 days at 50° gummy, brown solid material was obtained. From this a few colourless needles of m-nitrobenzobenzene could be isolated but the bulk of the brown solid was
insoluble in organic solvents and could not be purified.

N-(p-Cyanophenyl)azetidine

p-Bromobenzonitrile (0.38g., 0.0021M) was dissolved in azetidine (1.02g., 0.018M) to give a colourless solution. After 28 days in a sealed tube at 50°, the solution was treated with dilute potassium hydroxide (0.1g. in 5ml. water), whereupon a white, sticky solid precipitated and was filtered off. The solid, although soluble in ethanol, could not be recrystallized. Attempts to make the picrate by mixing hot ethanolic solutions of picric acid and the unknown material, resulted in the formation of a soft, tacky yellow solid from which no crystalline material could be obtained.

The action of HBr on N-iso-Propylazetidine

Gaseous hydrogen bromide, produced by dropping bromine (A.R.) on to tetralin and dried over calcium chloride and phosphorus pentoxide, was passed for 5 minutes into a dry ethereal solution (50ml.) of N-iso-propylazetidine (0.3g.). A flocculent white solid (0.29g) was precipitated. The solid was filtered, and dried by an air stream, both of these operations being carried out in a dry glove box. The solid melted at 135-136° and hydrolysed rapidly in the atmosphere. Analysis indicated the compound to be N-iso-propylazetidine
hydrobromide.

Analysis

| Calculated for C₆H₄Br₂N₂O₂⁺ | 46.85% |
| Found:                       | 47.11% |

The action of HBr on N-(p-Nitrophenyl)azetidine

(1) Hydrobromic Acid (aqueous)

Concentrated aqueous hydrobromic acid (10 drops, = 1.48 g./c.c.) was added to N-(p-nitrophenyl)azetidine (0.05 g.) The yellow crystals dissolved immediately to give a brown solution. The solution was left for 12 hours, and on cooling in an acetone/solid CO₂ bath, almost colourless crystals separated. The crystals (0.08 g.) were recrystallized from concentrated hydrobromic acid and dried in a vacuum desiccator. When dry the crystals were very pale yellow and melted at 128-132⁰. The 60% increase in weight could only be accounted for if the product had gained two bromine atoms, as would be expected for N-(3 bromopropyl)-p-nitroaniline hydrobromide.

Analysis

| Calculated for C₉H₁₂Br₂N₂O₂⁺ | 44.37% |
| Found:                       | 44.68% |

Attempted recrystallization of N-(3-bromo- propyl)-p-nitroaniline hydrobromide from hot 96% ethanol gave bright yellow crystals (m.p. 62.5-63.5⁰) which were
themselves recrystallized from hot 96% ethanol. Analysis indicated that the compound was likely to be N-(3-bromopropyl)_p-nitroaniline still contaminated by hydrogen bromide (7%).

**Analysis**

<table>
<thead>
<tr>
<th></th>
<th>Bromine</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated for 92.92% C₉H₈BrN₂O₂</td>
<td>35.66%</td>
<td>10.05%</td>
</tr>
<tr>
<td>Found:</td>
<td>35.65%</td>
<td>10.06%</td>
</tr>
</tbody>
</table>

Further recrystallization of the compound from hot ethanol would probably have removed the residual hydrogen bromide present. However, having only a small quantity (0.04g.) of N-(3-bromopropyl)_p-nitroaniline hydrobromide in hand, this hydrobromide was added to a solution of potassium hydroxide (0.01g. in 1ml. water). The almost colourless crystals gave yellow N-(3-bromopropyl)_p-nitroaniline which was filtered off and dried (m.p. 63°C). A mixed melting pt. of this compound with that obtained by the action of hot ethanol on N-(3-bromopropyl)_p-nitroaniline hydrobromide showed no depression. Furthermore, the infra red absorption spectra of the two samples of N-(3-bromo-propyl)_p-nitroaniline were identical.

