AD 269 695

(a) Mechanisms of the Oxidation of Organic Amines by Oxygen and by Free Radical Oxidizing Agents.

(b) Professor H.B. Henbest,
The Queen's University,
Belfast, Northern Ireland.

(c) Contract Number - DA-91-591-EUC-1594.

(d) Annual Technical Report.

(e) July 24, 1961 - October 31, 1961.

(f) The research reported in this document has been made possible through the support and sponsorship of the U.S. Department of Army, through its European Research Office.

62-1-5
XEROX

ABSTRACT

MECHANISMS OF THE OXIDATION OF AMINES

1. Oxidation of Amines by Ozone and other reagents.

By M.J.W. Stratford (Supervisor, H.B. Henbest).

A moderately detailed study of the oxidation of tributylamine by ozone and by active manganese dioxide has been made. The products from ozone oxidation depend on the reaction conditions. The N-Oxide is the main product in some solvents whereas attack of ozone at the carbon next to nitrogen occurs in other solvents. The α-Hydroxyamine appears to be formed in the latter reaction. This is fairly stable at low temperatures but gives dibutylamine on treatment with aqueous acid. The α-hydroxyamine dehydrates at 15° to the enamine so that N-formyldibutylamine is produced on oznolysis of the tertiary amine at room temperature.

Oxidation of tributylamine with manganese dioxide also gives N-formyldibutylamine, and similar oxidation occurs with other trialkylamines.

Further work on the tributylamine-oxygen reaction, and preliminary work on the oxidation of tertiary amines with cumene hydroperoxide is also reported.

2. Oxidation of Amines by Monovalent Radicals.

By R. Patton (Supervisor, H.B. Henbest).

Additional examples of the formation of substituted ethylene diamines by reaction of tertiary amines with t-butoxy radicals are given. In a competition experiment, dimethylaniline and dimethyl-t-butylamine showed similar reactivity towards t-butoxy radicals; cis- and trans-1,2,5-trimethylpyrrolidine also show little difference in reactivity.

Dehydrogenative coupling does not occur when t-butoxy-radicals react with dimethylaniline in acetic acid solution. The amine is demethylated, the ejected carbon linking two, then three aromatic rings together. Evidence for intermediate steps in the overall reaction has been obtained.

ABSTRACT

3. Reactions of Amines in Aqueous Solution with Polyvalent Metal Oxidants.

By W.J.W. Hanna (Supervisor, R.G.R. Bacon).

Among metal derivatives so far studied, argentic compounds, exemplified by argentic picolinate, or by the bivalent silver species present in $Ag^+/S_2O_8^{2-}$ mixtures, are uniquely effective for aliphatic amine oxidations in aqueous media; mercuric acetate has much lower activity. Polar organic solvents, such as alcohols or dioxan, may be successfully used in place of water as media for reactions between argentic picolinate and solid, water-insoluble substrates, but no reaction occurs in hydrocarbon solvents; t-butanol, being resistant to oxidation, is particularly suitable.

With aqueous solutions of primary amines, argentic picolinate gives aldehydes or ketones in 10-40% yield, while secondary amines give yields of 20-90%. Combination of amines with argentous ion, giving complexes which are stable to oxidation, may be a factor affecting this situation. Such an effect is clear in the case of ammonia oxidations, the stoichiometry of which indicates that each Ag^+ ion formed in the oxidation immobilises two ammonia molecules as $Ag(NH_3)_2^+$. Size and branching in the alkyl group of alhylamines has an important influence. Thus, 3,5,5-trimethylhexylamine is unique in losing four hydrogen atoms to give the corresponding cyanide, while di-(3,5,5-trimethylhexyl)amine gives 3,5,5-trimethylhexylidene-3,5,5-trimethylhexylamine which, unlike most aldimines, appears as the end product because of its high resistance to hydrolysis.

SECTION I

1. THE OXIDATION OF SOME TRIALKYLAMINES WITH MANGANESE DIOXIDE.

Introduction

Oxidations by active hydrated manganese dioxide in neutral media have been recently reviewed by Evans.[1]

Since the discovery in 1948, by Ball, Goodwin and Morton,[2] that active hydrated manganese dioxide oxidises Vitamin A, in light petroleum solution at room temperature, to retinene in 80% yield, the reagent has found considerable application in the exploration of the chemistry of polyenes and polyenynes in the oxidation of α,β-unsaturated alcohols generally, and in the oxidation of tertiary amines.[3,4]

The reactivity of manganese dioxide, a non-stoicheiometric compound, depends on its method of preparation and on its degree of hydration. A most reliable and highly active material containing about 4% of water can be prepared[5] in a finely divided state, by the oxidation of manganese sulphate with potassium permanganate in aqueous solution, i.e. under acid conditions, the resultant slurry being washed with water and dried at 100-120°.

The dioxide is usually shaken with the substrate in a neutral organic solvent, such as light petroleum, benzene, chloroform or ether, at room temperature. The yield of product is dependent on five main factors:-

(a) the ratio by weight of manganese dioxide to substrate
(b) the nature of the substrate
(c) the nature of the manganese dioxide
(d) the reaction time
(e) the solvent.

A large excess of manganese dioxide is always necessary to effect oxidation. This is sometimes a disadvantage, as some oxidations yield products which are very strongly adsorbed on to the surface of the dioxide.

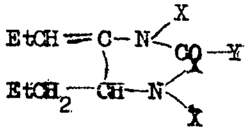
Solvents, such as alcohols, which compete with the substrate for the active sites on the surface cannot be used. The optimum conditions for the oxidation of some tertiary amines have been determined.[4]

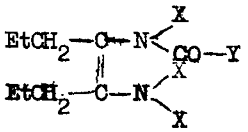
DISCUSSION OF RESULTS

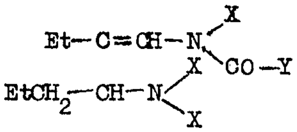
As an extension of the work of Curragh, Henbest and Thomas on the oxidation of tertiary amines,[3,4] it was of interest to study the manganese dioxide oxidation of trialkylamines. A detailed study was first carried out on the tributylamine-manganese dioxide reaction.

When tributylamine in cyclohexane was shaken with a twenty-five fold weight of manganese dioxide for 18 hr. at 19°, infrared analysis of the material, eluted from the dioxide surface, indicated the presence of oxidation products by the strong absorption at 1675 cm.$^{-1}$ and 1620 cm.$^{-1}$ and the weak absorption at 1565 cm.$^{-1}$ The crude product mixture, which was shown not to contain tributylamine N-oxide, was separated into neutral and basic fractions by extraction with dilute hydrochloric acid. By quantitative gas-liquid chromatography the neutral fraction, which absorbed strongly at 1675 cm.$^{-1}$, was found to contain only N,N-dibutylformamide, Bu_2NCHO, (36%). Likewise, the basic fraction, which absorbed strongly at 1620 cm.$^{-1}$ and weakly at 1655 cm.$^{-1}$ and 1565 cm.$^{-1}$, was shown to contain dibutylamine, Bu_2NH, (38%) and unreacted tributylamine. The yields of products are based on the amount of starting material not recovered.

As the carbonyl absorbing products in the basic fraction were not detected by gas-liquid chromatography, under the conditions used for the analysis of the amines, it was assumed that they had boiling points greater than 213°, the boiling point of tributylamine. Absorption chromatography of part of the basic fraction on deactivated alumina showed that, in addition to the dibutylamine, there were at least five other oxidation products some of which fluoresced in ultraviolet light. The low frequency carbonyl peaks at 1620 cm.$^{-1}$ and 1565 cm.$^{-1}$ indicated that some of the unidentified basic products were unsaturated amides, possibly formed by the oxidative coupling of two amine molecules. Since the work of Patton[6] and Leonard[7] has shown that oxidative α,α- and α,β-couplings of amines can be achieved, three possible basic structures can be drawn for the unsaturated amides:-







X = H and/or Bu, Y = H and/or Pr

An attempt was made to synthesise some of the possible chromophores responsible for absorption at 1620 cm.$^{-1}$ and 1565 cm.$^{-1}$ The manganese dioxide oxidation of N,N'-dimethyl-2,2'-dipiperidyl, the amine resulting from the oxidative α,α-coupling of two N-methylpiperidine molecules,[6] gave material which showed broad bands at 1545 cm.$^{-1}$ and 1645 cm.$^{-1}$ in the infrared.

Similarly the manganese dioxide oxidation of N,N'-dimethyl-Δ^2-tetrahydroanabasine, the amine resulting from the oxidative α,β-coupling of two N-methylpiperidine molecules,[7] gave material which showed a broad band at 1585 cm.$^{-1}$ in the infrared.

No definite conclusions could be drawn from these experiments, however, as the peaks were very broad in comparison with those shown by the crude tributylamine oxidation mixture.

When the tributylamine oxidation was repeated and the reaction mixture quantitatively analysed by gas-liquid chromatography, without separating into basic and neutral fractions by extraction with dilute hydrochloric acid, N,N-dibutylformamide (40%), dibutylamine (39.5%) and unreacted tributylamine were detected. It was noticed on analysing, however, that the dibutylamine had both a slightly longer retention time and a broader peak than that normally given. This suggested that the dibutylamine was formed by the thermal decomposition of some intermediate on passing through the hot chromatography column.

A more likely explanation of the longer retention time and broader peak, is that butyric acid and propionic acid, undoubtedly present in the reaction mixture, retarded the movement of the dibutylamine through the column. It was shown that pure dibutylamine mixed with a small quantity of propionic acid, was retained slightly longer on the column than pure dibutylamine and gave a peak which was broader than the normal peak. The dibutylamine behaved normally on the column in the first experiment described, as the butyric and propionic acids had been removed during the isolation procedure.

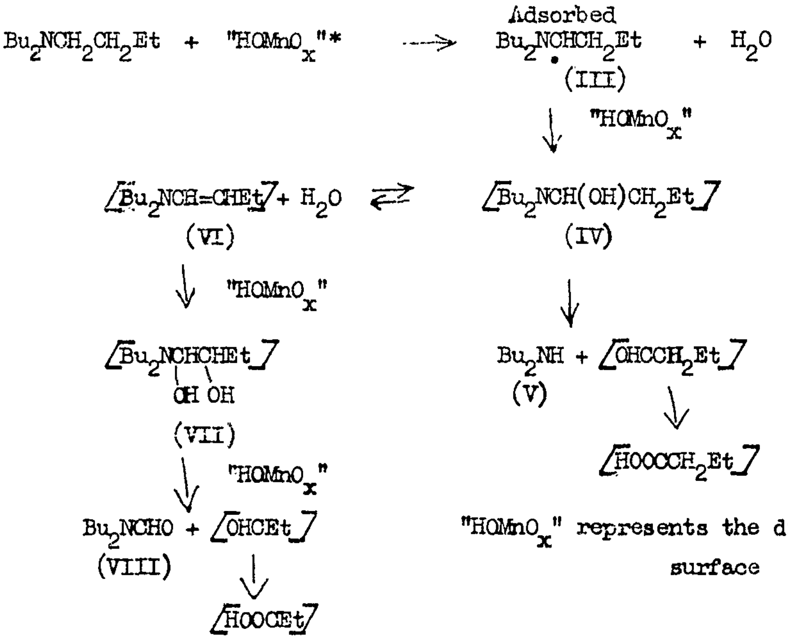
Reaction Mechanism

The critical effect of the moisture content on the activity of manganese dioxide has been mentioned above. Evans and co-workers[1] have found that the dioxide cannot be completely dehydrated without the removal of oxygen and that an excess moisture content of ca. 4-8% over that contained by material of constant weight, prepared by drying at 120° under vacuum, leads to the highest activity.

Henbest and Thomas[3] have suggested that the "water" is present as hydroxyl groups linked to the manganese and that these groups are responsible for the production of hydroxylated intermediates in the oxidation of dialkylanilines.

It is now thought that the properties of the oxidant, when suspended in organic media, are consistent with the proposal that its surface can act as a source of hydroxyl radicals and that species e.g. $(HO)_2MnO$, formed by the hydration of MnO_2, may exist at the surface. The hydroxyl radicals do not become free, however, but interact with the adsorbed substrate.

In accordance with the fact that amines react at the α-position in the primary step of their reactions with t-butoxy-radicals,[8] adsorbed tributylamine is believed to cause the successive detachment of two hydroxyl-radicals to form the adsorbed amine radical (III) and water and then the carbinolamine, 1-hydroxybutyl-dibutylamine (IV). The carbinolamine (IV) is a likely precursor of both the dibutylamine (V) and the enamine but-1-enyldibutylamine (VI).



"$HOMnO_x$" represents the dioxide surface

Work on the ozonisation of tributylamine[12] has shown that the carbinolamine (IV), in a nonpolar solvent in the presence of tributylamine, can be partially dehydrated at room temperature to give the enamine (VI). The enamine (VI) is a likely precursor of the N,N-dibutylformamide (VIII) as enamines are known to be cleaved with manganese dioxide to N-formyl compounds.[3] The oxidation of N,N-dibenzylstyrylamine (IX) gave benzaldehyde and N,N-dibenzylformamide (X).[3]

$$\underset{(IX)}{PhCH{=}CHN(CH_2Ph)_2} \longrightarrow PhCHO + \underset{(X)}{OHCN(CH_2Ph)_2}$$

Hydroxylation is an obvious initial stage in the enamine fission and vic-glycols[9] are known to be cleaved by manganese dioxide. The glycol, 1,2-dihydroxybutyldibutylamine (VII) is thus another likely precursor of the formamide (VIII).

The possibility of "active" oxygen adsorbed on the dioxide surface being responsible for the oxidations was excluded by Evans and co-workers.[1]

In support of the radical mechanism Henbest, Jones and Owen[10] showed that one commercial sample of manganese dioxide oxidised vitamin A to 3-hydroxyretinene in 16% yield and another gave a considerable proportion of 3-oxoretinene.

This latter oxidation can be considered as being analogous to the oxidation of dimethylaniline to N-methylformanilide[3] as it involves the conversion of an allylic methylene group into an unsaturated ketone. The fact that 2,4,6-trisubstituted phenols can be converted into stable phenoxy-radicals with manganese dioxide, is also consistent with a radical mechanism.[11]

The effect of increasing the weight ratio of manganese dioxide to tributylamine and the reaction time on the yields of dibutylamine (V) and the formamide (VIII) is shown in Table I.

Table I

Weight ratio MnO_2/tributylamine	Reaction Time hr.	Yield of (V) %	Yield of (VIII) %
25:1	18	39.5	40
50:1	72	33	51
75:1	48	25	32

Unreacted tributylamine was not detected at the end of the last two reactions in the Table. The results indicate that more dehydration of the carbinolamine (IV) to the enamine (VI) occurred using a 50:1 weight ratio of manganese dioxide to tributylamine than with a 25:1 ratio.

Table II shows that the addition of small quantities of either dichloromethane or isopropanol to the solvent, to increase the eluting power, makes no difference to the yields of products.

Table II

Solvent	Yield of (V) %	Yield of (VIII) %
cyclohexane	39.5	41
cyclohexane + 3% dichloromethane	39	40
cyclohexane + 3% isopropanol	39	40

Propionaldehyde is undoubtedly formed with the N,N-dibutylformamide (VIII) during the oxidation of tributylamine but probably undergoes further oxidation to propionic acid.

To determine whether or not the propionic acid was affecting the course of reaction, the oxidation was carried out in the presence of propionic acid (mole ratio of tributylamine to propionic acid 1:0·56). On working up the reaction mixture by separating into neutral and basic fractions using dilute hydrochloric acid, the formamide (VIII) (33.5%), dibutylamine (V) (53%) and unreacted tributylamine were detected indicating that the propionic acid aided the cleavage of the carbinolamine (IV), into dibutylamine (V) and butyraldehyde, to a small extent.

Technical difficulties prevented estimations being made of the aldehydes and acids formed during the oxidation of tributylamine.

On oxidation for 2½hrs. at 80°, tributylamine gave a high yield of the formamide (VIII). This indicated that the carbinolamine (IV) had been converted into the enamine (VI) to a large extent during reaction. Table III shows the results for oxidation in cyclohexane and benzene.

Table III

Solvent	Yield of (V) %	Yield of (VIII) %
cyclohexane	13	64.5
benzene	10	73.5

At the end of each reaction only a trace of tributylamine was detected.

The yields of dialkylformamides from the oxidations of a series of tri-n-alkylamines in cyclohexane at 19° are listed in Table IV. A 25:1 weight ratio of manganese dioxide to amine was used in every case except trioctylamine, where a 12.5:1 ratio was used.

Table IV

Amine R_3N	Yield of N,N-dialkylformamide %
R = C_2H_5	< 1.0
R = N-C_3H_7	27.5
R = N-C_4H_9	40.0
R = N-C_5H_{11}	48.2
R = N-C_8H_{17}	54.0

The yields of formamide thus improve as the length of chain to be severed increases; this is probably due to the stronger adsorption and/or further reaction of the lower molecular weight amides at the surface of the dioxide. Thus, on shaking N-formylpiperidine, a C_6amide, in light petroleum with a fifty fold weight of manganese dioxide for 15 min., Curragh[13] found that only 26.5% of the amide could be recovered from the dioxide surface by elution with light petroleum, methanol and water.

Triisobutylamine $[CH_3CH(CH_3)CH_2]_3$ N in cyclohexane was oxidised at 19° in the same way as tributylamine, N,N-diisobutylformamide and diisobutylamine being obtained in approximately equimolar quantity using a 25:1 weight ratio to dioxide to amine.

N,N,N',N'-Tetrabutyl-1,2-ethylenediamine, $Bu_2NCH_2CH_2NBu_2$, however, gave two unidentified neutral products in addition to the expected N,N-dibutylformamide, when oxidised in cyclohexane at 19° using a 25:1 weight ratio of dioxide to amine. This indicated that the methylene groups, α-to the nitrogen atoms, are attacked indiscriminately in aliphatic diamines. (cf. the oxidation of aromatic diamines[1,4])

To determine the affect of a bulky t-butyl-group close to the possible sites of oxidation, the oxidation of N,N-dimethyl-t-butylamine $(CH_3)_3CN(CH_3)_2$ was studied. Patton has shown that this amine is attacked in the usual fashion by t-butoxy-radicals to give a dimer.[6]

$$2(CH_3)_3CH(CH_3)_2 \quad + \quad 2(CH_3)_3CO \longrightarrow (CH_3)_3CH(CH_3)\ CH_2CH_2(CH_3)N(CH_3)_3 \; + \; 2(CH_3)_3COH$$

If manganese dioxide can be regarded as a very bulky oxidant, in comparison with a t-butoxy-radical, then steric hindrance between it and the t-butyl-group of the amine might alter the course of or prevent oxidation. When the amine, in light petroleum, was treated with a fifty-fold weight of manganese-dioxide for 18 hr. at 19°, N-methyl-t-butylamine (12%) was obtained, showing that oxidation had taken place possibly by the following route:-

$$(CH_3)_3CN(CH_3)_2 \longrightarrow (CH_3)_3CN(CH_3)\ CH_2OH \longrightarrow (CH_3)_3CNHCH_3 + CH_2O.$$

As unreacted amine (34%) was detected by quantitative gas-liquid chromatography when a twenty-five-fold weight of dioxide was used, the above yield of secondary amine was calculated assuming all the starting material to have reacted. The N-methyl-t-butylamine was estimated by measurement of the optical density of the blue quinone, formed by treating the reaction mixture with a mixture (molar ratio 1:10) of 2:3-dichloronaphthaquinone and acetaldehyde in benzene.[14]

The absence of carbonyl absorption in the infrared spectrum of the reaction mixture indicated that the amide, N-methyl-N-t-butylformamide $(CH_3)_3CN(CH_3)CHO$ was not present. It is possible that the amide was formed, however, but due to strong adsorption and/or further reaction on the dioxide surface it was not detected. N-methyl-N-t-butylformamide is of the same molecular complexity as N-formylpiperidine, an amide which Curragh showed to be strongly adsorbed on manganese dioxide.[13] Thus the results of the N,N-dimethyl-t-butylamine oxidation do not indicate the operation of a steric affect.

Curragh [13] has oxidised N-methylpiperidine, $[\mathrm{CH_2}]_5{>}\mathrm{NCH_3}$, to N-formylpiperidine, $[\mathrm{CH_2}]_5{>}\mathrm{NCHO}$, in 7% yield using a 70:1 weight ratio of dioxide to amine, showing that a dehydration step is not necessary for the production of an N-formyl group from an N-methyl group in a saturated tertiary amine.

$$[\mathrm{CH_2}]_5{>}\mathrm{NCH_3} \rightarrow [\mathrm{CH_2}]_5{>}\mathrm{NCH_2OH} \longrightarrow [\mathrm{CH_2}]_5{>}\mathrm{NCHO}$$

References

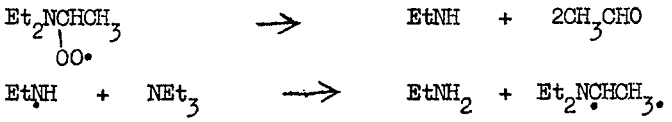
1. Evans, Quart. Rev., Vol.XIII, No.1, 1959,61.
2. Ball, Goodwin and Morton, Biochem. J., 1948, 42, 516.
3. Henbest and Thomas, J., 1957, 3032.
4. Curragh, Henbest and Thomas, J., 1950, 3559.
5. Mancera, Rosenkranz and Sondheimer, J., 1953, 2189.
6. Patton, Ph.D.Thesis, Belfast, 1961.
7. Leonard and Hauck, J. Amer. Chem. Soc., 1957, 79, 5279.
8. Henbest and Patton, J., 1960, 3557.
9. Padilla and Herran, Bol. Inst. Quim. Univ. nac. auton. Mexico, 1956, 8, 3.
10. Henbest, Jones and Owen, J., 1957, 4909.
11. Henbest, unpublished observations.
12. U.S. Army Report, 1960.
13. Curragh., M.Sc.Thesis, Belfast, 1959.
14. Buckley, Henbest and Slade, J., 1957, 4891.

