RAWALAY, Surjan Singh, 1933—
OXIDATION OF PRIMARY, SECONDARY, AND
TERTIARY ALIPHATIC AMINES WITH BUFFERED
PERMANGANATE.

The Ohio State University, Ph.D., 1962
Chemistry, organic

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substituted benzaldehydes, the reaction was accelerated by hydroxyl ions according to Equation 138.

$$\text{Rate} = k \left[ \text{PhCHO} \right] \left[ \text{MnO}_4^- \right]^{\frac{1}{2}} \left[ \text{OH}^- \right]^{\frac{3}{2}}$$  (138)

Furthermore, the decrease in rate which accompanied the replacement of hydrogen by deuterium in the aldehyde group became much smaller as the pH of the solution increased. Thus, at higher pH values, the rate-determining cleavage of the C-H bond to give a proton became less important. It is of interest that at low pH values (neutral) the oxygen introduced in the resulting benzoic acid is derived mainly from the oxidant; at higher pH values (alkaline) this oxygen came mainly from the solvent (water). The rate constant obeyed Hammett's equation, but while the reaction constant ($\rho$) for reaction in neutral solution was positive, its value for alkaline solution was large and negative, indicating that oxidation is facilitated by a high electron density at the reaction site.

The versatility of permanganate as an oxidant is even more impressive if permanganate oxidizes benzaldehydes in neutral and alkaline media by two different mechanisms.\textsuperscript{71} It has been suggested that reaction in neutral solution involves formation of a permanganate ester
of the hydrate of the aldehyde, followed by rate-determining loss of the aldehyde hydrogen as a proton.

\[ RCHO + H_3O^+ \leftrightarrow RCOOH + H_2O \]  \hspace{1cm} (139)

\[ RCOOH + MnO_4^- \leftrightarrow R - C - O MnO_3 \]  \hspace{1cm} (140)

\[ R - C - H : B \rightarrow RCO_2H + H^+ + MnO_3^- \]  \hspace{1cm} (141)

\[ 2MnO_3^- + H_2O \rightarrow 2MnO_2 + MnO_4^- + 2OH^- \]  \hspace{1cm} (142)

A free radical mechanism has also been suggested for reaction in basic solution:

**Initiation**  
\[ MnO_4^- + OH^- \rightarrow MnO_4^- + OH^- \]  \hspace{1cm} (143)

**Propagation**  
\[ HO^- + RCHO \rightarrow R - C - OH \]  \hspace{1cm} (144)

\[ R - C - OH + MnO_4^- \rightarrow RCO_2H + MnO_3^- + OH^- \]  \hspace{1cm} (145)
Termination \( 2\text{H}^0 \rightarrow \text{H}_2\text{O}_2 \)

\[
\text{H}_2\text{O}_2 + \text{MnO}_4^- \xrightarrow{\text{fast}} \text{O}_2 + \text{HMnO}_4^- + \dot{\text{H}} \quad (146)
\]

In general, under similar conditions, alcohols are oxidized by permanganate faster than are the corresponding hydrocarbons. For example, ethyl alcohol is oxidized by potassium permanganate, while ethane is not. Although ethane is resistant to permanganate, ethylbenzene is oxidized but at a slower rate than is \( \alpha \)-phenylethyl alcohol. Aliphatic amines are oxidized faster than alcohols. Also permanganate oxidizes \( \alpha \)-phenylethylamine faster than \( \alpha \)-phenylethyl alcohol under similar conditions.

The general rates of permanganate oxidation are summarized as:

\[
\text{Aliphatic amines} \gg \text{aliphatic alcohols} \gg \text{hydrocarbons.}
\]

\[
\begin{align*}
\text{R-NH}_2 & \gg \text{R-OH} \gg \text{R-C=CH}_2
\end{align*}
\]
On examination of the corresponding free radicals or carbonium ions, it is evident that their ease of formation will be in the order:

\[ R' \text{--NHR} > R' \text{--OH} > \emptyset \text{--CH}_2R \]

or

\[ R' \text{--NHR}^+ > R' \text{--OH} > \emptyset \text{--CH}_2R \]

On the other hand the order of ease of carbanion formation will be reversed:

\[ \emptyset \text{--CH}_2R > R' \text{--OH} > R' \text{--NHR} \]

It seems likely that permanganate oxidation (at least in buffered permanganate) of amines involves either removal

---

* Amines are better electron donor than alcohols and alcohols in turn better than hydrocarbons. This information is obtained from the quantitative measure of the polar effect of a substituent on an aromatic nucleus; \( \sigma \) values for \( \text{--N} \): more negative than those for \( \text{--O} \); and those of \( \text{--O} \): more negative than those for \( \text{--R} \).
of a hydrogen atom (H\(^+\)) or a hydride ion (H\(^-\)). The removal of hydrogen as a proton (H\(^+\)) and consequently involvement of carbanions in any rate-determining process is unlikely. The lone pair of electrons on nitrogen must play a very important role in this oxidation, since amines salts are resistant to permanganate. Amines salts are oxidized in solution only because the salt is in equilibrium with the free amine. In oxidation of aliphatic primary and secondary amines with permanganate, it is not clear whether the initial step involves removal of hydrogen from alpha carbon or from nitrogen. On assuming that the first step involves removal of hydrogen from the alpha carbon, rather than from nitrogen, then removal of the second hydrogen may be from nitrogen to give an imine or from beta carbon to give an enamine which in turn rearranges in a fast step to the corresponding imine (Chart C). These possibilities also exist for alcohols bearing beta-hydrogen; studies of the mechanisms of such oxidations have not been carried out however.

For aliphatic tertiary amines it appears that the initial step involves loss of hydrogen from the alpha-carbon and subsequent removal of hydrogen from beta-carbon or removal of an alkyl group from nitrogen (dealkylation) (Chart D). The results from the present study of oxidation of tributylamine indicate that whenever there is the
CHART C

\[ R - CH_2 - CH_2 - NH_2 \]

\[ \rightarrow R - CH(\cdot) - CH = NH \]

\[ \rightarrow R - CH = CH - NH \]

\[ \rightarrow R - CH = CH - NR \]

Products
CHART D

\[
\begin{align*}
R-\text{CH}_2-\text{CH}_2-N^+R \\
R-\text{CH}_2-\text{CH}-N^+R \\
R-\text{CH}==\text{CH}-N^+R \\
R^+ + R-\text{CH}_2-\text{CH}==N-R + R^-
\end{align*}
\]
possibility that an enamine can be formed, removal of hydrogen rather than dealkylation takes place. With aliphatic tertiary amines in which the formation of enamine is structurally inhibited as in tribenzylamine dealkylation occurs.
EXPERIMENTAL

General Procedure and Techniques

Melting points. All melting points reported are for samples which had been purified for elemental analyses. Melting points below 250° were determined in a stirred bath equipped with a calibrated thermometer. Melting points above 250° were obtained in a heated aluminum block which contained wells for the thermometer and capillary melting point tubes, and ports for illumination and observation of the sample. All melting points are uncorrected.

Infrared spectra. The infrared spectra of the compounds obtained in this research were determined with a Baird Associates, Model B, recording infrared spectrophotometer. The spectra of solid compounds were determined from potassium bromide wafers.

Ultraviolet spectra. All ultraviolet spectra were determined using a Cary recording spectrophotometer, Model 10.
Elemental analyses. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee, and some by J. A. Smith of this department.

Molecular weight determinations. Molecular weights of most of the new compounds reported were determined using a Mechrolab vapor pressure osmometer, Model 301 A. 1,2-Dichloroethane, benzene and in some cases chloroform were used as solvents for the molecular weight determinations.

Preparation of Cyclobutanecarboxylic Acid


A mixture of diethyl cyclobutanedicarboxylate (200 g., 1 mole) and dilute hydrochloric acid (25% by wt., 900 ml.) was refluxed and stirred for 7 hr. Solvents were removed from the stirred homogeneous mixture and the residue heated 160-175° to effect decarboxylation. After 1 hr. the mixture was cooled and the residue was distilled to yield crude cyclobutanecarboxylic acid, b.p. 192-195°. The product was redistilled in vacuo, b.p. 101-104°/20 mm.; yield 62 g., 0.62 mole, (62%).


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<td>A</td>
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<td>B</td>
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<td>C</td>
<td>94</td>
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<td>D</td>
<td>95</td>
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Preparation of Cyclobutylamine

Sodium azide (65 g., 1.0 mole) was added in small portions to a stirred mixture of cyclobutane-carboxylic acid (75 g., 0.75 mole) and concentrated sulfuric acid (400 ml.). Addition of sodium azide was regulated as to keep the temperature of the mixture about 40–50°C. After the sodium azide had been added and no more gas had been evolved, the mixture was stirred for 2 hr. The reaction mixture was first cooled to 0°C and then cold sodium hydroxide solution was added slowly and cautiously until the mixture was very alkaline. The alkalized reaction mixture was continuously extracted with diethyl ether. Ether was removed from the extract by fractional distillation. Cyclobutylamine was subsequently collected at 81–82°C, yield 34.5 g., (64.8%), \( n_D^{20} \) 1.4360; lit. \( n_D \) b.p. 81.5°C, \( n_D^{19} \) 1.4363.

(73) N. Zelinsky and J. Gutt, Ber., 40, 4746 (1907).

The present method is a new source of cyclobutylamine.

Oxidation of Cyclobutylamine

Cyclobutylamine (1.0 g., 0.014 mole) was added in one portion to a warm (≈65°C) stirred solution of potassium permanganate (3.75 g., 0.0237 mole, 2.5 equivalents), and calcium sulfate dihydrate (2.5 g., 0.0145 mole) in water:
t-butyl alcohol (8:5; 65 ml.). The mixture was heated rapidly and subsequently distilled into aqueous 2,4-dinitrophenylhydrazine. The crude cyclobutanone 2,4-dinitrophenylhydrazine was collected and dried; yield 2.51 g. (71%). The product was crystallized from ethanol to give orange yellow needles, m.p. 145-147°; lit. 147°. This melting point was not depressed by admixture with authentic cyclobutanone 2,4-dinitrophenylhydrazone.

(74) The reagent was prepared by diluting a solution of 2,4-dinitrophenylhydrazine (5 g.) in concentrated sulfuric acid (100 ml.) with water (1 liter). The aqueous solution was clarified by filtration.


Oxidation of Cyclohexylamine

Cyclohexylamine (1.0 g., 0.01 mole) was rapidly added to a warm (~ 78) stirred solution of potassium permanganate (3.3 g., 0.019 mole, ~ 3.0 equivalents) and calcium sulfate dihydrate (2.25 g., 0.013 mole) in water (30 ml.) and t-butanol (25 ml.). The mixture was heated rapidly and then distilled into 2,4-dinitrophenylhydrazine solution. The crude cyclohexanone 2,4-dinitrophenylhydrazone was collected and dried, yield 2.17 g. (75%). The crude hydrazone
was crystallized from grain alcohol to give yellow plates, m.p. and mixed m.p. 160-161°; lit. 162°.


Oxidation of Dicyclohexylamine

Dicyclohexylamine (1.0 g., 0.0055 mole) was rapidly added to warm (~75°) stirred solution of potassium permanganate (3.48 g., 0.022 mole, 3.0 equivalents) and calcium sulfate dihydrate (2.5 g., 0.0145 mole) in water: t-butyl alcohol (1:1, 60 ml.). The mixture was heated rapidly in order to effect distillation as soon as possible. The distillate was collected in 2,4-dinitrophenylhydrazine solution. 74 The crude product was filtered and dried; yield 77 2.6 g. (84.6%). Yellow plates, m.p. 160-

(77) Based on the fact that 1 mole of amine gives 2 moles of ketone.

162°, were obtained on crystallizing from ethanol. This melting point was not depressed by admixture with authentic cyclohexanone 2,4-dinitrophenylhydrazone; lit. 162°.

Oxidation of N-Ethylidicyclohexylamine

Potassium permanganate (5.5 g., 0.35 mole; ~3.5 equivalents), calcium sulfate dihydrate (3.5 g.; 0.0203 mole, water (35 ml.) and t-butyl alcohol (35 ml.) were
added to a 100 ml. round-bottomed flask. N-Ethylidicyclohexylamine (1.0 g., 0.0048 mole) was added to the warm (≈80°) stirred permanganate solution. The reaction mixture was heated rapidly in order to effect quick distillation. The distillate was received in 2,4-dinitrophenylhydrazine solution. The crude cyclohexanone 2,4-dinitrophenylhydrazone was crystallized from ethanol as yellow plates.

(78) Acetaldehyde 2,4-dinitrophenylhydrazone was not detected.

m.p. and mixed m.p. with authentic cyclohexanone 2,4-dinitrophenylhydrazone 161-162°, lit. 162°; yield 2.4 g. (89%).

Oxidation of Isopropylamine

Potassium permanganate (4.5 g., 0.0285 mole, 2.5 equivalents), calcium sulfate (3.0 g., 0.0174 mole), water (40 ml.) and t-butanol (25 ml.) were added to a 100-ml. round-bottomed flask. The mixture was stirred and warmed to ≈55°. Isopropylamine (1.0 g., 0.017 mole) was added in one portion to the mixture. The mixture was heated rapidly and distilled into 2,4-dinitrophenylhydrazine solution. The crude acetone 2,4-dinitrophenylhydrazone was collected and dried; yield 3.36 g. (82%).

The product was crystallized from grain alcohol to give yellow needles, m.p. 128°, lit. 126°. Its melting point when mixed with authentic acetone 2,4-dinitrophenylhydrazone was undepressed.
Oxidation of Diisopropylamine

Diisopropylamine (1.0 g., 0.0098 mole) was added (in one portion) to a warm (−70°) stirred solution of potassium permanganate (5.25 g., 0.033 mole, −2.5 equivalents) and calcium sulfate dihydrate (3.0 g., 0.0174 mole) in water:t-butanol (8:5; 65 ml.). The mixture was heated rapidly and then distilled into 2,4-dinitrophenylhydrazine reagent. The crude hydrazone was collected and dried; yield 4.1 g. (86%). The product when crystallized from grain alcohol gave acetone 2,4-dinitrophenylhydrazone as yellow needles, m.p. and mixed m.p. 127-128°; lit. 126°.

Oxidation of N-Methyldiisopropylamine

N-Methyldiisopropylamine was prepared from diisopropylamine and iodomethane.

N-Methyldiisopropylamine (1.0 g., 0.0087 mole) was poured into a warm (−70°) stirred solution of potassium permanganate (9.5 g., 0.06 mole, 3.5 equivalents) and calcium sulfate dihydrate (5.5 g., 0.032 mole) in water: t-butanol (50:50, 70 ml.). The reaction mixture was heated rapidly and the product was distilled into aqueous 2,4-dinitrophenylhydrazine solution. The crude hydrazone was

Formaldehyde 2,4-dinitrophenylhydrazone was not found.
collected and dried; yield 3.1 g. (74%). The crude product on crystallization from grain alcohol gave yellow needles, m.p. 127-128°; lit. 76 126°. This melting point remained unchanged by admixture with authentic acetone 2,4-dinitrophenylhydrazone.

**Oxidation of Sec-butylamine**

Sec-butylamine (1.0 g., 0.0137 mole) was poured into a warm (≈ 60°) stirred solution of potassium permanganate (4.0 g., 0.025 mole, ≈ 2.75 equivalents) and calcium sulfate dihydrate (2.5 g., 0.0145 mole) in water:t-butanol (6:5, 55 ml.). The reaction mixture was distilled rapidly into 2,4-dinitrophenylhydrazone solution. 74 The crude hydrazone was collected and dried; yield 3.14 g. (91%). Yellow crystals, m.p. 114-115°, lit. 76 117°, were obtained on crystallization from ethanol. The melting point was not depressed by admixture with authentic 2-butane 2,4-dinitrophenylhydrazone.

**Oxidation of Di-sec-butylamine**

Di-sec-butylamine (1.0 g., 0.0077 mole) was rapidly added to a warm (≈ 75°) stirred solution of potassium permanganate (4.0 g., 0.026 mole, ≈ 2.5 equivalents) and calcium sulfate dihydrate (2.5 g., 0.0145 mole) in water:
t-butyl alcohol (7:5, 65 ml.). The mixture was heated rapidly in order to effect distillation as quickly as possible. The distillate was collected in 2,4-dinitrophenylhydrazine solution. The crude 2-butanone 2,4-dinitrophenylhydrazone was filtered and dried; yield 3.75 g. (96%). Crystallization of the crude product from ethanol gave yellow crystals; m.p. and mixed m.p. 114-116°, lit. 117°.

**Oxidation of 2-Aminoheptane**

2-Aminoheptane (1.0 g., 0.0087 mole) was rapidly added to a warm (−75°) stirred solution of potassium permanganate (2.75 g., 0.0174 mole, −3.0 equivalents) and calcium sulfate dihydrate (1.75 g., 0.0101 mole) in water: t-butyl alcohol (1:1, 50 ml.). The reaction mixture was heated rapidly and distilled into aqueous 2,4-dinitrophenylhydrazine solution. The crude 2-heptanone-2,4-dinitrophenylhydrazone was collected and dried; yield 2.02 g., (79%). The crude product was crystallized from ethanol as orange-yellow crystals m.p. 88-89°, lit. 89°.

**Oxidation of α-Phenylethylamine**

α-Phenylethylamine (1.0 g., 0.00825 mole) was added (in one portion) to a stirred solution of potassium
permanganate (1.74 g., 0.011 mole, 2.0 equivalents) and calcium sulfate dihydrate (1.25 g., 0.0072 mole) in water: t-butanol (1:1, 50 ml.). After the reaction was complete (\( \sim 20 \) min.), the mixture was filtered. The filtrate was added to 2,4-dinitrophenylhydrazine solution. The crude acetophenone 2,4-dinitrophenylhydrazone was collected and dried; yield 1.93 g., (78%). The crude product was crystallized from ethanol as orange-yellow crystals, m.p. 247-249°, lit. 250°.

**Oxidation of Benzhydrylamine**

Benzhydrylamine (1.0 g., 0.00546 mole) was added (in one portion) to a warm (\( \sim 60^\circ \)) stirred solution of potassium permanganate (0.86 g., 0.0053 mole, 1.5 equivalents) and calcium sulfate dihydrate (0.5 g., 0.0029 mole) in water: t-butanol (1:1, 50 ml.). The mixture was refluxed until all the permanganate was reduced (\( \sim 1.5 \) hr.). The mixture was cooled and extracted with ether. The ether was removed and the residue added to 2,4-dinitrophenylhydrazine reagent. Crude benzophenone 2,4-dinitrophenylhydrazone was collected and dried; yield 1.66 g. (83%). The crude hydrazone was crystallized from ethanol as orange-red needles, m.p. 238-239°, lit. 239°.
Oxidation of n-Propylamine

n-Propylamine (1.0 g., 0.017 mole) was added (in one portion) to a warm (\(\sim 50^0\)) stirred solution of potassium permanganate (2.25 g., 0.016 mole, 1.25 equivalents) and calcium sulfate dihydrate (1.5 g., 0.0087 mole) in water:t-butanol (3:1, 50 ml.). The mixture was distilled rapidly into 2,4-dinitrophenylhydrazine solution.\(^74\) The precipitate which formed was filtered and dried; yield 1.7 g. (42%). The crude propionaldehyde 2,4-dinitrophenylhydrazone was crystallized from ethanol as yellow needles, m.p. 153-154\(^0\); lit.\(^76\) 154\(^0\).