(ii) **Hydrogen bromide (anhydrous)**

Gaseous hydrogen bromide (dried over calcium chloride and then phosphorus pentoxide) was passed into a solution of N-(p-nitrophenyl)acetidine (0.027g.) in ether (sodium dried; 30ml.). Immediately a bright
yellow precipitate was noticed (N-(3-bromopropyl)-p-nitro-aniline?) which turned white as soon as it was formed.

After passage of hydrogen bromide for 30 seconds the flask was stoppered and transferred to a dry glove box. The flask contents were filtered through a sintered glass funnel, and the white residue dried by a dry air stream. In moist air the white residue turned pale yellow, as it also did on heating (m.p. 122-124°). A mixed melting point with N-(3-bromopropyl)-p-nitroaniline hydrobromide, prepared from (aqueous) hydrobromic acid and N-(p-nitrophenyl) azetidine, showed no depression.

N-Butylpiperidine.

n-Butyl bromide (27.4g., 0.2 mole) and piperidine (105g., 1.21 mole) were refluxed together for about 4 days. The reaction mixture was cooled and piperidine hydrobromide (45g.) was filtered off. The filtrate was made strongly alkaline with potassium hydroxide (0.5M. solution) and then extracted with ether (2 x 100ml.). The ether extracts were dried over potassium hydroxide and the ether removed by flash distillation. The remainder was fractionally distilled to yield colourless, liquid N-n-butylpiperidine (19.5g., 69.4% yield); b.p. 175-178°, n_D^{25} 1.4435 (literature b.p. 175-178°, n_D^{25} 1.4442).

The infrared spectra of azetidines and other alkyleneimines have received little attention, and few references to them are to be found in the literature. There is only one report on azetidine itself and the paper containing it is also the only one recording an investigation into the effect of the alkyleneimine ring size on infrared spectra. Other workers have recorded the spectra of alkyleneimines other than azetidine, and some comparisons have been made between the spectra of this series and those of the cycloalkanes. In the case of ethyleneimine, comparisons with the infrared spectra of both cyclopropane and ethylene oxide have been made. However, with only one exception, published papers have restricted the comparisons of absorption bands to those arising from C-H and N-H stretching vibrations and hence the results recorded have been of only limited applicability to the present work.

Two Russian workers, Sheinker and Peresleni, have examined the infrared and Raman spectra of the unsubstituted alkyleneimines containing from two to six carbon atoms. They have published the spectrum of azetidine and have recorded its main absorption bands, but have assigned only the C-H and N-H stretching frequencies. With regard to these two vibrations, it was observed that the transition from multi-membered to
strained rings with few atoms was accompanied by a regular increase in the valency frequencies of the C-H bonds, a result in accord with that observed for the cycloalkanes. A decrease in the stretching frequencies of the N-H bonds, with decrease in ring size, was also observed.

The Russian workers attempted to correlate the basicity of the alkyleneimines with the value of the N-H vibrating frequencies, but concluded that no parallelism existed between these two properties. They further reported that, in the liquid state, the unsubstituted alkyleneimine molecules were associated by hydrogen bonding of the type N-H...N, the bond becoming weaker as the size of the ring increased. During the present work, it was considered that the breadth of a number of absorption bands might possibly be attributed to hydrogen bonding of this type, and this suggestion appeared to be strongly supported when it was observed that the spectra of the N-alkylazetidines were not similarly affected, being much more sharply resolved.