SECTION II

The Oxidation of Tributylamine with Oxygen at 100°

Introduction

Cullis and Waddington have shown that trimethylamine[1] and triethylamine[2] are oxidised in the gas phase at 165-215°. Triethylamine gives ethylamine, acetaldehyde and a small amount of diethylamine; the primary amine is suggested to arise largely from intramolecular decomposition of a peroxy-radical:



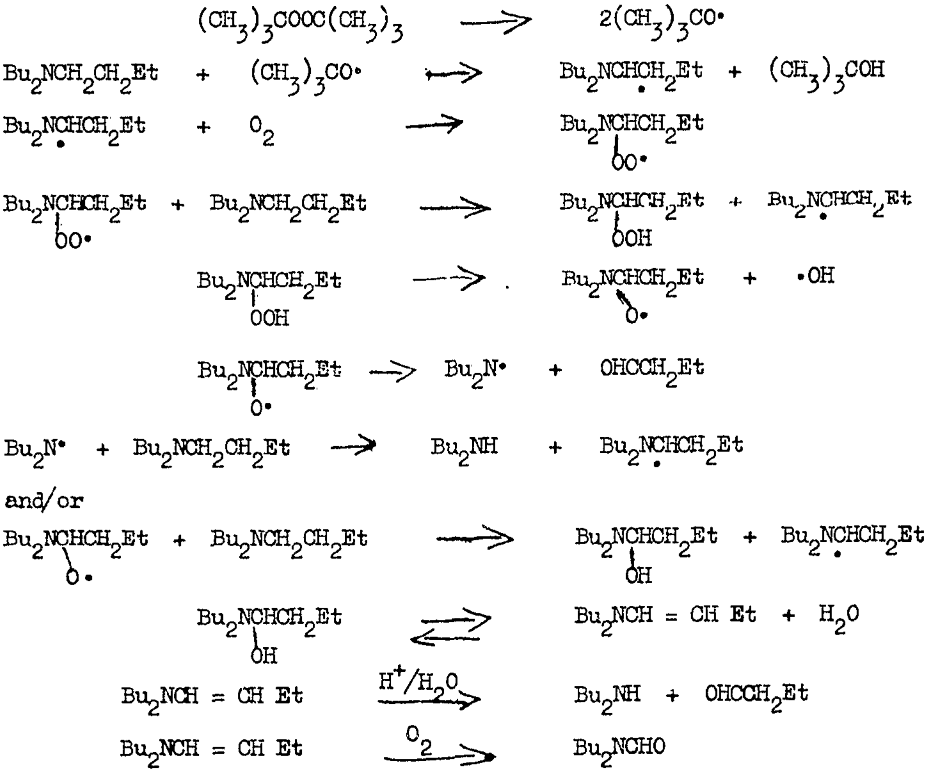
$$Et_2N\underset{OO\cdot}{C}HCH_3 \rightarrow Et\underset{\cdot}{N}H + 2CH_3CHO$$

$$Et\underset{\cdot}{N}H + NEt_3 \rightarrow EtNH_2 + Et_2N\underset{\cdot}{C}HCH_3.$$

Trimethylamine gives dimethylamine and formaldehyde as main products.

Discussion of results

When pure oxygen was passed for 36 hrs. in the absence of light, through tributylamine at 100° containing a catalytic amount of ditertiarybutyl peroxide as a radical initiator and the reaction mixture treated with dilute hydrochloric acid, N,N-dibutylformamide (5.5%), dibutylamine (17.5%) and other unidentified products were obtained. 61.5% of the tributylamine remained unreacted. The formation of the formamide and secondary amine may be explained by the following mechanism:-



$$(CH_3)_3COOC(CH_3)_3 \rightarrow 2(CH_3)_3CO\cdot \qquad \text{A.}$$

$$Bu_2NCH_2CH_2Et + (CH_3)_3CO\cdot \rightarrow Bu_2N\underset{\cdot}{C}HCH_2Et + (CH_3)_3COH \qquad \text{B.}$$

$$Bu_2N\underset{\cdot}{C}HCH_2Et + O_2 \rightarrow Bu_2N\underset{OO\cdot}{C}HCH_2Et \qquad \text{C.}$$

$$Bu_2N\underset{OO\cdot}{C}HCH_2Et + Bu_2NCH_2CH_2Et \rightarrow Bu_2N\underset{OOH}{C}HCH_2Et + Bu_2N\underset{\cdot}{C}HCH_2Et \qquad \text{D.}$$

$$Bu_2N\underset{OOH}{C}HCH_2Et \rightarrow Bu_2N\underset{O\cdot}{C}HCH_2Et + \cdot OH \qquad \text{E.}$$

$$Bu_2N\underset{O\cdot}{C}HCH_2Et \rightarrow Bu_2N\cdot + OHCCH_2Et \qquad \text{F.}$$

$$Bu_2N\cdot + Bu_2NCH_2CH_2Et \rightarrow Bu_2NH + Bu_2N\underset{\cdot}{C}HCH_2Et \qquad \text{G.}$$

and/or

$$Bu_2N\underset{O\cdot}{C}HCH_2Et + Bu_2NCH_2CH_2Et \rightarrow Bu_2N\underset{OH}{C}HCH_2Et + Bu_2N\underset{\cdot}{C}HCH_2Et \qquad \text{H.}$$

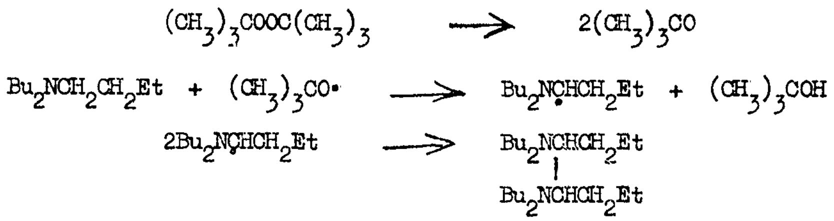
$$Bu_2N\underset{OH}{C}HCH_2Et \rightleftharpoons Bu_2NCH = CH\ Et + H_2O \qquad \text{I.}$$

$$Bu_2NCH = CH\ Et \xrightarrow{H^+/H_2O} Bu_2NH + OHCCH_2Et \qquad \text{J.}$$

$$Bu_2NCH = CH\ Et \xrightarrow{O_2} Bu_2NCHO \qquad \text{K.}$$

Reactions A and B are analogous to those suggested by Henbest and Patton[3] for the production of amine-radicals unambiguously with t-butoxy-radicals. Direct evidence for the production of the radical $Bu_2N\underset{\cdot}{C}HCH_2Et$ was provided by Raley, and

Seubold who found that ditetiarybutyl peroxide thermally decomposed in tributylamine gave 4,5-(dibutylamino) octane.[4]



$$(CH_3)_3COOC(CH_3)_3 \longrightarrow 2(CH_3)_3CO$$

$$Bu_2NCH_2CH_2Et + (CH_3)_3CO\cdot \longrightarrow Bu_2N\dot{C}HCH_2Et + (CH_3)_3COH$$

$$2Bu_2N\dot{C}HCH_2Et \longrightarrow \begin{array}{c} Bu_2NCHCH_2Et \\ | \\ Bu_2NCHCH_2Et \end{array}$$

The reaction sequence B.C.D. is analogous to the recognised process of hydrocarbon[7] or ether[8] autoxidation.

Reaction E may be considered to be analogous to the mechanism of the thermal decomposition of cumene hydroperoxide (see below).

The reaction sequence F,G,H is analogous to that suggested as part of the mechanism for the reaction of ozonised oxygen with ethers.[9]

Reaction J. has already been discussed.[5]

The formation of the formamide via the enamine (reaction K) is tentatively suggested by analogy with the mechanism proposed for its formation from tributylamine with solid (hydrated) manganese dioxide (see above) and with ozonised oxygen.[5]

It is of interest to note that Smith and Swan have obtained N,N-dimethylformamide by the irradiation of trimethylamine with γ-radiation.[6] The fact that N,N,N',N'-tetramethylethylenediamine $[(CH_3)_2NCH_2]_2$ was produced in the absence of oxygen suggests that the radical $(CH_3)_2NCH_2\cdot$ may have been involved in the production of the N,N-dimethylformamide.[6]

References

1. Cullis and Waddington, Proc. Roy. Soc., 1958, A.246, 91.
2. Cullis and Waddington, Proc. Roy. Soc., 1958, A.244, 110.
3. Henbest and Patton, J., 1960, 3557.
4. Raley and Seubold, U.S.P., 2,537,857. Chem. Abs., 45, 3414.
5. Our report of last year.
6. Smith and Swan, Chem. and Ind., 1961, 1221.
7. Walling, "Free Radicals in Solution", Wiley, New York, 1958, p.397.
8. Rieche, Angew. Chem., 1958, 70, 251.
9. Bailey, Chem. Rev., 1958, 58, 925.

SECTION III

THE OXIDATION OF TRIBUTYLAMINE AND OTHER AMINES WITH CUMENE HYDROPEROXIDE

Introduction

Hydroperoxides ROOH eg. R=t-butyl, cumyl, are among the most easily available organic derivatives of hydrogen peroxide and their ability to initiate polymerisation and autoxidation processes is clear evidence of their ability to split into free radicals.

When heated at 100° in certain solvents, eg., acetic or benzoic acids,[1] or alone[2], cumene hydroperoxide gives high yields of di-α,α-dimethylbenzyl peroxide, $PhC(CH_3)_2OOC(CH_3)_2Ph$, some acetophenone, CH_3COPh, and α,α-dimethylbenzylalcohol, $PhC(CH_3)_2OH$. Oxygen is also evolved. The α,α-dimethylbenzyl peroxide is probably formed by the dimerisation of two α,α-dimethylbenzyloxy-radicals,

$$2\ PhC(CH_3)_2O\cdot \longrightarrow PhC(CH_3)_2\ OOC(CH_3)_2Ph.$$

As Kharasch and co-workers[3] have shown that cumene hydroperoxide, thermally decomposed in decane at 140°, gives methane (30%), acetophenone (20%) and α,α-dimethylbenzyl alcohol (54%), it is evident that a considerable breakdown of the intermediate cumyloxy-radicals can occur.

$$PhC(CH_3)_2O\cdot \longrightarrow PhCOCH_3 + CH_3\cdot$$

$$PhC(CH_3)_2OOH + CH_3\cdot \longrightarrow PhC(CH_3)_2OO\cdot + CH_4$$

In cumene, $PhCH(CH_3)_2$, at 128° thermal decomposition of cumene hydroperoxide gave methane (32%), acetophenone (30%) and α,α-dimethylbenzyl alcohol (90%);[3] these results indicate attack of radicals on the cumene.

Capp and Hawkins first investigated the thermal decomposition of cumene hydroperoxide in a tertiary amine.[4] With triethylamine at 110-120° complete decomposition occurred in 0·5 hr. to form α,α-dimethylbenzyl alcohol in 88% yield. However, no nitrogenous product was identified.

It is of interest to note that de la Mare has recently published a paper[5] which includes the tripropylamine-tertiarybutyl hydroperoxide reaction. At 92° a 3:1 molar mixture of the amine and peroxide yielded t-butanol (80%) and dipropylamine (32%) as the main nitrogenous product. Two higher boiling fractions of the reaction mixture, which had empirical formulae $C_{9.9}H_{20}N\ O$ and $C_{12.8}H_{26}O\ N$, were probably $PrNHCH(OBu^t)Et$ and $Pr_2NCH(OBu^t)Et$ respectively.

By analogy with the well-known hydrogen peroxide-tertiary amine reaction, the triethylamine-cumene hydroperoxide and the tripropylamine-tertiarybutyl hydroperoxide reactions mentioned above might have been expected to yield triethylamine N-oxide and tripropylamine N-oxide respectively. It is possible that the N-oxides were formed but due to the high reaction temperatures, they may have been thermally decomposed.

Cope and Hiok-Huang Lee have shown that trialkylamine N-oxides, $R_3\overset{(+)}{N} - \overset{(-)}{O}$ eg. $R = C_2H_5$, C_3H_7, C_4H_9, are thermally decomposed at 100-150° to form

N,N-dialkylhydroxylamines and olefines containing the same number of carbon atoms as the side chain removed.[6]

A study of the tributylamine - cumene hydroperoxide reaction at 80° has consequently been carried out.

DISCUSSION OF RESULTS

When cumene hydroperoxide was thermally decomposed at 80°, in tributylamine, tributylamine N-oxide and dibutylamine were obtained. The details of the reactions carried out are summarized in the following table:-

					Products	
	Bu_3N g.,[a] mole[b]	$PhC(CH_3)_2OOH$ g.,[a] mole[b]	Reaction time (hr)	Unreacted Bu_3N g.,[a] mole[b]	$\overset{(+)}{Bu_3N} - \overset{(-)}{O}$ g.,[a] mole[b] %[c]	Bu_2NH g.,[a] mole[b] %[c]
(1)	3.94[a] 0.0213[b]	1.56[a] 0.0103[b]	24	2.61[a] 0.0141[b]	0.246[a] 0.00132[b] 18[c]	0.19[a] 0.00147[b] 20.5[9]
(2)	2.02 0.0109	3.06 0.0201	9	0.80 0.00432	0.425 0.00212 32	-
(3)	3.64 0.0197	1.44 0.00947	4	2.38 0.0129	0.38 0.00191 28	0.198 0.00154 22.5

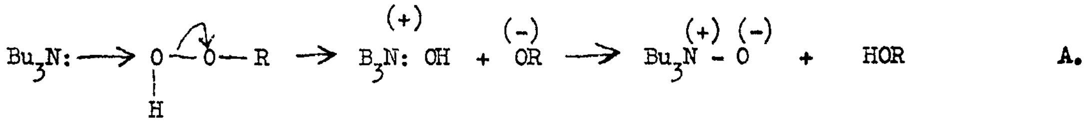
α.α-Dimethylbenzyl alcohol (1.15g., 0.0084 mole, 82.5%) was detected in the reaction mixture of experiment (1). The results of experiments (1) and (3) indicate that a short reaction time favours the formation of N-oxide. Thermal decomposition of the N-oxide probably occured during the 24-hr. reaction time used in experiment (1). Changing the ratio of amine to peroxide made only a small difference in the yield of N-oxide (experiment (2).

In an attempt to obtain a higher yield of N-oxide in the tertiary amine - cumene hydroperoxide reaction, the oxidation of N-ethylpiperidine, a stronger nucleophile than tributylamine, was carried out. Due to volatility an accurate estimation of the amount of unreacted N-ethylpiperidine would not have been possible using a 2:1 molar ratio of amine to peroxide. By using an excess of cumene hydroperoxide, it was hoped that all of the amine would react. When N-ethylpiperidine (0.005 mole) and cumene hydroperoxide (0.020 mole) were mixed and heated to 80°, the reaction mixture rapidly turned dark red-brown in colour indicating that considerable secondary reactions had taken place. However, by reacting N-ethylpiperidine (0.005 mole) with cumene hydroperoxide (0.020 mole) at room temperature for 24-hrs. a colourless reaction mixture was obtained from which N-ethylpiperidine N-oxide (29%) was isolated. The yield is based on the amount of starting material used.

By heating cumene hydroperoxide (0.0076 mole) in triethylenediamine, $N \leqslant [CH_2]_3 \geqslant N$, (0.0112 mole) at 80° for 4-hrs., α,α-dimethylbenzyl alcohol (100%) was formed. The fate of the amine was not determined.

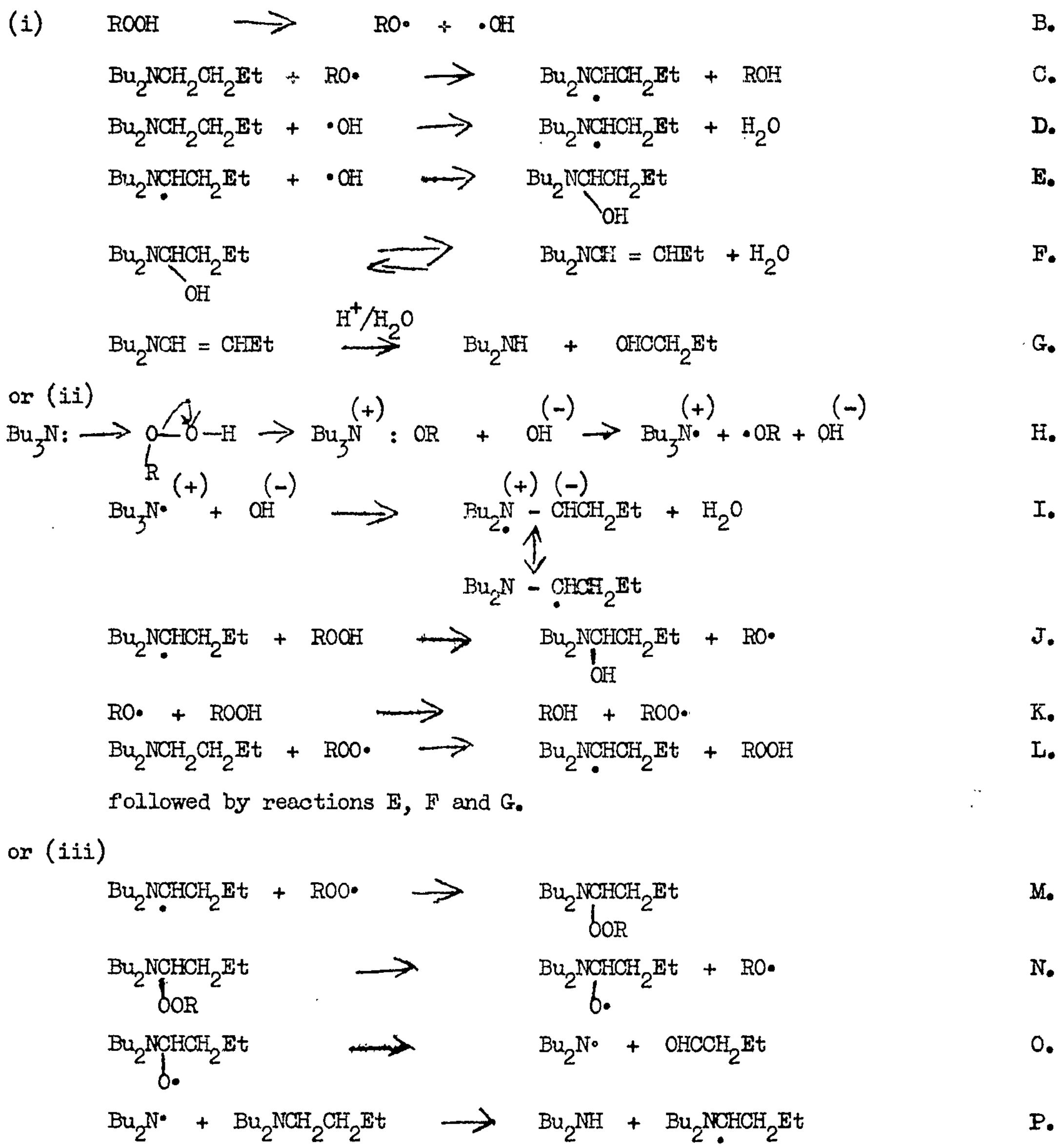
The following mechanism for the oxidation of tributylamine with cumene hydroperoxide may be considered. (R = cumyl).

(a) Formation of the N-oxide



$$\mathrm{Bu_3N\colon} \longrightarrow \mathrm{\underset{\displaystyle H}{O}-O-R} \longrightarrow \mathrm{B_3\overset{(+)}{N}\colon OH} + \overset{(-)}{\mathrm{OR}} \longrightarrow \mathrm{Bu_3\overset{(+)}{N}-\overset{(-)}{O}} + \mathrm{HOR} \qquad \mathrm{A.}$$

(b) Formation of the secondary amine.



(i)

$$\mathrm{ROOH} \longrightarrow \mathrm{RO\cdot} + \mathrm{\cdot OH} \qquad \mathrm{B.}$$

$$\mathrm{Bu_2NCH_2CH_2Et} + \mathrm{RO\cdot} \longrightarrow \mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{ROH} \qquad \mathrm{C.}$$

$$\mathrm{Bu_2NCH_2CH_2Et} + \mathrm{\cdot OH} \longrightarrow \mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{H_2O} \qquad \mathrm{D.}$$

$$\mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{\cdot OH} \longrightarrow \mathrm{Bu_2N\underset{\displaystyle OH}{C}HCH_2Et} \qquad \mathrm{E.}$$

$$\mathrm{Bu_2N\underset{\displaystyle OH}{C}HCH_2Et} \rightleftarrows \mathrm{Bu_2NCH=CHEt} + \mathrm{H_2O} \qquad \mathrm{F.}$$

$$\mathrm{Bu_2NCH=CHEt} \xrightarrow{\mathrm{H^+/H_2O}} \mathrm{Bu_2NH} + \mathrm{OHCCH_2Et} \qquad \mathrm{G.}$$

or (ii)

$$\mathrm{Bu_3N\colon} \longrightarrow \mathrm{\underset{\displaystyle R}{O}-O-H} \longrightarrow \mathrm{Bu_3\overset{(+)}{N}\colon OR} + \overset{(-)}{\mathrm{OH}} \longrightarrow \mathrm{Bu_3\overset{(+)}{N}\cdot} + \mathrm{\cdot OR} + \overset{(-)}{\mathrm{OH}} \qquad \mathrm{H.}$$

$$\mathrm{Bu_3\overset{(+)}{N}\cdot} + \overset{(-)}{\mathrm{OH}} \longrightarrow \mathrm{Bu_{\underset{\bullet}{2}}\overset{(+)}{N}-\overset{(-)}{C}HCH_2Et} + \mathrm{H_2O} \qquad \mathrm{I.}$$

$$\updownarrow$$

$$\mathrm{Bu_2N-\underset{\bullet}{C}HCH_2Et}$$

$$\mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{ROOH} \longrightarrow \mathrm{Bu_2N\underset{\displaystyle OH}{C}HCH_2Et} + \mathrm{RO\cdot} \qquad \mathrm{J.}$$

$$\mathrm{RO\cdot} + \mathrm{ROOH} \longrightarrow \mathrm{ROH} + \mathrm{ROO\cdot} \qquad \mathrm{K.}$$

$$\mathrm{Bu_2NCH_2CH_2Et} + \mathrm{ROO\cdot} \longrightarrow \mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{ROOH} \qquad \mathrm{L.}$$

followed by reactions E, F and G.

or (iii)

$$\mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} + \mathrm{ROO\cdot} \longrightarrow \mathrm{Bu_2N\underset{\displaystyle OOR}{C}HCH_2Et} \qquad \mathrm{M.}$$

$$\mathrm{Bu_2N\underset{\displaystyle OOR}{C}HCH_2Et} \longrightarrow \mathrm{Bu_2N\underset{\displaystyle O\cdot}{C}HCH_2Et} + \mathrm{RO\cdot} \qquad \mathrm{N.}$$

$$\mathrm{Bu_2N\underset{\displaystyle O\cdot}{C}HCH_2Et} \longrightarrow \mathrm{Bu_2N\cdot} + \mathrm{OHCCH_2Et} \qquad \mathrm{O.}$$

$$\mathrm{Bu_2N\cdot} + \mathrm{Bu_2NCH_2CH_2Et} \longrightarrow \mathrm{Bu_2NH} + \mathrm{Bu_2N\underset{\bullet}{C}HCH_2Et} \qquad \mathrm{P.}$$

Reaction A is analogous to the mechanism formulated by Walling for the production of tertiary amine N-oxides from tertiary amines and hydrogen peroxide.[7]

Reaction B has been discussed above in the introduction and the reaction sequence C to G in Section II and in our report of last year.