Oxidation of n-Butylamine

To a warm (\(\sim 65^0\)) stirred solution of potassium permanganate (1.8 g., 0.0114 mole, \(\sim 1.25\) equivalents) and zinc sulfate heptahydrate (1.75 g., 0.0061 mole) in water:t-butanol (8:5, 65 ml.), n-butylamine (1.0 g., 0.0137 mole) was added in one portion. The reaction mixture was heated rapidly in order to distill the product as quickly as possible. The distillate was collected in 2,4-dinitrophenylhydrazine solution.\(^74\) The precipitate formed was filtered and dried; yield, 1.6 g. (46%). The crude product was crystallized from ethanol as yellow needles, m.p. 122-123\(^0\); lit.\(^76\) 122\(^0\). There was no
depression on admixture with an authentic sample of butyraldehyde 2,4-dinitrophenylhydrazone.

**Oxidation of Di-n-butylamine**

Di-n-butylamine (1.0 g., 0.0077 mole) was added to a warm (75°C) stirred solution of potassium permanganate (2.0 g., 0.0127 mole, ~1.25 equivalents) and calcium sulfate dihydrate (1.5 g., 0.0087 mole) in water: t-butanol (1:1, 70 ml.). The mixture was heated rapidly and distilled into 2,4-dinitrophenylhydrazine solution. The dry crude butyraldehyde 2,4-dinitrophenylhydrazone weighed 1.96 g., (49.8%). The crude product was crystallized from ethanol as yellow needles, m.p. 121-122°C; lit. 122°C.

**Oxidation of Tri-n-butylamine**

Tri-n-butylamine (1.0 g., 0.00539 mole) was added to a warm (80°C) stirred solution of potassium permanganate (1.7 g., 0.0107 mole, 1.0 equivalent) and calcium sulfate dihydrate (1.0 g., 0.0058 mole) in water: t-butanol (1:1, 50 ml.) in one portion. The temperature of the bath was raised considerably in order to effect rapid distillation. The distillate was collected in 2,4-dinitrophenylhydrazine solution. The crude dry butyraldehyde 2,4-dinitrophenyl-
INTRODUCTION

The present research consists of a systematic investigation of oxidation of aliphatic and alicyclic amines with permanganate. Although potassium permanganate has been used for oxidation of certain aliphatic amines, the scope, utility, and mechanism of such reactions have not been investigated.
hydrazone weighed 1.36 g., yield $^{81} 33\%$. Yellow needles,

(81) Based on the fact that 1 mole of amine gives 3 moles of aldehyde.

m.p. 121-122°, were obtained on crystallization of the derivative from ethanol; lit. $^{76} 122°$.

**Oxidation of Isobutylamine**

Isobutylamine (1.0 g., 0.0137 mole) was poured into a warm ( ~ 60°) stirred solution of potassium permanganate (1.8 g., 0.0114 mole, ~ 1.25 equivalents) and calcium sulfate dihydrate (1.0 g., 0.0058 mole) in water: t-butanol (2:1, 45 ml.). The mixture was distilled rapidly into 2,4-dinitrophenylhydrazine. $^{74}$ The crude product was collected and dried; yield: 1.76 g. (50.5%). Crude isobutyraldehyde 2,4-dinitrophenylhydrazone, when crystallized from grain alcohol, gave yellow needles, m.p. 182-183°; lit. $^{76} 182°$.

**Oxidation of Diisobutylamine**

Diisobutylamine (1.0 g., 0.0077 mole) was poured into a warm ( ~ 80°) stirred solution of potassium permanganate (1.7 g., 0.0107 mole, ~ 1.0 equivalent) and calcium sulfate dihydrate (1.25 g., 0.0072 mole) in water: t-butanol (1:1, 60 ml.). The mixture was heated rapidly
so as to effect distillation as quickly as possible. The distillate was received in 2,4-dinitrophenylhydrazine solution. The crude product was collected and dried; yield: 2.19 g. (56%). The derivative was crystallized from ethanol to give isobutyraldehyde 2,4-dinitrophenylhydrazone as yellow needles, m.p. 181-182°; lit. 182°.

**General Procedure of Oxidation of Benzylamines on Small Scale**

The amine (1.0 g.) was added rapidly to a stirred solution of potassium permanganate (1.25 equivalents) and calcium sulfate (about 60-70% of potassium permanganate by weight) in water: t-butanol (1:1, 50 ml.) at room temperature. After reaction was complete (5-10 min.), the mixture was filtered. The filtrate was added to 2,4-dinitrophenylhydrazine solution. The crude 2,4-dinitrophenylhydrazone was collected and dried. The crude hydrazone was crystallized from ethanol. The experimental results are summarized in Table 3.

**Oxidation of Cyclohexylamine**

**Isolation of Cyclohexanone**

Cyclohexylamine (20 g., 0.202 mole) was rapidly added to a warm ( 〜 55°) and stirred water:t-butanol (1:1, 1 l.) solution of potassium permanganate (78 g.,
### TABLE 3

**OXIDATION OF BENZYLAMINES**

<table>
<thead>
<tr>
<th>Amine</th>
<th>Aldehyde 2,4-DNPH&lt;sup&gt;a&lt;/sup&gt; g.</th>
<th>Yield %</th>
<th>M.P.&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M.P. Lit.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benzylamine</strong></td>
<td>1.65</td>
<td>61</td>
<td>235-237</td>
<td>237&lt;sup&gt;76&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>p-Methylbenzylamine</strong></td>
<td>1.66</td>
<td>67</td>
<td>231-233</td>
<td>232-234&lt;sup&gt;75&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>p-Chlorobenzylamine</strong></td>
<td>1.53</td>
<td>68</td>
<td>266-268</td>
<td>267-268&lt;sup&gt;96&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>p-Methoxybenzylamine</strong></td>
<td>1.62</td>
<td>70</td>
<td>253-254</td>
<td>254&lt;sup&gt;75&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>p-Nitrobenzylamine&lt;sup&gt;b&lt;/sup&gt;</strong></td>
<td>1.29</td>
<td>59</td>
<td>319-320</td>
<td>320&lt;sup&gt;75&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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(a) Weight of dried crude derivative precipitated from an initially saturated solution of the dinitrophenylhydrazone.

(b) Generated in situ from p-nitrobenzylamine sulfate.

(c) Melting point of the derivative after crystallization from ethanol.
0.49 mole) and calcium sulfate dihydrate (50 g., 0.29 mole). The oxidation was quite exothermic, raising the temperature of the mixture to 75° almost immediately. The reaction mixture was heated rapidly in order to effect distillation as quickly as possible. Manganese dioxide soon began to precipitate. The stirred mixture was distilled to dryness; the inorganic residue made stirring rather difficult towards the end of distillation. The distillate was extracted with petroleum ether (30-60°). Solvents were evaporated from the extract and the residual liquid was fractionated to give cyclohexanone (11.5 g., 56%).

(82a) An aliquot from the distillate gave cyclohexanone 2,4-dinitrophenylhydrazone in 65% yield when treated with 2,4-dinitrophenylhydrazine.

b.p. 153-156°; lit.76 155° (2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 160-161°; lit.76 162°) and a high boiling material (4.5 g.).

Cyclohexylamine was oxidized under varied experimental conditions. The following experiments failed to give cyclohexanone in any reasonable yield:

1. Dropwise addition of cyclohexylamine to permanganate solution over a longer period of time gave very small amounts of cyclohexanone. Adipic acid (26%) was isolated from the reaction mixture;
2. When permanganate solution was added to cyclohexylamine dropwise in \( \sim 0.5 \) hr., cyclohexanone was obtained in very low yields (5-10%);

3. When the reaction was effected at room or lower temperatures and steam distillation was avoided, an unidentified high boiling material was obtained. Only very small amounts of cyclohexanone was formed;

4. Cyclohexylamine when oxidized with one to two equivalents of permanganate gave again high boiling material and only 5-15% of cyclohexanone.

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(83) This material gave cyclohexanone 2,4-dinitrophenylhydrazone when treated with 2,4-dinitrophenylhydrazine solution but was not investigated further.

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**Oxidation of Dicyclohexylamine**

**Isolation of Cyclohexanone**

Dicyclohexylamine (15 g., 0.0826 mole) was rapidly added to a warm (\( \sim 55^\circ \)) stirred solution of potassium permanganate (60 g., 0.38 mole) and calcium sulfate dihydrate (43 g., 0.25 mole) in water: \( t \)-butyl alcohol (1:1, 750 ml.). The temperature of the mixture rose to 75\(^\circ\) immediately as a result of exothermic oxidation. The reaction mixture was heated rapidly in order to effect
distillation as quickly as possible. Manganese dioxide soon began to precipitate. The reaction mixture was distilled to dryness while stirred; the inorganic residue made the stirring difficult towards the end of distillation. The distillate was extracted with petroleum ether (30-60°). Solvents were removed through a fractionating column and the residue distilled to give cyclohexanone (10.9 g., 67%), b.p. 154-156°; lit. 76, 155°, (2,4-dinitro-

(82b) An aliquot of the distillate gave cyclohexanone 2,4-dinitrophenylhydrazone in 76% yield when treated with 2,4-dinitrophenylhydrazine solution.

phenylhydrazone, m.p. and mixed m.p. 160-162°; lit. 76 162°) and a high boiling material (2.5 g.).

Oxidation of 2-Aminoheptane

Isolation of 2-Heptanone

2-Aminoheptane (20 g., 0.174 mole) was rapidly added to a warm (∼50°) stirred solution of potassium permanganate (55 g., 0.35 mole, ∼3.0 equivalents) and calcium sulfate dihydrate (30 g., 0.17 mole) in water:butyl alcohol (1:1, 800 ml.). The mixture was heated in order to effect distillation to dryness as rapidly as possible. The distillate was extracted exhaustively with ether. The product, obtained after removal of solvents through a fractionating
column, was distilled to give 2-heptanone (11.8 g., 59\%\(^\text{82c}\))

(82c) An aliquot from the distillate gave 2-heptanone 2,4-dinitrophenylhydrazone in 69\% yield when treated with 2,4-dinitrophenylhydrazine solution.

b.p. 149-152\(^\circ\); lit. 76 89\(^\circ\) and a high boiling material (5.0 g.).

Preparation of Diphenylmethyl Bromide

A mixture of diphenylmethane (168 g., 1.0 mole), N-bromosuccinimide (185 g., 1.04 mole) and carbon tetrachloride (1.0 l.) was refluxed for 7 hr. The reaction mixture was filtered to remove succinimide. The filtrate was evaporated and the crude product crystallized from ethanol to give diphenylmethyl bromide, yield: 167 g., (66\%); m.p. 44-45\(^\circ\); lit. 75 45\(^\circ\).

Preparation of N-Phenylbenzhydrylamine\(^\text{84}\)


Diphenylmethyl bromide (44 g., 0.177 mole) was added over a period of 1 hr. to a hot (\(\sim 90\)^\circ) stirred suspension of aniline (20 g., 0.215 mole) and sodium bicarbonate (21 g., 0.25 mole) in water (50 ml.). After 4 hr. the
layers were separated and the organic product vacuum distilled to give N-phenylbenzhydramine; b.p. 182-185°/ 2mm.; m.p. 56-58°; lit. 58°; yield 28 g. (61%).

**Oxidation of N-Phenylbenzhydramine**

**Isolation of N-(Diphenylmethyl)-N,N',1,1-tetraphenylmethanediamine**

N-Phenylbenzhydramine (1.0 g., 0.00385 mole) was rapidly added to a stirred water:acetone (1:20, 42 ml.) solution of potassium permanganate (0.41 g., 0.0026 mole, 1.0 equivalent) and zinc sulfate (0.5 g., 0.0017 mole). After 4 hr., the mixture was filtered and solvents evaporated. Crude N-(diphenylmethyl)-N,N',1,1-tetraphenylmethanediamine was crystallized from ethanol as colorless prisms: m.p. 82-83°, lit. 83°; yield 0.78 g., (78.5%). This melting point was not depressed by admixture with a sample which was prepared by mixing equimolar quantities of N-phenylbenzhydramine and N-diphenylmethyleneaniline in acetone and subsequent crystallization from ethanol.

**Anal. Calcd. for C_{38}H_{32}N_{2}:** N, 5.42. Found: N, 5.41.


The infrared spectrum (given in Appendix) showed an absorption band at 3.05 μ (NH); there was no absorption for a carbon double bond nitrogen linkage.
Oxidation of Benzhydrylamine

A water:acetone (1:10, 44 ml.) solution of benzhydrylamine (2.0 g., 0.0109 mole), potassium permanganate (1.2 g., 0.0076 mole, 1.0 equivalent) and zinc sulfate (1.0 g., 0.0035 mole) was stirred for 0.75 hr. The reaction mixture was filtered and the filtrate evaporated. The oily residue decomposed on storage for about 15 days to give ammonia and N-diphenylmethylenebenzhydrylamine; yield 1.4 g., (74%), m.p. and mixed m.p. 150-151°; lit. 152-153°.


Oxidation of Benzhydrylamine

Isolation of Benzophenone Azine

Benzhydrylamine (5.0 g., 0.0272 mole) was added in one portion to a warm (~70°) stirred solution of potassium permanganate (4.5 g., 0.0285 mole, 1.5 equivalents) and calcium sulfate dihydrate (2.5 g., 0.0145 mole) in water:t-butanol (1:1, 100 ml.). The mixture was refluxed for 8 hr. and then filtered. The inorganic residue was washed with a small amount of ether. The combined filtrates were evaporated and benzophenone azine was crystallized.
from ethanol as bright yellow needles, m.p. 159-162°, lit. 162°, yield 3.6 g. (73%).


Anal. Calcd. for C26H20N2: C, 86.66; H, 5.59; N, 7.77.
Found: C, 87.10; H, 5.55; N, 7.67.

Oxidation of Diphenylmethaneimine

Isolation of Benzophenone Azine
And Benzophenone

Diphenylmethaneimine hydrochloride was prepared in 45% yield from benzophenone oxime. Diphenylmethaneimine hydrochloride (4.0 g., 0.0184 mole) was rapidly added to a warm and stirred water:tert-butyl alcohol (1:1, 50 ml.) solution of potassium permanganate (1.0 g., 0.006 mole, 0.5 equivalent), calcium sulfate (0.6 g., 0.00348 mole) and sodium hydroxide (0.78 g., 0.0195 mole) and the mixture refluxed for about 8 hr. The mixture was extracted with ether and filtered. The filtrate was evaporated and the residue chromatographed on neutral alumina using petroleum ether (30-60°) as an eluent to give benzophenone (1.85 g.,
HISTORICAL

Amines have been oxidized by many different reagents. The chemistry of such oxidations will be presently reviewed. The available literature is classified according to the oxidizing agent employed.

I. Oxidations with Potassium Permanganate*

Ethylamine on oxidation with potassium permanganate was reported in 1863 to give acetaldehyde.\(^1\) Diethylamine and triethylamine give acetic acid, n-butylamine yields butyric acid, and N-methylpropylamine gives propionic and formic acids on oxidation with potassium permanganate.\(^2\)

\(^1\) E. Carstanjen, J. prakt. Chem., 89, 486(1863).

\(^2\) O. Wallach and L. Claisen, Ber., 8, 1237(1875).

* Almost all the carbonyl compounds reported were isolated as 2,4-dinitrophenyldrazones or as similar derivatives.
55%; m.p. 46-48°; lit. 76 48°) and benzophenone azine (1.05 g., 32%; m.p. 160-162°; lit. 86 162°).

**Oxidation of Benzylamine**

**Isolation of N-[α-(Benzyldieneamino)benzyl] Benzamide, N,N'-(Iminodibenzylidene)bis-[Benzamide] and Benzoic Acid**

t-Butanol (50 ml.) was added to a stirred solution of potassium permanganate (6.25 g., 0.04 mole, 1.25 equivalents) and calcium sulfate (Drierite; 3.5 g., 0.0257 mole) in water (50 ml.). Benzylamine (5.0 g., 0.0466 mole) was then added in one portion to the resultant solution. As the reaction proceeded, a white precipitate began to appear on the surface. After 0.25 hr., the mixture was cooled in ice and triturated with ether. The ether insoluble product, N,N'(iminodibenzylidene)bis[benzamide] (which remained in ether as a white suspension) was filtered, washed with water, dried and crystallized from benzene as white pyramids; yield, 0.46 g. (9%); m.p. 158-160°.

**Anal. Calcd. for C_{28}H_{25}N_{3}O_{2}:** C, 77.22; H, 5.79; N, 9.64.

**Found:** C, 77.23; H, 5.88; N, 9.36.

**Mol. Wt. Calcd.:** 435.5. **Found:** 429.3.

Its infrared spectrum (given in Appendix) showed strong absorption bands for a NH grouping at 2.98 μ and an amide carbonyl at 6.07 μ.
The ether filtrate was washed with water and evaporated (at room temperature) to give \( \text{N-}[\alpha-(benzylideneamino)benzyl}\)-benzamide as white fluffy crystals: yield; 2.5 g. (51%); m.p. 146-149\(^\circ\); \( \lambda_{\text{max}} \) 248 \( \mu \) (log \( \varepsilon \) 4.35) in 95\% ethanol.

**Anal. Calcd. for C\(_{21}\)H\(_{18}\)N\(_2\)O:** C, 80.21; H, 5.78; N, 8.91.

**Found:** C, 79.57; H, 5.79; N, 9.17.

**Mol. Wt. Calcd.:** 314.4. **Found:** 298.7.

The infrared spectrum of the product (given in Appendix) exhibited absorption bands at 3.05 \( \mu \) (NH), at 6.07 \( \mu \) (amide carbonyl) and at 6.19 \( \mu \) (C=\( N \)).

The inorganic residue (after trituration with ether) was extracted with water. The water extract after acidification gave benzoic acid (1.1 g., 19.3\%), m.p. 121-122\(^\circ\). The melting point of the acid was undepressed by admixture with an authentic sample.