In the search for infra red bands which could be characteristic of compounds carrying an azetidine ring, the compounds listed below were examined. All spectra were measured with a Perkin-Elmer 221 spectrophotometer equipped with sodium chloride optics. The spectra are reproduced following p. 77.
<table>
<thead>
<tr>
<th>Compound</th>
<th>b.p.</th>
<th>$n_D^{25}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azetidine</td>
<td>61°</td>
<td>1.4220</td>
</tr>
<tr>
<td>N-Ethylazetidine</td>
<td>74°</td>
<td>1.4020</td>
</tr>
<tr>
<td>N-iso-Propylazetidine</td>
<td>94-96°</td>
<td>1.4120</td>
</tr>
<tr>
<td>N-n-Butylazetidine</td>
<td>124-130°</td>
<td></td>
</tr>
<tr>
<td>N-phenylazetidine</td>
<td>104-112°/11 mm.</td>
<td>1.5695</td>
</tr>
<tr>
<td>Pyrrolidine</td>
<td>88-89°</td>
<td></td>
</tr>
<tr>
<td>N-Phenylpyrrolidine</td>
<td>137-139°/20 mm.</td>
<td></td>
</tr>
<tr>
<td>Piperidine</td>
<td>105-106°</td>
<td></td>
</tr>
<tr>
<td>N-n-Butylpiperidine</td>
<td>173.5°/769 mm.</td>
<td>1.4435</td>
</tr>
</tbody>
</table>

A few absorption bands could be assigned with reliability to a particular vibration. These bands are given in Table III. Analytically, the most useful of these assignable absorption bands was that due to the N-H stretching vibration (3240 cm$^{-1}$). This band was completely absent when the alkyleneimine nitrogen atom was substituted and such absence provided positive evidence for the authenticity of the N-alkyl-azetidines prepared during the course of the work.

The C-H stretching band (2975-2730 cm$^{-1}$) was present consistently in the alkyleneimines. This was usually a wide band of high intensity and was sometimes resolved into two or three adjacent peaks. A strong band in the range
<table>
<thead>
<tr>
<th></th>
<th>NH</th>
<th>Et</th>
<th>i-Pr</th>
<th>t-Bu</th>
<th>V.S.</th>
<th>Cyclopyrrolidone</th>
<th>S.</th>
<th>D-8u</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-H stretching</td>
<td>M.</td>
<td>V.S.</td>
<td>3340</td>
<td>3240</td>
<td>V.S.</td>
<td>S. 3030</td>
<td>V.S.</td>
<td>V.S.</td>
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<td></td>
<td>3240</td>
<td></td>
<td>3240</td>
</tr>
<tr>
<td>C-H stretching</td>
<td>V.S.</td>
<td>V.S.</td>
<td>2975-</td>
<td>2940-</td>
<td>V.S.</td>
<td>V.S. 2930</td>
<td>V.S.</td>
<td>V.S.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2640</td>
<td>2640</td>
<td></td>
<td>2860</td>
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<td>2910-</td>
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<td>2960</td>
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<td></td>
<td></td>
<td>2750</td>
<td></td>
<td>2770</td>
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<tr>
<td>C-H bending</td>
<td>W.-M.</td>
<td>S.</td>
<td>S.-M.</td>
<td>S.</td>
<td>V.S.</td>
<td>W.-M.</td>
<td>S.</td>
<td>V.S.</td>
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<tr>
<td>CH₂ rocking</td>
<td>V.S.</td>
<td>V.S.</td>
<td>1440</td>
<td>1445</td>
<td>V.S.</td>
<td>N. 1195</td>
<td>N.</td>
<td>N. 1190</td>
</tr>
<tr>
<td>Aromatic C-H out of plane deformation</td>
<td>V.S.</td>
<td>1200</td>
<td>1200</td>
<td>1195</td>
<td>V.S.</td>
<td>750-745, 685</td>
<td>V.S.</td>
<td>745, 690</td>
</tr>
<tr>
<td>(CH₃)₂CH-Skeletal</td>
<td>V.S.</td>
<td></td>
<td>1235</td>
<td></td>
<td>V.S.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-N stretching (aromatic amines)</td>
<td>V.S.</td>
<td>1340</td>
<td></td>
<td></td>
<td>V.S.</td>
<td>1340</td>
<td>S. 1340</td>
<td></td>
</tr>
<tr>
<td>C=C skeletal (in plane)</td>
<td>V.S.</td>
<td>1600</td>
<td>1500</td>
<td>1480</td>
<td>V.S.</td>
<td>1600</td>
<td>1500</td>
<td>1480</td>
</tr>
</tbody>
</table>