Reaction H, involving the formation of the aminium radical $\mathrm{Bu_3\overset{(+)}{N}\cdot}$, is analogous to that suggested by Horner[8] for the first step of the oxidation of N,N-dimethylaniline with benzoyl peroxide in chloroform solution to form

N-methylaniline, formaldehyde and other products. The formation of aminium radicals is by no means a new concept. In the case of some aryl and alkyl aryl amines, stable aminium salts have been prepared.[9]

For the tripropylamine-tertiarybutyl hydroperoxide reaction (mentioned in the introduction) de la Mare has suggested a similar reaction sequence to HIJ for the formation of the carbinolamine N-(1-hydroxypropyl)-dipropylamine, $Pr_2NCH(OH)Et$, from which he suggests dipropylamine, one of the nitrogenous products of the oxidation, may be formed. As a result of electron spin resonance measurements, he has further suggested that chain propagation may occur with the species $Pr_2NO\cdot$, which presumably arises to some extent from the dipropylamine formed in the reaction.

Reaction J. may be important as radical displacement on the O - O bond of benzoyl peroxide has recently received strong experimental support.[10]

$$CH_3.CHOCH_2CH_3 \quad + \quad BzO - OBz \longrightarrow CH_3CH(OBz)OCH_2CH_3 \quad + \quad \cdot OBz$$

Reactions K and L may also be important as de la Mare has used 2,6-ditertiarybutyl-4-methylphenol to capture tertiarybutylperoxy-radicals formed during the tripropylamine - tertiarybutyl hydroperoxide reaction.

The reaction sequence M,N,O,P, with R = H has already been discussed in Section II. Reaction N may be considered to be analogous to the thermal decomposition of di-a,a-dimethylbenzyl peroxide into a,a-dimethylbenzyloxy-radicals.[11]

$$PhC(CH_3)_2OOC(CH_3)_2Ph \longrightarrow 2\ PhC(CH_3)_2O\cdot$$

References

1. Kharasch, Fono and Nudenberg, J. Org. Chem., 1950, 15, 748.
2. Lorand and Reese, U.S.P., 2, 691, 683/1954.
3. Kharasch, Fono and Nudenberg, J. Org. Chem, 1951, 16, 113
4. Capp and Hawkins, J., 1953, 4106.
5. De La Mare, J. Org. Chem., 1960, 25, 2114.
6. Cope and Hiok-Huang Lee, J. Amer. Chem. Soc., 1957, 79, 964.
7. Walling, "Free Radicals in Solution", Wiley, New York, 1957, P.595.
8. Homer and Schwenk, Angew. Chem., 1949, 61, 411; Annalen, 1949, 566, 69., and subsequent papers.
9. Franzen, Ber., 1955, 88, 1697; Walter, J. Amer. Chem. Soc., 1955, 77, 5999.
10. Drew and Martin, Chem. and Ind., 1959, 925; Denney and Feig, J. Amer. Chem Soc., 1959, 81, 5323.
11. Pfordte and Leuschner, Annalen, 1961, 646, 25.

EXPERIMENTAL SECTION

GENERAL NOTES

Quantitative analyses of amines and amides by gas-liquid chromatography were carried using the method of internal standardisation of a Griffin and George "V.P.C. Apparatus", Mk.IIa. A linear relationship between peak area and concentration was found over the range of concentrations used. The peak areas were determined using a planimeter. A 6 ft. colum of 8% by weight of silicone oil on celite (80-120 mesh) was used with nitrogen as carrier gas (flowrate Ca. 1:8 l. per hr.).

Abbreviations:-

G.L.C. = gas-liquid chromatography
i.s. = internal standard
r.t. = retention time

Tributylamine N-oxide was separated from mixtures of tributylamine, dibutylamine, N,N-dibutylformamide by extracting the cyclohexane solutions of the mixtures with water.

The yields of products are based on the amount of starting material not recovered.

Light petroleum refers to the fraction boiling between 40° and 60°.

Solutions were concentrated by rotary evaporation at 20°/14 m.m. unless otherwise stated.

Manganese dioxide

The manganese dioxide used was a commercial sample from Messrs. J. Woolley Sons and Co. Ltd., who state that it was prepared by mixing solutions of a bivalent manganese salt and a permanganate, i.e., under acid conditions.

General Oxidation Procedure using manganese dioxide

For oxidations at room temperature (ca.19°), the amine, in a solvent, was shaken with manganese dioxide in a stoppered flask. For oxidations at 80°, the amine, in the refluxing solvent, was stirred with manganese dioxide.

After reaction the manganese dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol. The solvent was then removed either by distillation at atmospheric pressure or under reduced pressure by rotary evaporation at 20°/14 mm.

Oxidation of tributylamine

(i) Tributylamine (2.00g.) in cyclohexane (250 ml.) was shaken with manganese dioxide (50 g.) for 18 hr. at 19°. The dioxide was filtered off the washed with a 3:1 mixture of dichloromethane and methanol (400 ml). The filtrate was concentrated to about 5 ml. The infrared spectrum of the resulting solution indicated the presence of oxidation products by the strong absorption at 1675 $cm.^{-1}$ and 1620 $cm.^{-1}$ and the weak absorption at 1565 $cm.^{-1}$

When the solution, in cyclohexane (100 ml), was extracted with water and the aqueous extract treated with cold saturated aqueous picric acid, no tributylamine N-oxide picrate was formed.

The cyclohexane solution was extracted with 0.7% hydrochloric acid (100 ml) and water (100 ml). It was then washed with dilute sodium bisulphite solution and water, to remove aldehydes, dried ($MgSO_4$) and concentrated to about 5ml. The resulting solution absorbed at 1675 cm^{-1} but not at 1620 cm^{-1} and 1565 cm^{-1} in the infrared. On analysis by G.L.C., N,N-dibutylformamide (0.448g., 36.4%) was detected.

The aqueous acidic extract was basified with ice-cold concentrated sodium hydroxide solution and extracted with ether (4 x 50 ml.). The combined ether extracts were dried ($MgSO_4$) and concentrated to about 5 ml. by distillation at atmospheric pressure. To reduce volatility cyclohexane (5 ml.) was added and the solution again concentrated to about 5 ml. by distillation at atmospheric pressure. This solution absorbed strongly at 1620 cm^{-1} and weakly at 1565 cm^{-1} and 1655 cm^{-1} in the infrared. On analysis by G.L.C., only dibutylamine (0.382g., 37.7%) and unreacted tributylamine (0.554g.) were detected.

Isolation and identification of products.

The formamide, $n_D^{18} = 1.4430$, was isolated from the remainder of the neutral fraction by distillation at 0.1 m.m. and identified by comparison of its infrared spectrum with that of the authentic compound. The formamide exhibited a strong band at 1675 cm^{-1}. (Found: C,68.4; H,12.1; N,8.9; Calc. for $C_9H_{19}NO$: C,68.7; H,12.2; N,8.9%).

The remainder of the basic fraction was divided into two parts. One part was treated with phenylisothiocyanate (1 ml.) and refluxed for 15 min. The phenylthiourea of dibutylamine, $C_6H_5NHCSNBu_2$, formed was isolated by chromatography on deactivated alumina (100g.) - the derivative being eluted by 50% benzene in light petroleum. Crystallisation from aqueous ethanol gave material m.p. and mixed m.p. 83°.

The other part was chromatographed on deactivated alumina (50g.). Elution with benzene removed the tributylamine and dibutylamine. Elution with dichloromethane showed the presence of at least five other products some of which fluoresced in ultraviolet light.

G.L.C. Analysis

N,N-dibutylformamide estimation:
Column temperature 125°.
N,N-dibutylformamide r.t. 20 min.
N,N-dibutylacetamide (i.s.), r.t. 28 min.

Amine estimation:
Column temperature 100°.
Decalin (i.s.), r.t. 11 min.
Tributylamine r.t. 24 min.
Dibutylamine r.t. 6 min.

(ii) Tributylamine (2.08g.) in cyclohexane (250 ml.) was shaken with manganese dioxide (50 g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400 ml.) The filtrate was concentrated to about 5 ml.

On analysis by G.L.C. as in experiment (i), N,N-dibutylformamide (0.47 g., 40.0%), dibutylamine (0.382g., 39.5%) and unreacted tributylamine (0.68g.) were detected in the solution. The dibutylamine had both a slightly longer r.t. and a broader peak than that normally given.

(iii) Tributylamine (0.99g.) in cyclohexane (250 ml.) was shaken with manganese dioxide (50g.) for 72 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400 ml.) The filtrate was concentrated to about 5 ml.

On analysis by G.L.C. as in experiment (i), N,N-dibutylformamide (0.426g., 51.0%) and dibutylamine (0.231g., 33.0%) were detected in the solution. Unreacted tributylamine was not detected.

(iv) Tributylamine (0.98g.) in cyclohexane (300 ml.) was shaken with manganese dioxide (75g.) for 48 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (500 ml.). The filtrate was concentrated to about 5 ml.

On analysis by G.L.C. as in experiment (i), N,N-dibutylformamide (0.266g., 32.0%) and dibutylamine (0.172g., 25.0%) were detected in the solution. Unreacted tributylamine was not detected.

(v) Tributylamine (1.97g.) in cyclohexane, contaiņining 3% of dichloromethane (250 ml.) was shaken with manganese dioxide (50g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400ml. The filtrate was concentrated to about 5 ml.

On analysis by G.L.C. as in experiment (i), N,N-dibutylformamide (0.505g., 40.4%), dibutylamine (0.403g., 39.2%) and unreacted tributylamine (0.498g.) were detected in the solution.

(vi) Tributylamine (1.98g.) in cyclohexane, containing 3% of isopropanol (250 ml.) was shaken with manganese dioxide (50g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400 ml.). The filtrate was concentrated to about 5 ml.

On analysis by G.L.C. as in experiment (i), N,N-dibutylformamide (0.392g., 40.0%), dibutylamine (0.314g., 39.2%) and unreacted tributylamine were detected in th solution.

(vii) Tributylamine (2.00g.) in cyclohexane (250ml.), containing propionic acid (0.45g.), was shaken with manganese dioxide (50g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400ml The filtrate was concentrated to about 5ml., and the resulting solution separated into neutral and basic fractions by extraction with dilute hydrochloric acid as in experiment (i).

On analysis of each fraction by G.L.C., as in experiment (i), N,N-dibutylformamide (0.372g., 33.5%), dibutylamine (0.488g., 53.4%) and unreacted tributylamine (0.688g.) were detected.

(viii) Tributylamine (2.00g.) in benzene (250ml.) was stirred with manganese dioxide (50g.) for 2½hr. at 80°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400 ml.). The filtrate was concentrated to about 5ml., and the resulting solution separated into neutral and basic fractions by extraction with dilute hydrochloric acid as in experiment (i).

On analysis of each fraction by G.L.C., as in experiment (i), N,N-dibutylformamide (1.23g., 73.5%), dibutylamine (0.14g., 10.0%), and unreacted tributylamine (trace) were detected.

(ix) Tributylamine (2.00g.) in cyclohexane (250ml.) was stirred with manganese dioxide (50g.) for 2½hr. at 80°. The dioxide was filtered off and washed with a 3:1

mixture of dichloromethane and methanol (400ml.). The filtrate was concentrated to about 5ml. and the resulting solution separated into neutral and basic fractions by extraction with dilute hydrochloric acid as in experiment (i).

On analysis of each fraction by G.L.C., as in experiment (i), N,N-dibutylformamide (1.08g., 64.5%), dibutylamine (0.178g., 13.0%), and unreacted tributylamine (trace) were detected.

Preparation of triisobutylamine.

Diisobutylamine (6g.) and isobutyliodide (18g.), i.e., mole ratio 2:1, were heated on a steam bath for 3 hr. The reaction mixture was treated with ice cold concentrated sodium hydroxide solution and extracted with ether (4 x 50 ml.). The combined ether-extracts were dried and concentrated. The residue was fractionally distilled, first at atmospheric pressure to remove diisobutylamine, and then at 14mm. to give triisobutylamine (1.5g.), $n_D^{18} = 1.4245$ (lit.$n_D^{17.5} = 1.4252$).[1] G.L.C. indicated that the material was ca.90% pure, the impurities probably being isomers.

Oxidation of triisobutylamine.

Triisobutylamine (0.378g.) in cyclohexane (50 ml.) was shaken with manganese dioxide (9.4g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (100 ml.). The filtrate was concentrated to about 3 ml.

On analysis by G.L.C., diisobutylformamide, diisobutylamine and unreacted triisobutylamine were detected. The diisobutylformamide and diisobutylamine were produced in approximately equimolar quantity. The diisobutylamine had both a slightly longer r.t. and a broader peak than that normally given. c.f. the dibutylamine analysis in experiment (ii).* The amine behave normally, however, when first extracted from the reaction product with dilute hydrochloric acid.

Preparation of N,N,N',N'-tetrabutyl-1,2-ethylenediamine.

Dibutylamine (51.6g) and ethylene dibromide (18.8g.), i.e., mole ratio 2:1, were refluxed for 1 hr. The reaction mixture was basified with ice cold concentrated sodium hydroxide solution and extracted with ether (4 x 50ml.). The combined ether extracts were dried ($MgSO_4$) and concentrated. The residue was fractionally distilled first at 14mm. to remove dibutylamine and then at 0.1 mm. to yield N,N,N',N'-tetrabutyl-1,2-ethylenediamine (8.5g.), b.p. 90°/0.1mm., $n_D^{21} = 1.4454$. (lit. b.p. 156-8°/12mm., $n_D^{25} = 1.4438$)[2] (Found: C,76.2; H,13.8; N,9.8. Calc. for $C_{18}H_{40}N_2$: C,76.0; H,14.2; N.9.8%).

Oxidation of N,N,N',N'-tetrabutyl-1,2 -ethylenediamine.

The amine (1.91g.) in cyclohexane (250ml.) was shaken with manganese dioxide (50g.) for 18hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400ml.) The filtrate was concentrated to about 5ml.

The infrared spectrum of the resulting solution indicated the presence of oxidation products which absorbed at 1675cm^{-1} and 1655cm^{-1}. The solution, in cyclohexane (100ml.), was extracted with 0.7% hydrochloric acid (200ml.) and water (100ml.), dried ($MgSO_4$) and concentrated to about 5 ml.

On analysis by G.L.C., N,N-dibutylformamide and two other neutral compounds of higher boiling point were detected in the solution.

* (see page 17)

Oxidation of triethylamine.

Triethylamine (2.01g.) in cyclohexane (250ml.) was shaken with manganese dioxide (50g.) for 18hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400ml.) The filtrate was concentrated to about 5ml. by distillation through a 12 inch Fenske column.

On analysis by G.L.C., N,N-diethylformamide (0.09g., $<1\%$) was detected in the solution. Unreacted triethylamine was not estimated because of losses due to volatility.

G.L.C. Analysis

Column temperature 78°.
m-xylene (i.s.), r.t. 9 min.
N,N-diethylformamide r.t. 16 min.

Oxidation of tripropylamine.

Tripropylamine (2.05g.) in cyclohexane (250ml.) was shaken with manganese dioxide (50g.) for 18hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400ml.). The filtrate was concentrated to about 5ml. by distillation through a 12 inch Fenske column.

On analysis by G.L.C., N,N-dipropylformamide (0.34g., 27.5%) and tripropylamine (0.675g.) were detected in the solution.

G.L.C. Analysis

Column temperature 130°.
Tributylamine (i.s.), r.t. 38min.
Tripropylamine r.t. 7 min.
N,N-dipropylformamide r.t. 19 min.

Oxidation of tripentylamine.

Tripentylamine (2.04g.) in cyclohexane (250 ml.) was shaken with manganese dioxide (50g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (400 ml.). The filtrate was concentrated to about 5 ml.

The infrared spectrum of the resulting solution indicated the presence of oxidation products by the strong absorption at 1675 cm^{-1} and 1620 cm^{-1} and by the weak absorption at 1565 cm^{-1}. Cf. the oxidation of tributylamine. The solution in cyclohexane (100 ml.) was extracted with 0.7% hydrochloric acid (400 ml), dried ($MgSO_4$) and concentrated to about 5 ml.

On analysis by G.L.C., N,N-dipentylformamide (0.60g., 48.2%) was detected in the solution. The aqueous acidic extract was basified with ice cold concentrated sodium hydroxide solution and extracted with ether (4 x 50 ml.). The combined ether extracts were dried ($MgSO_4$) and concentrated to about 5ml. by distillation at atmospheric pressure. On analysis by G.L.C., tripentylamine (0.39g.) and dipentylamine were detected in the solution. The dipentylamine was not estimated.

G.L.C. Analysis

N,N-dipentylformamide estimation:
Column Temperature 171°.
Tributylamine (i.s.), r.t. 3 min.
N,N-dipentylformamide r.t. 11 min.

Tripentylamine estimation:
Column Temperature 171°.
Tributylamine (i.s.), r.t. 3 min.
Tripentylamine r.t. 10 min.

Isolation and identification of the N,N-dipentylformamide.

The remainder of the neutral fraction was washed with dilute sodium bisulphite solution to remove aldehydes. The formamide $n_D^{18} = 1.4470$ (lit. $n_D^{25} = 1.4462$)[3], which isolated by distillation at 0.1 mm., exhibited a strong band at 1675 cm^{-1} in the infrared. (Found: C,70.9; H, 12.4; N,6.6. Calc. for $C_{11}H_{23}NO$: C,71.3; H,12.5; N,7.5%)

Oxidation of trioctylamine.

Trioctylamine (1.99g.) in cyclohexane (150 ml.) was shaken with manganese dioxide (25g.), for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (250 ml.). The filtrate was concentrated to about 5 ml. The infrared spectrum of the resulting solution indicated the presence of oxidation products by the strong absorption at 1675 cm^{-1} and 1620 cm^{-1} and the weak absorption at 1565 cm^{-1}. Cf. the oxidations of tributylamine and tripentylamine.

The solution was chromatographed on activated alumina (100g.) Elution with light petroleum gave unreacted trioctylamine (0.741g.) and with 5% benzene in light petroleum, N,N-dioctylformamide (0.513g., 54.0%). The oxidation products which absorbed at 1620 cm^{-1} and 1565 cm^{-1} were eluted with methylene chloride.

The N,N-dioctylformamide, which exhibited a strong band at 1675 cm^{-1} in the infrared, was distilled at -.1 mm. $n_D^{18} = 1.4534$ (lit. $n_D^{25} = 1.4523$)[3]. (Found: C,75.3; H, 12.6; N,5.3. Calc. for $C_{17}H_{35}NO$: C,75.8; H,13.1; N,5.2%).

Oxidation of N,N'-dimethyl-Δ²-tetrahydroanabasine.

The amine (0.14g.) in cyclohexane (20 ml.) was shaken with manganese dioxide (3.5 g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (50 ml.) The filtrate was concentrated to about 5 ml. The infrared spectrum of the resulting solution showed a broad band at 1585 cm^{-1}.

Oxidation of N,N'-dimethyl-2,2'-dipiperidyl.

The amine (0.16g.) in cyclohexane (20 ml.) was shaken with manganese dioxide (4g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (50 ml.) The filtrate was concentrated to about 5 ml. The infrared spectrum of the resulting solution showed broad bands at 1645 cm^{-1} and 1545 cm^{-1}.

Oxidation of N,N-dimethyl-t-butylamine.

(i) The amine (0.98g.) in light petroleum b.p.30-40° (150 ml.) was shaken with manganese dioxide (25 g.) for 18 hr. at 19°. The dioxide was filtered off and washed with dichloromethane (200 ml.). The filtrate was concentrated to about 5 ml. by distillation through a 12-inch Fenske column. On analysis by G.L.C. unreacted N,N-dimethyl-t-butylamine (0.338g.) and two unidentified products were detected in the solution. The infrared spectrum of the solution showed no carbonyl absorption.

G.L.C. Analysis

Column temperature 19°.
Toluene (i.s.), r.t. 17 min.
N,N-dimethyl-t-butylamine r.t. 9 min.
Product A. r.t. 7 min.
Product B. r.t. 5 min.

(ii) The amine (1.0g.) in light petroleum b.p. 30-40° (150 ml.) was shaken with manganese dioxide (25g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (300 ml.). The filtrate was concentrated to about 5 ml. by distillation through a 12-inch Fenske column. The solution showed no carbonyl absorption in the infrared.

(iii) The amine (1.00g.) in light petroleum b.p. 30-40° (250 ml.) was shaken with manganese dioxide (50g.) for 18 hr. at 19°. The dioxide was filtered off and washed with a 3:1 mixture of dichloromethane and methanol (300 ml.). The filtrate was concentrated to about 200 ml. by distillation through a 12-inch Fenske column and treated with a mixture (mole ratio 1:10) of 2,3-dichloronaphthaquinone (1.12g.) and acetaldehyde (2.20g.) in benzene (100 ml.)^4.

After 18 hr. in the dark at 19°, the resulting blue solution was concentrated to about 50 ml. After washing with 0.5N sulphuric acid to extract the amine hydrochloride, the blue solution was dried ($MgSO_4$) and made up to 500 ml. with benzene. From the optical density of this solution at 5720Å, the amount of 2-chloro-3,2'-N-methyl-N-t-butylaminovinyl-1,4-naphthaquinone formed was 0.186g. The yield of N-methyl-t-butylamine was thus 0.0534g., 12.4%, assuming all the N,N-dimethyl-t-butylamine to have reacted.

The solution was evaporated to dryness and chromatographed on deactivated alumina (50g.). Rapid elution with benzene gave first unreacted 2,3-dichloronaphthaquinone and then the blue 2-chloro-3,2'-N-t-butylaminovinyl-1,4-naphthaquinone. The blue quinone was crystallised twice from toluene and dried at 60° for 15 hr. at 0.1mm. to remove toluene of crystallisation. m.p.157°. (Found: C,65.5; H,6.1; N,4.0. $C_{17}H_{18}O_2NCl$ requires: C,67.2; H,5.9; N,4.6%). Ultraviolet absorption (in benzene): λ max 5720Å., ε max = 12,750.

The ultraviolet absorption of a solution of the blue quinone in pure dioxan was measured in the range 2,000 - 5,800Å. Three maxima were found:

Band I	Band II	Band III
λ max 2,360Å.	λ max 3,200Å	λ max 5,660Å
ε max = 10,110	ε max = 26,800	ε max = 12,720

2-Chloro-3,2'-dimethylaminovinyl-1,4-naphthaquinone (A)
and 2-chloro-3,2'-diethylaminovinyl-1,4-naphthaquinone (B)
under the same conditions each give three maxima:-^{4}

	Band I	Band II	Band III
(A)	λ max 2,380Å	λ max 3,230Å	λ max 5,640Å
	ε max 10,200	ε max 27,600	ε max 13,300
(B)	λ max 2,380Å	λ max 3,210Å	λ max 5,580
	ε max 10,100	ε max 26,600	ε max 12,200

Oxidation of tributylamine with oxygen at 100°.