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**Acid Hydrolysis of \( \text{N-}[\alpha-(benzylideneamino)benzyl]\)-benzamide**

\( \text{N-}[\alpha-(benzylideneamino)benzyl]\)-benzamide (2.0 g., 0.00636 mole) was refluxed with dilute hydrochloric acid (25\% by wt., 12 ml.) for 0.25 hr. The mixture was cooled and extracted exhaustively with ether. The aqueous layer gave a positive test for ammonia (Nessler's reagent). The ether layer was evaporated and the residue added to sodium
bisulfite reagent. The bisulfite addition compound was prepared by addition of ethanol (10 ml.) to an aqueous solution of sodium bisulfite (50%, 40 ml.) and subsequent filtration.

(88) Sodium bisulfite reagent was prepared by addition of ethanol (10 ml.) to an aqueous solution of sodium bisulfite (50%, 40 ml.) and subsequent filtration.

filtered, washed with ether and added to 2,4-dinitrophenylhydrazine solution to give benzaldehyde 2,4-dinitrophenylhydrazone (3.55 g., 97.7%, 0.0124 mole, m.p. 236-237°C; lit. 237°C). The filtrate was extracted with ether; the ether extract gave benzamide (0.67 g., 86.5%, 0.0055 mole, m.p. and mixed m.p. 127-128°C; lit. 128°C).

Acid Hydrolysis of N,N'(iminodibenzyldene)bis[benzamide]

A mixture of N,N'(iminodibenzyldene)bis[benzamide] (1.0 g., 0.0023 mole) and dilute hydrochloric acid (25% by wt., 10 ml.) was refluxed for 0.25 hr. On working up the reaction mixture, benzaldehyde (0.45 g., 92%, 0.00424 mole, m.p. 236-237°C; lit. 237°C) and benzamide (0.49 g., 88%, 0.00406 mole, m.p. and mixed m.p. 127-128°C; lit. 128°C) was obtained.

(89) The procedure is described in the previous experiment.

(90) Estimated as the 2,4-dinitrophenylhydrazone; the reported weight of aldehyde was calculated from the weight of 2,4-dinitrophenylhydrazone obtained.
mixed m.p. 127-128°; lit.\textsuperscript{76} 128°) were isolated. The reaction mixture gave a positive test for ammonia (Nessler reagent).

**Benzoylation of**

\textbf{N-[a-(Benzyldieneamino)benzyl]benzamide}

A mixture of benzoyl chloride (1.0 g., 0.0071 mole), \textbf{N-[a-(benzyldieneamino)benzyl]benzamide} (1.0 g., 0.0032 mole) and pyridine (15 ml.) was warmed on a steam bath for 10 min. The reaction mixture was then poured into ice-cold 5\% sodium bicarbonate solution (150 ml.). The oily product solidified on standing. The mixture was filtered and the residue crystallized from ethanol to give \textbf{N,N'-benzyldinebies[benzamide]}; yield 0.74 g., (68\%) as colorless needles; m.p. 229-230°; lit.\textsuperscript{91} 231-232.5°.


**Anal. Calcd. for C\textsubscript{21}H\textsubscript{18}N\textsubscript{2}O\textsubscript{2}:** C, 76.31; H, 5.49; N, 8.48.

**Found:** C, 75.77; H, 5.50; N, 8.67.

**Mol. Wt. Calcd.:** 330.37. **Found:** 317.8.

The infrared spectrum exhibited strong absorption bands at 3.0 \(\mu\) (NH) and at 6.0 \(\mu\) (amide carbonyl).

The filtrate was added to 2,4-dinitrophenylhydrazine solution\textsuperscript{74} to give benzaldehyde 2,4-dinitrophenylhydrazone, yield 0.71 g. (25\%), m.p. 236-237°, lit.\textsuperscript{76} 237°.
**Acid Hydrolysis of**

**N,N'-Benzyldene bis[benzamide]**

A mixture of N,N'-benzyldene bis[benzamide] (1.0 g., 0.00302 mole) in dilute hydrochloric acid (25% by wt., 10 ml.) was refluxed for 0.25 hr. The reaction mixture on work-up gave benzaldehyde (0.298 g., 91%, 0.00276 mole, 2,4-dinitrophenylhydrazone 0.786 g., m.p. 236-237°, lit. 237°) and benzamide (0.662 g., 90%, 0.00545 mole, m.p. and mixed m.p. 127-128°, lit. 128°).

**Acetylation of**

**N-[α-(Benzyldieneamino)benzyl] benzamide**

N-[α-(Benzyldieneamino)benzyl] benzamide (0.5 g., 0.0016 mole) was dissolved in dilute hydrochloric acid (5%, 50 ml.). After the excess acid had been neutralized by addition of 5% sodium hydroxide solution, the mixture was cooled in ice and treated with acetic anhydride (5 ml.). The mixture was stirred vigorously and an aqueous solution of sodium acetate trihydrate (10%, 50 ml.) then added. The product which separated was filtered, washed and dried. The crude N-[α-acetamidobenzyl] benzamide was crystallized from ethanol; yield 0.34 g. (79%), m.p. 211-212°, lit. 206°.

Sodium Borohydride Reduction of N-\([\alpha-(benzylideneamino)benzyl]benzamide\)

Sodium borohydride (240 mg., 0.0064 mole) was added in one portion to a solution of N-\([\alpha-(benzylideneamino)benzyl]benzamide\) (2.0 g., 0.0064 mole) in absolute methanol (100 ml.) at room temperature. After a period of about 0.75 hr., water (200 ml.) was introduced. The white precipitate which appeared on addition of water, crystallized on storing the reaction mixture overnight in a freezer. The product was filtered, washed with water, dried and recrystallized from benzene to give N-\([\alpha-(dibenzylamino)benzyl]benzamide\) (1:1 g., 84%) as white feathery needles, m.p. 179-181°.

Anal. Calcd. for C\(_{28}\)H\(_{26}\)N\(_2\)O\(_2\): C, 82.73; H, 6.45; N, 6.89.

Found: C, 82.62; H, 6.16; N, 7.02.


Its infrared spectrum (given in Appendix) exhibited strong absorption bands at 2.98 μ (NH) and at 6.05 μ (amide carbonyl).
The aqueous filtrate on work-up yielded benzamide (0.32 g., 0.0026 mole, 82%, m.p. and mixed m.p. 127-128°, lit.76 128°).

**Acid Hydrolysis of N-α-(Dibenzy lamino)benzyl]benzamide**

N-α-(Dibenzy lamino)benzyl]benzamide (1.0 g., 0.00246 mole) was refluxed with dilute hydrochloric acid (25% by wt., 10 ml.) for 0.25 hr. The mixture was cooled and extracted exhaustively with ether. The aqueous layer was made basic and extracted with ether to give dibenzy lamine93

(93) Estimated as N-phenyl-N,N-dibenzylthiourea. The reported weight of amine was calculated from the weight of phenylthiourea obtained.

(0.43 g., 0.00218 mole, 88.6%, phenylthiourea, 0.73 g., m.p. and mixed m.p. 144-145°, lit.94 145-146°). The ether


layer on work-up89 gave benzaldehyde90 (0.24 g., 0.00226 mole, 92.5%, 2,4-dinitroph enylhydrazone 0.65 g., m.p. 236-237°, lit.76 237°) and benzamide (0.28 g., 0.00231 mole, 93.9%, m.p. and mixed m.p. 127-128°, lit.76 128°).
Sodium Borohydride Reduction of
\[ N\{a-(\text{benzylideneamino})\text{benzyl}\}\text{benzamide} \]

A solution of \[ N\{a-(\text{benzylideneamino})\text{benzyl}\}\text{benzamide} \] (0.5 g., 0.0016 mole) in absolute methanol (40 ml.) was added dropwise in 0.5 hr. to a stirred solution of sodium borohydride (60 mg., 0.0016 mole) in absolute methanol (25 ml.). The mixture was kept for 0.75 hr. and diluted with water (225 ml.). The reaction mixture was stored in a freezer overnight and the white crystalline \[ N\{a-(\text{benzylamino})\text{benzyl}\}\text{benzamide} \] collected, washed with water and dried, yield 0.365 g. (73%), m.p. 127-129°.

**Anal. Calcd. for C\(_{21}\)H\(_{20}\)N\(_2\)O:** C, 79.71; H, 6.37; N, 8.85.
**Found:** C, 79.92; H, 6.23; N, 8.63.

**Mol. Wt. Calcd.:** 316.4. **Found:** 317.3.

The infrared spectrum of the product (see Appendix) showed absorption for NH (3.05 µ) and amide carbonyl (6.05 µ) groups.

**Acid Hydrolysis of**
\[ N\{a-(\text{benzylamino})\text{benzyl}\}\text{benzamide} \]

\[ N\{a-(\text{benzylamino})\text{benzyl}\}\text{benzamide} \] (0.5 g., 0.00158 mole) was refluxed with dilute hydrochloric acid (25% by wt., 8 ml.) for 0.25 hr. The mixture was cooled and extracted exhaustively with ether. The aqueous layer on basification followed by ether extraction gave benzylamine\(^{93}\) (0.136, 0.00127 mole, 80.4%, phenylthiourea 0.308 g.,
m.p. and mixed m.p. 154-156°, lit. 76 156°). On working up the ether layer, benzaldehyde (0.151 g., 0.00141 mole, 89.5%, 2,4-dinitrophenylhydrazone 0.405 g., m.p. and mixed m.p. 236-237°, lit. 76 237°) and benzamide (0.174 g., 0.00144 mole, 91%, m.p. and mixed m.p. 127-128°, lit. 76 128°) were isolated.

Oxidation of p-Methylbenzylamine

Isolation of N-{p-Methyl-α-[p-methylbenzylidene]-
   amino}benzyl]-p-toluamide and N,N'-(Iminobis-
   (p-methylbenzylidene))bis[p-toluamide]

t-Butanol (50 ml.) was added to a stirred solution of potassium permanganate (5.5 g., 0.0348 mole, 1.25 equivalents) and calcium sulfate (Drierite, 3.25 g., 0.0238 mole) in water (50 ml.) and the mixture further stirred for about 5 min., followed by addition of p-methylbenzylamine (5.0 g., 0.0412 mole) in one portion. As the reaction proceeded, a white precipitate began to appear on the surface. After 10 min., the mixture was cooled in ice and triturated with ether. The ether insoluble product (a white suspension) was filtered, washed, dried and crystallized from benzene to give N,N'-(iminobis[p-methylbenzylidene])bis[p-toluamide] as a white crystalline solid; yield 0.56 g. (11%), m.p. 140-142°.
Anal. Calcd. for \( \text{C}_{32}\text{H}_{33}\text{N}_{3}\text{O}_{2} \): C, 78.17; H, 6.77; N, 8.55.
Found: C, 78.20; H, 6.87; N, 8.35.
The infrared spectrum (given in Appendix) exhibited strong absorption bands for NH (3.02 \( \mu \)) and amide carbonyl (6.07 \( \mu \)) groups.

The ether filtrate was washed with water, evaporated and the product crystallized from ether to give \( \text{N}-\left[p\text{-methyl}-\alpha-\left[(p\text{-methylbenzylidene})\text{amino}\right]\text{benzyl}\right]-p\text{-toluamide} \) as white fluffy needles; m.p. 125-129°, yield 3.71 g. (74%), \( \lambda_{\text{max}} 257 \text{ m} \mu \) (log \( \varepsilon \) 4.43) in 95% ethanol.

Anal. Calcd. for \( \text{C}_{24}\text{H}_{24}\text{N}_{2}\text{O} \): C, 80.87; H, 6.79; N, 7.85.
Found: C, 81.06; H, 6.97; N, 7.67.
The infrared spectrum (given in Appendix) exhibited absorption bands for a NH grouping (3.0 \( \mu \)), an amide carbonyl (6.03 \( \mu \)), and a Schiff base linkage (6.18 \( \mu \)).

**Acid Hydrolysis of \( \text{N}-\left[p\text{-Methyl}-\alpha-\left[(p\text{-methylbenzylidene})\text{amino}\right]\text{benzyl}\right]-p\text{-toluamide} \)**

A mixture of \( \text{N}-\left[p\text{-methyl}-\alpha-\left[(p\text{-methylbenzylidene})\text{amino}\right]\text{benzyl}\right]-p\text{-toluamide} \) (1.0 g., 0.0028 mole) and hydrochloric acid (37% by wt., 10 ml.) was refluxed for 0.25 hr. On work-up of the reaction mixture, \( p\text{-methylbenzaldehyde} \)
Acid permanganate has little action on tertiary amines except under conditions which are so vigorous that the amines are completely disrupted. Tetramethylammonium and tetraethylammonium salts are not affected by permanganate.\(^3\)


Benzylamine on oxidation with alkaline potassium permanganate gives benzaldehyde,\(^4,5\) benzoic acid\(^4,5\) and benzamide.\(^4\)


Work of the present dissertation proved this report to be in error.

Potassium permanganate is reported to oxidize dibenzylamine\(^5\) to tribenzylbenzoylhydrazine, dipropylamine\(^5\) to \(\alpha,\beta\)-dipropyl-\(\alpha,\beta\)-dipropionylhydrazine and piperidine\(^5\) to \(1,1'\)-bipiperidin]-2-one.

On oxidation with potassium permanganate in acetone benzhydrylamine yields benzophenone imine and 9-amino-fluorene gives 9-iminofluorene.\(^6\)

(0.65 g., 0.0054 mole, 96%, 2,4-dinitrophenylhydrazone 1.65 g., m.p. 232-234°C, lit. 75 232-234°C), and p-toluamide (0.34 g., 0.00251 mole, 89%, m.p. and mixed m.p. 158-160°C, lit. 76 160°C) were isolated. The aqueous layer gave a positive test for ammonia (Nessler's reagent).

Acid Hydrolysis of N,N'-[Iminobis(p-methyl-
benzylidene)]bis[p-toluamide]

N,N'-[Iminobis(p-methylbenzylidene)]bis[p-toluamide]
(0.5 g., 0.00102 mole) was refluxed with hydrochloric acid (37% by wt., 8 ml.) for 0.25 hr. On working up the reaction mixture, p-methylbenzaldehyde (0.229 g., 0.00191 mole, 95%, 2,4-dinitrophenylhydrazone 0.575 g., m.p. 231-233°C, lit. 75 232-234°C), and p-toluamide (0.243 g., 0.00178 mole, 88%, m.p. and mixed m.p. 158-160°C, lit. 76 160°C) were obtained. The aqueous layer gave a positive test for ammonia (Nessler's reagent).

Sodium Borohydride Reduction of N-[p-Methyl-
α-[p-methylbenzylidene)amino]-
benzyl]-p-toluamide

Sodium borohydride (0.113 g., 0.003 mole) was added in one portion to a solution of N-[p-methyl-α-[p-methyl-
benzylidene)amino]benzyl]-p-toluamide (1.07 g., 0.003 mole)
in absolute methanol (125 ml.) at room temperature. After 0.75 hr., water (200 ml.) was added; a white precipitate crystallized on storing the reaction mixture overnight in a freezer. The product was filtered, washed with water, dried and recrystallized from benzene to give \( N-[\alpha-[\text{bis-} (p\text{-methylbenzyl})\text{amino}]_2-p\text{-methylbenzyl}]_p\text{-toluamide} \) as a white crystalline solid; m.p. 146-148°, yield 0.458 g. (65%).

**Anal.** Calcd. for \( C_{32}H_{34}N_2O \): C, 83.08; H, 7.41; N, 6.05.

Found: C, 83.05; H, 7.37; N, 5.91.


Its infrared spectrum (given in Appendix) exhibited absorption bands for NH (3.07 \( \mu \)) and amide carbonyl (6.05 \( \mu \)) groups.

The aqueous filtrate on work-up gave \( p\text{-toluamide} \) (0.167 g., 0.00124 mole, 83%, m.p. and mixed m.p. 157-159°, lit. \( 160° \)).

Attempts\(^95\) to get \( p\text{-methyl-}N-[p\text{-methyl-}\alpha-[p\text{-methyl-benzyl}]\text{benzamido} \) benzamido on sodium borohydride reduction of \( N-[p\text{-methyl-}\alpha-[p\text{-methylbenzylidene})\text{amino}]_2-p\text{-toluamide} \) resulted in the formation of \( N-[\alpha-[\text{bis-} (p\text{-methylbenzyl})\text{amino}]_2-p\text{-methylbenzyl}]_p\text{-toluamide} \).

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(95) Reductions were effected at 25° and at 5° using sodium borohydride:substrate (1:1, 3:2, and 2:1) mole ratios in absolute methanol at each temperature.
irrespective of the order of addition of sodium borohydride.

**Oxidation of p-Chlorobenzylamine**

Isolation of p-Chloro-N-\([p\text{-chloro-\(\alpha\)-[(p-chloro-
benzylidene)aminobenzyl]benzamide}\) and
N,N'-[iminobis(p-chlorobenzylidene)]-
bis[p-chlorobenzamide]

\(t\)-Butyl alcohol (50 ml.) was added to a stirred
(\(\sim 15\) min.) solution of potassium permanganate (4.5 g.,
0.0285 mole, \(\sim 1.25\) equivalents) and calcium sulfate
(Drierite, 2.75 g., 0.0202 mole) in water (50 ml.). The
mixture was stirred for about 5 min. followed by addition
of \(p\)-chlorobenzylamine (5.0 g., 0.0352 mole) in one por-
tion. As the reaction proceeded, a white precipitate be-
gan to appear on the surface of the reaction mixture. After
10 min., the mixture was cooled in ice and tritiated with a
mixture of ether and methylene chloride (1:1). The ex-
tract was washed with water. Evaporation of solvents gave
a crude mixture of ether soluble and ether insoluble pro-
ducts. The crude product was added to ether (350 ml.) and
stirred. The ether insoluble product, N,N'-[iminobis-
(p-chlorobenzylidene)]bis[p-chlorobenzamide], was filtered,
washed, dried and crystallized from benzene as a white micro-
crystalline solid, m.p. 171-173\(^\circ\), yield 0.505 g. (10.4%).
Anal. Calcd. for $C_{28}H_{21}N_3O_2Cl_4$: C, 58.65; H, 3.66; N, 7.35.

Found: C, 58.85; H, 3.56; N, 7.56.


Its infrared spectrum (given in Appendix) showed the presence of NH (3.0 μ) and amide carbonyl (6.07 μ) functions.

The ether filtrate on evaporation and crystallization from ether gave $p$-chloro-$\bar{N}$-[p-chloro-$\alpha$-[(p-chlorobenzylidene) amino] benzyl] benzamide (3.68 g., 75%), a white crystalline solid (spheres), m.p. 154-157°, $\lambda_{max}$ 255 μ (log $\varepsilon$ 4.48) in 95% ethanol.