* Three intense bands in this region

Very strong band also present at 1370.
1440-1470 cm\(^{-1}\) was also observed in the spectra of all the alkyleneimines studied. Such a band in the spectrum of pyrrolidine has recently been assigned to a C-H deformation vibration; in the spectra of the azetidines, apart from N-phenylazetidine, it has now been found to be a particularly definite band at about 1450 cm\(^{-1}\). A further strong band at 1195-1200 cm\(^{-1}\) occurred in the spectra of the N-alkylazetidines, piperidine and pyrrolidine. A recent paper assigns this band in pyrrolidine to a CH rocking vibration, and it is assumed that the origin of this band is the same in the N-alkylazetidines.

The other assignable frequencies were those specifically characteristic of the substituents on the alkyleneimine nitrogen atom. The CH\(_3\)-CH-CH\(_3\) skeletal vibration was expected for N-iso-propylazetidine and this was assigned to a very intense band at 1380 cm\(^{-1}\). The spectra of N-phenylazetidine and N-phenylpyrrolidine showed the bands expected for aromatic vibrations. The "C=C in plane skeletal" vibration gave rise to three very strong absorption bands at 1600 cm\(^{-1}\), 1500 cm\(^{-1}\), and 1480 cm\(^{-1}\), while the C-H aromatic, out of plane deformation, vibration gave two very intense bands at 745 cm\(^{-1}\) and 685 cm\(^{-1}\). The aromatic C-N stretching vibration gave a strong band at 1340 cm\(^{-1}\).

The aliphatic C-N stretching frequency was
looked for in the spectra of the N-alkylalkyleneimines but could not be assigned, although two consistent bands in the spectra of these compounds were observed. Bellamy reports the normal aliphatic C-N stretching vibration to occur between 1020 and 1220 cm\(^{-1}\). The strong band at 1120-1130 cm\(^{-1}\), which appeared to be characteristic of N-alkylalkyleneimines (as distinct from N-arylalkyleneimines and the unsubstituted ring compounds) may correspond to the C-N stretching frequency of aliphatic amines. However, because this band, and a similarly consistent band for the N-alkylalkyleneimines at 1330 cm\(^{-1}\), occurred in a densely-packed region of the spectrum, it could not be reliably assigned to the C-N stretching vibration.

Both N-ethylazetidine and N-iso-propylazetidine exhibited strong absorption at 740 cm\(^{-1}\), but, since other azetidines and pyrrolidine and piperidine showed continuous absorption in this region this band may not be peculiar to N-ethylazetidine and N-iso-propylazetidine. It seems likely that it arose from the combination of bands which occurred in the lower range of the spectra.

Within the spectral region 1500 cm\(^{-1}\) to 1600 cm\(^{-1}\) detailed analysis was impossible because of the large number of absorption bands. However, the spectra of the N-alkylazetidines all showed strong absorption bands at approximately 1300 cm\(^{-1}\), 1235 cm\(^{-1}\), 1150 cm\(^{-1}\), 1120 cm\(^{-1}\), although, as was to be expected, there were slight individual variations in these band
positions.

It can be seen that, although it was hoped to find absorption bands characteristic of this type of compound which could be recognised in the spectra of the new N-aryiazetidines, much difficulty was met in the attempt to pick up a recognisable pattern in the spectra of N-substituted azetidines. When the N-aryiazetidines were included in the correlation of individual absorption bands, any analogies that might have been drawn were completely unreliable. Outside the crowded spectral range 1500-1000 cm.⁻¹, where some useful correlation of bands might have been expected, the only band characteristic of N-alkylazetidines, that at 740 cm.⁻¹, was absent from the spectrum of N-phenylazetidine. It is true that an absorption band appears in the spectra of N-(nitrophenyl)azetidines at about 750 cm.⁻¹, but this was assigned to the NO₂ valence vibration.