In the absence of light a slow stream of pure oxygen was passed for 36-hrs. through tributylamine (26.41g., 0.143 mole) and a 0.01 mole equivalent of ditertiarybutyl peroxide at 100° in a 100 ml. flask filted with a double surface condenser. The reaction mixture which was dark red-brown in colour was cooled, taken up in cyclohexane (200 ml.), and extracted with water. On treating the aqueous extract with cold saturated aqueous picric acid, a crystalline picrate was not obtained. The residual cyclohexane solution was extracted with dilute hydrochloric acid to remove basic material, dried ($MgSO_4$) and concentrated to about 10 ml. On analysis by G.L.C. N,N-dibutylformamide (0.49g., 0.0031 mole, 5.6%) and two other unidentified products were detected in the solution. Infrared absorption at 1675 cm^{-1} confirmed the presence of the formamide. The acid extract of the reaction mixture was basified with cold concentrated sodium hydroxide solution and extracted with ether (4 x 200 ml.) The combined extracts were dried ($MgSO_4$) and concentrated to about 25 ml. Unreacted tributylamine (16.2g., 0.0876 mole) and dibutylamine (1.24g., 0.0096 mole, 17.4%) were detected in the solution on analysis by G.L.C.

Cumene hydroperoxide from Laporte Chemicals Limited was purified by distillation at 53°/0.0005mm. $n_D^{20} = 1.5242$ (Lit. $n_D^{20} = 1.5242$).[5]

α,α-Dimethylbenzyl alcohol[6] was prepared by the action of cumene hydroperoxide on tributylamine at 110°. m.p. 34° (from light petroleum).

Oxidation of tributylamine with cumene hydroperoxide.

(i) Tributylamine (3.94g., 0.0213 mole) and cumene hydroperoxide (1.56g., 0.0103 mole) were mixed and heated at 80° for 24-hr. The reaction mixture was cooled and taken up in cyclohexane (100 ml.) The cyclohexane solution was extracted with water and the aqueous extract treated with cold saturated picric acid. Tributylamine N-oxide picrate (m.p. and mixed m.p. 110°) was formed representing tributylamine N-oxide (0.264g., 0.00132 mole, 18%). The cyclohexane solution was extracted with dilute hydrochloric acid to remove basic material, dried ($MgSO_4$), and concentrated to about 5 ml. On analysis by G.L.C. α,α-dimethylbenzyl alcohol (1.15g., 0.0084 mole, 82.5%) was detected but not N,N-dibutylformamide and N,N-dibutylbutyramide. The acid extract of the reaction mixture was basified with cold concentrated sodium hydroxide solution and extracted with ether (4 x 100 ml.). The combined extracts were dried ($MgSO_4$) and concentrated to about 5 ml. Unreacted tributylamine (2.61g., 0.0141 mole) and dibutylamine (0.19g., 0.00147 mole, 20.5%) were detected on analysis of the solution by G.L.C.

G.L.C. Analysis of α,α-dimethylbenzyl alcohol.

The α,α-dimethylbenzyl alcohol was estimated on a 6ft. column of 8% by weight of silicone oil on elite at 110° using tributylamine as internal standard.

Tributylamine (i.s.), r.t. 12 min.
α,α-dimethylbenzyl alcohol r.t. 25 min.

(ii) Tributylamine (3.64g., 0.0197 mole) and cumene hydroperoxide (1.44g., 0.00947 mole) were mixed and heated at 80° for 4-hr. The reaction mixture was worked up and analysed as in experiment (i).

Unreacted tributylamine (2.38g., 0.0129 mole), dibutylamine (0.198g., 0.00154 mole, 22.5%) and tributylamine N-oxide (0.38g., 0.00191 mole, 28%) were obtained.

(iii) Tributylamine (2.02g., 0.0109 mole) and cumene hydroperoxide (3.06g., 0.0201 mole) were mixed and heated at 80° for 9 hr. The reaction mixture was worked up and analysed as in experiment (i).

Unreacted tributylamine (0.80g., 0.00432 mole) and tributylamine N-oxide (0.425g., 0.00212 mole, 32%) were obtained.

Oxidation of N-ethylpiperidine with cumene hydroperoxide.

(iv) N-Ethylpiperidine (0.559g., 0.00495 mole) and cumene hydroperoxide (2.96g., 0.0194 mole) were mixed and heated to 80°. Almost immediately the reaction mixture turned a dark brown colour. The reaction was not investigated further.

(v) N-Ethylpiperidine (0.559g., 0.00495 mole) and cumene hydroperoxide (2.96g., 0.0194 mole) were mixed and allowed to stand for 24 hr. The reaction mixture was taken up in cyclohexane (100 ml.) and extracted with water. The aqueous extract, on treatment with cold saturated aqueous picric acid yielded N-ethylpiperidine N-oxide picrate (m.p. and mixed m.p. 144°. Found: C,43.7; H,4.9; N,16.00. Calc. for $C_{13}H_{18}O_8N_4$ C,43.6; H,5.1; N,15.6%) representing N-ethylpiperidine N-oxide (0.198g., 0.00142 mole, 29%0.

Oxidation of triethylenediamine with cumene hydroperoxide.

(vi) Triethylenediamine (1.12g., 0.0112 mole) and cumene hydroperoxide (0.76g., 0.0076 mole) were mixed and heated at 80° for 4 hr. Although the reaction mixture was worked up as in experiment (i), the fate of the amine could not be determined due to the extreme solubility of triethylenediamine in water. *a,a*-Dimethylbenzyl alcohol (0.68g., 0.0076 mole, 100%) was obtained.

References.

1. Handbook of Chemistry and Physics, 30th Ed., Chemical Rubber Publishing Co.
2. Armbrecht, Rice, Grogan and Reid, J. Amer. Chem. Soc., 1953, 75, 4829.
3. Piquett, Gersdorff and Gertler, Chem. Abs., 1956, 50, 8125^e.
4. Buckley, Henbest and Slade, J., 1957, 4891.
5. Armstrong, Hall and Quin, J., 1950, 666.
6. Capp and Hawkins, J., 1953, 4106.

2. OXIDATION OF TERTIARY AMINES BY MONOVALENT RADICALS.

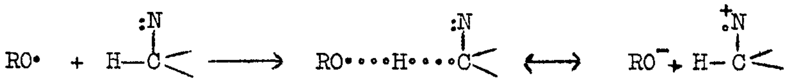
In our previous reports the oxidation of dimethylaniline by t-butoxy radicals formed by thermal or photochemical decomposition of di-t-butyl peroxide in an excess of dimethylaniline has been discussed in detail. The products of the reaction indicated that N-methylanilinomethyl radicals ($\mathrm{PhMeN{\cdot}CH_2{\cdot}}$) were generated and that these dimerised to give the main product. Other products were the triamine and tetramine formed by further dehydrogenative coupling with the N-methyl groups of the diamine and triamine respectively. The oxidation of other amines has also been discussed and attempts to find other sources of radicals described. The work of the present report continues the oxidation of amines with di-t-butyl peroxide using an excess of the amine as solvent and also using acetic acid as solvent. Comparison is made with the products of oxidation using other oxidising agents.

The oxidation of N,N-dimethyl-t-butylamine by di-t-butyl peroxide in mole ratio 5:1 by reaction at 132° for 87 hours was described in the last report. N,N'-Dimethyl-N,N'-di-t-butylethylenediamine was formed in 47% yield. The reaction has been repeated and the formation of a triamine noted in 27% yield. Gas chromatography showed that the trimeric fraction consisted of two compounds (ratio about 95:5). By analogy with the trimer and tetramer in the dimethylaniline case it may be assumed that the lesser peak corresponds to the trimer resulting from dehydrogenative coupling with the N-methylene group of the diamine, $\mathrm{Bu^{Y}(Me)NCH_2CH[CH_2N(Me)Bu^{Y}]N(Me)Bu^{Y}}$, and that the major peak corresponds to the trimer resulting from coupling with the N-methyl group, $\mathrm{Bu^{Y}(Me)NCH_2CH_2N(Bu^{Y})CH_2CH_2N(Me)Bu^{Y}}$. The results with N,N-dimethyl-t-butylamine show that it is attacked by t-butoxy radicals in the usual fashion and that there is no steric hindrance between the entering t-butoxy radical and the bulky t-butyl group of the amine.

The reaction between N-methylpiperidine and di-t-butylperoxide with the formation of 2,2'-dipiperidyl and an enamine was discussed in the report of last year. In order to obtain more evidence on the route of enamine formation experiments were done using N,N-dimethylisobutylamine and N,N-dimethylisopropylamine. When N,N-dimethylisobutylamine and di-t-butyl peroxide were reacted together no N,N-dimethyl-2-methyl-prop-1-enylamine $\mathrm{Me_2C{:}CHNMe_2}$ was found. This compound would be the monomeric enamine expected. The higher-boiling products of the reaction showed only a weak band in the infrared at 1675 $\mathrm{cm.^{-1}}$ and this appeared to be a carbonyl impurity rather than an enamine of a dimeric product. Gas chromatography indicated a single compound and spectra in the near infrared region indicated that the product was N,N'-dimethyl-N,N'-diisobutylethylenediamine i.e. dehydrogenative coupling occurred <u>via</u> the N-methyl group of the amine and not on the N-methylene group. The results with N,N-dimethylisopropylamine were similar. A weak band was again observed at 1675 $\mathrm{cm.^{-1}}$ in the infrared spectrum of the product. Spectra in the near infrared region indicated that a substituted ethylenediamine had been formed. Further evidence that this may be the structure is that another possible dehydrogeno-dimer, 2,3-bis(dimethylamino)-2,3-dimethylbutane has a lower boiling point than that of the product. Thus these two amines are attacked at the N-methyl group in the usual fashion by the t-butoxy radical to form an aminomethyl radical and t-butanol.

Enamines do not seem to have been formed.

The reactivity of methyl groups towards t-butoxy radicals increases in the order CMe, OMe, NMe. Thus the yield of t-butanol when di-t-butyl peroxide is decomposed in substrates is 26% from t-butylbenzene,[1] 55% from anisole,[2] and 100% from dimethylaniline. Competitive experiments were therefore done on N,N-dimethyl-t-butylamine, t-butylmethylether, and dimethylaniline and the results compared with other work in this department on parallel experiments with dimethylaniline, anisole and t-butylmethylether. The results are illustrated in tabular form in the experimental section, where it may be seen that amines are very much more reactive than ethers. However, dimethylaniline was not much more reactive than dimethyl-t-butylamine. Thus the additional possible stabilization of the initial radical by the benzene ring does not contribute much to the reactivity. The greater reactivity of amines compared with ethers is probably due to the greater capacity of amines to contribute a polar structure to the transition state. Electron donation from the hetero-atom with consequently lowering of the activation energy, occurs more readily for nitrogen than for oxygen:

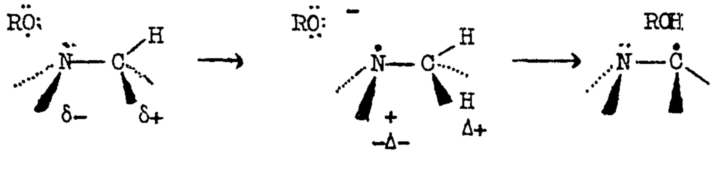


Resonance stabilization by electron donation must also be greater for $R_2N\cdot CR_2\cdot$ then for $RO\cdot CR_2\cdot$ radicals as dimers are formed by the former radicals.

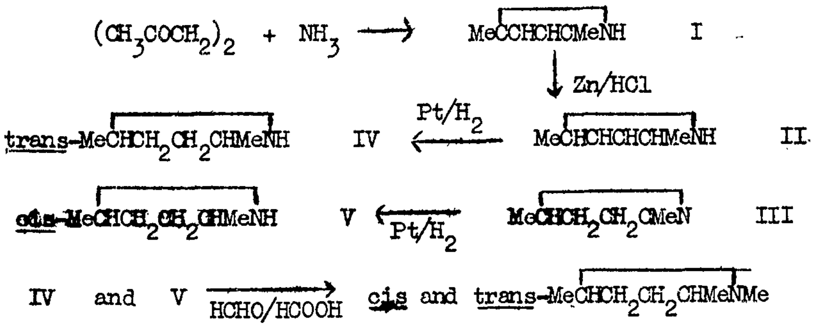
Stereochemical Aspect of Hydrogen Removal

For amines it may be expected that, for a particular oxidising agent, there will be a preferred conformation for the removal of hydrogen. The problem is to determine the preferred angle between the leading hydrogen and the characteristic unbonded electron pair on nitrogen. If alkoxyl radicals are electron accepting in character then their reaction with amines may be due to electron donation from nitrogen in the transition state. Walling[3] has suggested that the t-butoxy radical is electrophilic in character. However Moore[4] has found that the α-position in ketones is activated towards attack by t-butoxy radicals for butan-2-one and cyclohexanone, and Beckwith[5] from the reaction of di-t-butyl peroxide with aliphatic acids has suggested that the t-butoxy radical has negligible electron accepting properties and that polar effects do not influence the course of its reactions. Johnston and Williams[6] and Huang and Yeo[7] however have concluded that hydrogen abstraction by t-butoxy radicals may involve some degree of polarization in the transition state.

If electron donation from nitrogen in the transition state is a step in the reaction of amines with t-butoxy radicals then the removal of *cis*-hydrogen will be the preferred path.



Competitive reactions of cis- and trans-1,2,5-trimethylpyrrolidine with t-butoxy radicals may be informative. These amines were synthesised according to the scheme:



$$(CH_3COCH_2)_2 + NH_3 \longrightarrow MeCCHCHCMeNH \quad I$$

$$\downarrow Zn/HCl$$

$$trans\text{-}MeCHCH_2CH_2CHMeNH \quad IV \xleftarrow{Pt/H_2} MeCHCHCHCHMeNH \quad II$$

$$cis\text{-}MeCHCH_2CH_2CHMeNH \quad V \xleftarrow[Pt/H_2]{} MeCHCH_2CH_2CMeN \quad III$$

$$IV \text{ and } V \xrightarrow[HCHO/HCOOH]{} cis \text{ and } trans\text{-}MeCHCH_2CH_2CHMeNMe$$

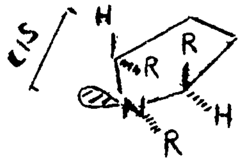
Reduction of 2,5-dimethylpyrrole I by zinc and hydrochloric acid gives a mixture of 2,5-Δ^3-pyrroline II and 2,5-Δ^1-pyrroline III. These were separated by the differences in solubility of their picrates and the amines were regenerated from the picrates. Hydrogenation of the pyrrolines gave the cis- and trans-isomers of 2,5-dimethylpyrrolidine (V and IV) and these were methylated using formic acid/formaldehyde to give the cis- and trans-isomers of 1,2,5-trimethylpyrrolidine.

In the reactions of the isomers of 1,2,5-trimethylpyrrolidine with di-t-butyl peroxide it was found that isomerisation of cis to trans or vice versa did not occur. Thus the reaction of the molecule RX with the corresponding radical R• according to the equation

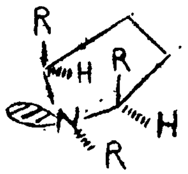
$$RX + R\bullet \longrightarrow R\bullet + RX$$

does not occur. This is in accord with the unimportance of similar reactions with benzylic radicals.[8]

In the experiments, both by thermal decomposition and by photolysis of the peroxide, it was found that the trans-isomer reacted slightly more quickly than the cis-isomer. This is in agreement with the theory as the trans-isomer contains the hydrogen of the α-carbon and the lone pair of the nitrogen in a more cis-configuration. However, it should be emphasized that the reactivity difference is not large.



trans-1,2,5-trimethylpyrrolidine



cis-1,2,5-trimethylpyrrolidine

Dimethyl-p-toluidine and di-t-butyl peroxide in acetone.

In order to compare the reaction of t-butoxy radicals with that of 3,5,3',5'-tetrachloro-4,4'-diphenoquinone (t.c.d.), di-t-butyl peroxide was decomposed photochemically in the presence of dimethyl-p-toluidine in acetone. With t.c.d. the main product of the reaction was 5,6,11,12-tetrahydro-2,5,8,11-tetramethylphenhomazine. This was not formed in the present case, the main product being the expected N,N'-dimethyl-N,N'-di-p-tolylethylenediamine (40%). A small amount of monomethyl-p-toluidine was also formed. Thus the mechanisms of the two reactions are different. The t.c.d. mechanism will be discussed later.

Dimethylaniline and di-t-butylperoxide in acetic acid.

The reaction of dimethylaniline and di-t-butyl peroxide in acetic acid as solvent has been studied. Initial work was done using 50% aqueous acetic acid as solvent. The products were essentially the same as in those using glacial acetic acid but were in lower yields. The latter system was therefore used most often. With dimethylaniline and peroxide in mole ratio 5:1 and decomposed in glacial acetic acid the products of the reaction were 4,4'-bis(dimethylamino)-diphenylmethane I (54%), 4,4',4"-tris(dimethylamino)triphenylmethane II, (leuco-crystal violet) (12%), N-methylacetanilide (84%), 4-dimethylamino(4'-methyl-4'-acetyl)aminodiphenylmethane III (20%). The yield of the last-named compound is based on the amount of N-methylacetanilide from which it could theoretically be formed. The yields are based on the equations:

$$3PhNMe_2 + (Me_3CO)_2 \longrightarrow \underset{\text{I}}{(C_6H_4NMe_2)_2CH_2} + PhNHMe + 2Me_3COH \qquad (1)$$

$$4PhNMe_2 + 2(Me_3CO)_2 \longrightarrow \underset{\text{II}}{(C_6H_4NMe_2)_3CH} + PhNHMe + 4Me_3COH \qquad (2)$$

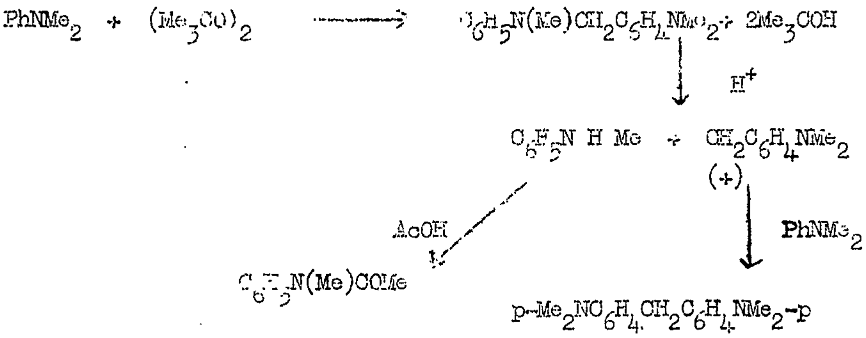
The yield of methylaniline, as N-methylacetanilide, is based on equation (2).

The amide III was recognised by hydrolysis to 4-dimethylamino-4'-methylaminodiphenylmethane IV, the secondary amine being synthesized as follows:

$$\begin{tikzcd} p\text{-}Me_2NC_6H_4CH_2OH + p\text{-}H_2NC_6H_4Me \arrow[r, "H^+"'] & p\text{-}Me_2NC_6H_4CH_2NHC_6H_4Me\text{-}p \arrow[d, "C_6H_5NHMe.HCl \text{ in } C_6H_5NHMe"] \\ \underset{\text{III}}{p\text{-}Me_2NC_6H_4CH_2C_6H_4N(Me)COMe} \arrow[r, "H_2O"'] & p\text{-}Me_2NC_6H_4CH_2C_6H_4NH(Me)\text{-}p \quad \text{IV} \end{tikzcd}$$

The reaction of dimethylaniline, 4,4'-bis(dimethylamino)diphenylmethane, and di-t-butylperoxide (mole ratios 2:2:1) in glacial acetic acid was also studied. N-methylacetanilide (11%), the amide III (85%) and leuco crystal violet (15%) were formed. From the amount of 4,4'-bis(dimethylamino)diphenylmethane returned it was evident that some was formed during the reaction. The results of this experiment suggest that N-methyl groups rather than the central CH_2 of the 4,4'-bis(dimethylamino) diphenylmethane are attacked by the butoxy radicals.

The formation of 4,4'-bis(dimethylamino)diphenylmethane in these experiments suggests, by analogy with the formation of IV above from p-dimethylaminobenzyl-p-toluidine $p\text{-}Me_2NC_6H_4CH_2NHC_6H_4Me\text{-}p$, that p-dimethylaminobenzyl-methylaniline VI $p\text{-}Me_2NC_6H_4CH_2N(Me)C_6H_5$, may be an intermediate in the reaction of the peroxide with dimethylaniline in acetic acid as solvent. This compound has been reported earlier in the reaction of the peroxide in dimethylaniline when the concentration of the generated N-methylanilinomethyl radicals was relatively low. Thus it may be suggested



Reactions using p-dimethylaminobenzylmethylaniline were therefore tried.

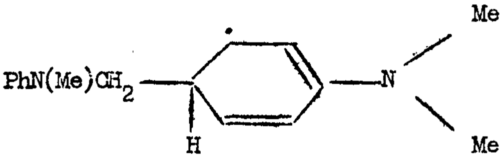
From work previously carried out in this department it was thought that 3,5,3',5'-tetrachloro-4,4'-diphenoquinol (t.c.d.h$_2$), a reduction product of t.c.d. in the oxidations using that product, would provide the acidic conditions thought necessary for the splitting of the intermediate, as methylaniline and 4,4'-bis(dimethylamino)diphenylmethane had been obtained in the T.C.D oxidation of dimethylaniline. However, experiments with dimethylaniline, t.c.d.h$_2$ and p-dimethylaminobenzylmethylaniline under various conditions showed the intermediate to be unchanged. Monomethylaniline seemed to react under the same conditions but the products were not identified.

When dimethylaniline, p-dimethylaminobenzylmethylaniline and t.c.d.h$_2$ (catalytic amount) were refluxed in glacial acetic acid, 4,4'-bis(dimethylamino)-diphenylmethane (100%), N-methylacetanilide (94%), and a small amount of leuco crystal violet were formed. Further experiments showed that the presence of t.c.d.h$_2$ was not required.

If the carbonium ion $^{+}CH_2C_6H_4NMe_2$-p is formed, then a mixed diamine should be formed on refluxing p-dimethylaminobenzylmethylaniline and N-phenylpyrrolidine in acetic acid. In fact, N-methylacetanilide (67%) was obtained together with an amine whose properties indicated that it was the expected 4-(dimethylamino)-4'-(N-pyrrolidino)diphenylmethane (58%).

The formation of the acetyl compound III in the reactions of dimethylaniline and peroxide may be due to the above carbonium ion attacking a methylaniline molecule (or its acetyl derivative), or it may be due to attack of a methylanilinomethyl radical on an N-methyl group of 4,4'-bis(dimethylamino)diphenyl methane.