Anal. Calcd. for $C_{21}H_{15}N_2OCl_3$: C, 60.31; H, 3.63; N, 6.69.

Found: C, 60.20; H, 3.75; N, 6.81.


The infrared spectrum (given in Appendix) exhibited absorption bands for NH (3.05 μ), amide carbonyl (6.07 μ), and Schiff base linkages (6.21 μ).

**Acid Hydrolysis of $p$-Chloro-$\bar{N}$-[p-chloro-$\alpha$-[(p-chlorobenzylidene) amino] benzyl] benzamide**

A mixture of $p$-chloro-$\bar{N}$-[p-chloro-$\alpha$-[(p-chlorobenzylidene) amino] benzyl] benzamide (1.0 g., 0.0024 mole) and hydrochloric acid (37% by wt., 10 ml.) was refluxed for 0.25 hr. On working up the reaction mixture, $p$-chlorobenzaldehyde (0.62 g., 0.0044 mole, 92%, 2,4-dinitro-
phenylhydrazone 1.44 g., m.p. 266-268°, lit. 267-268°),

and p-chlorobenzamide (0.314 g., 0.00202 mole, 84%, m.p. and mixed m.p. 179-180°, lit. 179°) were obtained. The aqueous layer gave a positive test for ammonia (Nessler's reagent).

A mixture of N,N'-[iminobis(p-chlorobenzylidene)]bis[p-chlorobenzamide] (0.5 g., 0.000873 mole) and hydrochloric acid (37% by wt., 8 ml.) was refluxed for 0.25 hr. The work-up of the reaction mixture gave p-chlorobenzaldehyde (0.228 g., 93%, 0.00163 mole, 2,4-dinitrophenylhydrazone 0.48 g., m.p. 266-268°, lit. 267-268°) and p-chlorobenzamide (0.235 g., 86%, 0.00151 mole, m.p. and mixed m.p. 178-179°, lit. 179°). The reaction mixture gave a positive test for ammonia (Nessler's reagent).
Sodium Borohydride Reduction of p-Chloro-
N-[p-chloro-a-[p-chlorobenzylidene]-
amino]benzylbenzamide

Sodium borohydride (0.076 g., 0.002 mole) was added in one portion to a solution of p-chloro-N-[p-chloro-a-
[p-chlorobenzylidene]amino]benzylbenzamide (0.836 g., 0.002 mole) in absolute methanol (100 ml.) at room temperature. After 0.75 hr., water (200 ml.) was introduced. The white precipitate which appeared on addition of water, crystallized on storing the reaction mixture overnight in a freezer. The product was filtered, washed with water, dried and recrystallized from benzene to give p-chloro-N-[p-chloro-a-[p-chlorobenzyl]amino]benzylbenzamide as a white microcrystalline solid; m.p. 166-168°, yield 0.589 g. (70.4%).

Anal. Calcd. for C_{21}H_{17}N_{2}O_{2}Cl_{3}: C, 60.05; H, 4.06; N, 6.67. Found: C, 60.08; H, 4.03; N, 6.53.


The infrared spectrum (given in Appendix) exhibited absorption bands for NH (3.05 μ) and amide carbonyl (6.05μ) groups.

Attempts\(^{97}\) to obtain N-[α-[bis(p-chlorobenzyl)amino]-

\(^{97}\) Reductions were effected at room temperature using equimolar quantities of sodium borohydride and substrate in absolute methanol.

**Sodium Borohydride Reduction of p-Chloro-N-**

\[ p\text{-chloro-}\alpha\text{-}[(p\text{-chlorobenzyl})\text{amino}]\text{benzyl}]\text{benzamide and p-Chloro-N-} \]

\[ p\text{-chloro-}\alpha\text{-}[(p\text{-chlorobenzylidene})\text{amino}]\text{benzyl}]\text{benzamide Mixture} \]

Sodium borohydride (0.04 g., 0.001 mole) was added in one portion to a solution of p-chloro-N-[p-chloro-α-[p-chlorobenzyl]amino]benzyl]benzamide (0.42 g., 0.001 mole) and p-chloro-N-[p-chloro-α-[p-chlorobenzylidene]-amino]benzyl]benzamide (0.418 g., 0.001 mole) in absolute methanol (100 ml.) at room temperature. After 0.75 hr., water (200 ml.) was introduced. The product crystallized out on storing the reaction mixture overnight in a freezer. The product was filtered, washed with water, dried and re-crystallized from benzene to give p-chloro-N-[p-chloro-α-[p-chlorobenzyl]amino]benzyl]benzamide; yield 0.63 g. (75%), m.p. and mixed m.p. 165-167°.
Oxidation of p-Methoxybenzylamine

Isolation of $N\{p$-Methoxy-$\alpha-[$(p-methoxybenzylidene)amino]benzyl$]-p$-anisamide$^9\$

(98) A compound believed to be $N,N'$-[iminobis($p$-methoxybenzylidene)]bis[$p$-anisamide] on the basis of nitrogen analysis, was formed in trace amounts but was not investigated.

$t$-Butanol (50 ml.) was added to a stirred solution of potassium permanganate (4.75 g., 0.03 mole, $\sim 1.25$ equivalents) and calcium sulfate dihydrate (3.0 g., 0.0174 mole) in water (50 ml.). p-Methoxybenzylamine (5.0 g., 0.0364 mole) was then added in one portion. After 10 min., the mixture was cooled and extracted with ether. The ether extract was washed with water. Evaporation of ether and subsequent crystallization from ether gave $N\{p$-methoxy-$\alpha-[$(p-methoxybenzylidene)amino]benzyl$]-n$-anisamide as white crystalline spheres, m.p. 130-133, yield 4.33 g. ($^8\$); $\lambda_{max}$ 275 m$\mu$ (log e 4.57) in 95% ethanol. $\lambda_{max}$.

Anal. Calcd. for $C_{24}H_{24}N_2O_4$: C, 71.27; H, 5.98; N, 6.94.

Found: C, 71.34; H, 5.97; N, 7.15.


Its infrared spectrum (given in Appendix) exhibited absorption bands at 3.0 μ (NH grouping), at 6.12 μ (amide carbonyl grouping), and at 6.23 μ (imino linkage).
Acid Hydrolysis of $N$-$[p$-Methoxy-$\alpha$-
$[(p$-methoxybenzylidene)amino]$-
benzyl]-$p$-anisamide

A mixture of $N$-$[p$-methoxy-$\alpha$-
$[(p$-methoxybenzylidene)amino]$-
benzyl]-$p$-anisamide (1.0 g., 0.00247 mole) and
hydrochloric acid (37% by wt., 10 ml.) was refluxed for
0.25 hr. On working up the reaction mixture, $p$-methoxy-
benzaldehyde (0.598 g., 90%, 0.0044 mole, 2,4-dinitro-
phenylhydrazone 1.38 g., m.p. and mixed m.p. 253-254°,
lit. 254°) and $p$-anisamide (0.318 g., 86%, 0.00213 mole, m.p. and mixed m.p. 165-166°, lit. 167°) were
isolated. The aqueous layer gave a positive test for
ammonia (Nessler's reagent).

(99) J. W. Williams, W. T. Rainey and R. S. Leopold,

Sodium Borohydride Reduction of $N$-$[p$-Methoxy-
$\alpha$-$[(p$-methoxybenzylidene)amino]$-
benzyl]-$p$-anisamide

Sodium borohydride (0.095 g., 0.00248 mole) was
added in one portion to a solution of $N$-$[p$-methoxy-$\alpha$-
$[(p$-methoxybenzylidene)amino]$benzyl]-$p$-anisamide (1.0 g.,
0.00247 mole) in absolute methanol (100 ml.) at room
temperature. After a period of 0.75 hr., water (250 ml.)
was introduced. The product crystallized on storing the
reaction mixture for 4 days in a freezer. The solid was filtered, washed with water, dried and recrystallized from benzene to give $N-$[α-[bis(p-methoxybenzyl)amino]-p-methoxybenzyl]-p-anisamide as white tiny needles, m.p. 123-124°, yield 0.417 g. (64%).

Anal. Calcd. for $C_{32}H_{34}N_2O_5$: C, 72.98; H, 6.51; N, 5.32.

Found: C, 72.76; H, 6.73; N, 5.27.


Its infrared spectrum showed absorption bands at 3.0 μ (NH) and at 6.12 μ (amide carbonyl).

Attempts to obtain p-methoxy-N-[p-methoxy-α-[p-methoxybenzyl]amino]benzyl]benzamide on sodium borohydride reduction of $N-$[p-methoxy-α-[p-methoxybenzylidene)amino]-benzyl]-p-anisamide resulted in the formation of $N-$[α-[bis(p-methoxybenzyl)amino]-p-methoxybenzyl]-p-anisamide irrespective of the order of addition of the sodium borohydride.

**p-Nitrobenzylamine Sulfate**

*p-Nitrophenylacetic acid was obtained from p-nitrobenzyl cyanide (94% conversion) by the procedure**

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Secondary and tertiary amines containing substituted benzyl groups have been oxidized by potassium permanganate in acid media. In all cases the substituted benzylamino groups were oxidized to the corresponding benzaldehydes. Frequently acids corresponding to the substituted benzaldehydes were produced. The N-methyl group of such secondary and tertiary amines was resistant to oxidation.\(^7\)


Cyclohexylamine is oxidized to nitrosocyclohexane and cyclohexanone oxime by potassium permanganate in the presence of formaldehyde\(^8\) and acetaldehyde.\(^9\) Potassium permanganate oxidizes \(t\)-carbinamines to the corresponding nitro compounds in good yields.\(^{10}\)


\(^{9}\) I. Okamura and R. Sakurai, ibid., 2, 434(1952).

previously described. Sodium azide (40 g., 0.62 mole) was added in small portions to a stirred mixture of p-nitrophenylacetic acid (90.5 g., 0.5 mole) and concentrated sulfuric acid (500 ml.). Addition of sodium azide was regulated as to keep the temperature of the mixture about 35-55°. After sodium azide had been added and no more gas had been evolved, the mixture was stirred for 5 hr. The reaction mixture was then cooled to ~5°, and cold sodium hydroxide solution was added slowly and cautiously until the mixture was very alkaline. The alkalized reaction mixture was extracted with ether. On removal of ether a dark brown liquid was obtained which did not crystallize on standing overnight in a freezer, but gave a solid product (p-nitrobenzylamine sulfate) on treatment with sulfuric acid. Crude p-nitrobenzylamine sulfate was crystallized from ethanol as yellow tinged prisms, m.p. 230-232°, yield 54 g. (27%).

**Anal.** Calcd. for C_{14}H_{18}N_{4}O_{8}: N, 13.93.

**Found:** N, 14.06.

The identity of p-nitrobenzylamine sulfate was further proved by its conversion to N-p-nitrobenzylbenzamide (92% yield), m.p. 156-157°, lit. 75 155-156°, and N-p-nitrobenzylacetamide (89% yield), m.p. 132-133°, lit. 75 133°. Attempts to convert p-nitrobenzylamine sulfate into
p-nitrobenzylamine did not succeed. When p-nitrobenzylamine sulfate was treated with aqueous sodium hydroxide, a dark brown resinous material was obtained.

Oxidation of p-Nitrobenzylamine

Isolation of p-Nitro-\(N\)-[p-nitro-\(\alpha\)-[p-nitrobenzylidene]amino]benzyl]-benzamide, \(N,N'\)-[iminobis(p-nitrobenzylidene)]bis[p-nitrobenzamide], and p-Nitrobenzoic Acid

\(t\)-Butyl alcohol (50 ml.) was added to a stirred solution of potassium permanganate (3.4 g., 0.0215 mole, \(\sim 1.25\) equivalents), calcium sulfate dihydrate (2.5 g., 0.0145 mole) and sodium hydroxide (1.0 g., 0.025 mole) in water (50 ml.). The mixture was further stirred for about 5 minutes followed by addition of p-nitrobenzylamine sulfate (5.0 g., 0.0124 mole) in one portion. After the reaction was complete (\(\sim 10\) min.), the mixture was cooled (\(\sim 25^\circ\)) in ice and triturated with a mixture of ether:methylene chloride (1:1). The product in suspension, was filtered, washed well with ether, methylene chloride, dichloroethane and benzene successively and dried to give \(N,N'\)-[iminobis(p-nitrobenzylidene)]bis[p-nitrobenzamide] (0.381 g., 10.4%), as a grey powdery substance, m.p. 184-186\(^\circ\).
Because of its insolubility its molecular weight could not be determined. Its infrared spectrum (given in Appendix) exhibited strong absorption bands at 3.01 μ (NH) and at 6.07 μ (amide carbonyl).

The filtrate was washed with water. Evaporation of ether and methylene chloride gave p-nitro-N-[p-nitro-α-[(p-nitrobenzylidene)amino]benzyl]benzamide (2.06 g., 46%), a yellow micro-crystalline solid, m.p. 153-156°, \( \lambda_{\text{max.}}^{\text{EtOH}} 269 \text{ mp} \) (log \( \varepsilon \) 4.56).

Its infrared spectrum (given in Appendix) showed absorption bands for NH (3.0 μ), amide carbonyl (6.05 μ) and imine groups (6.23 μ).

The inorganic residue (after trituration with organic solvents) on washing with water and subsequent acidification gave p-nitrobenzoic acid (0.52 g., 12.7%), m.p. and mixed m.p. 240-241°; lit. 76-241°.
Acid Hydrolysis of \( p \)-Nitro-\( N \)-[\( p \)-Nitro-\( \alpha \)-[\( p \)-Nitrobenzylidene]amino]benzyl]benzamide

A mixture of \( p \)-Nitro-\( N \)-[\( p \)-Nitro-\( \alpha \)-[\( p \)-Nitrobenzylidene]amino]benzyl]benzamide (1.0 g., 0.00222 mole) and hydrochloric acid (37% by wt., 10 ml.) was refluxed for 0.25 hr. On working up the reaction mixture, \( p \)-Nitrobenzaldehyde \( ^{90} \) (0.604 g., 90%, 0.00399 mole; 2,4-Dinitrophenylhydrazone 1.34 g., m.p. 318-320\(^\circ\), lit. \( 75 \) 320\(^\circ\)) and \( p \)-Nitrobenzamide (0.33 g., 85.5%, 0.0019 mole, m.p. and mixed m.p. 201-202\(^\circ\), lit. \( 76 \) 201\(^\circ\)) were isolated. The aqueous layer gave a positive test for ammonia (Nessler's reagent).

Acid Hydrolysis of \( N,N' \)-[Iminobis(\( p \)-Nitrobenzylidene)]bis[\( p \)-Nitrobenzamide]

\( N,N' \)-[Iminobis(\( p \)-Nitrobenzylidene)]bis[\( p \)-Nitrobenzamide] (0.5 g., 0.00081 mole) was refluxed with hydrochloric acid (37% by wt., 8 ml.) for 20 min. On working up the reaction mixture, \( p \)-Nitrobenzaldehyde \( ^{90} \) (0.231 g., 94%, 0.00153 mole, 2,4-Dinitrophenylhydrazone 0.51 g., m.p. 317-319\(^\circ\), lit. \( 75 \) 320\(^\circ\)) and \( p \)-Nitrobenzamide (0.23 g., 86%, 0.0014 mole, m.p. and mixed m.p. 201-202\(^\circ\) lit. \( 76 \) 201\(^\circ\)) were obtained. The aqueous layer gave a positive test for ammonia (Nessler's reagent).
Sodium Borohydride Reduction of p-Nitro-N-
[(p-nitro-a-[(p-nitrobenzylidene)amino]benzyl)benzamide

Sodium borohydride (0.019 g., 0.0005 mole) was
added in one portion to a solution of p-nitro-N-
[p-nitro-a-[(p-nitrobenzylidene)amino]benzyl]benzamide (0.225 g.,
0.0005 mole) in absolute methanol (100 ml.). The reaction
mixture was allowed to stand for 1 hr. Water (250 ml.)
was then added. A pale yellow precipitate crystallized
from the mixture on standing in a freezer for 4 days. The
product was filtered, washed with water, dried and recry-
stallized from benzene to give p-nitro-N-[p-nitro-a-
[(p-nitrobenzyl)amino]benzyl]benzamide (0.108 g., 47%),
a pale yellow micro-crystalline solid, m.p. 124-126°C.

Anal. Calcd. for C21H17N5O7: C, 55.87; H, 3.80; N, 15.52.
Found: C, 56.05; H, 3.94; N, 15.59.


The infrared spectrum (given in Appendix) exhibited absorp-
tion bands at 2.9 μ (NH) and at 6.0 μ (amide carbonyl).

Attempts to obtain N-[α-[bis(p-nitrobenzyl)amino]-
p-nitrobenzyl]-p-nitrobenzamide by sodium borohydride
reduction of p-nitro-N-[p-nitro-a-[(p-nitrobenzylidene)-
amino]benzyl]benzamide gave p-nitro-N-[p-nitro-a-[(p-
nitrobenzyl)amino]benzyl]benzamide irrespective of the
order of addition of the reducing agent.
Oxidation of Dibenzylamine

Isolation of \( N-\{\alpha-(\text{Dibenzylamino})-\text{benzyl}\}\text{benzamide} \)

t-Butyl alcohol (40 ml.) was added to a stirred (\(\sim 15\) min.) solution of potassium permanganate (2.65 g., 0.0168 mole) and calcium sulfate dihydrate (1.8 g., 0.01 mole) in water (40 ml.). After the mixture had been stirred 5 min., dibenzylamine (5.0 g., 0.025 mole) was added in one portion (but not rapidly). After 10 min., the mixture was cooled and extracted with ether.\(^{101}\) The ether extract was washed with water. Evaporation of ether and crystallization of the residue from benzene gave \( N-\{\alpha-(\text{dibenzylamino})\text{benzyl}\}\text{benzamide} \) (3.21 g., 62.3\%), as white fine needles, m.p. 179-181°. Its identity was proved by the mixed melting point and comparison of its infrared spectrum with an authentic sample of \( N-\{\alpha-(\text{dibenzylamino})-\text{benzyl}\}\text{benzamide} \) obtained on sodium borohydride reduction of \( N-\{\alpha-(\text{benzylideneamino})\text{benzyl}\}\text{benzamide} \).
Preparation of Benzoyltribenzylhydrazine

Tribenzylhydrazine hydrochloride was prepared in 62% yield from benzyl chloride and hydrazine hydrate. Benzoyl chloride (4.0 g., 0.028 mole) was added to a warm (≈80°) stirred suspension of tribenzylhydrazine hydrochloride (2.0 g., 0.0084 mole) and anhydrous sodium carbonate (4.0 g., 0.038 mole) in pyridine (50 ml.). The mixture was refluxed for 1 hr., cooled and added to water (250 ml.). An oily material soon separated which solidified on standing. The product was filtered, dried and crystallized from ethanol to give benzoyltribenzylhydrazine (2.11 g., 88%) as colorless plates, m.p. 108-109°.