However, in the spectra of N-(nitrophenyl)-azetidines the assignment of a few absorption bands to particular molecular vibration was possible. Table IV includes those bands which occurred consistently within the series of N-(nitrophenyl)azetidines. The corresponding absorption bands in N(⁻p-nitrophenyl)-piperidine and N-(3-bromopropyl)-p-nitroaniline are also included.

Absorption bands characteristic of C-H stretch-
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<tbody>
<tr>
<td><strong>N-H stretching</strong></td>
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<tr>
<td>C=O aromatic</td>
<td>V.S. 1600-1590</td>
<td>V.S. 1600-1590</td>
<td>V.S. 1615-1600</td>
<td>S. 1500-1600</td>
<td>S. 1610-1570</td>
<td>S. 1500-1560</td>
</tr>
<tr>
<td>Skeletal in plane</td>
<td>M. 1500</td>
<td>M. 1500</td>
<td>M. 1500</td>
<td>M. 1500</td>
<td>M. 1500</td>
<td>M. 1500</td>
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<tr>
<td>C-H deformation</td>
<td>S. 815</td>
<td>V.S. 820</td>
<td>S. 810</td>
<td>S. 810</td>
<td>S. 810</td>
<td>S. 810</td>
</tr>
<tr>
<td>(2-free adjacent</td>
<td></td>
<td></td>
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<tr>
<td>Hydrogens)</td>
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<td>C-H deformation</td>
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<tr>
<td>(4-free adjacent</td>
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<tr>
<td>Hydrogens)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>NO₂ valence</strong></td>
<td>S. 750</td>
<td>S. 750</td>
<td>S. 750</td>
<td>S. 740</td>
<td>M. 750</td>
<td>M. 750</td>
</tr>
</tbody>
</table>
ing vibrations were not observed because these spectra were obtained using Nujol mulls, and the C-H stretching band was consequently masked. C-H Deformation aromatic vibrations characteristic of 1,4-disubstitution or 1,2,4-trisubstitution gave a strong band at about 810 cm\(^{-1}\) in the spectra of all the N-(nitrophenyl)azetidines except that of N-(p-nitrophenyl)azetidine which gave the expected strong absorption at 770 cm\(^{-1}\), characteristic of ortho-substitution. Strong absorption bands due to aromatic "C=C skeletal in plane" vibrations were observed at 1500 cm\(^{-1}\) and 1600 cm\(^{-1}\) for all the N-(nitrophenyl)-azetidines. The strong absorption band characteristic of the aromatic NO\(_2\) valence vibration was also observed at about 750 cm\(^{-1}\). The only unassigned absorption band occurring consistently in Table IV was a strong band close to 1110 cm\(^{-1}\). That this band had its origin in a vibration of the nitroaromatic ring seems to be indicated by the fact that it was given by N-(p-nitrophenyl) piperidine, N-(p-nitrophenyl)azetidine, and N-(3-bromo-propyl)-p-nitroaniline. It may finally be noted that the occurrence of the N-H absorption band (3300 cm\(^{-1}\)) in the spectrum of N-(3-bromo-propyl)-p-nitroaniline is illustrative of the analytical value of this band because the spectra of N-(3-bromo-propyl)-p-nitroaniline and N-(p-nitrophenyl)azetidine are otherwise closely similar throughout the region 660-3500 cm\(^{-1}\).
5. REFERENCES


b. M. Kohn, Monatsh., 28, 423 (1907).


17. A. Litherland and F.G. Mann, J., 141, 1588 (1938).
33. L. Knorr, Ber., 37, 3507 (1904).