The resulting molecule would be analogous to p-dimethylaminobenzylmethylaniline and on hydrolysis in acetic acid would lead to the acetyl compound III and the carbonium ion previously postulated. This latter mechanism leads to the consideration of the initial formation of p-dimethylaminobenzylmethylaniline. In view of the strength of an aromatic CH bond it is unlikely that direct abstraction of a para hydrogen of a dimethylaniline molecule occurs either by a methylanilinomethyl radical or a t-butoxy radical. Such a radical would then combine with a methylanilinomethyl radical to give the product directly. Work with ring-deuterated toluene[9] has shown that radicals react by addition followed by abstraction of hydrogen. Similarly in this case it is more likely that a methylanilinomethyl radical first adds to the benzene ring to give a radical;

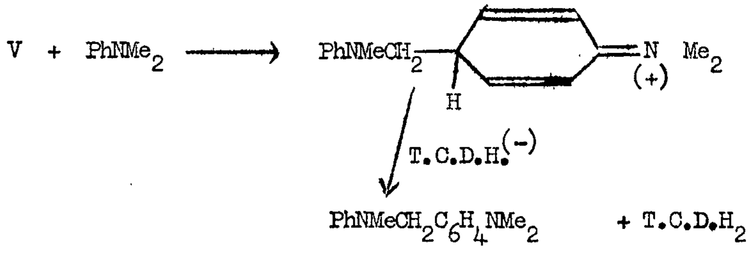


which then undergoes hydrogen abstraction by another methylanilinomethyl radical or a t-butoxy radical to give p-dimethylaminobenzylmethylaniline.

The reaction of 3,5,3',5'-tetrachloro-4,4'-diphenoquinone with dimethylaniline in acetone has also been studied. Previous work[10] had shown that 4,4'-bis(dimethylamino)diphenylmethane and methylaniline were formed. It has now been shown that p-dimethylaminobenzylmethylaniline (VI) is also formed as a major product of the reaction. This diamine is presumably the intermediate in the formation of the other two products. Its formation may be represented:

V.

$$\mathrm{PhNMe_2} \quad + \quad \mathrm{T.C.D.} \longrightarrow \underset{(+)}{\mathrm{PhN(Me)CH_2}} \quad + \quad \mathrm{(T.C.D.H)}^{(-)}$$



VI

This work finds agreement in the work on dimethyl-p-toluidine and t.c.d. (Henbest - unpublished work) where 5,6,11,12-tetrahydro-2,5,8,11-tetramethylphenhomazine is the main product. This must be formed via an intermediate of the type VI.

The reaction of dimethylaniline and cumene hydroperoxide in acetic acid was also studied. Previous work[10] had shown that methylaniline (as N-methylacetanilide) and 4,4'-bis(dimethylamino)diphenylmethane were formed. Experiments now showed that leuco crystal violet and 4-dimethylamino-(4'-methyl-4'-acetyl)aminodiphenylmethane were also formed. As the basic products of the reaction are the same as for di-t-butyl peroxide it is reasonable to assume that the mechanism of the radical attack on the amine is similar. The initial breakdown of the hydroperoxide into a cumyloxy and a hydroxy radical is, however, a complicating factor.

Reaction of t-butoxy radicals with a mixture of dimethylaniline and 4,4'-bis-(dimethylamino)diphenyl methane in acetic acid gave, as already mentioned, N-methylacetanilide, the amide III and leuco crystal violet. Similar reaction in the absence of acetic acid gave t-butanol and 4-dimethylamino-4'-methylamino-diphenylmethane (87%). Also formed was 1,1,2,2,-tetrakis(4-dimethylaminophenyl)ethane(19%). The formation of a demethylated product has been noted in an earlier report in the reaction of N-methyldiphenylamine with di-t-butyl peroxide when diphenylamine was the main product. The other amine is formed by hydrogen abstraction from the central methylene group with subsequent dimerization of the radicals so formed. This suggestion is supported by the following reaction carried out in the absence of dimethylaniline.

4,4'-Bis(dimethylamino)diphenylmethane and di-t-butyl peroxide in mole ratio 3:1 gave 4-dimethylamino-4'-methylaminodiphenylmethane (19%), 1,1,2,2,-tetrakis(4-dimethylaminophenyl)ethane (17%), A,and N,N'-di-[4-p -dimethylaminobenzyl)-phenyl]-N,N'-dimethylethylenechamine (24%), B.

The last named compound B is the dehydrogenodimer resulting from coupling of radicals formed by hydrogen abstraction from the N-methyl group of 4,4'-bis(dimethylamino)diphenylmethane. As the yields of A. and B. are approximately equal, the central methylene group must be activated by the presence of two adjacent dimethylaminophenyl groups as statistically the chance of attack on N-Me should be four times that of attack on the central CH$_2$.

EXPERIMENTAL

N,N-Dimethyl-t-butylamine and di-t-butyl peroxide.

(i) N,N,-Dimethyl-t-butylamine (2.53g.) and di-t-butyl peroxide (0.73g.), (i.e., 5 moles:1 mole), were heated in a sealed tube for 87 hours at 132°. Gas chromatography using 6ft. silicone oil/celite column at 19° showed that t-butanol and no acetone had formed. Distillation at reduced pressure at the water pump gave N,N'-dimethyl-N,N'-di-t-butylethylenediamine, b.p. 95°/15 mm., n^{20}_D 1.4448. [Found: C,70.7; H,13.8; N,13.55%. $C_{12}H_{28}N_2$ requires C, 71.9; H,14.1; N,14.0%]. The yield of substituted ehtylenediamine (0.47g., 47%) was found by gas chromatography on the above column at 122° with dibutylformamide as the internal standard.

(ii) N,N-Dimethyl-t-butylamine (5.05g.) and di-t-butylperoxide (1.46g.), (i.e., 5 moles: 1mole) were heated in a sealed tube at 125° for 24 hours. Gas chromatography using 6ft. silicone oil/celite column at 37° showed that t-butanol had been formed and that some peroxide still remained. Low-boiling products were removed from the reaction mixture (4.52g.) by distillation and N,N'-dimethyl-N,N'-di-t-butylethylenediamine collected at 86°/12 m.m (0.43g., 31%). Distillation at the oil pump gave a higher boiling product corresponding to a dehydrogenotrimer, b.p. 85°/0.05mm (0.28g., 27%). [Found: C,71.8, H, 13.6; N, 13.4% $C_{18}H_{41}N_3$ requires C,72.2; H,13.8; N,14.0%]. A residue (0.15g.) remained. Gas chromatography using 6ft. silicone oil/celite at 191° with a flow rate 1.7 litres N_2/hour showed that three high-boiling products had been formed. N,N'-dimethyl-N,N'-di-t-butylethylenediamine had a retention time of 4.6 minutes, and the product b.p. 85°/0.05 mm. showed two peaks. The largest (95%) had a retention time of 30 minutes, whilst the other (5%) had a retention time of 21.8 minutes.

N,N-Dimethylisobutylamine.

Isobutylamine (73g.), 90% formic acid (260g.) and 40% formaldehyde (165g.) (i.e. 1:5:2.2 moles respectively) were mixed by adding a mixture of the aldehyde and acid dropwise to the amine with ice-cooling and the mixture refluxed for 17 hours. Concentrated hydrochloric acid (45g.) was then added and the mixture boiled for 15 mins. The mixture was then made alkaline with sodium hydroxide solution, extracted with ether, dried with magnesium sulphate and distilled. The product b.p. 78-83° was collected and was refluxed with benzoic anhydride (20g.) for two hours and then distilled b.p. 80-81°. This product was redistilled from solid potassium hydroxide and stored over sodium, b.p. 80-81°, n^{18}_D 1.3935.

N,N-Dimethyl-2-methyl-prop-1-enylamine.

Isobutyraldehyde (36g.) in pentane (100 ml.) with much anhydrous magnesium sulphate were cooled to 0°. Anhydrous dimethylamine (22.5g.) in pentane (50 mls), also cooled to 0°, was added dropwise with stirring. After two hours the magnesium sulphate was replaced by anhydrous calcium sulphate and stirred for one hour before being filtered. The infrared spectrum of the filtrate showed a very strong aldehyde peak at 1729 cm^{-1} and no enamine peak at 1670 cm^{-1}. The solvent was distilled off slowly over two hours and the excess of aldehyde collected at 55-61°. The product, N,N-dimethyl-2-methyl-prop-1-enylamine distilled at 85-87°, (9g.). This product showed the enamine peak at 1670 cm^{-1} in the infrared and was shown to contain a little aldehyde (5%) by gas chromatography using 6ft. silicone oil/celite column at 20° with a flow rate of 2 litres N_2/hour. The retention time of isobutyraldehyde was 3.5 min, the enamine 12.4 minutes, and N,N-dimethylisobutylamine 9.5 minutes.

Addition of dinitrophenylhydrazine solution to a solution of the enamine in methanol gave crystals of the derivative of isobutyraldehyde m.p. 183-5°.

N,N-Dimethylisobutylamine and di-t-butyl peroxide.

(i) N,N,- Dimethylisobutylamine (11.50g.) and di-t-butyl peroxide (3.32g.), i.e., 5 moles:1 mole), were heated in a sealed tube under nitrogen at 126° for 90 hours. Gas chromatography of the reaction mixture using 6 ft. silicone oil/celite column at 20° showed that t-butanol and no acetone were formed. There was also no N,N-dimethyl-2-methyl-prop-1-enylamine present in the chromatograph. The reaction mixture (12.33g.) was then distilled at atmospheric pressure (bath 140°) to leave a residue (3.43g. , 88% if assumed to be dehydrogenodimer). The distillate did not show an enamine band in its infrared spectrum. The higher-boiling residue showed a weak band at 1675 cm^{-1}. However, on hydrogenation with Adam's Platinum Oxide Catalyst (0.13g.) in methanol for 21 hours at 20° at atmospheric pressure the residue (1.08g.) had only taken up a small amount (170 c.c.) of hydrogen and this was probably the amount taken up by the catalyst. Gas chromatography on the silicone oil column at 121° indicated a single high-boiling product. With 4 ft. silicone oil/celite column at 100° (flow 27ml/min) using the Pye-Argon Gas Chromatograph the presence of a small amount of a second high-boiling compound which had a retention time close to that of the main peak (24 minutes) was indicated. This second compound thus appears to be a carbonyl compound rather than an enamine.

(ii) N,N-Dimethylisobutylamine (2.64g.) and di-t-butyl peroxide (0.79g.) were heated in a sealed tube under nitrogen for 49 hours at 122°. Low-boiling products (2.5g.) were removed by distillation at atmospheric pressure (bath temperature 130°). The higher-boiling products were then distilled at reduced pressure (water pump). The product N,N-dimethyl-N,N'-diisobutylethylenediamine (0.26g., 24%), b.p. 80°/15 mm., n^{19}_D 1.4370, was collected in four fractions with the bath temperature 120-200°. All fractions had identical refractive indices and infrared spectra thus indicating a single compound, and gas chromatography of each fraction showed a single peak, retention time 30 mins. using 6ft. silicone oil/celite column at 113°, flow 1.9 litres N_2/ hour. Spectra of the product in the near infrared were done using the Perkin-Elmer Model 21 spectrophotometer with a lithium fluoride prism. The spectra were compared with those of N,N-dimethylisobutylamine, N,N-dimethylisopropylamine, and the product of the latter reacted with di-t-butyl peroxide. From these it was concluded that a band corresponding to CH_2 had appeared in the "dimeric" product at 2869 cm^{-1} and that the region 2844-2750 cm^{-1} had altered in the "dimeric" structures and was the same for both the isobutyl and the isopropyl cases. It was then probably associated with the substituted ethylenediamine structure and not with the structure with attack initially on the N-methylene group.

N,N-Dimethylisopropylamine.

Isopropylamine (59g.), 90% formic acid (260g.), and 40% formaldehyde (165g.) (i.e., 1:5:2.2 moles respectively), were mixed and refluxed for 10 hours. The mixture was worked up as before in the methylation of N,N-dimethylisobutylamine, to give

N,N-dimethylisopropylamine b.p. 66°, $n_D^{19.5}$ 1.3921, picrate m.p. 245°, (lit.[11] b.p. 67-67.5°).

N,N-Dimethylisopropylamine and di-t-butyl peroxide.

N,N-Dimethylisopropylamine (4.3g.) and di-t-butyl peroxide (1.46g.), (i.e. 5 moles: 1 mole) were heated in a sealed tube under nitrogen at 122° for 72 hours. About half of the contents of the tube were above the oil level of the heating bath. The reaction mixture was distilled at a bath temperature of 100° to give a distillate (4.29g.), b.p. 70°. The residue was distilled at reduced pressure (water pump) to give a high-boiling product, N,N'-dimethyl-N,N'-diisopropylethylenediamine (0.186g., 11%), b.p. 60°/15 mm., $n_D^{19.5}$ 1.4392. Di-t-butyl peroxide would have been lost at the pump. Gas chromatography of the reaction mixture using 6 ft. silicone oil/celite column at 18°, flow rate 2 litres N_2/hour showed that much di-t-butyl peroxide (not estimated quantitatively) still remained and that t-butanol had been formed. Gas chromatography at 112°, flow rate 1.9 litres N_2/hour showed that the high-boiling product consisted of a single compound and had retention time 19.5 minutes. The infrared spectrum of the product showed a weak band at 1675 cm^{-1} similar to that of the product of the N,N-dimethylisobutylamine oxidation. Spectra in the near infrared region had a band at 2869 cm^{-1} corresponding to CH_2 and not present in the parent amine. Comparison with the product of N,N-dimethylisobutylamine oxidation suggested the substituted ethylenediamine structure. Further evidence that this is the structure is supplied by the fact that another possible dehydrogenodimer, 2,3-bis(dimethylamino)-2,3-dimethylbutane has a lower boiling point, 149°.[12]

Competitive experiments.

Competitive experiments have been done on N,N-dimethyl-t-butylamine, t-butylmethylether, and dimethylaniline using di-t-butyl peroxide as the oxidising agent. The results are compared with parallel experiments, by A. Reid of this department, on dimethylaniline, anisole and t-butylmethylether. The experiments were done in sealed tubes with the liquid-containing portion immersed in an oil bath at 125-129° for 168 hours. The substrates were estimated using gas chromatography at the experimental conditions given below. The yields are based on the amount of substrate which has been used compared with the amount which could have been used if all of the peroxide had attacked it specifically in the stoiciometric ratio of one mole of peroxide to two moles of substrate. The term "dimer" in the tables refers to this latter amount.

In the experiments with amines acetone was formed only in trace amount. The experiments were heated for a long time in order that all of the peroxide would have been decomposed. This had happened in all cases except in that of $Bu^{\gamma}NMe_2$ and $Bu^{\gamma}OMe$ in table II where it was shown that (0.01g., 1.4%) still remained.

Gas Chromatographic Analysis:

TABLE I			TABLE II	
Substrate	Column	Internal Standard	Column	Internal Standard
$Bu^{Y}OMe$	6ft. Silicone oil/celite 19°. 6ft. T.X.P./ celite, 19°.	Dioxane Cyclohexane	6ft. T.X.P.*/ celite, 19°.	Cyclohexane
$Bu^{Y}NMe_2$	6ft. Silicone oil/celite 19°.	Toluene	6ft. Silicone oil/celite 19°.	Cyclohexane
$PhNMe_2$	6ft. Silicone oil/celite 122°.	Dibutyl-formamide	6ft. Silicone oil/celite 126°.	Diethyl-aniline
$(Me_3CO)_2$	6ft. Silicone oil/celite 30°.	Amyl bromide	6ft. Silicone oil/celite 30°.	Amyl bromide

* T.X.P.= trixylylphosphate.

The competitive experiments in Table I have been done with mole ratios of 2.5:2.5:1 where the peroxide is in the least concentration. An exception is the anisole:dimethylaniline:peroxide experiment where the ratio is 25:2.5:1. In Table II all the experiments were done with mole ratios of 5:5.1 where the peroxide is again in the least concentration.

TABLE I

	$Bu^{Y}NMe_2$	$Bu^{Y}OMe$	$Bu^{Y}NMe_2$	$PhNMe_2$
Start	2.525g.	2.20g.	1.26g.	1.51g.
Finish	1.225g.	1.96g.	0.885g.	0.95g.
Used	1.30g.	0.24g.	0.38g.	0.56g.
% used (based on weights)	51.6%	10.9%	29.9%	36.9%
Peroxide used	1.46g.		0.73g.	
"Dimer"	2.02g.	1.76g.	1.01g.	1.21g.
% used (based on peroxide)	64.4%	13.7%	37.4%	46%

TABLE I (contd.)

Reid's	PhOMe	PhNMe	Bu^{Y}OMe	PhOMe
Start	6.75g.9	0.76g.	1.75g.	2.13g.
Finish	6.53g.	0.39g.	1.26g.	1.13g.
Used	0.22g.	0.37g.	0.49g.	1.00g.
% used (based on weights)	3.3%	49%	25.7%	47%
Peroxide used	0.365g.		1.15g.	
"Dimer"	0.54g.	0.605g.	1.37g.	1.70g.
% used (based on peroxide)	40.5%	61.6%	35.7%	58.5%

TABLE II

	Bu^{Y}NMe$_2$	Bu^{Y}OMe	Bu^{Y}NMe$_2$	PhNMe$_2$
Start	2.52g.	2.20g.	2.525g.	3.02g.
Finish	1.90g.	2.24g.	2.36g.	2.53g.
Used	0.62g.	-	0.165g.	0.49g.
% used (based on weights)	24.7%	-	6.5%	16.3%
Peroxide used	0.72g.		0.73g.	
"Dimer"	0.99g.	0.87g.	1.01g.	1.21g.
% used (based on peroxide)	62.7%	-	16.3%	40.8%

Reid's	PhOMe	PhNMe$_2$	Bu^{Y}OMe	PhOMe
Start	2.66g.	2.95g.	2.20g.	2.67g.
Finish	2.67g.	2.00g.	1.33g.	2.32g.
Used	-	0.95g.	0.87g.	0.35g.
% used (based on weights)	-	32%	39.7%	13%
Peroxide used	0.71g.		0.71g.	
"Dimer"	1.02g.	1.16g.	0.85g.	1.02g.
% used (based on peroxide)	-	82%	100%	34%

Dimethyl-p-toluidine, di-t-butyl peroxide in acetone.

Dimethyl-p-toluidine (6.76g.), di-t-butyl peroxide (1.47g.), and acetone (22.3g.), (i.e. in mole ratios 5:1:40 respectively), were irradiated for 65 hours. Gas chromatography using 6ft. silicone oil/celite column at 55° with m-xylene as internal standard showed that 0.67g. of the peroxide had decomposed. Gas chromatography at 110° showed that the peak corresponding to dimethyl-p-toluidine was altered from that of the pure amine in that the peak did not cut off sharply. This behaviour was repeated on adding methyl-p-toluidine to the pure amine. Acetone and t-butanol were removed from the reaction mixture (28.5g.) by distillation at atmospheric pressure, and the excess of amine (3.3g.) collected at 106°/15 mm. Acetic anhydride (5 mls.) and acetic acid (5mls.) were added to this distillate and the mixture warmed on the steam bath for 1 hour. Water was then added, the solution made acidic with dilute hydrochloric acid and extracted with dichloromethane. The organic layer was dried with magnesium sulphate and the solvent evaporated. The residue was the acetate of methyl-p-toluidine (0.15g.) m.p. and mixed m.p. 83°. This yield corresponds to 0.11g. of dimethyl-p-toluidine having been demethylated.

The residue (2.56g.) from the distillation was chromatographed on activated alumina (100g.). Dimethyl-p-toluidine (0.4g.) eluted with petrol, and elution with benzene/petrol (1:20) gave N,N'-dimethyl-N,N'-di-p-tolylethylenediamine, (0.46g., 40%), m.p. and mixed m.p. 80°. The infrared spectrum was identical with that of the authentic and there was no trace of any of the characteristic bands of 5,6,11,12-tetrahydro-2,5,8,11-tetramethylphenhomazine.

Further elution with benzene/petrol and benzene gave a brown liquid (1.27g.).

SYNTHESIS OF CIS-AND TRANS- 1,2,5-TRIMETHYLPYRROLIDINE.

2,5-Dimethylpyrrole.

2,5-Hexanedione (190g, 1.7 mole) and ammonium carbonate (400g., 3.5 mole), were placed in a 2-litre flask and the mixture heated on an oil bath at 100° for 2 hours. Sublimed carbonate was not allowed to block the air condenser. The air condenser was then replaced by a water-cooled condenser and the mixture refluxed gently for one hour at a bath temperature of 115°. The mixture was cooled and the upper, yellow layer of the pyrrole separated. The lower layer was extracted with chloroform (50 ml.) which was added to the crude pyrrole and the whole was dried over calcium chloride in an atmosphere of nitrogen in a tightly stoppered flask.

The chloroform was then distilled under reduced pressure and the dimethylpyrrole (137g., 87%) collected at 72-73/25 mm., n_D^{20} 1.4997, (lit.[13] n_D^{22} 1.550). Nitrogen was admitted to the distillation apparatus after pressure release and the product was stored under nitrogen in the dark.

Reduction of 2,5-Dimethylpyrrole.

The reduction was done by the method of Andrews and McElvain.[14]

Hydrochloric acid (1500 ml. of 20%) was placed in a 5-litre flask and cooled to 0°. Zinc dust (600g.) was then added with stirring and 2,5-dimethylpyrrole added dropwise with the temperature of reaction kept between 0-10°. When all of the pyrrole had been added concentrated hydrochloric acid (900 ml.) was added and the mixture stirred for 4 hours at room temperature. The liquid was then filtered using a Buchner funnel to remove zinc, and was made alkaline by the cautious addition of sodium hydroxide flakes. The mixture was steam distilled until about one litre of distillate was collected and there was no smell of amine in the distillate. Anhydrous potassium carbonate was added to the distillate until it was saturated but did not have solid carbonate present. The upper pyrroline layer was separated and the lower layer extracted with ether. The organic layers were combined, shaken with solid potassium hydroxide, filtered and dried with magnesium sulphate and then with calcium sulphate. Distillation gave the product (72.7g.) b.p. 103-110°.

The 2,5-dimethyl-Δ'-pyrroline and 2,5-dimethyl-Δ^3-pyrroline formed during the reduction of 2,5-dimethylpyrrole may be separated by the differences in solubility of their picrates. It was found that the calculated amount of picric acid for formation of the picrates must be used as an excess of picric acid subsequently interfered with the separation.