Anal. Calcd. for C₂₈H₂₆N₂O₂: C, 82.73; H, 6.45; N, 6.89.
Found: C, 82.89; H, 6.29; N, 6.89.

Its infrared spectrum (given in Appendix) showed the absence of NH but the presence of amide carbonyl groups (6.04 μ). Addition of benzoyltribenzylhydrazine (0.5 g., 0.00123 mole) in ethanol (10 ml.) to 2,4-dinitrophenylhydrazine reagent gave no benzaldehyde 2,4-dinitrophenylhydrazone.

Benzoyltribenzylhydrazine remained unchanged in dilute hydrochloric acid on standing for 4 hr. Hence contrary to a literature report benzoyltribenzylhydrazine did not give benzaldehyde, benzamide and dibenzylamine in dilute acid.
Oxidation of Tribenzylamine

t-Butanol (50 ml.) was added to a stirred solution of potassium permanganate (5.0 g., 0.032 mole) and calcium sulfate dihydrate (3.0 g., 0.017 mole) in water (50 ml.). Tribenzylamine (5.0 g., 0.0174 mole) was rapidly added after stirring the mixture for 5 min. After 20 min., the mixture was cooled and extracted with ether. The ether extract was washed with water. Tribenzylamine (2.1 g., 42%, m.p. and mixed m.p. 90-92°, lit. 76 91°) and benzaldehyde (0.94 g., 17%; 2,4-dinitrophenylhydrazone

(102) Estimated as the 2,4-dinitrophenylhydrazone of an aliquot.

2.55 g., m.p. and mixed m.p. 235-237°, lit. 76 237°) were isolated on removal of the ether. The infrared spectrum of the crude product showed a weak band at 6.07 μ indicating the presence of an unidentified amide (small amounts). There was no NH absorption in the infrared spectrum of the crude product, giving a clue to the absence of dibenzylamine as an oxidation product. The absence of dibenzylamine was confirmed by gas-liquid chromatographic analysis. 103, 104

(103) The help rendered by Mr. Peter Sargeant and Mr. George Baum of this department in running G.L.C. analysis is thankfully acknowledged.

(104) A 5 ft. column of 23% by weight of silicone grease on fire brick (42-60 mesh) with helium as carrier gas was used at 180°.
The inorganic residue (after ether extraction) was washed with water. The aqueous extract on acidification and subsequent ether extraction gave benzoic acid (1.96 g., 31%; m.p. and mixed m.p. 121-122°, lit. 121°).

**Oxidation of Tributylamine**

Tributylamine (50 g., 0.27 mole) was added to a cold (\(\sim 10^\circ\)) and stirred solution of potassium permanganate (85 g., 0.54 mole) and calcium sulfate dihydrate (50 g., 0.29 mole) in water: \(\frac{1}{2}\)-butanol (1:1, 1 l.) over a period of 2 min. After the reaction was complete (\(\sim 7\) min.), the mixture was filtered, the inorganic residue washed with ether, and the combined filtrates extracted with ether. The mixture of products obtained on removal of solvents was fractionated to give tributylamine (21.3 g., 42.6%, b.p. 53-54°/1 mm., lit. 216.5°) and N,N-dibutylbutyramide (5.1 g., 95%, b.p. 74-76°/0.5 mm., \(n^2_{D} \) 1.4442; lit. 105 b.p. 142°/17 mm., \(n^2_{D} \) 1.4443). The infrared


spectra of N,N-dibutylbutyramide exhibited strong bands
at 3.45 μ and 6.05 μ. Gas-liquid chromatography\textsuperscript{103, 106}

(106) A 15 ft. column of 5% by weight of silicone oil No. 550 on flouropack with helium as carrier gas was used at 125°.

confirmed the presence of tributylamine, N,N-dibutyl-
butyramide and revealed the presence of dibutylamine
(\sim 8\%) in the ether soluble fraction of oxidation products
of tributylamine. Only very small amounts of N,N-dibutyl-
formamide were detected. The aqueous layer was concen-
trated, acidified and extracted with ether to give butyric
acid 12.5 g., 17\%). The identity of butyric acid\textsuperscript{107} was

(107) The butyric acid was converted into methyl butyrate
for G.L.C. analysis.

further proved by gas-liquid chromatographic analysis.\textsuperscript{108}

(108) A 5 ft. column of 23% by weight of silicone grease
on firebrick (42-60 mesh) with helium as carrier
gas was used at 46°.

Only small amounts of propionic acid were detected. Butyr-
aldehyde\textsuperscript{102} (6.9 g., 12\%; 2,4-dinitrophenylhydrazone 31.5 g.,
m.p. 120-122°, lit.\textsuperscript{76} 122°) was also obtained.
II. Oxidations with Manganese Dioxide

Solid manganese dioxide oxidizes benzylamine, N-methyl-benzylamine and N-methylpiperonylamine to the corresponding Schiff bases.\(^ {11} \) \( \text{N,N-Dialkylanilines react with manganese} \)


Manganese dioxide at room temperature. Dimethylaniline gives N-methylformanilide; diethylaniline yields formanilide and acetaldehyde; \( \text{N,N-diphenylpiperazine is converted to N,N-diformyl-N,N-diphenylethlenedihamine.} \)\(^ {12} \)

\(^ {12} \) H. B. Henbest and A. Thomas, Chem. and Ind., 1097 (1956).

The three reactions discernable in oxidation of \( \text{N-alkyl- and N,N-dialkylanilines with manganese dioxide are:} \)

(a) formation of amides (Equation 1);

(b) dealkylation with formation of an aliphatic aldehyde (Equation 2);

(c) dehydrogenation followed by oxidative cleavage of the resultant enamine\(^ {13} \) (Equation 3).

Oxidation of Tributylamine Under Anhydrous Conditions

Tributylamine (50 g., 0.27 mole) was added to a cold (\(\sim 10^\circ\)) stirred mixture of potassium permanganate (85 g., 0.54 mole) and calcium sulfate dihydrate (50 g., 0.29 mole) in anhydrous acetone (700 ml.) in 2 min. After 0.25 hr., the mixture was filtered and the residue washed with water. The combined filtrates were extracted with ether. The aqueous layer was concentrated, acidified and extracted with ether to give small amounts of organic acids (\(\sim 1.0\) g., \(\sim 1.5\text{-}2.0\%\)). The ether layer on removal of solvents gave tributylamine (\(\sim 23.0\) g., \(\sim 46\%\)), dibutylamine (\(\sim 3.25\) g., \(\sim 9\%\)), N,N-dibutylformamide (\(\sim 6.5\) g., \(\sim 15\%\)) and N,N-dibutylbutyramide (\(\sim 2.0\) g., \(\sim 4\%\)) as analysed by gas-liquid chromatography.\(^{103, 106}\)

The infrared spectrum of the crude product exhibited strong bands at 3.45 \(\mu\) and 6.02 \(\mu\).

Oxidation of Cyclopropylamine

Experiment A

Cyclopropylamine (1.0 g., 0.0175 mole) was rapidly added to a warm (\(\sim 50^\circ\)) stirred solution of potassium permanganate (2.0 g., 0.0127 mole) and calcium sulfate dihydrate (1.5 g., 0.0087 mole) in water: \(t\)-butanol (2:1,
The mixture was heated rapidly and distilled into 2,4-dinitrophenylhydrazine solution. The crude 2,4-dinitrophenylhydrazone was collected and dried; yield 0.29 g. (7.1%). The product was crystallized from ethanol to give an orange yellow micro-crystalline solid, m.p. 114-120°. This material was slightly soluble in carbon tetrachloride, chloroform and ether; soluble in dimethylsulfoxide. Its solution in dimethylsulfoxide turned dark on standing. This substance may be cyclopropanone 2,4-dinitrophenylhydrazone.

Found: C, 46.07; H, 3.61; N, 23.61.

Acrolein 2,4-dinitrophenylhydrazone (0.128 g., 3.12%, m.p. and mixed m.p. 163-165°, lit. 76 165°) was obtained as an insoluble material during crystallization. This residue was insoluble in grain alcohol.

**Experiment B**

The above was repeated. The crude 2,4-dinitrophenylhydrazone, instead of crystallizing from ethanol was cleaned with ether, to give a yellow micro-crystalline solid, m.p. 83-88°.

Found: N, 23.76.
Experiment C

Cyclopropylamine (1.0 g., 0.0175 mole) was added (in one portion) to a warm (~50°) stirred solution of potassium permanganate (2.0 g., 0.0127 mole) and calcium sulfate dihydrate (1.5 g., 0.0087 mole) in water: t-butyl alcohol (2:1, 60 ml.). The mixture was distilled into p-nitrophenylhydrazine reagent. The crude product was collected and dried, yield 0.225 g. (6.7%). The crude hydrazone was crystallized from benzene to give orange-red micro-crystalline solid, m.p. 88-91°.

Anal. Calcd. for C₉H₉N₃O₂: C, 56.54; H, 4.75; N, 21.98.

Found: C, 56.46; H, 4.69; N, 21.68.
APPENDIX

Infrared Spectra
\[
\ce{N-CH_3} \rightarrow \ce{N-CHO} \quad (1)
\]
\[
\ce{N-CH_2R} \rightarrow \ce{NH + ROHO} \quad (2)
\]
\[
\ce{N-CH_2-CH_2R} \rightarrow \ce{N-CH=CHR} \rightarrow \ce{NCHO + ROHO} \quad (3)
\]

Manganese dioxide converts \(N,N\)-dimethylbenzylamine, \(N,N\)-diethylbenzylamine and tribenzylamine to benzaldehyde, \(N,N\)-dimethylcyclohexylamine, \(N,N\)-diethylcyclohexylamine and cyclohexylamine to cyclohexanone, triethylenediamine to 1,4-diformylpiperazine, 1,2-dipiperidinoethane to 1-formylpiperidine and 1,4-dibenzylpiperazine to \(N,N\)-dibenzyl-\(N,N\)-diformylethlenediamine.\(^{14}\)


III. Oxidation with Ozone

Methylamine and dimethylamine give formaldehyde and trimethylamine yields trimethylamine-N-oxide when reacted with ozone at low temperatures; reaction is violent at
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room temperature.\textsuperscript{15, 16} Trimethylamine, triethylamine

\begin{enumerate}
\item W. Manchot, \textit{Ber.}, \textbf{46}, 1089(1913).
\item W. Strecker and H. Thienemann, \textit{ibid.}, \textbf{53}, 2096(1920).
\end{enumerate}

and tripropylamine are oxidized by ozone in various solvents; N-oxides, aldehydes, and secondary amines are the principal products formed.\textsuperscript{17} Recently amine oxides

\begin{enumerate}
\item W. Strecker and M. Baltes, \textit{ibid.}, \textbf{54}, 2693(1921).
\end{enumerate}

have been obtained in high yields on oxidation of aliphatic tertiary amines with ozone in chloroform at -50\textdegree. The reaction is believed to occur by the electrophilic attack of a terminal atom of ozone followed by loss of oxygen\textsuperscript{18}

\begin{enumerate}
\end{enumerate}

(Equation 4).

\begin{equation}
R_3N + O_3 \rightarrow R_3N^+ - \overset{0}{\underset{0^-}{2}} - R_3N^+ - O^- + O_2 \tag{4}
\end{equation}

Ozonolysis of alkylamines and arylalkylamines resulted in the corresponding acids.\textsuperscript{19}

\begin{enumerate}
\item F. P. Florentine, \textit{U. S. 2}, 793, 221, May 21(1957).
\end{enumerate}
IV. Oxidations with Hydrogen Peroxide

Ethylamine, amylamine and benzylamine hydrosulfates are converted to their corresponding aldehydes by hydrogen peroxide and ferrous sulfate.²⁰

(20) K. Suto, Biochem. Z., 71, 169(1915).

Oxidation of diethylamine²¹ by 30% hydrogen peroxide leads to ethyl acetate, acetic acid, ammonia and acetohydroxamic acid. 1-Diethylamino-4-aminopentane²² yields


(22) V. S. Smirnov and E. A. Shklyaruk, ibid., 20, 331 (1950).

ethanol, acetic acid, formaldehyde, hydroxamic acids, ammonia and succinic acid. Butylamine²² reacts with hot hydrogen peroxide to give butyric acid, the corresponding hydroxamic acid and ammonia. Potassium permanganate or chromic acid gives results similar to hydrogen peroxide; the same products result from oxidations of dibutylamine.²²
OXIDATION OF PRIMARY, SECONDARY, AND TERTIARY ALIPHATIC AMINES WITH BUFFERED PERMANGANATE

DISSERTATION
Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By
Surjan Singh Rawalay, B. Sc., M. Sc.

* * * * *

The Ohio State University
1962

Approved by
Adviser
Department of Chemistry
Oximes$^{23,24}$ have been prepared by oxidizing primary


(24) I. V. Antipina and S. N. Kazarnovskii, U.S.S.R.,

or secondary amines with hydrogen peroxide catalyzed by
alkali salts of tungstic, molybdic or uranic acids. Cyclo-

hexylamine$^{25}$ is converted to nitrosocyclohexane and


cyclohexanone oxime by hydrogen peroxide in sulfuric acid.
Aliphatic amines and ammonia are oxidized by hydrogen per-
oxide in the presence of sodium tungstate to form products
of the amine oxide type.$^{26}$

(26) O. L. Lebedeva and S. N. Kazarnovskii, Zhur. Obshchei

V. Oxidations with Peroxymonosulfuric Acid

Peroxymonosulfuric acid oxidizes benzylamine$^{27}$ to

(27) E. Bamberger and T. Scheutz, Ber., 34, 2262(1901).
benzaldoxime, phenylhydroxamic acid, benzonitrile and phenylnitromethane; methylamine\textsuperscript{28} yields formaldoxime,

\begin{equation}
\begin{array}{c}
\text{CH-NH}_2 \\
\xrightarrow{\text{HO-SO}_2-0-OH}
\text{C-NOH}
\end{array}
\end{equation}

Nitrosocyclohexane\textsuperscript{30, 31} and cyclohexanone oxime\textsuperscript{30} are formed in oxidation of cyclohexylamine; phenylacetic acid\textsuperscript{31} is obtained from 2-phenylethylamine.
VI. Oxidations with Oxygen

Reactions of methylamine, \(^{32}\) ethylamine \(^{32}\) and cyclopropanemethylamine \(^{33}\) with oxygen in the presence of copper have been studied. Methylamine and ethylamine give formaldehyde ammonia and acetaldehyde ammonia respectively; cyclopropanemethylamine yields cyclopropanecarboxaldehyde. Vapor-phase oxidation of methylamine, ethylamine, propylamine and butylamine \(^{34}\) bears a close similarity to hydrocarbon oxidation.

VII. Oxidations with Mercuric Acetate

Oxidation of substituted tertiary amines of the piperidine type with mercuric acetate has been studied. \(^{35}\)

1,2-Substituted bases yield \(\Delta^2\)-tetrahydropyridines
exclusively regardless of other substituents. 1,3-Di-
substituted piperidines yield mixtures of products of 
oxidation on each side of the ring. Secondary amines such 
as piperidine and pyrrolidine are not oxidized. N,N-Di-
methylbenzylamine and N,N-dimethylcyclohexylamine yield 
benzaldehyde and cyclohexanone respectively. These carbonyl 
compounds result from hydrolysis of intermediate enamines.

Mercuric acetate dehydrogenation of 1,2,3 and 
4-methylquinolizidines results in introduction of a double 
bond at the bridgehead carbon. The course of mercuric

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acetate oxidation of tertiary amines has been studied 
with a series of piperidines in which alkyl substituents 
on the ring have been varied with respect to position and 
degree. As a result of this study the authors are in a 
position to predict with some degree of assurance the 
fate of a given substituted piperidine when subjected to 
mercuric acetate oxidation. 11-Methyl-11-azabicyclo-

---


(5.3.1)hendecane, a tertiary amine in which the hydrogens 
on the equivalent α-tertiary carbons are sterically
prevented from attaining trans coplanarity with the N-Hg bond in the mercurated complex, undergoes demethylation with mercuric acetate. The importance of steric requirements in determining the site of mercuric acetate oxidation is thereby demonstrated.38


Pyrrolidines39 and methyl-substituted pyrrolidines40 are


oxidized by mercuric acetate to the corresponding \( \Delta^1 \)-pyrrolines and \( \Delta^2 \)-pyrrolines respectively. Mercuric acetate oxidation of many piperidino-alcohols can be controlled to give bicyclic oxazolidines and tetrahydro-1,3-oxazines in which the masked aldehyde or ketone carbon atom is at a bridgehead. The main side reaction is oxidation to give amidoalcohols.\(^4^1\)

\( (41) \) N. J. Leonard and W. K. Musker, \textit{ibid.}, 82, 5148(1960).