The pyrroline distillate (32g.) was treated with a solution of picric acid (81g.) in ether. A yellow precipitate m.p.122° immediately formed and this was recrystallised twice from n-butanol to give 2,5-dimethyl-Δ'-pyrroline picrate (37g.), m.p. 135-136°. Evaporation of the butanol mother liquor and addition of n-butyl ether afforded a few grams of the Δ' product. Evaporation of the ethereal filtrate afforded an oil more dense than ether. On standing this oil solidified to give a product (37g.) which on crystallisation from ether corresponded to 2,5-Δ^3-pyrroline picrate m.p. 105-107°,

The pyrrolines were regenerated from their picrates. 2,5-Dimethyl-Δ'-pyrroline picrate (54g.) was crushed to a powder and suspended in water (650 ml.) Concentrated hydrochloric acid (51 ml.) was added and the mixture stirred for several hours. The precipitated picric acid was filtered off under pressure and the filtrate extracted with ether until the ethereal layer was not yellow thus showing that all the picric acid had been extracted. The aqueous acidic solution was made basic with potassium carbonate and the product was extracted with ether and dried with magnesium sulphate. Distillation gave 2,5-dimethyl-Δ'-pyrroline b.p. 110-112°, $n_D^{20.5}$ 1.4362. The infrared spectrum of the product was consistent with the structure, the main feature of the spectrum being the C=N band at 1645 cm^{-1}.

2,5-Dimethyl-Δ^3-pyrroline was obtained by a similar regeneration from the picrate as for the Δ'-compound. The product had b.p. 103-105° $n_D^{20.5}$ 1.4427, and the infrared spectrum was consistent with the structure. There was no band at 1645 $cm.^{-1}$

The retention times on 6ft. silicone oil/celite column at 44°, flow 1.9 litres N_2/hour were for the Δ'-pyrroline, 16 minutes, and for the Δ^3-pyrroline, 11 minutes. Gas chromatography showed that both products were essentially pure.

Reduction of 2,5-Dimethylpyrrolines.

2,5-Dimethyl-Δ^3-pyrroline (4.8g) were dissolved in glacial acetic acid (50 ml) and Adam's Platinum Oxide Catalyst (0.23g.) added. The mixture was then shaken in an atmosphere of hydrogen in a medium-pressure hydrogenator at pressures between 3.7 and 2.5 atmospheres at room temperature. Uptake of hydrogen was rapid, the hydrogenation being virtually complete in two hours. The mixture was, however, shaken for 24 hours. The volume of hydrogen absorbed was approximately that required theoretically (1 litre).

The catalyst was filtered off and the filtrate was made alkaline with potassium hydroxide solution with cooling. The amine was extracted with ether and the ethereal solution dried with magnesium sulphate. The ether was distilled through a Fenske column to leave a residue which on gas chromatography using 6ft. silicone oil/celite column at 44° had the same retention time (11 minutes) as had the starting material. However, the picrate, made in ether, had m.p. 125-127° (Lit.[15] 128-130°), and so hydrogenation to trans-2,5-dimethylpyrrolidine had taken place. As only a small ether peak was present in the gas chromatograph it was decided to use this material without further purification.

Cis-2,5-Dimethylpyrrolidine was made by reduction of 2,5-dimethyl-Δ'-pyrroline (6.9g) using 0.47g. of catalyst in acetic acid in a manner similar to that of the reduction of the Δ^3-compound. Approximately the theoretical amount of hydrogen (1.5 litres) was again absorbed. Gas chromatography using 6ft. silicone oil/celite column at 43° showed that the product had a shorter retention time (11.5 minutes) than had the Δ'-compound. A small amount ($<$ 5%) of the Δ'-compound still remained but the product was considered pure enough for the next stage. Cis- and trans-2,5-Dimethylpyrrolidine have b.p. 106 and 104°[15] respectively and so would be expected to have almost identical retention times.

1,2,5-Trimethylpyrrolidines.

trans-2,5-Dimethylpyrrolidine (20g.) formic acid (10.2g. of 90%), and aqueous formaldehyde (20g. of 30%), were mixed and refluxed for 12 hours. Concentrated hydrochloric acid (12 ml.) and water (12 ml.) were added and the mixture boiled for 20 minutes. The solution was made alkaline with sodium hydroxide and extracted with ether. Gas chromatography of the ethereal solution showed that two amine peaks were present in the mixture. The ether was distilled off from the mixture and the methylation stage repeated using the same quantities of formic acid and formaldehyde and refluxing for 4 hours. On working up as before the gas chromatograph again showed two peaks. The amine product was then refluxed with benzoic anhydride (10.g) and distilled. The gas chromatograph again showed two peaks of the same relative intensity as before. The peak present in smaller amount (20%) corresponded to the product obtained from the methylation of the cis-2,5-dimethyl-pyrrolidine (retention time 12 minutes on 6ft. silicone oil/celite column at 43°) whilst the major peak had retention time of 18 minutes. Repeated distillation using a Fenske column gave trans-1,2,5-trimethylpyrrolidine, b.p. 116°, n_D^{18} 1.4325. [Found: C,72.6; H,12.7%. $C_7H_{15}N$ required C,74.3; H,13.4%]. The picrate was made using ethereal picric acid and was recrystallised from ethanol, m.p. 125°. [Found: C,45.8; H, 5.5; N, 16.3% $C_{13}H_{18}N_4O_7$ requires C, 45.6; H, 5.3; N, 16.4%] . The infrared spectrum as a liquid film showed strong bands at 2945, 2780, 1450, 1370, 1320, 1215, 1200 cm^{-1}, and weaker bands at 1340, 1175, 1120, 1080 and 1040 cm^{-1}.

Cis-2,5-Dimethylpyrrolidine (8g.), formic acid (4.2g. of 90%) and aqueous formaldehyde (8g. of 30%) were mixed and refluxed for 17 hours. The solution was worked up as for the *trans*-compound. Distillation gave *cis*-1,2,5-trimethylpyrrolidine b.p. 108°, $n_D^{18.5}$ 1.4260. [Found: C,73.0; H, 13.4%. $C_7H_{15}N$ required C, 74.3; H, 13.4%]. The picrate was made using ethereal picric acid and was recrystallized from ethanol, m.p. 125°. [Found: C,45.6; H, 5.4; N, 16.4%. $C_{13}H_{18}N_4O_7$ requires C,45.6; H, 5.3; N, 16.4%]. The infrared spectrum as a liquid film showed strong bands at 2945, 2780, 1450, 1370, 1320, 1205 cm^{-1}, and weaker bands at 1340, 1305, 1115, 1055 cm^{-1}. The product was pure ($>$ 95%) as shown by gas chromatography on 6ft. silicone oil/celite column at 43° and 72°. The retention time at 43° was 12 minutes.

1,2,5-Trimethylpyrrolidine and di-t-butyl peroxide.

cis-1,2,5-Trimethylpyrrolidine (0.232g.) and di-t-butyl peroxide (0.063g.), (i.e., 4.8 moles: 1 mole), were heated in a sealed tube under nitrogen at 126° for 36 hours. The reaction mixture was analysed by gas chromatography on the Griffon and George V.P.C. apparatus using 6ft. silicone oil/celite column at 58°, flow 1.9 litres N_2/hour. t-Butanol was formed and the amine was estimated using o-xylene as internal standard to show that 0.060g. (62%) had been used in the reaction.

The experiment was repeated using the *trans*-isomer and also a mixture of *cis* and *trans*. The competitive experiment was also done by irradiation of the mixture in a quartz sealed tube using the Hanovia ultra-violet lamp at a distance of 9 cms. for 5 hours. The results of the experiments are shown in the table.* Higher-boiling products of the oxidation were not looked for because of the small scale of the experiments but a preliminary gas chromatographic survey using 6ft. silicone oil/celite at 90° showed the presence of a product with a retention time of 15 minutes.

A criticism of the experiments is that the *trans*-isomer "tails" under the gas chromatographic conditions used. Attempts to use other columns such as polyethylethylene glycol succinate, apiezon, and silicone oil on the Pye Argon apparatus did not allow a differentiation of the *cis* and *trans* forms. The amounts of materials used in the experiments are too small for very accurate results as the changes in the absolute amounts are very small and accuracy is probably to 3%. The results do, however, show that there is no interchange of *cis* - *trans* forms during reaction as the experiments with the single amines did not show production of the other. In the competitive experiments more of the *trans*-form reacted.

---

* Table III.

TABLE III

1,2,5-TRIMETHYLPYROLIDINE AND DI-T-BUTYL PEROXIDE

Decomposition	Thermal	Thermal	Thermal	U.V.
Peroxide	0.0626g.	0.0315g.	0.0475g.	0.1014g.
Amine at start	0.2322g. cis	0.1493g. trans	0.0866g. cis 0.0912 trans	0.1600g. cis. 0.1599g. trans
Amine used	0.0603g.	0.0176g.	0.0206g. cis 0.0250g. trans	0.0332g. cis 0.0441g. trans
Amine calc'd to have been used	0.0969g.	0.0489g.	0.0735g.	0.157g.
% amine used	62%	36%	28% cis 34% trans	21% cis 28% trans
Mole ratio Amine:peroxide	4.8:1	6 : 1	2.35 cis 2.48 trans :1	2.0 cis 2.0 trans :1

Dimethylaniline and di-t-butyl peroxide in acetic acid.

(i) Dimethylaniline (6.05g) and di-t-butyl peroxide (1.46 g.), (i.e. 5 moles: 1 mole), in a mixture of acetic acid (30 ml.) and water (30 ml.) were refluxed for 17 hours. The solution became violet after a few minutes. The acetic acid and water was distilled at atmospheric pressure. Water was then added and the mixture made alkaline with sodium hydroxide and extracted with ether. The ethereal solution was acidified with dilute hydrochloric acid and the organic layer dried with magnesium sulphate and the solvent evaporated. There was no residue of amide. The acidic solution was made alkaline with sodium hydroxide and extracted with dichloromethane. The organic layer was dried with magnesium sulphate and distilled to give dimethylaniline (4.6g.). This distillate on gas chromatography on 6 ft. silicone oil/celite column at 139° showed no peak corresponding to monomethylaniline. The residue (0.30g.) was dissolved in benzene/petrol and chromatographed on activated alumina (100g.) Elution with benzene/petrol (1:3) gave dimethylaniline (0.02g.), n_D^{20} 1.5509. Further elution with benzene/petrol (3:1) and with benzene gave 4,4'-bis(dimethylamino)diphenylmethane, (0.177g, 5%), m.p. and mixed m.p. 88°. The infrared spectrum was identical with that of the authentic material. Elution with benzene gave a solid m.p. 176° (0.028g., 1%). With N,N,N',N'-tetramethylbenzidine the mixed m.p. was 155°, and mixed crystallization of 4,4'-bis(dimethylamino)diphenylmethane and tetramethylbenzidine gave a product m.p. 84°. The infrared spectrum of this mixture was the same as a superposition of the infrared spectra of the separate components and was different from that of the solid m.p. 176°. On recrystallization from ether/benzene the m.p. was 179°, mixed m.p. with 4,4'4"-tris(dimethylamino)triphenylmethane (leuco crystal violet) was 179°. The infrared spectra were identical. [Found: C,80.3; H, 8.2; N, 11.2%. Calc.for $C_{25}H_{31}N_3$: C,80.4; H, 8.4; N, 11.25%]. The authentic leuco crystal violet was made by the sodium borohydride reduction of crystal violet in methanol. Elution with ether gave a small amount of oil (0.02g.) which in acetone gave a violet solution. Total amount eluted from the column was 0.28g.

(ii) The experiment was repeated using dimethylaniline (36.30g.), di-t-butyl peroxide (8.76g), and aqueous acetic acid (360 ml. of 50%) refluxed for 50 hours. On working up as before the products obtained were 4,4'-bis(dimethylamino)diphenylmethane (1.62g., 11%) and leuco crystal violet (0.22g., 1%). Other products were a yellow oil (0.14g.) eluted with ether/benzene (1:1) and a purple oil (0.13g.) eluted with ether/methanol (20:1). Other coloured oxidation products were removed from the column on elution with more polar ether/methanol solutions.

Yields are calculated according to the equations.

$$3PhNMe_2 + (Me_3CO)_2 \rightarrow (C_6H_4NMe_2)_2\ CH_2 + PhNHMe + Me_3COH$$

$$4PhNMe_2 + 2(Me_3CO)_2 \rightarrow (C_6H_4NMe_2)_3\ CH + PhNHMe + 4Me_3COH$$

$$PhNHMe + MeCOOH \longrightarrow PhNMeCOMe + H_2O$$

(iii) Dimethylaniline (6.06g.) and di-t-butyl peroxide (1.46g.) (i.e., 5 moles : 1 mole) in glacial acetic acid (58 ml.) and acetic anhydride (2 ml.) were heated for 17 hours at reflux. The acetic acid was removed by distillation and water added and the solution made alkaline with sodium hydroxide. The solution was extracted with ether and the ethereal solution washed with dilute hydrochloric acid. The ethereal layer after drying with magnesium sulphate and distillation gave N-methylacetanilide (0.355g.) m.p. and mixed m.p. 100°. The infrared spectra were identical.

The aqueous acidic extract was basified with sodium hydroxide and extracted with dichloromethane. Distillation gave dimethylaniline (1.86g.) and a residue (2.86g.) which was dissolved in benzene/petrol and was chromatographed on activated alumina (150g.). Elution with benzene/petrol (1:9) gave dimethylaniline (0.16g.), n_D^{20} 1.5578, and with benzene/petrol (1:4) gave 4,4'-bis(dimethylamino) diphenylmethane (1.37g., 54%), m.p. and mixed m.p. 87°; infrared spectra identical. Benzene/petrol (3:1) gave leuco crystal violet (0.22g., 12%), m.p. and mixed m.p. 176°. The column had developed a series of purple, yellow and white bands, and so was cut into sections and each section eluted separately. In order of appearance as they would have come from a complete column were a purple non-crystalline solid (0.04g.) eluted with ether; N-methylacetanilide (0.27g.) m.p. and mixed m.p. 100°, infrared spectra identical eluted with benzene/ether (1:1). The total yield of N-methylacetanilide was then 0.62g. (84%). From further up the column was eluted with benzene/ether (3:1 another solid (0.27g., 20%), m.p. 117-119°. It was recrystallized from benzene/petrol to give m.p. 124°. [Found: C,76.0; H,7.7; N, 10.0%. 4-Dimethylamino-(4'-methyl-4'acetyl)aminodiphenylmethane, $C_{18}H_{22}ON_2$ requires C, 76.6; H, 7.85; N, 9.9%]. Further elution with the coloured top section gave an oil (0.15g.) which in acetone or methanol gave a violet solution.

The amide m.p. 117-119° showed a strong amide band in its infrared spectrum at 1645 cm^{-1}. Other strong bands were at 1520, 1370, 1350, 828 and 797 cm^{-1}. The amide was refluxed with 20% sulphuric acid for several hours but did not hydrolyse and refluxing with concentrated sulphuric acid produced charring and no identifiable products. Hydrolysis was achieved thus: the amide (0.07g.) was refluxed with 70% sulphuric acid (2 ml) for 40 minutes. The solution was basified with aqueous potassium hydroxide and extracted with dichloromethane. The organic solution was dried with magnesium sulphate and the dichloromethane distilled to leave a solid residue m.p. 50°. This was recrystallized from light petroleum (b.p. 40-60°) to give m.p. 52°. The infrared spectrum showed an NH band at 3340cm^{-1}. The mixed m.p. with 4-dimethylamino-4'-methylaminodiphenylmethane was 52° and the infrared spectra were identical.

4-Dimethylamino-4'-methylaminodiphenylmethane.

p-Dimethylaminobenzyl alcohol (1.5g.) and p-toluidine (0.75g.) with 1 drop of concentrated hydrochloric acid as catalyst were allowed to sit at 37° for 12 hours. The product was crystallized from methylated spirits to form pale yellow crystals of p-dimethylamino-p-tolylamine, p-$Me_2NC_6H_4CH_2NH$ C_6H_4Me-p, m.p.101°. (Lit.[16] m.p. 101°). The infrared spectrum had an NH band at 3420 cm^{-1}. A characteristic group of bands indicative of the aromatic substitution were at 825, 816 and 807 cm^{-1}.

p-Dimethylamino-p-tolylamine (0.09g.), methylaniline hydrochloride (0.06g.) and methylaniline (0.217g.), (i.e., in mole ratios 1:1:5 respectively), were heated for 2 hours on a steam bath. The mixture was made strongly alkaline by the addition of sodium hydroxide and was extracted with dichloromethane. The organic layer was dried with magnesium sulphate, the solvent was evaporated, and the residue chromatographed on activated alumina (10g.). Elution with benzene/petrol (1:1) and with benzene gave 4-dimethylamino-4'-methylaminodiphenylmethane (0.09g., 90%), m.p. 52°. (Lit [17] m.p. 57°). The infrared spectrum had a strong NH band at 3380 cm^{-1}, and a set of characteristic bands at 848, 827, 810 and 770 cm^{-1}, the band at 810 cm^{-1} being about twice as strong as the others in the set.

Dimethylaniline, 4,4'-bis(dimethylamino)diphenylmethane, and di-t-butyl peroxide in acetic acid.

Dimethylaniline (1.21g.), 4,4'-bis(dimethylamino)diphenylmethane (2.54g.) and di-t-butyl peroxide (0.73g.), (i.e., in mole ratios 2:2:1 respectively), were refluxed in glacial acetic acid (30 ml.) containing acetic anhydride (2 ml.). The acetic acid (25 ml.) was distilled and the residue made alkaline with sodium hydroxide and extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and then dried with magnesium sulphate and the solvent evaporated to leave a residue of N-methylacetanilide (0.08g., 11%), m.p. 100°. The acidic solution from the HCl washing was basified with sodium hydroxide and extracted with dichloromethane to give a red solution. The solution was distilled at reduced pressure (water pump) to leave a residue (3.44g.) which was dissolved in benzene/petrol and chromatographed on activated alumina (200g.). Elution with benzene/petrol (1:1) and benzene gave 4,4'-bis(dimethylamino)diphenylmethane (2.30g.,) m.p. and mixed m.p. 88°, and elution with benzene/ether (1:1) gave leuco crystal violet (0.27g. 15%), m.p. and mixed m.p. 176°. Further elution with ether gave 4-dimethylamino-(4'-methyl-4'-acetyl)aminodiphenylmethane (0.572g. 85%), m.p. 122°, identified by its infrared spectrum. The yield of this amide is based on the amount of N-methylacetanilide from which it could be assumed to have been formed compared with the amount of N-methylacetanilide expected according to the equations.

$$4PhNMe_2 + 2(Me_3CO)_2 \longrightarrow (C_6H_4NMe_2)_3\,CH + PhNHMe + 4Me_3COH$$

$$PhNHMe + MeCOOH \longrightarrow PhNMeCOMe + H_2O$$

Thus 0.572g. of the amide m.p. 122° corresponds to 0.318g. of N-methylacetanilide which is 85% of the theoretical yield.

p-Dimethylaminobenzylmethylaniline.

This amine, prepared by the reaction of methylaniline and p-dimethylaminobenzyl benzoate as described previously, is a stable crystalline solid m.p. 69°. It can be recrystallized from solvents such as benzene, light petroleum, ether and nitromethane without decomposition. However, it is decomposed in acid media and on standing in a mixture of acetic acid/acetic anhydride, N-methylacetanilide is formed in high yield. It is unchanged on towering through activated alumina.

p-Dimethylaminobenzylmethylaniline, 3,5,3',5'-tetrachloro-4,4'-diphenoquinol ($t.c.d.h_2$), and methylaniline.

(i) p-Dimethylaminobenzylmethylaniline (0.037g.), $t.c.d.h_2$ (0.002g.), and methylaniline (0.116g.), (i.e. in mole ratios 1.56:0.059:10.87 respectively), were left at 25° for 4 days. The mixture was then chromatographed on activated alumina (10g.). Elution with benzene/petrol (1:10) gave p-dimethylaminobenzylmethylaniline (0.02g.) m.p. and mixed m.p. 68°. Elution with benzene and ether gave no other recognizable product. 0.1g. of material was eluted from the column.

(ii) p-Dimethylaminobenzylmethylaniline (0.071g.), $t.c.d.h_2$(0.014g.), and methylaniline (0.409g.), (i.e. in mole ratios 2.9: 0.4: 38.3 respectively), were heated on a steam bath for 2 hours and left for 2 days at room temperature. The reaction mixture, red-brown in color, was chromatographed on activated alumina (15g.). Methylaniline (0.29g.) eluted with petrol and with benzene/petrol (1:10) p-dimethylaminobenzylmethylaniline (0.019g.) m.p. 68° was obtained. Benzene/petrol (1:5) eluted small amounts (0.017g.) of a liquid continuously. With benzene/petrol (1:1) and benzene a yellow oil (0.073g.) was obtained. This eluate showed no band corresponding to NH in its infrared spectrum but had a strong band at 1750 cm^{-1}. The usually strong aromatic bands at 1600 and 1510 cm^{-1} are very weak. Stronger bands are present at 1460, 1360, 1280, 1220, 1180, 1140 and 1060 cm^{-1}. Bands below 900 cm^{-1} are very weak.

p-Dimethylaminobenzylmethylaniline, t.c.d.h., and dimethylaniline.

(i) p-Dimethylaminobenzylmethylaniline (0.218g.), $t.c.d.h_2$ (0.009g.), and dimethylaniline (1.12g.), (i.e. in mole ratios 1.8: 0.06: 18.5 respectively), were heated at 77° for 4 hours. The mixture was chromatographed on activated alumina (30g.). Elution with petrol afforded dimethylaniline (0.99g.), n_D^{17} 1.5562, (authentic dimethylaniline had n_D^{17} 1.5592). Benzene/petrol (1:9) afforded p-dimethylaminobenzylmethylaniline (0.208g.) m.p. 69°, infrared spectrum identical with the authentic material. Further elution with benzene and ether afforded only a small amount (0.02g.) of a liquid.

(ii) p-Dimethylaminobenzylmethylaniline (0.025g.), $t.c.d.h_2$ (0.034g.), and dimethylaniline (0.696g.), (i.e. in mole ratios 1.0: 1.0: 57.4), were allowed to sit for 48 hours at room temperature (20°). The mixture was then triturated with petrol to give $t.c.d.h_2$ (0.027g.), m.p. 230°. The solution was then chromatographed on activated alumina (10g.). Elution with petrol gave dimethylaniline (0.63g.), $n_D^{18.5}$ 1.5562, and with benzene/petrol (1:20) gave p-dimethylaminobenzylmethylaniline (0.023g.), m.p. 68.5°, indentical in infrared spectrum with the authentic material. Further elution with benzene gave a yellow oil (8 mgs.).

(iii) p-Dimethylaminobenzylmethylaniline (0.104g.), $t.c.d.h_2$(0.006g.), and dimethylaniline (1.049g.), (i.e. in mole ratios 1.1: 0.05: 21.7) were dissolved in glacial acetic acid (10ml.) containing acetic anhyrdide (0.5ml.) and refluxed for 5 hours. The mixture, initially light green in color, turned blue and finally violet as the temperature was raised. The acetic acid was distilled slowly at atmospheric pressure and the violet residue was made alkaline with sodium hydroxide and extracted with ether. The ethereal solution was dried with magnesium sulphate and the ether evaporated to leave a blue residue which was dissolved in benzene/petrol and chromatographed on activated alumina (20g.). Elution with petrol gave dimethylaniline (0.50g.), $n_D^{19.5}$ 1.5571, and with benzene/petrol (1:9) gave 4,4'-bis(dimethylamino)-diphenylmethane (0.109g., 100%) m.p. and mixed m.p. 88°. The infrared spectrum was identical with that of the authentic compound. Elution with benzene/petrol (3:1) gave a compound (0.015g.) m.p. 100-140°, whose infrared spectrum was the same as that of leuco crystal violet except that it contained an extra weak band at 1720cm^{-1}. On recrystallization this band disappeared and the m.p. was that of leuco crystal violet 179°. Elution with benzene and benzene/ether (9:1) gave N-methylacetanilide (0.061g., 94%), m.p. and mixed m.p. 100°, infrared spectra identical. Further elution with solvents of increasing polarity gave a small amount of a blue liquid (4 mg.).

(iv) p-Dimethylaminobenzylmethylaniline (0.082g.) and dimethylaniline (0.862g.) (i.e. in mole ratio 1:21), were dissolved in glacial acetic acid (4 ml.) containing acetic anhydride (0.3 ml.) and refluxed for 4 hours. The color changes noted previously were again observed. The acetic acid was then distilled and the residue made alkaline with sodium hydroxide and extracted with ether as before to give a residue which was chromatographed on activated alumina (20g.). Elution with petrol gave dimethylaniline (0.47g.) and with benzene/petrol (1:9) gave 4,4'-bis(dimethylamino)diphenylmethane (0.827g., 95%) m.p. and mixed m.p. 88°, infrared spectra identical. Elution with benzene gave N-methylacetanilide (0.039g., 76%), m.p. and mixed m.p. 100°, infrared spectra identical. This yield was slightly low as it was suspected that some N-methylacetanilide was present in the previous fraction. Coloured residues remained on the column.

When 4,4'-bis(dimethylamino)diphenylmethane was heated with glacial acetic acid, the color changed slowly from green via red to a red-purple. p-Dimethylaminobenzylmethylaniline when treated similarly underwent the same color changes but in the presence of dimethylaniline the system changed color very quickly. The first system was unaffected by the presence of dimethylaniline.

p-Dimethylaminobenzylmethylaniline and N-phenylpyrrolidine.

p-Dimethylaminobenzylmethylaniline (0.185g.) and N-phenylpyrrolidine (0.34g.), (i.e. in mole ratio 1:3), were dissolved in glacial acetic acid (14 ml.) containing acetic anhydride (1 ml.) and refluxed for 18 hours. The color changed from green, through blue, to red. The acetic acid was distilled and the residue was made alkaline with sodium hydroxide and was extracted with dichloromethane. After drying with magnesium sulphate the solvent was distilled and the residue dissolved in benzene and chromatographed on activated alumina (30g.). Elution with petrol gave a liquid (0.26g.), n_D^{20} 1.5790 (N-phenylpyrrolidine had n_D^{20} 1.5825). Elution with benzene petrol gave 4-(dimethylamino)-4'-(N-pyrrolidino)diphenylmethane (0.126g., 58%), m.p. 75° (from light petroleum (b.p. 40-60°)). [Found: C,81.7; H,8.9; N,9.8%. $C_{19}H_{14}N_2$ requires C,81.4; H, 8.6; N, 10.0%]. Further evidence that this is the compound is supplied by the infrared spectrum. On comparison with the spectrum of 4,4'-bis(dimethylamino)diphenylmethane, many of the bands in both spectra correspond. Those which differ notably are at 1370, 1182, 972 and 770 cm^{-1}. These bands are present in the spectrum of 4,4'-di(N-pyrrolidino)diphenylmethane. Thus all the bands can be accounted for and fit the assigned structure. Further elution with benzene/petrol (1:1) gave a compound (0.047g.), m.p. 124°. [Found: C, 72.0; H, 9.5; N, 6.5%]. The infrared spectrum of this compound is quite different from that of the earlier compound. There is a strong band at 1660 cm^{-1} corresponding to an amide band. Infrared spectra of different fractions did not show any diminution of any band. Bands characteristic of N-methylacetanilide at 782 and 712 cm^{-1} were not present. There was only a single band in the region 850-680 cm^{-1} at 830 cm^{-1}, thus showing that any aromatic rings present are still para-disubstituted. Elution with benzene gave N-methylacetanilide (0.078g. 67% , m.p. and mixed m.p. 100°, infrared spectrum identical. Further elution with benzene/ether (3:1) gave an oil (0.03g.) and with ether gave a small amount (22 mg.) of a purple solid.

<u>Dimethylaniline and 3,5,3',5'-tetrachloro-4,4'-diphenoquinone in acetone.</u>

The quinone (abbrev. t.c.d.) was prepared thus: Sodium nitrite (30.8g.) in water (125 ml.) was gradually added to a stirred solution of benzidine (41.6g.) in water (5 litres) containing concentrated hydrochloric acid (166 ml.). The mixture was left at room temperature for 2 hours and then boiled for 1 hour and filtered hot. The filtrate on cooling gave 4,4'-dihydroxydiphenyl (28g.), m.p. 272°.

Chlorine was passed into a stirred suspension of the 4,4'-dihydroxyphenyl in glacial acetic acid (400 ml.). The solution was cooled in ice and filtered and chlorine passed into the filtrate until no more solid was deposited. The solid was recrystallized from acetic acid to give 3,5,3', 5'-tetrachloro-4,4'-diphenoquinol, (abbrev. t.c.d.h_2.),(20g.), m.p. 232°.

Concentrated nitric acid (10 ml.) was added to a solution of t.c.d.h_2 (10g.), in hot glacial acetic acid (400 ml.). Violet crystals were initally formed but on further addition of acid these disappeared. On cooling no crystals were deposited. Concentrated nitric acid (5 ml.) in glacial acetic acid (5 ml.) were added to another solution of t.c.d.h_2 (10g.) in hot glacial acetic acid (400 ml.). Addition of the nitric acid mixture was stopped when crystals formed in the solution. On cooling and filtration and washing with water t.c.d. (2g.), m.p. 360°[23] was collected.

Dimethylaniline (2.265g.), t.c.d. (1.98g.) in acetone (3.60g.), (i.e. in mole ratios 3:1:10 respectively), were shaken for 18 hours at room temperature. The quinone had been decolorized. The acetone was removed by rotary evaporation and the residue dissolved in benzene/petrol and chromatographed on activated alumina (100g.). Elution with benzene gave a liquid, mainly dimethylaniline, (0.64g) $n_D^{17.5}$ 1.5569. Elution with benzene/petrol (1:19) gave p-dimethylaminebenzylmethylaniline (0.3448g., 23%), m.p. and mixed m.p. 69°, infrared spectra identical. Further elution with benzene/petrol (1:1) gave 4,4'-bis(dimethylamino)diphenylmethane (0.296g., 19%). Benzene/ether (9:1) gave a yellow oil (0.11g.). Yields are based on the equations:

$$\text{t.c.d.} + 3PhNMe_2 \longrightarrow \text{t.c.d.}h_2 + (Me_2NC_6H_4)_2CH_2 + PhNHMe$$

and

$$\text{t.c.d.} + 2PhNMe_2 \longrightarrow \text{t.c.d.}h_2 + PhN(Me)CH_2C_6H_4NMe_2$$

Dimethylaniline and cumene hydroperoxide in acetic acid.

Dimethylaniline (6.052g.) and cumenehydroperoxide (1.529g.),(i.e. 5 moles: 1 mole) were dissolved in glacial acetic acid (60 ml.) containing acetic anhydride (2 ml.) and refluxed for 70 minutes. The solution went an intense violet. The solution was diluted to approximately 1 litre with water and acidified with hydrochloric acid. The solution was now green and was extracted with ether. The acidic solution was then made alkaline with sodium hydroxide flakes and the solution extracted with ether. The ethereal solution was dried with magnesium sulphate and distilled, the excess of dimethylaniline being removed at the water pump at 80°. The residue was dissolved in benzene/petrol and chromatographed on activated alumina (60g.). Elution with petrol gave dimethylaniline (0.90g.), $n_D^{17.5}$ 1.5569. Elution with benzene/petrol (1:1) gave 4,4'bis(dimethylamino)diphenylmethane (1.037g. 41%), m.p. and mixed m.p.88°, infrared spectra identical. Elution with benzene/petrol (3:1) gave leuco crystal violet (0.123g. 6.5%), m.p. and mixed m.p. 178°, infrared spectra identical. Elution with benzene gave N-methylacetanilide (0.146g., 19.6%) m.p. and mixed m.p. 100°, infrared spectra identical, and elution with benzene/ether (3:1) gave 4-dimethylamino-(4'methyl-4'-acetyl)aminodiphenylmethane (0.097g., 7%), m.p. and mixed m.p. 120°, infrared spectra identical. Further elution with ether gave a small amount of a blue dye (20 mg.). Yields are based on the equations.

$$\mathrm{ROOH} + 3\,\mathrm{PhNMe_2} \longrightarrow \underset{\mathrm{I}}{(\mathrm{Me_2NC_6H_4})_2\,\mathrm{CH_2}} + \underset{+\mathrm{ROH}}{\mathrm{PhNHMe}} + \mathrm{H_2O}$$

for calculation of I.

and

$$4\mathrm{PhNMe_2} + 2\mathrm{ROOH} \longrightarrow \underset{\mathrm{II}}{(\mathrm{C_6H_4NMe_2})_3\,\mathrm{CH}} + \underset{\mathrm{III}}{\mathrm{PhNHMe}} + 2\mathrm{H_2O} + 2\mathrm{ROH}$$

for calculation of II, and of III, as its acetyl derivative.
The yield of the other amide is again based on the equivalent amount of N-methylacetanilide.

Dimethylaniline, 4,4'-bis(dimethylamino)diphenylmethane, and di-t-butyl peroxide.

Dimethylaniline (0.305g.), 4,4'-bis(dimethylamino)diphenylmethane (0.635g.), and di-t-butyl peroxide (0.126g.), (i.e. in mole ratios 3:3:1 respectively), were heated in a sealed tube under nitrogen for 37 hours at 126°. It was noted that t-butanol had been formed and was crystallized around the top of the tube. On trituration of the reaction mixture with petrol, a solid (0.0105g.) m.p. > 300° which had been deposited during the reaction, was recovered by filtration. This compound was again obtained later in the chromatograph and was identified as 1,1,2,2-tetrakis(4-dimethylaminophenyl)ethane. The solution of the reaction mixture was chromatographed on activated alumina. Elution with petrol gave dimethylaniline (0.164g.) and with benzene/petrol (1:4) gave 4,4'-bis(dimethylamino)diphenylmethane, m.p. and mixed m.p. 88°. The infrared spectrum showed no trace of any N,N'-dimethyl-N,N'-diphenylethylenediamine. Elution with benzene/petrol (1:1) gave 4-dimethylamino-4'-methylaminodiphenylmethane (0.102g., 87%), m.p. and mixed m.p. 50°, infrared spectra identical. Elution with benzene gave 1,1,2,2-tetrakis(4-dimethylaminophenyl)ethane (0.0126g., i.e. total 0.023g., 19%) m.p. > 320°. The m.p. was not depressed < 320° on admixture with the authentic compound, and the infrared spectra of the chromatographic fraction and of the insoluble material from the reaction mixture were identical with that of the authentic material. Further elution with benzene and with benzene/ether gave a blue liquid (0.05g.) which gave a violet solution in chloroform or methanol. The yields are based on the amount of 4,4'-bis(dimethylamino)diphenylmethane not returned.

4,4'-bis(dimethylamino)diphenylmethane and di-t-butyl peroxide.

(i) 4,4'-Bis(dimethylamino)diphenylmethane (2.858g) and di-t-butyl peroxide (0.545g.), (i.e. 3 moles : 1 mole), were heated in a sealed tube under nitrogen for 37 hours at 126°. On adding benzene/petrol to the reaction mixture 1,1,2,2-tetrakis(4-dimethylaminophenyl)ethane (0.065g.) separated, m.p. > 320°. [Found: C,80.4; H,8.4; N,10.7% Calc. for $C_{34}H_{42}N_4$: C, 80.6; H, 8.4; N,11.1%]. The reaction mixture was chromatographed on activated alumina (120g.) Elution with benzene/petrol (1:9) gave 4,4'-bis(dimethylamino)diphenylmethane (2.124g.), m.p. and mixed m.p. 88°, infrared spectra identical. Elution with benzene/petrol (3:1) gave 4-dimethylamino-4'-methylaminodiphenylmethane (0.170g., 25%), m.p. and mixed m.p. 50°, and infrared spectra identical. Further elution with benzene gave N,N'-di-[4-(p-dimethylaminobenzyl)-phenyl]-N,N'-dimethylethylenediamine(0.12g.,16%), m.p. 106°. [Found: C, 80.4; H, 8.4; N, 10.6%. $C_{34}H_{42}N_4$ requires C, 80.6; H, 8.4; N, 11.1%]. The infrared spectrum is consistent with the assigned structure. The region 950-670 cm^{-1} differs from the other compounds found and has a strong band at 805 cm^{-1}, weaker bands of equal intensity at 950 and 820 cm^{-1}, and weak bands at 840, 757, and 749 cm^{-1}. Attempts to synthesise this compound using 4-dimethylamino-4'-methylaminodiphenylmethane and ethylenedibromide in mole ratio 1:2 at 60° for 3 hours have proved unsuccessful.

Continued elution with benzene gave 1,1,2,2,-tetrakis(4-dimethylaminophenyl)-ethane (0.0615g., i.e. total 0.126g., 17%), m.p. > 320°, infrared spectra identical. Benzene/ether (1:1) gave a yellow oil (0.013g.) and ether gave a brown oil (0.07g.).

(ii) The above experiment was repeated using 4,4'-bis(dimethylamino)diphenylmethane (2.86g.) and di-t-butyl peroxide (0.550g.), (i.e. 3 moles : 1 mole) in a sealed tube for 24 hours at 126°. The yields were 4,4'-bis(dimethylamino)diphenylmethane (2.311g.), 4-dimethylamino-4'-methylaminodiphenylmethane (0.097g., 19%), substituted ethylenediamine (0.13g., 24%), and substituted ethane (0.096g., 17.5%).

1,1,2,2-Tetrakis(4-dimethylaminophenyl)ethane.

4,4'-Bis(dimethylamino)benzophenone, i.e, Michler's ketone, (5g.) and tinfoil (9g.) were dissolved in concentrated hydrochloric acid (75 ml.) and allowed to sit for an hour[18]. The solution was made alkaline with sodium hydroxide to give a blue solution which was extracted with dichloromethane to give a red solution which fluoresced green. The solvent was evaporated and light petroleum (b.p. 40-60°) added to the residue to give a white solid m.p. 195-205°. This is probably the pinacol (Lit.[19] m.p. 195-210°). The reduction was repeated on the product using tin (6.4g.) and hydrochloric acid (50 ml.). On working up, the product still had m.p. 195-205°. The infrared spectrum was very different from that of the ketone and had a strong broad band at 810 and other strong bands at 950, 1155, 1345, 1515 and 1610 cm^{-1}.

The CO band of Michler's ketone is at 1600 cm^{-1}, so that the band at 1610 cm^{-1} may be due to the presence of some pinacolone. In case this is so the product was treated with zinc amalgam thus:[20]

Zinc (4g.), mercuric chloride (0.3g.), concentrated hydrochloric acid (0.2 ml.) and water (5 ml.) were shaken for 15 minutes. The aqueous layer was decanted and the Zn/Hg covered with water (3 ml.) and hydrochloric acid (4 ml.). The pinacol product was added and shaken at room temperature for two hours and for one hour at 60°. The zinc remaining was filtered off and the filtrate made alkaline by the addition of sodium hydroxide. The solution was extracted with dichloromethane dried with magnesium sulphate, and the dichloromethane evaporated to give a product which melted mainly at 195-205° but which had a trace of a compound, m.p. ~290°. This latter was probably 1,1,2,2,tetrakis(4-dimethylaminophenyl)ethylene, m.p. 296°.[21]

This reaction product (0.362g.) was refluxed in amyl alcohol (40 ml.) whilst sodium (1g.) was added slowly over half an hour. The mixture was then refluxed for an hour. Water was then added and the solution extracted with dichloromethane, dried with magnesium sulphate and the solvent evaporated to give a solid residue m.p. 320°. This was washed with methanol and dried at 80° for 6 hours to give 1,1,2,2-tetrakis(4-dimethylaminophenyl)ethane (0.3g.), m.p. 330°. (Lit.[22] m.p. 334°). The infrared spectrum had strong bands of almost equal intensity at 811 and 798 cm^{-1}., weaker bands at 954 and 756 cm^{-1}.

References:-

1. Raley, Rust and Vaughan, *J. Amer. Chem. Soc.*, 1948, *70*, 1336.
2. Henbest, Reid and Stirling, J., in press.
3. Walling, "Free Radicals in Solution", John Wiley & Sons, Inc., London, 1957, p.470.
4. Moore, *J.*, 1951, 236.
5. Beckwith, *Austral. J. Chem.*, 1960, *13*, 244.
6. Johnston & Williams, *J.*, 1960, 1446.
7. Huang & Yeo, *J.*, 1959, 3190.
8. Eliel, Wilken, Fang & Wilen, *J. Amer. Chem. Soc.*, 1958, *80*, 3303.
9. Wilen and Eliel, *J. Amer. Chem. Soc.*, 1958, *80*, 3309.
10. Thomas, Ph.D. Thesis, London 1958.
11. Skita and Keil, *Monatsh*, *53/54*, 762.
12. Velghe, *Bl. Acad. Belgique* [5] II 305. *Chem. Zentr.*, 1926, I, 875.
13. Blatt, "Organic Syntheses", John Wiley and Sons, Inc., London, 1943. Vol. II, p.219.
14. Andrews and McElvain, *J. Amer. Chem. Soc.*, 1929, *51*, 887.
15. Evans, *J. Amer. Chem. Soc.*, 1951, *73*, 5230.
16. Smith and Welch, *J.*, 1934, 1136.
17. Von Braun, *Ber.*, 1908, *41*, 2145.
18. Willstatter and Goldmann, *Ber.*, 1906, *39*, 3775.

References (contd.)

19. Cohen, Rec. Trav. Chim., 1919, 38, 113.

20. Fischl, Monatsh, 1914, 35, 528.

21. Tadros and Latif, J., 1953, 189.

22. Schenk and Bergmann, Annalen, 1928, 463, 41.

23. Magatti, Ber., 1880, 13, 227.

3. AMINE OXIDATIONS: REACTIONS OF AMINES IN AQUEOUS SOLUTION WITH OXIDANTS UNDERGOING ONE-ELECTRON TRANSFER.

Introduction

The background to this project has been discussed in considerable detail in the reports for 1958-59 (pp. 31-34) and for 1959-60 (p.32). During the 1960-61 session the studies contained in this and the previous two reports have been presented in a Ph.D. thesis. A short summary follows, briefly outlining the results of the previous sessions and their relationship to those described in this report.

Stewart[1] had examined the oxidation of primary amines and some amino-acids by sodium persulphate catalysed by silver nitrate; he also carried out some uncatalysed reactions with sodium persulphate solutions, irradiated by ultraviolet light. In the former system possible oxidants are the argentic ion Ag^{2+}, the sulphate radical-ion, $SO_4^{\cdot -}$ and the hydroxyl radical[2]:

$$S_2O_8^{2-} + Ag^+ \longrightarrow Ag^{2+} + SO_4^{2-} + SO_4^{\cdot -}$$

$$SO_4^{\cdot -} + H_2O \longrightarrow SO_4^{2-} + \cdot OH + H^+$$

$$Ag^{2+} + H_2O \longrightarrow Ag^+ + \cdot OH + H^+$$

In the second system only the sulphate radical-ion and the hydroxyl radical are possible; the greatly reduced yields of aldehyde from primary amines obtained with this system (e.g. isobutylamine gave only 4% of isobutyraldehyde as compared with 20% with the $Ag^+ - S_2O_8^{2-}$ system) suggested that $SO_4^{\cdot -}$ and $\cdot OH$ do not play so important a part in oxidation by the $Ag^+ - S_2O_8^{2-}$ system as had been supposed by some workers.[3,4]

Investigations were accordingly undertaken to determine the oxidative effects of divalent silver. This was conveniently obtained as argentic picolinate, a square-planar complex in which the divalent silver ion is linked to the 2-carboxylate groups and to the nuclear nitrogen of the picolinate ligands.

The oxidative effects of this compound form the subject of the present investigations, which are in continuation of those previously reported. Briefly, the oxidant has been found to oxidise all those classes of compounds which are oxidised by the $Ag^+ - S_2O_8^{2-}$ system, but the order of reactivities is different. This is attributed to the need for association of substrate molecules and Ag^{2+}, and for displacement of the picolinate ligands to occur, when argentic picolinate is the oxidant, whereas in aqueous $Ag^+ - S_2O_8^{2-}$ the argentic ion is presumably only loosely complexed with water molecules or anions such as OH^-. Inorganic displacement reactions of square-planar complexes have been the subject of a good deal of study.[5] Argentic picolinate can effect the following types of oxidation: primary amines to aldehydes (or occasionally to a nitrile) or ketones; secondary amines to aldehydes or ketones; alcohols to aldehydes; glycols to carbonyl compounds by fission; phenols to quinones; carboxylic acids to carbonyl compounds, with loss of carbon dioxide; arylalkyl hydrocarbons to carbonyl compounds.

Discussion of Results obtained 1960-61.

A. Oxidation of Ammonia by Argentic Picolinate.

Since the postulated scheme for the oxidation of primary amines (see below) produces ammonia, experiments were carried out to determine the effect of ammonia, in various proportions, on argentic picolinate. A suspension of the oxidant in aqueous ammonia was stirred in a closed vessel connected to a gas burette, in which the amount of nitrogen evolved was measured. Typical results, obtained with 100 ml. of solution, are shown in Table I.

TABLE I.