\( \) 

\section*{VIII. Oxidations with Alkyl Peroxides}

Thermal decomposition of di-tertiarybutyl peroxide in tributylamine results in 4,5-bis(dibutylamino)octane\(^4^2\) (Equation 6).


\[ \begin{align*}
2\text{Bu}_2\text{NCH}_2\text{Pr} + (\text{CH}_3)_3\text{C} - 00 - \text{C(}\text{CH}_3)_3 & \rightarrow 2(\text{CH}_3)_3\text{C} - \text{OH} + \\
\text{Pr} & \ | \ | \\
\text{Bu}_2\text{N} - \text{CH} - \text{CH} - \text{N} & \text{Bu}_2
\end{align*} \] (6)
Benzoyl peroxide effects dehydrogenation of triethylamine\(^4\(^3\)) (Equation 7).

\[
\text{Et}_3\text{N} + \text{Bz}_2\text{O}_2 \rightarrow \text{Et}_2\text{N}-\text{CH} = \text{CH}_2 + 2\text{BzOH} \quad (7)
\]

Oxidation of 4-methyl-2-pentylamine, 2,4,4-trimethyl-2-pentylamine, diisopropylamine and tri-n-propylamine with tert-butyl hydroperoxide has been studied\(^4\(^4\))

\[\text{(44) H. E. De La Mare, J. Org. Chem., 25, 2114(1960).}\]

at 60-110\(^0\). Primary and secondary amines possessing at least one alpha hydrogen give substituted ketimines (or aldimes) as the principal nitrogenous products when the oxidation is carried out in excess amine. Imines are produced when di-tert-butyl peroxide is decomposed in primary and secondary amines. A tertiary amine, tri-n-propylamine undergoes dealkylation on reaction with tert-butyl hydroperoxide; di-n-propylamine is the major nitrogenous product. Evidence has been obtained which indicates that free radicals are involved in these reactions;\(^4\(^4\))
this has also been confirmed by electron paramagnetic resonance techniques.\(^{45}\)


\section{Oxidations with Miscellaneous Agents}

Ethylamine\(^{46}\) and benzylamine\(^{47}\) are oxidized to acetaldehyde and benzaldehyde by potassium dichromate. Nitrogen and acetic acid are also obtained as oxidation products of ethylamine. Acetic acid, propionic acid and pentanoic acid are formed on oxidation of ethylamine, propylamine and amylamine\(^{48}\) respectively, with potassium dichromate. Cyclopentylamine\(^{49}\) is converted by copper and


\[(47)\] O. Coninck and A. Combe, Compt. rend., 127, 1221(1898).


osmium tetroxide to cyclopentanone. Cyclopropylamine on long exposure to oxygen yields acrolein, probably by isomerization of initially formed cyclopropanone. By oxidizing cyclopropylamine with osmium tetroxide without subsequent exposure to oxygen, a product similar to the hydrate of cyclopropanone was obtained, but the identity could not be proved. 2,2,2-Triphenylethylamine hydrochloride is converted to 2,2,2-triphenyl-N-2,2,2-


triphenylethyldeneethylamine when heated with mercuric oxide. Diethylamine is dehydrogenated by 2,3-dichloronaphthoquinone. The initial intermediate, N-ethyldiene-


ethyldiene, reacts with unchanged diethylamine to give ethylamine and N,N-diethylvinylamine. N-Bromosuccinimide effects dehydrogenation of tertiary amines to aldehydes and secondary amines. Acetaldehyde and benzaldehyde are

(52) S. Dunstan and H. B. Henbest, ibid., 4905 (1957).
obtained on oxidation of ethylamine and benzylamine respectively, with sodium 1,2-naphthoquinone-4-sulfonate.\(^{53}\)


Argentic picolinate\(^{54}\) and persulfate\(^{55, 56}\) oxidize


primary and secondary amines to their corresponding carbonyl derivatives. Primary amines containing an alpha methylene group are oxidized by iodine pentafluoride to the corresponding nitriles in good yields.\(^{57}\) Peracetic


acid\(^{58}\) has been employed in certain cases for oxidation


of aliphatic amines to nitroalkanes.
ACKNOWLEDGMENTS

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Helpful suggestions from my friend, Dr. S. Ranganathan are thankfully acknowledged.

Grateful appreciation is expressed to the Office of Ordnance Research for extending financial aid.
DISCUSSION OF RESULTS

Permanganate Oxidation of Aliphatic Amines

A number of aliphatic amines have been oxidized with permanganate in an attempt to develop a method for conversion of amines to the corresponding carbonyl compounds and to elucidate the mechanisms of the various oxidation reactions.

Amines are readily oxidized by aqueous potassium permanganate. The oxidations may be effected in many different ways to yield various products depending on which reactant is used in excess. Acids and bases affect the strength of potassium permanganate as an oxidant and thus the course and products of reaction; certain control of the oxidant was effected by its use under neutral conditions. Neutrality during oxidation with permanganate was attained with calcium sulfate as a buffer; zinc sulfate was also used in a few cases. Magnesium sulfate has been previously used as a buffer in potassium permanganate oxidations of other organic compounds; it was unsatisfactory in the present work.
Equivalents of oxidant were calculated on the basis that in neutral solution potassium permanganate is reduced to manganese dioxide (Equation 8).

$$2\text{KMnO}_4 + \text{H}_2\text{O} \rightarrow 2\text{KOH} + 2\text{MnO}_2 + 3(0) \quad (8)$$

Equation 8 shows that as the reaction proceeds the solution becomes alkaline; in the presence of calcium sulfate Equation 8 is modified to Equation 8a.

$$2\text{KMnO}_4 + \text{CaSO}_4 + \text{H}_2\text{O} \rightarrow \text{Ca(OH)}_2 + 2\text{MnO}_2$$

$$+ \text{K}_2\text{SO}_4 + 3(0) \quad (8a)$$

The calcium hydroxide produced is only slightly soluble in the solvent system and the solution remains practically neutral.

The various amines have been oxidized homogeneously in a mixture of water and tert-butanol. Water alone was unsatisfactory because of the insolubility of most of the amines (and their oxidation products) investigated. Under the experimental conditions tert-butanol is completely resistant to permanganate oxidation. All the reported yields of 2,4-dinitrophenylhydrazones have been corrected for solubility losses.
Oxidation of Benzylamine

Oxidation of benzylamine with buffered permanganate (1.25 equivalents) in water:1-butanol (1:1) at room temperature yielded \(N-[\alpha-(benzylideneamino)benzyl]benzamide\) (I, 51%), \(\text{N,N}'(\text{iminodibenzylidene})\text{bis[benzamide]}\) (II, 9%), benzoic acid (19.3%) and ammonia.

\[
\begin{align*}
\text{I} & : \text{O-} - \text{NH-CH-N=CH-} \text{O} \\
\text{II} & : \text{O-} - \text{NH-OH-NH-OH-NH-OH-} \text{O}
\end{align*}
\]

Separation of I and II was readily effected by utilizing the facts that I is ether soluble whereas II is ether insoluble. The infrared spectrum of I exhibited absorption bands at 3.05\(\mu\) for the NH grouping, at 6.07\(\mu\) for an amide carbonyl and at 6.19\(\mu\) for the imino (Schiff base) linkage. The ultraviolet spectrum of I displayed maximum absorption at 248 \(\mu\) in 95% ethanol and was identical with the ultraviolet spectrum of an equimolar mixture of benzamide and \(\text{N}-\text{benzylidenebenzylamine}\) in 95% ethanol. The molecular weight of I was 298.7; theory 314.4. Hydrolysis of I with
refluxing hydrochloric acid gave benzaldehyde (97.7%), benzamide (86.5%), and ammonia on the basis of the stochiometry indicated in Equation 9.

\[
\phi-\phi-\text{NH}-\phi-\text{CH}-\phi + 2\text{H}_2\text{O} \rightarrow \phi-\phi-\text{NH}_2 + 2\phi\text{CH}=0 + \text{NH}_3
\]

I

(9)

The infrared spectrum of II showed strong absorption bands for NH at 2.98 μ and for amide carbonyl at 6.07 μ. The molecular weight of II was 429.3; theory 435.5. As expected from the structure assigned, benzaldehyde (92%), benzamide (88%), and ammonia were formed on refluxing II with hydrochloric acid. The stoichiometry for hydrolysis of II, as summarized in Equation 10, indicates that 1 mole of II gives 2 moles of benzaldehyde, 2 moles of benzamide, and ammonia (Equation 10).

\[
\phi-\phi-\text{NH}-\phi-\text{NH}-\phi-\phi + 2\text{H}_2\text{O} \rightarrow 2\phi-\phi-\text{NH}_2 + 2\phi\text{CH}=0 + \text{NH}_3
\]

II

(10)
Due to the presence of an imino (Schiff base) group in I, it was of interest to investigate its chemistry in some detail. An excellent method for reduction of Schiff bases of the N-benzylideneaniline type with sodium borohydride has been reported.\(^{59}\) This method with minor modifications has been employed for selective reduction of the more complex Schiff bases obtained in the present investigation. Previously there has been no experimental evidence as to the mechanism of sodium borohydride reduction of Schiff bases, other than that the corresponding secondary amines are produced.

One of the important observations of this investigation is that reduction of N-benzylidene derivatives with sodium borohydride may give a simple reduction product (the secondary amine), or a more complex reduction product (a tertiary amine) depending on the nature of the substrate or the experimental conditions. The isolation of tertiary amines as products of reaction of sodium borohydride and Schiff bases gives insight into the possible mechanisms of these reductions. On addition of sodium borohydride (powder)
to an equimolar solution of I in absolute methanol, \( \text{N-} \left[ \alpha- \text{(dibenzylamino)benzyl} \right] \text{benzamide} \) (III, 84\%) and benzamide (82\%) (Equation 11) were obtained.

\[
\begin{align*}
2\Phi-\text{NH-CH-N}=\text{CH-}\Phi & \xrightarrow{\text{NaBH}_4} \Phi-\text{NH-CH-N}=\text{CH-CH}_2-\Phi \\
\text{I} & \rightarrow \text{III} \\
+ \Phi-\text{NH}_2 & + \left[ \Phi\text{CH}_2\text{NH}_2 \right]
\end{align*}
\]

A mechanism for this reaction is proposed in Equations 12 - 14.

\[
\begin{align*}
\text{I} & \xrightarrow{\text{NaBH}_4} \Phi-\text{NH-CH-NH-CH}_2-\Phi \\
\text{IV} & \rightarrow \\
\text{IV} + \text{I} & \rightarrow \Phi-\text{NH-CH-NH-CH}_2-\Phi \\
\text{V}
\end{align*}
\]
The infrared spectrum of III contained strong absorption bands at 2.98 μ (NH) and at 6.05 μ (amide carbonyl). The molecular weight of III was 396.3; theory 406.5. The structure of III was proved upon its hydrolysis with hydrochloric acid to benzamide (93.9%), benzaldehyde (92.5%) and dibenzylamine (88.6%) according to the stoichiometry of Equation 15.

\[
\phi-\phi-\text{NH-CH-N}^\text{CH}_2-\phi + \text{H}_2\text{O} \rightarrow \phi-\phi-\text{NH}_2 + \phi\text{CH}=\phi + \text{NH}^\text{CH}_2-\phi
\]

Surprisingly enough when an equimolar solution of I in methanol was added dropwise to a solution of sodium borohydride in methanol (instead of adding powdered sodium
borohydride to a methanol solution of I) N-\(\alpha\)-(benzyl-
aminobenzyl)benzamide (IV) was obtained in 73% yield
(Equation 15).

\[
\begin{align*}
\phi\phi\phi\text{-NH-CH-N=CH-}\phi & \xrightarrow{\text{NaBH}_4} \phi\phi\phi\text{-NH-CH-NH-CH}_2\phi \\
\text{I} & \quad \text{IV}
\end{align*}
\]

The reduction mechanism in this case may be simple or
complex (Equations 17 - 20).

**Possibility a --**

\[
\begin{align*}
\text{I} & \xrightarrow{\text{NaBH}_4} \text{IV} \\
(17)
\end{align*}
\]

**Possibility b --**

\[
\begin{align*}
\text{I} & \xrightarrow{\text{NaBH}_4} \text{IV} \\
(18)
\end{align*}
\]

\[
\begin{align*}
\phi\phi\phi\text{-NH-CH-N=CH-}\phi & \xrightarrow{\text{I + IV}} \phi\phi\phi\text{-NH-CH-}\phi \\
\phi\phi\phi\text{-NH-CH-NH} & \quad \text{V}
\end{align*}
\]

\[
\begin{align*}
\phi\phi\phi\text{-NH-CH-NH} & \xrightarrow{\text{NaBH}_4} 2\phi\phi\phi\text{-NH-CH-NH-CH}_2\phi \\
\text{V} & \quad \text{IV}
\end{align*}
\]
In the present investigation, it has been observed that amines add rapidly to imine functions; for this reason possibility b is preferred over possibility a. Further investigation is required to clarify this point.

The structure of IV was proved by its infrared spectrum, its molecular weight and its hydrolysis by hydrochloric acid to benzamide (91%), benzaldehyde (89.5%) and benzylamine (80.4%) in accordance with Equation 21.

\[
\begin{align*}
\phi-\text{NH-CH-NH-CH}_2-\phi & + H_2O \rightarrow \phi-\text{NH}_2 + \phi\text{OH}=0 + \phi\text{CH}_2-\text{NH}_2 \\
\text{IV} & 
\end{align*}
\]

(21)

Treatment of I in pyridine with benzoyl chloride, followed by addition of water gave \(N,N\)-benzylidene-bis[benzamide] (VI, 68%) and benzaldehyde (25%) (Equation 22).

\[
\begin{align*}
\phi-\text{NH-CH-N=CH-}\phi & \xrightarrow{\phi-\text{CH}_2-\text{Cl}} \phi-\text{NH-CH-NH-CH}_2-\phi + \phi\text{CH}=0 \\
\text{I} & \quad \text{VI}
\end{align*}
\]

(22)

A possible mechanism for this conversion is proposed in Chart A.
CHART A

\[ \phi-C-NH-CH-N=CH-\phi + \text{pyridine} + \phi-C-Cl \]

\[ \xrightarrow{H_2O} \]

\[ \left[ \phi-C=O \right] \quad \phi-C=O \]

\[ \xrightarrow{H_2O} \]

\[ \left[ \phi-C-NH-CH-NH-CH-\phi \right] \quad + \text{pyridine} \cdot \text{HCl} \]

\[ \xrightarrow{} \]

\[ \phi-C-NH-CH-NH-C-\phi \quad + \phiCH=O \]

VI
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The infrared spectrum of VI exhibited strong absorption bands at 3.0 \( \mu \) (NH) and at 6.0 \( \mu \) (amide carbonyl). Its experimental molecular weight agreed with that calculated. The structure was further substantiated by its hydrolysis to benzamide (90%) and benzaldehyde (91%) with hydrochloric acid. Stoichiometrically, 1 mole of VI gave 2 moles of benzamide and 1 mole of benzaldehyde within experimental error, as expected from Equation 23.

\[
\phi-\phi-NH-CH-NH-\phi + H_2O \rightarrow \phi-CH=0 + 2\phi-\phi-NH_2 \quad (23)
\]

Survey of the literature indicated that there was no previous example of benzoylation of a Schiff base as shown. To test the generality of this reaction, authentic N-benzylideneaniline, N-benzylidenebenzylamine and N-diphenylmethyleneaniline were each treated with benzoyl chloride and pyridine and then diluted with water to give N-phenylbenzamide (78%), N-benzylbenzamide (75%) and N-phenylbenzamide (71%) respectively (Equations 24 - 26).
Acetylation of I in cold 5% hydrochloric acid was effected by addition of acetic anhydride and then 10% sodium acetate to give \( \text{\textit{N}}-(\alpha\text{-acetamidobenzyl})\text{benzamide} \) (VII, Equation 27) in 79% yield.

\[
\begin{align*}
\phi\text{CH}=\text{N}-\phi & \xrightarrow{\text{\phi-\phi-Cl}} \phi\text{\textit{N}}_{-}\phi + \phi\text{CH}=0 \\
\phi\text{CH}=&\text{NCH}_{2}-\phi & \text{\phi-\phi-Cl} & \xrightarrow{\text{\phi-\phi-Cl}} \phi\text{\textit{N}}\text{CH}_{2}-\phi + \phi\text{CH}=0 \\
\phi\text{CO}=\text{N}-\phi & \xrightarrow{\text{\phi-\phi-Cl}} \phi\text{\textit{N}}_{-}\phi + \phi\text{C}=0
\end{align*}
\]

A sequence for the conversion is indicated in Chart B.
CHART B

\[ \phi-C-\text{NH-CH-N} = \text{CH}\phi + \text{CH}_3\text{C-O-C-CH}_3 \]

I

\[ \begin{array}{c}
\phi-C-\text{NH-CH-N} = \text{CH}\phi \\
\phi-C-\text{O-C-CH}_3
\end{array} \]

\[ \text{H}_2\text{O} \]

\[ \begin{array}{c}
\phi-C-\text{NH-CH-N} = \text{CH}\phi \\
\phi-C-\text{OH}
\end{array} \]

\[ \phi-C-\text{NH-CH-NH-C-CH}_3 + \phi\text{CH}=\text{O} \]

VII
The infrared absorption of VII showed the presence of NH (3.03 μ) and amide carbonyl (6.04 μ) groups. The experimental molecular weight was 256.7; theory 268.3.

Oxidation of benzyline to benzoic acid with potassium permanganate is well known though the mechanism of this oxidation is obscure. The isolation of I and II as intermediate oxidation products gives some help in possibly understanding the mechanism of oxidation of benzyline to benzoic acid with excess permanganate since both I and II are oxidized to benzoic acid with permanganate. One of various possible reaction sequences for the formation of I and II from benzyline on permanganate oxidation is indicated (Equations 28 - 33). Other sequences are not included because of the very tentative nature of any single scheme.

\[
\text{OCH}_2\text{NH}_2 \xrightarrow{[0]} \text{OCH}=\text{NH} + \text{H}_2\text{O} \tag{28}
\]

\[
\text{OCH}_2\text{NH}_2 + \text{OCH}=\text{NH} \rightarrow \text{O}\text{-CH}_2\text{-NH-CH-} \frac{\text{NH}_2}{\phi} \tag{29}
\]

\[
\text{OCH}_2\text{NH}_2 + \text{OCH}_2\text{NH-CH-} \frac{\text{NH}_2}{\phi} \rightarrow \text{OCH}_2\text{NH-CH-NHCH}_2-\phi + \text{NH}_3 \tag{30}
\]
The reason for the formation of the double bond (Schiff base linkage) in I by permanganate at the indicated position is not clear. The experimental facts from oxidation of other benzylamines are that the products arise from dehydrogenation of the methanemonoamine rather than the methanediamicine functions wherever there is competition between the two possibilities (Equations 34a - 34b).

\[
\phi CH_2-\text{NH}-\text{CH}-\text{NHCH}_2-\phi + \text{MnO}_4^- \rightarrow \phi-\text{NH}-\text{CH}-\text{N}=\text{CHR} \quad (34a)
\]

\[
\phi-\text{NH}-\text{CH}-\text{NH}-\text{CH}-\text{NHCH}_2-\phi + \text{MnO}_4^- \rightarrow \phi-\text{NH}-\text{CH}-\text{NH}-\text{NHCH}_2-\phi \quad (33)
\]

\[
\phi CH_2-NH_2 + I \rightarrow \phi-\text{NH}-\text{CH}-\text{NH}-\text{CH}-\text{NHCH}_2-\phi \quad (32)
\]

\[
\phi CH_2-NH_2 \quad \text{H}_2\text{O} \quad [0] \quad \phi CH_2-\text{NH}-\text{CH}-\text{NHCH}_2-\phi \quad (31)
\]
Oxidation of \( p \)-Methylbenzylamine

Oxidation of \( p \)-methylbenzylamine with buffered permanganate (1.25 equivalents) in water: \( t \)-butanol (1:1) at room temperature yielded \( N-\{p\)-methyl-\( \alpha-\[(p\)-methylbenzylidene)amino\]benzyl\] \(-p\)-toluamide (VIII, 74\%), \( N,N\)-benzylideneamino]benzyl\] \(-p\)-toluamide (VIII, 74\%), \( (IX_{N,N'}\)iminobis\( (p\)-methylbenzylidene\)]bis\[p\)-toluamide\] (IX, 11\%) and ammonia.

Oxidation product VIII is ether soluble whereas IX is ether insoluble; hence their separation is effected readily. The infrared spectrum of VIII showed absorption bands for a NH grouping (3.0 \( \mu \)), for amide carbonyl (6.03 \( \mu \)) and for an imino linkage (6.18 \( \mu \)). Product VIII exhibited ultraviolet absorption (\( \lambda_{\text{max}} \)) at 257 \( \mu \) (log \( \varepsilon \) 4.43) in 95\% ethanol. The structure assigned corresponds satisfactorily with the experimental molecular weight.
Hydrolysis of VIII with refluxing hydrochloric acid gave p-methylbenzaldehyde (96%), p-toluamide (89%), and ammonia according to the stoichiometry of Equation 35.

\[
\text{VIII} \quad + \quad 2\text{H}_2\text{O} \quad \rightarrow \quad \text{IX} \quad \text{NH}_2 \quad + \quad \text{CH}=\text{O} \quad + \quad \text{NH}_3
\]

Product IX exhibited strong infrared absorption bands for NH (3.02 μ) and amide carbonyl (6.07 μ) groups. Its molecular weight agreed with the structure assigned. As expected from the proposed structure, p-methylbenzaldehyde (95%), p-toluamide (88%) and ammonia were formed on hydrolysis of IX with refluxing hydrochloric acid. The stoichiometry for hydrolysis of IX, as in Equation 36, indicates that 1 mole of IX gives 2 moles of p-methylbenzaldehyde, 2 moles of p-toluamide and ammonia (Equation 36).

\[
\text{IX} \quad + \quad 2\text{H}_2\text{O} \quad \rightarrow \quad 2\text{NH}_2 \quad + \quad 2\text{CH}=\text{O} \quad + \quad 2\text{NH}_3
\]
Since VIII is a Schiff base, its reduction by sodium borohydride was of interest. When sodium borohydride (powder) was added to an equimolar solution of VIII in absolute methanol, \( N\left\{\alpha\left[\text{bis}(p\text{-methylbenzyl})\text{amino}\right]\text{p-methylbenzyl}\}\right\}_p\text{toluamide} (X, 65\%) \) and \( p\text{-toluamide} (83\%) \) (Equation 37) were obtained.

\[
\begin{align*}
\begin{array}{c}
\text{VIII} \\
2 \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3
\end{array}
\xrightarrow{\text{NaBH}_4, \text{CH}_3\text{OH}}
\begin{array}{c}
\text{X} \\
\text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3
\end{array}
\end{align*}
\]

A sequence for the conversion is indicated in Equations 38 - 40.

\[
\begin{align*}
\text{VIII} \xrightarrow{\text{NaBH}_4}
\begin{array}{c}
\text{XI} \\
\text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3
\end{array}
\end{align*}
\]
VIII + XI \rightarrow \text{(39)}

\[
\begin{align*}
\text{XII} & \quad \text{X}
\end{align*}
\]

XII $\text{NaBH}_4$ \rightarrow \text{(40)}
The infrared spectrum of X indicated the presence of
NH (3.07 μ) and amide carbonyl (6.05 μ) functions. Its
experimental molecular weight (453.8) agreed with that
calculated (462.6). It is interesting (but hard to explain)
that attempts to prepare \(^p\)-methyl-N-[\(^p\)-methyl-\(\alpha\)-[\(^p\)-methyl-
benzyl]amino]benzyl]benzamide (XI) on sodium borohydride
reduction of VIII resulted in X irrespective of the order
of addition of the reducing agent. The reduction experi-
ments were carried out at 25° and at 5° using various
mole ratios of sodium borohydride to substrate in absolute
methanol. The methyl group in the \(\text{para}\) position of XII in
some way directs the course of reductive cleavage of the
aminal linkage to give specifically the tertiary amine (X).

A tentative explanation for this fact is as follows:
intermediate XII contains a weak bonded aminal center;
one of its nitrogens is tertiary (\(-\text{N}-\)) whereas the other
is secondary (\(-\text{NH}-\)). The tertiary nitrogen is linked to
three \(^p\)-methylbenzyl groups whereas the secondary nitrogen
is attached to only two \(^p\)-methylbenzyl groups. Since a
\(^p\)-methyl group is electron donating, the nitrogen bonded
to the three \(^p\)-methylbenzyl groups is more electron rich
than that linked to only two such groups. Nucleophilic
attack of the borohydride ion on carbon effects displacement
of the \(-\text{NH}\) derivative rather than the \(-\text{N}\)- derivative since
the former is comparatively less electron rich and thus
a better leaving group.
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p-Methylbenzylamine may be oxidized to p-methylbenzoic acid or terephthalic acid with potassium permanganate. The mechanism of this oxidation is not clear. Isolation of VIII and IX as intermediates gives some insight to the mechanism of this oxidation and also confirms the results obtained on permanganate oxidation of benzylamine. As expected the methyl group of p-methylbenzylamine is resistant to permanganate under the experimental conditions. One of the possible oxidation sequences for formation of VIII and IX from p-methylbenzylamine is indicated (Equations 41 - 46). Other sequences are not given because of the speculation involved in any single scheme.

\[
\begin{align*}
\text{CH}_2\text{-NH}_2 & \xrightarrow{[0]} \text{CH=NH} + \text{H}_2\text{O} \\
\end{align*}
\] (41)

\[
\begin{align*}
\text{CH}_2\text{-NH}_2 + \text{CH=NH} & \rightarrow \text{CH}_2\text{-NH-CH-NH}_2 \\
\end{align*}
\] (42)
Although a specific reason for the formation of the imino linkage at the indicated position is not apparent, the
results of oxidation of \( p \)-methylbenzylamine are similar to that of benzylamine. The previous hypothesis that products result from dehydrogenation of a methanemonoamine rather than of a methanediamine function, is supported.

**Oxidation of \( p \)-Chlorobenzylamine**

\( p \)-Chlorobenzylamine on oxidation with buffered permanganate (1.25 equivalents) in water: \( t \)-butyl alcohol (1:1) at 25-30° gave \( p \)-chloro-\( N \)-[\( p \)-chloro-\( \alpha \)-\( p \)-chlorobenzylidene)amino] benzyl] benzamide (XII, 75%), \( \text{N,N}' \)-[iminobis-\( \beta \)-(\( p \)-chlorobenzylidene)] bis[\( p \)-chlorobenzamide] (XIV, 10.4%) and ___.

Separation of XIII and XIV was effected by their differences in solubility. XIII is fairly soluble in ether whereas XIV is very ether insoluble. The infrared spectrum of XIII agrees with the assigned structure; there are absorption bands for a NH group at 3.05 \( \mu \), an amide carbonyl at 6.07 \( \mu \), and an imino linkage at 6.21 \( \mu \).
Product XIII exhibited maximum absorption at 255 μm (logε 4.48) in 95% ethanol. Its experimental molecular weight was 424.2; theory 417.8. The structure of XIII was substantiated by its hydrolysis with hydrochloric acid to p-chlorobenzaldehyde (92%), p-chlorobenzamide (84%) and ammonia on the basis of the stoichiometry of Equation 47.

\[
8\text{-NH-CH-N=CH} + 2\text{H}_2\text{O} \rightarrow 8\text{-NH}_2 + \text{CH}=0 + \text{NH}_3
\]

(XIII)

Infrared absorption in XIV occurred for NH at 3.0 μ and amide carbonyl at 6.07 μ. The molecular weight of XIV (osmometry) was 556.7; theory 573.2. The structure of XIV was further substantiated by its hydrolysis with refluxing hydrochloric acid to p-chlorobenzaldehyde (93%), p-chlorobenzamide (86%) and ammonia as in Equation 48.

\[
8\text{-NH-CH-NH-CH-NH-} + 2\text{H}_2\text{O} \rightarrow 8\text{-NH}_2 + \text{CH}=0 + \text{NH}_3
\]

(XIV)
The possible reduction of the imino linkage of XIII with sodium borohydride was of interest. Previous attempts to obtain \( p \)-methyl-\( N-[p\)-methyl-\( \alpha-[p\)-methylbenzyl]amino]benzyl\)-benzamide (XI) on sodium borohydride reduction of \( N-[p\)-methyl-\( \alpha-[p\)-methylbenzylidene]amino]benzyl\)-\( p \)-toluamide (VIII) gave \( N-[\alpha-[\text{bis}(p\)-methylbenzyl]amino]-\( p \)-methylbenzyl\)-\( p \)-toluamide. The unexpected result was explained tentatively on the basis of a positive inductive effect of the \( p \)-methyl group. Sodium borohydride reduction of XIII, in which the \( p \)-chloro group has an electron withdrawing effect, might give the corresponding secondary amine specifically if the reduction is extremely sensitive to electrical factors.

When powdered sodium borohydride was added to an equimolar solution of XIII in absolute methanol at 25-30\(^\circ\), \( p \)-chloro-\( N-[p\)-chloro-\( \alpha-[p\)-chlorobenzyl]amino]benzyl\)-benzamide (XV, 70.4\%) was obtained (Equation 49).

\[
\text{III} \xrightarrow{\text{NaBH}_4} \text{XV} \quad (49)
\]
Possible mechanisms for this conversion are indicated in Equations 50 - 52.

\[
\text{XIII} + \text{XV} \rightarrow \text{XVI} \quad (51)
\]
The infrared spectrum of XV exhibited absorption bands for a NH grouping (3.05 μ) and an amide carbonyl (6.05 μ). Its experimental weight was 408.6; theory 419.8.

Attempts to obtain N-\([\alpha-\text{bis(p-chlorobenzyl)amino}]\text{-p-chlorobenzyl}\)-p-chlorobenzamide (XVII) on sodium borohydride reduction of XIII resulted in XV, irrespective of the order of addition of sodium borohydride.

With respect to reduction of XIII to XV it can be argued that XIII is reduced to XV at a faster rate than that of addition of XV to XIII to give postulated intermediate XVI. Sodium borohydride reduction of an equimolar mixture of authentic XIII and XV (after allowing sufficient time for probable formation of XVI) gave XV; XVII was not formed. These results can be explained tentatively on the basis of the negative inductive effect of the p-chloro group of XVI. Intermediate XVI consists of a weakly bonded aminal center; one of the nitrogens of the amino acetal linkage is tertiary (\(-\text{N}^{-}\)) whereas the other is secondary (\(-\text{NH}^{-}\)).
Nucleophilic attack of the borohydride ion on carbon brings about the displacement of the -N-derivative (Equation 52) rather than the -NH derivative since the former is comparatively more electron deficient and consequently a better leaving group. Although such sensitivity of sodium borohydride reduction to an inductive effect is difficult to rationalize, the results are consistent with the mechanism proposed.

One of the possible paths for formation of XIII and XIV on permanganate oxidation of p-chlorobenzylamine is given (Equations 53 - 58); other tentative sequences may be devised.

\[
\begin{align*}
\text{CH}_2\text{-NH}_2 & \xrightarrow{[0]} \text{CH}=\text{NH} + \text{H}_2\text{O} \\
\end{align*}
\]

(53)

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

(54)
The selective formation of the Schiff base function at the indicated position by the mechanism suggested is quite surprising. The results of permanganate oxidation of p-chlorobenzylamine are in agreement with those for benzylamine and
p-methylbenzylamine in that the products arise from dehydrogenation of the methanemonoamine rather than the methanediamine functions.

Oxidation of p-Methoxybenzylamine

Oxidation of p-methoxybenzylamine with buffered permanganate (1.25 equivalents) in water:t-butanol (1:1) at 25-30° yielded N-[p-methoxy-a-[(p-methoxybenzylidene)-amino]benzyl]-p-anisamide (XVIII, 89%) and ammonia. A compound believed to be N,N'-[iminobis(p-methoxybenzylidene)]-bis[p-anisamide] (XIX) on the basis of nitrogen analysis, was formed in trace amounts but was not characterized.

\[
\begin{align*}
&\text{XVIII} & & \quad \text{XIX} \\
&\begin{array}{c}
\text{OCH}_3 \\
\text{OCH}_3 \\
\text{OCH}_3 \\
\end{array} & & \begin{array}{c}
\text{OCH}_3 \\
\text{OCH}_3 \\
\text{OCH}_3 \\
\end{array}
\end{align*}
\]

The infrared spectrum of XVIII contained absorption bands at 3.0 μ (NH), at 6.12 μ (amide carbonyl) and at 6.23 μ (imino linkage); its ultraviolet spectrum displayed maximum absorption at 275 μν (log ε 4.57) in 95% ethanol. The molecular weight (osmometry) agreed with the structure.
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assigned to XVIII. Its structure was proved by hydrolysis with hydrochloric acid to p-methoxybenzaldehyde (90%), p-anisamide (86%) and ammonia as summarized in Equation 59.

\[
\begin{align*}
\text{XVIII} + 2\text{H}_2\text{O} & \rightarrow \text{ammonia} + \text{hydrochloric acid} + \text{hydroxide} \\
\end{align*}
\]

Reduction of XVIII was effected by addition of sodium borohydride to an equimolar solution of XVIII in methanol to give \( N\left[\alpha\left\{\text{bis}(p\text{-methoxybenzyl})\text{amino}\right\}\text{p-methoxybenzyl}\right] - p\text{-anisamide} \) (XX, 64%; Equation 60).
A reaction sequence for this reduction is suggested in Equations 61 - 63.

$$\text{XVIII} \xrightarrow{\text{NaBH}_4} \text{XXI}$$  \hspace{1cm} (61)

$$\text{XVIII} + \text{XXI} \rightarrow \text{XXII}$$  \hspace{1cm} (62)
The fate of XXIII was not determined.

It is interesting that attempted preparation of XXI resulted in XX. These results are consistent with those obtained from sodium borohydride reduction of VIII and XIII. The results further indicate the sensitivity of sodium borohydride reduction of Schiff bases to inductive effects.
One of the possible sequences for the formation of XVIII from permanganate oxidation of p-methoxybenzylamine is indicated in Equations 64 - 67.

\[
\text{CH}_2-\text{NH}_2 + \text{OHH} \quad \xrightarrow{[0]} \quad \text{CH}=\text{NH} + \text{H}_2\text{O} \quad (64)
\]

\[
\text{CH}_2-\text{NH}_2 + \text{CH}=\text{NH} \quad \rightarrow \quad \text{CH}_2-\text{NH-CH-NH}_2 \quad (65)
\]

\[
\text{CH}_2-\text{NH}_2 + \text{CH}_2-\text{NH-CH-NH}_2 \quad \rightarrow \quad \text{CH}_2-\text{NH-CH-NH-CH}_2 + \text{NH}_3 \quad (66)
\]

\[
\text{CH}_2-\text{NH-CH-NH-CH}_2 \quad \xrightarrow{[0]\text{H}_2\text{O}} \quad \text{8-NH-CH-N}=\text{CH} \quad (67)
\]

XVIII
The results and the sequence suggested are similar to those for permanganate oxidation of benzylamine, p-methylbenzylamine and p-chlorobenzylamine.

**Oxidation of p-Nitrobenzylamine**

p-Nitrobenzylamine (generated in situ from its sulfate) is oxidized by buffered permanganate (1.25 equivalents) in water:t-butanol (1:1) to p-nitro-N-[p-nitro-a-[(p-nitrobenzylidene)amino]benzyl]benzamide (XXIV, 46%, 46%), N,N'-[iminobis(p-nitrobenzylidene)]bis[p-nitrobenzamide] (XXV, 10.4%), p-nitrobenzoic acid (12.7%) and ammonia.

XXIV is soluble and XXV is insoluble in a 1:1 mixture of ether and methylene chloride; separation was effected readily. The infrared spectrum of XXIV showed absorption bands at 3.0 μ for the NH grouping, at 6.05 μ for amide carbonyl and at 6.23 μ for the imino (Schiff base) group.
The ultraviolet absorption of XXIV in 95% ethanol is: 
\[ \lambda_{\text{max}} = 269 \text{ nm (log}\varepsilon = 4.56) \]. Its experimental molecular weight (osmometry) is 442.3; theory 449.37. Hydrolysis of XXIV with refluxing hydrochloric acid gave \( p \)-nitrobenzaldehyde (90%), \( p \)-nitrobenzamide (85.5%) and ammonia on the basis of the stoichiometry indicated in Equation 68.

\[
\begin{align*}
\text{8-NH-OH-N=CH} + 2\text{H}_2\text{O} & \rightarrow \text{8-NH}_2 + 2\text{H}=0 + \text{NH}_3 \\
\text{XXIV}
\end{align*}
\]

Reduction of XXIV was effected by addition of sodium borohydride to an equimolar solution of XXIV in methanol to give \( p \)-nitro-\( \text{N-[p-nitro-}\alpha-[p-nitrobenzyl]amino}-\)benzyl benzamide (XXVI, 47.0%, Equation 69).

\[
\begin{align*}
\text{8-NH-CH-N=CH} \underset{\text{NaBH}_4}{\rightarrow} \text{8-NH-CH}_2
\end{align*}
\]
A possible reaction sequence for this conversion is proposed in Equations 70 - 72.

\[
\text{XXIV} \quad \xrightarrow{\text{NaBH}_4} \quad \text{XXVI} \quad (70)
\]

\[
\text{XXIV } + \text{XXVI} \quad (71)
\]

\[
\text{XXVII} \quad (72)
\]
It is of significance that attempts to obtain \( N\left[\alpha\left(\text{bis-(p-nitrobenzyl)amino}\right)\text{p-nitrobenzyl}\right]\text{p-nitrobenzamide} \) (XXVIII) from sodium borohydride reduction of XXIV gave XXVI.

![Chemical structure of XXVIII](image)

It seems unlikely that reduction of XXIV to XXVI occurs only as indicated in Equation 70. The reduction results can be explained tentatively via Equations 71 and 72 on the basis of the negative inductive effect of the p-nitro group. Since a p-nitro group is electron withdrawing, the nitrogen attached to the three p-nitrobenzyl groups in XVII is relatively more electron deficient than that linked to only two such groups. Nucleophilic attack of the borohydride ion on carbon effects the displacement of the -N- derivative rather than the -NH derivative since the former is relatively more electron deficient and consequently a better leaving group.
The structure of XXV was established by its hydrolysis with refluxing hydrochloric acid to p-nitrobenzaldehyde (94%), p-nitrobenzamide (86%) and ammonia. The stoichiometry of hydrolysis of XXV is given in Equation 73.

\[
\begin{align*}
\text{XXXVII} & \rightarrow \text{XXXV} + 2\text{H}_2\text{O} + \text{NH}_3 \\
\text{XXXVII} & \rightarrow \text{XXXV} + 2\text{H}_2\text{O} + \text{NH}_3
\end{align*}
\]

The infrared spectrum of XXV showed absorption bands at 3.01 μ (NH) and at 6.07 μ (amide carbonyl). Because of the insolubility of XXV in organic solvents its molecular weight could not be determined. One of the various possible sequences for the formation of XXIV and XXV on permanganate oxidation of p-nitrobenzylamine is shown in Equations 74 - 79. Other sequences are not given because of very tentative nature of every single scheme.