Oxidation of Ammonia by Argentic Picolinate

Argentic Picolinate (mole)	Ammonia (mole)	Nitrogen evolved (ml.)	Nitrogen evolved (mole)	Yield of Nitrogen (%)
0.01	0.44	34.05	0.001522	91.0
0.01	0.44	37.50	0.001675	100.6
0.01	0.01	12.13	0.000541	32.4
0.01	0.01	12.40	0.000554	33.2

The yields in the last column have been calculated from the amount of argentic picolinate added, assuming the equation:

$$6\ Ag^{2+} + 2NH_3 \longrightarrow 6\ Ag^{+} + N_2 + 6\ H^{+}$$

The results show that at low concentrations of ammonia this relationship is inadequate, but the argentic ion will release the theoretical amount of nitrogen from ammonia when the latter is present in much larger quantity than is required by the above equation. Experiments in which a standard solution of ammonia was added dropwise to a stirred suspension of argentic picolinate in water, until the red color of the oxidant disappeared, showed that 2.36 moles of ammoniawere necessary to decompose 1 mole of argentic picolinate. It is well known[5] that argentous silver combines with ammonia to form very stable complex ions $Ag(NH_3)_2^{+}$. It appears that ammonia thus bonded to silver will not displace the picolinate ligands from argentic picolinate and is therefore effectively removed from the reaction system. On this basis the equation for the reduction of ammonia by argentic picolinate is:-

$$6\ Ag^{2+} + 14\ NH_3 \longrightarrow 6Ag(NH_3)_2^{+} + 6\ H^{+} + N_2$$

From this equation, the number of moles of ammonia equivalent to one mole of argentic picolinate is 2.33, which is comparable with the figure (2.36) obtained experimentally,

B. Oxidation of Primary Amines by Argentic Picolinate.

A number of primary amines were oxidised by argentic picolinate in aqueous suspension; the results obtained are summarised in Table 2.

TABLE 2

Oxidation of Primary Amines by Argentic Picolinate

Amine	Argentic Picolinate (mol)	Reaction temp.	Reaction time (hr.)	Aldehyde or ketone produced	Yield (%)
Isopropylamine	2	70°	3	acetone	16
n-Butylamine	2	70°	1	n-butyraldehyde	14
Isobutylamine	2	70°	1	isobutyraldehyde	9
s-Butylamine	2	70°	2.5	butanone	27
Cyclohexylamine	2	75	2	cyclohexanone	41
Benzylamine	2	70	1	benzaldehyde	35
2-Ethylhexylamine	2	70	1	2-ethylhexanal	1.2

In all cases the yields obtained were lower, and the reaction rate slower, than those for secondary amines. It is possible that this is at least partly due to complexing of the primary amines with Ag^+ ions, analogously to the case of ammonia (see above). Primary amines form complexes of the type $Ag(NH_2R)_2^+$ which are more stable than those formed by ammonia. Since the formation of the complex $Ag(NH_3)_2^+$ may prevent the oxidation of ammonia by argentic picolinate, it seems likely that a high proportion of a primary amine may be removed from the reaction system analogously. There is a further complication in that ammonia produced in the oxidation of primary amines may destroy some of the argentic picolinate:

$$RCH_2 : NH_2 \longrightarrow RCH : NH$$

$$RCH : NH + H_2O \longrightarrow RCHO + NH_3$$

A further possible contributory cause of low yields of carbonyl compound may be that some of the presumed intermediate, RCH:NH, may undergo polymerisation or oxidation. Resinous products were formed in the case of 2-ethylhexylamine, which gave only a 1.2% yield of 2-ethylhexanal.

Features of special interest were observed in the oxidation of the branched primary amine, 3,3,5-trimethylhexylamine. No aldehyde was obtained, but there was a 10% yield (in addition to polymeric material) of 3,3,5-trimethylhexanonitrile, identical with an authentic sample prepared from the corresponding carboxylic acid. In this oxidation 4 atoms of hydrogen have been removed from the amine: $RCH_2 \cdot NH_2 \longrightarrow R \cdot C \equiv N$. Such dehydrogenations can be effected over catalysts in the vapour phase, but, so far as liquid-phase oxidations are concerned, the only case found in the literature was Bamberger's observation that oxidations of benzylamine and ethylamine by Caro's acid (peroxymonosulphuric acid) produce mixtures of products which include very small amounts of the corresponding nitriles. Under the conditions used for the argentic picolinate oxidations, 3,3,5-trimethylhexanal underwent substantial oxidation to the corresponding acid; the nitrile gave little evidence for conversion into acid.

Oxidation of Secondary Amines by Argentic Picolinate.

Oxidations of di-s-butylamine, di-2-ethylhexylamine, dibenzylamine, and 2-benzylamino-2,4,4-trimethylpentane by argentic picolinate, are examples of secondary amine conversions which appear in the previous reports. Other results are shown in Table 3.

TABLE 3

Oxidation of Secondary Amines by Argentic Picolinate in Aqueous Suspension

Amine Oxidised	Argentic Picolinate (mol.)	Reaction Time (min.)	Reaction Temp.	Product Formed	Yield (%)
Di-isopropylamine	2	15	70°	acetone	31
Di-n-butylamine	2	15	70°	n-butyraldehyde	67
Di-isobutylamine	2	15	70°	isobutyraldehyde	73
Di-s-butylamine	2	5	70°	butanone	62
Dicyclohexylamine	2	15	75°	cyclohexanone	61
Dibenzylamine	2	15	70°	benzaldehyde	76
Di-3,5,5-trimethylhexylamine	2	5	70°	3,5,5-trimethylhexanal	17
-do-	2	5	70°	3,5,5-trimethylhexylidene-3,5,5-trimethylhexylamine.	78
N-Triphenylmethylbenzylamine	2	24 hr.	70°	benzaldehyde	15

For the series of secondary amines examined, yields of aldehyde or ketone were, in general, much higher than for the corresponding primary amines. The times required for the complete decomposition of the argentic picolinate were also much lower, and in some cases the reaction was almost instantaneous.

The initially formed product, in the oxidation of secondary amines by argentic picolinate, is believed to be an aldimine or ketimine, which does not contain imino-hydrogen, and so cannot undergo the further oxidation to nitrile which is exemplified by the primary amine, 3,5,5-trimethyl-hexylamine:

$$\mathrm{RCH_2{\cdot}NH{\cdot}CH_2R} \longrightarrow \mathrm{RCH{:}N.CH_2R}$$

Possible reactions of such an imine are hydrolysis to the carbonyl compound and primary amine:

$$\mathrm{RCH{:}N.CH_2R + H_2O} \longrightarrow \mathrm{RCHO + NH_2.\ CH_2R}$$

or polymerisation.[7,8.] However, the reaction mixture rapidly attains pH 4-5, at which hydrolysis occurs readily and gives good yields of aldehyde or ketone, except in a few cases where the stability of the imine to hydrolysis, even under acid conditions, is high. One such case is that of di-2-ethylhexylamine (Report for 1958-59) where the yield of 2-ethylhexanal was only 9% and a considerable amount of resinous material was obtained. In the recently investigated case of di-3,5,5-trimethylhexylamine, the resulting imine, 3,5,5-trimethylhexylidene-3,5,5-trimethylhexylamine, was so unusually stable that it could be isolated in 78% yield even after the reaction mixture had been brought to ~ pH1 with dilute hydrochloric acid. The infrared absorption spectrum of the product was identical with that of a sample of authentic imine prepared from the aldehyde and amine; the -C:N- peak occurs at 1660 cm^{-1}.

C. Oxidations by Argentic Picolinate in Non-aqueous Solvents.

Reaction conditions which are suitable for most amines, i.e., oxidation in aqueous solution at 0-~85°, with a suspension of argentic picolinate, are unfavourable in the case of substrates which are insoluble and solid under such conditions. The use of non-aqueous reaction media was therefore investigated. Argentic picolinate proved to be stable for long periods in light petroleum (b.p. 40-60°), benzene, carbon tetrachloride, chloroform, glacial acetic acid, and t-butanol. In ethanol the red color of the argentic complex was discharged during 5 min. at boiling temperature (78°); this indicated that it might be possible to use ethanol as solvent for fast reactions at room temperature, though not for oxidations in which reaction times were in the order of days, nor for oxidation at elevated temperatures, since the result would be complicated by the oxidation of ethanol to acetaldehyde:

$$CH_3CH_2OH + 2Ag^{2+} \longrightarrow CH_3CHO + 2H^+ + 2Ag^+$$

When argentic picolinate was stirred in dioxan for 2 days at room temperature, a brown precipitate formed and a silver mirror was deposited on the sides of the reaction vessel. The nature of this decomposition was not investigated; the deposition of metallic silver indicates that a more extensive oxidation than usual had taken place. It appeared that dioxan might be used for fast oxidations at room temperature, but not for reactions requiring a number of days.

Reaction in different solvents was tested in the case of 2-benzylamino-2,4,4-trimethylpentane, since this amine had already been found to give high yields of benzaldehyde when oxidised in water. When it was stirred with argentic picolinate in light petroleum or in benzene for 24-hrs. at room temperature, the red color of the argentic salt was not discharged and unchanged amine was recovered nearly quantitatively as the hydrochloride.

The oxidation of 2-benzylamino-2,4,4-trimethylpentane by argentic picolinate in ethanol resulted in a 93% yield of benzaldehyde in 3 hr. at room temperature; in water the yield was 88.5% at 70°. N-Triphenylmethylbenzylamine had been found to give a poor yield (14%) of benzaldehyde when oxidised in water, even at elevated temperature (see above); this was presumably due, not only to steric effects, but to the solid state of the amine (m.p.91°) at the reaction temperature (70°). Oxidation of this amine dissolved in ethanol gave benzaldehyde (36%), after stirring for 24 hr. at room temperature, but the 2,4-dinitrophenylhydrazone from the product was impure (m.p. 175° rising to 237° after one recrystallisation from dioxan). A likely contaminant is the 2,4-dinitrophenylhydrazone (m.p. 168°) of acetaldehyde, formed by oxidation of the solvent during the long period of reaction.

Oxidations in t-butanol have the advantage that this alcohol contains no α-hydrogen atoms and so is not susceptible to oxidation by argentic picolinate. In this solvent, 2-benzylamino-2,4,4-trimethylpentane gave benzaldehyde (93%) at a slower rate than in ethanol but, in view of the stability of the solvent, oxidation could be carried out at 65°, when the reaction time (3 hr.) was similar to that observed in ethanol at room temperature.

Oxidation of 2-benzylamino-2,4,4-trimethylpentane in dioxan gave benzaldehyde (72%) when stirred with argentic picolinate at 65° for 3 hr. This reaction was slow compared with the oxidation of the amine in water, but the rate was comparable to that in t-butanol. The yield of benzaldehyde, however, was lower than that in water, ethanol, or t-butanol, and so the solvent does not seem to have any particular advantages. In glacial acetic acid, oxidation of 2-benzylamino-2,4,4-trimethylpentane was not complete in 24 hr. at 20°, but on raising the temperature to 70°, reaction was complete in 10 min., giving benzaldehyde in 80% yield.

D. Comparative Experiments with Other Heavy-metal Ions.

In the Report for 1959-60, details were given of experiments designed to assess the oxidative power of various heavy-metal ions and oxides towards amines. The substrate was 2-benzylamino-2,4,4-trimethylpentane and only argentic oxide proved to be an oxidant. Further reactions have been carried out with ceric ammonium sulphate and with mercuric acetate. The former was ineffective but the latter, under the conditions used by Leonard[9] for the oxidation of tertiary amines, gave benzaldehyde (6%) from 2-benzylamino-2,4,4-trimethylpentane after 24 hr.

EXPERIMENTAL DATA

In general, experimental conditions used for the examples quoted above were similar to those given in previous reports. The following descriptions concern cases showing various special features.

Preparation of N-triphenylmethylbenzylamine.

Triphenylchloromethane (0.018 mole; 5g.) was dissolved in dry dioxan (about 50 ml.) and benzylamine (0.036 mole) was added. The mixture was boiled under reflux for 2 hr., cooled, filtered, and the dioxan was evaporated from the filtrate to leave a gummy residue, which did not dissolve completely in hot light petroleum (b.p. 40-60°). The residue was filtered off and added to the previous precipitate. The combined precipitates (2.3g.) showed m.p. 260°, not depressed by admixture with an authentic sample of benzylamine hydrochloride (m.p. 261° ; lit., m.p. 255 - 258°). The light petroleum extract was concentrated and cooled, when N-triphenylmethylbenzylamine (6.15g., 98%) separated as a white crystalline solid; after one recrystallisation from light petroleum it was obtained analytically pure, m.p. 91°.

Oxidation of N-triphenylmethylbenzylamine.

(a) N-Triphenylmethylbenzylamine (0.01 mole, 3.49g.) and argentic picolinate (0.02 mole) were stirred in water (150 ml.) at 70° for 24 hr; the mixture, which still contained some unreacted argentic picolinate, was cooled and filtered. The filtrate, after treatment with sufficient 2N-hydrochloric acid to convert all silver present into the chloride, was steam distilled. Benzaldehyde in the distillate was estimated by precipitation as the 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 235°, obtained in 15% yield.

(b) A similar reaction was carried out in ethanol (150 ml.) at room temperature for 24 hr; the white precipitate of argentous picolinate was filtered off, the filtrate poured into water (750 ml.), and sufficient hydrochloric acid added to precipitate all silver as chloride, which was removed by filtration. The filtrate was distilled and aldehyde in the distillate was estimated in the normal way, as the 2,4-dinitrophenylhydrazone (36%). The derivative thus obtained was impure, showing m.p. 175°, but after one recrystallisation from dioxan the m.p. was 234°, and was not depressed by admixture with authentic benzaldehyde 2,4-dinitrophenylhydrazone, m.p. 237°.

Stability of argentic picolinate in various non-aqueous media.

Argentic picolinate (1g.) and the solvent under test (50 ml.) were stirred together. The time required for discharge of the red argentic color was noted; results obtained are as follows:-

In light petroleum (b.p. 40-60°), benzene, carbon tetrachloride, or chloroform, no decomposition of the argentic picolinate was visible during eight days stirring at room temperature and in 5 min. at the boiling point. In dioxan, a brown precipitate and a silver mirror appeared during 2 days stirring at room temperature. In t-butanol, no change was visible during long periods at 0-82°. In acetic acid, no change was observed during two weeks at room temperature, but at the boiling point a brown solution and a silver mirror were formed in 15 min.

Oxidation of 2-benzylamino-2,4,4-trimethylpentane in organic solvents.

(a) 2-Benzylamino-2,4,4-trimethylpentane (0.01 mole, 2.19g.), argentic picolinate (0.02 mole) and ethanol (150 ml.) were stirred at room temperature (20°) for 3 hrs., when the red colour was discharged. The mixture was filtered, the filtrate added to 1 litre of water, followed by sufficient hydrochloric acid to precipitate all silver as the chloride. The solution was steam distilled and benzaldehyde in the distillate was estimated as the 2,4-dinitrophenylhydrazone, (93%), m.p. 237°.

(b) Reaction was carried out in t-butanol for 3-hr. at 65°; conditions were otherwise similar to those used for ethanol. Benzaldehyde 2,4-dinitrophenylhydrazone (93%) was obtained, m.p. 235°, after recrystallisation from dioxan.

(c) Reaction was carried out in dioxan for 3-hr. at 65°; conditions were otherwise similar to those used for ethanol. Benzaldehyde 2,4-dinitrophenylhydrazone (72%), was obtained, m.p. 237° after recrystallisation from dioxan.

(d) A suspension of argentic picolinate (0.02 mole) in a solution of the amine (0.01 mole, 2.19g.) in light petroleum, b.p. 40-60° (150 ml.), was stirred at room temperature for 24 hr. The red argentic color had not been discharged during this time. The mixture was filtered and the filtrate was shaken with 6N hydrochloric acid (100 ml.). This gave a white crystalline precipitate of 2-benzylamino-2,4,4-trimethylpentane hydrochloride (88%), m.p. and mixed m.p. 237° after recrystallisation from isopropanol. Its infrared absorption spectrum was identical with that of the authentic hydrochloride. The petroleum layer left no residue on evaporation.

(e) Repetition of experiment (d) in benzene resulted in no decomposition of argentic picolinate. 2-Benzylamino-2,4,4-trimethylpentane hydrochloride (88%) was recovered and no benzaldehyde was found.

(f) A suspension of argentic picolinate (0.02 mole) in a solution of the amine (0.01 mole, 2.19g.) in glacial acetic acid (150 ml.) was stirred at room temperature for 24 hr., during which the argentic picolinate was not decomposed. When the temperature was raised to 70° the red color disappeared in 10 min., giving a greenish-brown viscous mixture. Sufficient 2N-hydrochloric acid was added to precipitate all silver present as the chloride and the filtered solution was diluted to 1 litre with water and extracted with ether. The ether extract, freed from acetic acid with alkali, left crude benzaldehyde on evaporation. When this residue was taken up in methanol and an aliquot was treated with an excess of a saturated solution of 2,4-dinitrophenyl-hydrazine in 2N hydrochloric acid, benzaldehyde 2,4-dinitrophenylhydrazone (80%), m.p. and mixed m.p. 235°, was obtained.

Oxidation of primary and secondary amines by argentic picolinate.

The following general procedure was followed for the oxidations summarised in Tables 2 and 3. The amine (0.01 mole), argentic picolinate (0.02 mole) and water were stirred at the requisite temperature until the red color of the suspended argentic picolinate had been discharged. The argentous picolinate was filtered off and the filtrate was treated with sufficient 2N hydrochloric acid to ensure complete precipitation of dissolved argentous picolinate. After removal of the silver chloride, the filtrate was steam-distilled and aldehyde or ketone in the distillate was estimated, in the normal way, as the 2,4-dinitrophenylhydrazone.

Oxidation of 3,5,5-trimethylhexylamine.

Mixtures of 3,5,5-trimethylhexylamine (0.01 mole) and argentic picolinate (0.02 mole) in water (150 ml.) underwent complete reaction in less than 2 hr. at 20° or 70°. No aldehyde was detected. The gelatinous mixture left on cooling was treated with excess of 2N-hydrochloric acid and ether extracted. Distillation of ether yielded an oil, b.p. 90°/10 mm., and left some polymer. Analysis and comparison of the infrared spectrum with that of an authentic sample (see below) showed the product to be 3,5,5-trimethylhexanonitrile, isolated in 10% yield.

3,5,5-Trimethylhexanonitrile.

Treatment of 3,5,5-trimethylhexanoic acid with excess of thionyl chloride under reflux gave the acid chloride (90%), b.p. 185°/760 mm. on distillation. It was converted into the amide (98%), m.p. 94°, by adding its solution in ether to liquid ammonia at the temperature of solid carbon dioxide; aqueous ethanol was used for recrystallisation. The amide was intimately mixed with phosphorus pentoxide (1 mol.) and 3,5,5-trimethylhexanonitrile was distilled out of the mixture at 10 mm. pressure. Redistillation gave the pure nitrile (86%), b.p. 95-100°/15 mm. When it was stirred in water with argentic picolinate (2 mol.) for 24 hr. at 75°, the red color was not discharged and recovered organic material (73%) showed a strong nitrile peak, but only a very weak carbonyl peak, in the infrared spectrum.

Oxidation of 3,5,5-trimethylhexanal.

The aldehyde (0.01 mole) and argentic picolinate (0.02 mole) were stirred in water (150 ml.) at 70° for 4 hr., when the red color was discharged. After treatment with hydrochloric acid, ether extraction, and evaporation of solvent, 3,5,5-trimethylhexanoic acid (62%), b.p. 92-95°/15 mm., was isolated by distillation.

Oxidation of di-3,5,5-trimethylhexylamine.

Di-3,5,5-trimethylhexylamine (0.01 mole), argentic picolinate (0.02 mole), and water (150 ml.) were stirred at 70° for 5 minutes. On cooling, the white reaction mixture formed a viscous sludge, which was broken up by treating it with sufficient 2N-hydrochloric acid to precipitate all silver present as the chloride. The filtrate was extracted with ether and the extract mixed with ether washings of the silver chloride. Evaporation of the ether left a brown oil, which could not be distilled, due to excessive frothing, and was therefore chromatographed on alumina. Elution with a 5% mixture of ether in light petroleum, b.p. 40-60°, gave an orange-red oil (78%), the infrared spectrum of which was identical with that of an authentic sample of 3,5,5-trimethylhexylidene-3,5,5-trimethylhexylamine (see below).

3,5,5-Trimethylhexylidene-3,5,5-trimethylhexylamine.

3,5,5-Trimethylhexylamine (0.01 mole, 14.2g.) and 3,5,5-trimethylhexanal (0.1 mole, 14.3g.) were stirred together while refluxing for 3 hr. The reaction mixture was cooled and the upper layer was dried and purified by distillation. Pure 3,5,5-trimethylhexylidene-3,5,5-trimethylhexylamine, b.p. 95-100°/0.7 mm., was obtained in 95% yield. The infrared absorption spectrum showed a -C=N- peak at 1660 cm^{-1}.

Evaluation of ceric ammonium sulphate as oxidant.

Ceric ammonium sulphate (0.02 mole), 2-benzylamino-2,4,4-trimethylpentane (0.01 mole), and water (150 ml.) were stirred at 70° for 12 hr. Benzaldehyde formed was estimated as the 2,4-dinitrophenylhydrazone (1.5%), m.p. and mixed m.p. 236°; a blank test, without oxidant, gave a similar yield.

Evaluation of mercuric acetate as oxidant.

2-Benzylamino-2,4,4-trimethylpentane (0.02 mole) and mercuric acetate were stirred in 5/95 acetic acid/water mixture, heated on a steam-bath for 24 hr. After cooling, and acidification to about pH2 with glacial acetic acid, the reaction mixture was distilled. From the distillate benzaldehyde 2,4-dinitrophenylhydrazone, m.p. 235°, was obtained in 6% yield.

References:

1. D. Stewart, Ph.D. Thesis, Queen's University of Belfast, 1960.
2. Bawn and Margerison, Trans. Faraday Soc., 1955, 51, 925.
3. Fordham and Williams, J. Amer. Chem. Soc., 1951, 73, 4855.
4. Kolthoff, Medolia and Raaen, J. Amer. Chem. Soc., 1951, 73, 1733.
5. Basolo and Pearson, "Mechanisms of Inorganic Reaction", Wiley & Sons, New York, 1958.
6. Bamberger, et al., Ber., 1902, 35, 4293, 4299; 1903, 36, 701.
7. Tiollais, Bull. Soc. Chim. France, 1947, 708, 716, 959.
8. Emerson, Hess and Uhle, J. Amer. Chem. Soc., 1941, 63, 872.
9. Leonard, et al., J. Amer. Chem. Soc., 1957, 79, 5279 and related papers.

Mr. M.J.W. Stratford, B.Sc.	Supervised by Professor H.B. Henbest
Mr. R. Patton, B.Sc.	
Mr. W.J.W. Hanna, B.Sc.	Supervised by Dr. R.G.R. Bacon

No major changes in research policies were made during the year.

The three men each worked about 2000 hours during the year, so that the total number of manhours can be put at 6000.

£960 was divided between the three men leaving a balance of £190 to cover the cost of chemicals and apparatus. No one item of expensive equipment was bought during the year at direct contract expense.