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

(75)

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

(76)

\[
\text{CH}_2\text{-NH-CH-NH-CH}_2 \rightarrow \text{CH}_2\text{-NH-CH-NH-CH}_2 + \text{NH}_3
\]

(77)

\[
\text{CH}_2\text{-NH-CH-NH-CH}_2 \rightarrow \text{CH}_2\text{-NH-OH-NH-CH}_2
\]

(78)

\[
\text{CH}_2\text{-NH-CH-NH-CH}_2 \rightarrow \text{CH}_2\text{-NH-OH-NH-CH}_2 + \text{NH}_3
\]

(79)
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Oxidation of Dibenzylamine

Oxidation of dibenzylamine with potassium permanganate has been previously reported to give benzoyltribenzylhydrazine (XXX) m.p. 181°. The authors postulated tetrabenzylhydrazine (XXIX) as an intermediate and proposed the following mechanism for formation of XXX from dibenzylamine (Equations 80 - 82).

\[
2 \left[ \phi-\text{CH}_2 \right]_2 \text{NH} \xrightarrow{[O]} 2 \left[ \phi-\text{CH}_2 \right]_2 \text{N}^* \quad (80)
\]

\[
2 \left[ \phi-\text{CH}_2 \right]_2 \text{N}^* \rightarrow \left[ \phi-\text{CH}_2 \right]_2 \text{N-N} \left[ \text{CH}_2-\phi \right]_2 \quad (81)
\]

XXIX

\[
\left[ \phi-\text{CH}_2 \right]_2 \text{N-N} \left[ \text{CH}_2-\phi \right]_2 \xrightarrow{[O]} \left[ \phi-\text{CH}_2 \right]_2 \text{N-N} \phi-\phi \quad (82)
\]

XXIX     XXX

The authors claimed to have proved the structure of XXX by its melting point, its mixed melting point with an authentic sample, and by its reduction with zinc dust in acetic acid to dibenzylamine and N-benzylbenzamide. The formation of benzaldehyde, dibenzylamine and benzamide on treatment of XXX with cold dilute acid was also reported. In the light of the results and knowledge obtained in the
present work on permanganate oxidation of aliphatic amines, it was quite difficult to rationalize the results of the previous report.\(^5\)

From the present investigation it is general that permanganate oxidation of amines results initially wherever possible, in formation of an imino linkage as a result of dehydrogenation. In no case when there is hydrogen on carbon alpha to the NH group of an amine was there isolated a hydrazine arising from coupling of amine radicals (Equations 83 - 84).

\[
\begin{align*}
R'R''CH-NHR & \xrightarrow{MnO_4^-} \left[ R'R''C=NR \right] \rightarrow \text{Products} \\
\xrightarrow{\text{Products}} & \left[ R'R''CH-NR \right] \xrightarrow{\text{Products}} \left[ R'R''CH-NR \right]
\end{align*}
\]

Moreover examination of structure XXX reveals that there might be something wrong with its assigned structure if it gives benzaldehyde, dibenzylamine and benzamide readily on treatment with dilute (cold) acids.

For these reasons, it was of interest to reinvestigate the permanganate oxidation of dibenzylamine. When dibenzylamine was oxidized with buffered permanganate in water:tit-butanol (1:1) at room temperature, \(N\left[\alpha-(\text{dibenzylamino})\text{benzyl}\right]\text{benzamide (III, m.p. 179-181}^\circ)\) was obtained
in 62.3% yield. Other products if formed in this reaction were not looked for.

\[
\phi-\phi-NH-CH-NCH_2-\phi
\]

III

Oxidation product III gave benzaldehyde, benzamide and dibenzylamine on treatment with dilute acid. The infrared spectrum of III exhibited strong absorption bands at 2.98 μ for a NH group and at 6.05 μ for an amide carbonyl function. (The infrared spectrum of XXX cannot exhibit absorption for a NH group.) Benzoyltribenzylhydrazine (XXX) was then prepared from benzoyl chloride and tribenzylhydrazine in 88% yield; tribenzylhydrazine was prepared from benzyl chloride and hydrazine hydrate.\(^6\) Amazingly enough

\[\text{(60) J. Kenner and J. Wilson, J. Chem. Soc., 1112(1927).}\]

benzoyltribenzylhydrazine, XXX, melted at 108-109° instead of 181° as reported.\(^5\) Furthermore XXX gave neither benzaldehyde, nor dibenzylamine nor benzamide on treatment with dilute acids. The identity of III was proved by its mixed melting point and comparison of its infrared spectrum with that of an authentic sample of \(\text{N-}[\alpha-(\text{dibenzylamino})-\text{ion benzyl}]\) benzamide obtained from sodium borohydride reduction
of N-α-(benzylideneamino)benzyl benzamide (see page 24).

A possible mechanism for conversion of dibenzylamine to III is proposed in Equations 85 - 89.

\[
\phi-\text{CH}_2\text{NH}-\text{CH}_2-\phi \xrightarrow{[\text{O}]} \phi-\text{CH}_2\text{-N=CH}-\phi \\
\phi-\text{CH}_2\text{-NH}-\text{CH}_2-\phi + \phi\text{CH}_2\text{-N}=\text{CH}-\phi \rightarrow \phi-\text{CH}_2\text{-NH}-\text{CH}-\text{N}\phi\text{CH}_2-\phi \\
\phi-\text{CH}_2\text{-NH}-\text{CH}-\text{N}\phi\text{CH}_2-\phi \xrightarrow{[\text{O}]} \phi\text{CH}=\text{N}-\text{CH}-\text{N}\phi\text{CH}_2-\phi \\
\phi\text{CH}=\text{N}-\text{CH}-\text{N}\phi\text{CH}_2-\phi + \text{H}_2\text{O} \rightarrow \phi-\text{CH}-\text{NH}-\text{CH}-\text{N}\phi\text{CH}_2-\phi \\
\phi-\text{CH}-\text{NH}-\text{CH}-\text{N}\phi\text{CH}_2-\phi \xrightarrow{[\text{O}]} \phi-\phi-\text{CH}-\text{NH}-\text{CH}-\text{N}\phi\text{CH}_2-\phi
\]

III

The same authors\(^5\) report the formation of [1,1-bi-piperidin]-2-one and α,β-dipropyl-α-β-dipropionylhydrazine.
from permanganate oxidation of piperidine and dipropylamine (Equations 90 - 93).

\[
2 \text{NH} \rightarrow 2 \left[ \text{N.} \right] \rightarrow \text{N} - \text{N} \quad (90)
\]

\[
\text{N} - \text{N} \rightarrow \left[ \text{N.} \right] \rightarrow \text{N} - \text{N} \quad (91)
\]

\[
2\text{Pr}_2\text{NH} \rightarrow 2 \left[ \text{Pr}_2\text{N.} \right] \rightarrow \text{Pr}_2\text{N-N-Pr}_2 \quad (92)
\]

\[
\text{Pr}_2\text{NH} - \text{NH}_2 \rightarrow \left[ \text{Pr}_2\text{N.} \right] \rightarrow \text{Pr}_2\text{N-N-Pr}_2 \quad (93)
\]

Although piperidine and dipropylamine were not oxidized in the present study, in light of the facts on permanganate oxidation of aliphatic secondary amines obtained during this investigation, the previous work cannot be believed. It seems reasonable that piperidine is oxidized according to sequences indicated in Equations 94 - 99.

\[
\text{NH} \rightarrow \left[ \text{N.} \right] \rightarrow \text{N} \quad (94)
\]
\[ \text{Equation 95} \]

\[ \text{Equation 96} \]

\[ \text{Equation 97} \]

\[ \text{Equation 98} \]

\[ \text{Equation 99} \]

XXXIII
Possibility b for oxidation of piperidine seems more likely since hydrolysis of XXXIII should give tetrahydropyridine and α-piperidone. Tetrahydropyridine and α-piperidone were reported by previous authors to be formed from their product of oxidation of piperidine.

A reaction sequence similar to that for dibenzylamine may be given for the oxidation of dipropylamine (Equations 100 - 103).

\[
\begin{align*}
C_3H_7-NH-CH_2-C_2H_5 & \xrightarrow{[0]} C_3H_7-N=CH-C_2H_5 & (100) \\
C_3H_7-N=CH-C_2H_5 + C_3H_7-NH-C_2H_7 & \rightarrow C_3H_7-NH-CH-N\overset{0}{\underset{3}{H}} C_2H_5 & (101) \\
C_2H_5CH_2-NH-CH-N\overset{0}{\underset{3}{H}} C_2H_5 & \xrightarrow{2[0]} C_2H_5-OH=N-OH-N\overset{0}{\underset{3}{H}} C_2H_5 & (102) \\
C_2H_5-OH=N-OH-N\overset{0}{\underset{3}{H}} C_2H_5 & \xrightarrow{2[H_2O]} 2[0] \rightarrow C_2H_5-\overset{0}{\underset{3}{H}}-NH-CH-N\overset{0}{\underset{3}{H}} C_3H_7 \\
\end{align*}
\]

XXXIV (103)
It is interesting that hydrolysis of XXXIV will give N-propylpropionamide and N-propylidenepropionamide. The previous authors report formation of N-propylpropionamide and N-propylidenepropionamide from the hydrazine which they claimed as the oxidation product of dipropylamine.

A number of secondary amines containing substituted benzyl groups have been previously⁷ oxidized by potassium permanganate in acid media. In all cases the corresponding aldehydes were reported as oxidation products as isolated as 2,4-dinitrophenylhydrazones. It is quite possible that amides corresponding to III also were oxidation products.

**Oxidation of Tributylamine**

Oxidation of tributylamine has been studied extensively with various oxidants.⁶¹ When tributylamine in

---


...cyclohexane was oxidized with manganese dioxide, N,N-dibutylformamide (36%), dibutylamine (38%) and unreacted tributylamine were obtained. Tributylamine and cumene hydroperoxide gave tributylamine-N-oxide (18%), di-butylamine (20.5%) and unreacted tributylamine. Photooxidation of tributylamine in water yields butyraldehyde, dibutylamine and unreacted tributylamine; it is important
that neither propionaldehyde, propionic acid nor N,N-di-butyldiformamide were formed. When the photooxidation of tributylamine was effected in cyclohexane, the products were N,N-dibutylformamide, dibutylamine, N,N-dibutyl-butyramide (traces) and recovered tributylamine. When tributylamine in cyclohexane was ozonized, tributylamine N-oxide, N,N-dibutylformamide, N,N-dibutylbutyramide, dibutylamine and unreacted tributylamine were isolated. It has been postulated that an enamine (XXXV, Equation 104) is formed as an intermediate in all of these oxidations of tributylamine.

\[
\text{Bu}_2\text{N}-\text{CH}_2\text{CH}_2\text{-Et} \xrightarrow{\text{oxidant}} \left[ \text{Bu}_2\text{N}-\text{CH}=\text{CH-Et} \right]
\]  

XXXV

Mercuric acetate oxidation of aliphatic tertiary amines also involves enamines as intermediates (Equation 105). 35, 36, 37, 38, 40, 41

\[
\text{RR'}\text{N}-\text{CH}_2\text{CH}_2\text{-R} \xrightarrow{\text{Hg(OAc)}_2} \left[ \text{RR'}\text{N}-\text{CH}=\text{CHR} \right]
\]

With this background, it was desired to obtain information concerning the mechanism of oxidation of aliphatic tertiary amines with permanganate. When tributylamine was oxidized with buffered permanganate in water: t-butanol,
N,N-dibutylbutyramide (9.5%), dibutylamine (~8%), butyraldehyde (12%), butyric acid (17%) and unreacted tributylamine (42.6%) were obtained. Only trace amounts of N,N-dibutylformamide and propionic acid were detected.

A gross sequence for this oxidation is indicated in Equations 106 - 110.

\[
\begin{align*}
\text{Bu}_2\text{N}-\text{CH}_2\text{-OH} & \quad \xrightarrow{[\text{O}]} \quad \text{Bu}_2\text{N}-\text{CH}=\text{OH}-\text{Et} \quad (106) \\
\text{Bu}_2\text{N}-\text{CH}=\text{CH}-\text{Et} & \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{Bu}_2\text{N}-\text{CH}=\text{OH}-\text{CH}_2-\text{Et} \quad (107) \\
\text{Bu}_2\text{N}-\text{OH}-\text{CH}_2-\text{Et} & \quad \xrightarrow{\text{PrCHO}} \quad \text{Bu}_2\text{NH} + \text{PrCHO} \quad (108) \\
\text{PrCHO} & \quad \xrightarrow{[\text{O}]} \quad \text{PrC}O\text{OH} \quad (109) \\
\end{align*}
\]

If this sequence is correct, water adds to the carbon carbon double bond of the enamine faster than is the enamine oxidatively-cleaved. To test this hypothesis, the oxidation was carried out in the absence of water. When tributylamine was oxidized with buffered permanganate in anhydrous acetone, N,N-dibutylformamide (~15%), N,N-dibutylbutyramide (~4%) and dibutylamine (~9%) were formed.
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as analysed by gas-liquid chromatography. Tributylamine (~ 46%) was recovered unchanged. Acids were formed only in small amounts (~ 2%) and were not characterized. Aldehydes were also formed but were not identified because formation of N,N-dibutylformamide, as predicted from the previous sequence, is the result of greatest importance. The mechanism for oxidation of tributylamine under anhydrous condition may be visualized as (Equations 111 - 116):

(a)

(a)  \[
\begin{align*}
\text{Bu}_2\text{N}-\text{CH}_2-\text{CH}_2\text{Et} & \quad [\text{O}] \quad \rightarrow \quad \text{Bu}_2\text{N}-\text{CH}=\text{CH}-\text{Et} \\
\text{Bu}_2\text{N}-\text{CH}=\text{CH}-\text{Et} & \quad [\text{O}] \quad \rightarrow \quad \text{Bu}_2\text{NOH} + \text{EtCHO} \\
\text{Bu}_2\text{N}-\text{CH}=\text{CH}-\text{Et} & \quad \overset{\text{H}_2\text{O}}{\text{of reaction}} \quad \rightarrow \quad \text{Bu}_2\text{N}-\text{CH}-\text{Pr} + \text{OH} \\
\end{align*}
\]

(b)

(b)  \[
\begin{align*}
\text{Bu}_2\text{N}-\text{CH}_2\text{Pr} & \quad [\text{O}] \quad \rightarrow \quad \text{Bu}_2\text{N}-\text{CH}-\text{Pr} + \text{OH} \\
\text{Bu}_2\text{N}-\text{CH}-\text{Pr} & \quad [\text{O}] \quad \rightarrow \quad \text{Bu}_2\text{NH} + \text{PrCHO} \\
\end{align*}
\]
The reaction indicated by Equation 110 is a relatively minor process in oxidation of tributylamine in the absence of water as a solvent.

**Oxidation of Tribenzylamine**

Tribenzylamine when oxidized with buffered permanganate in water: t-butanol gave benzaldehyde (17%), benzoic acid (31%), an unidentified amide (small amounts) and unreacted tribenzylamine (42%). Dibenzylamine was not formed on oxidation of tribenzylamine.

In a system in which formation of an enamine is prevented, oxidation thus results in dealkylation. Dealkylation may be accompanied by a minor side reaction in which one of the methylene group of tribenzylamine is oxidized possibly to an alcohol function, which in turn is dehydrogenated to \( N,N\)-dibenzylbenzamide (XXXVI) (Equations 117 - 119). If indeed this is true then the unidentified amide (small amounts) reported here must be XXXVI.

\[
\begin{align*}
\text{CH}_2\text{CH}_2\text{N-CH}_2\text{-O} & \quad \text{O} \quad \text{CH}_2\text{CH}_2\text{N-CH}_2\text{-O} \\
\text{CH}_2\text{CH}_2\text{-N} & \quad \text{OH}
\end{align*}
\]  

(117)

* Tribenzylamine on oxidation with manganese dioxide\(^{14}\) in chloroform for 40 hr. gave benzaldehyde (23%) and unchanged tribenzylamine (70%).
Oxidation of Benzhydrylamine

When benzhydrylamine was oxidized with buffered permanganate (1.0 equivalent) in water:acetone (1:10) at room temperature, an oily product was formed which decomposed on standing for several days to ammonia and N-diphenylmethylenebenzhydrylamine (XXXVIII, 74%). It is reasonable to assume that the unstable intermediate was N-(diphenylmethyl)-1,1-diphenylmethanediamine (XXXIX), an addition product of benzhydrylamine and diphenylmethylenimine (XL). The results are summarized in Equations 120 - 122.

\[
\begin{align*}
\phi\text{CH}_2\text{N-CH-}\phi & \xrightarrow{[\text{O}]} \phi\text{CH}_2\text{N-O-}\phi \\
\phi\text{CH}_2\text{OH} & \xrightarrow{X} \phi\text{CH}_2\text{NH} + \phi\text{OH}=0
\end{align*}
\]
The fact that XXXVIII and ammonia are obtained from XXXIX only after several days possibly indicates that XL adds benzhydrylamine much faster than it hydrolyzes to benzo-phenone and ammonia.

When benzhydrylamine was oxidized by refluxing buffered permanganate (1.5 equivalents) in water:t-butanol (1:1), benzophenone azine (XLI, 73%) was obtained. To account for the formation of XLI, it appears almost certain that benzhydrylamine is initially oxidized to benzophenone-imine (XL). Oxidation of XL to the benzophenoneimine radical, followed by radical coupling can give XLI (Equations 123 - 124).

\[
\begin{align*}
\phi \text{CH-NH}_2 + \text{XL} & \rightarrow \phi \text{O-NH-CH}_2 \\
\text{XXXIX} \\
\text{XXXIX} & \rightarrow \phi \text{O=N-OH} + \text{NH}_3 \\
\text{XXXVIII}
\end{align*}
\]
If this reaction sequence is followed it is evident that the rate of oxidative coupling of XL to XLI is much faster than the hydrolysis of XL to benzophenone and ammonia. The oxidative coupling of XL to XLI suggested here is not unique. Formation of benzophenone azine (XLI, 91.6%) by oxidation of benzophenoneimine (XL) with oxygen in the presence of cuprous chloride has been reported. In an attempt to obtain evidence for the suggested mechanism of oxidation of benzhydrylamine to XLI, authentic benzophenoneimine was oxidized with permanganate under the experimental conditions used for oxidation of benzhydrylamine to XLI. Benzophenone azine (XLI) was thus obtained in 32% yield (Equation 125).

\[ \text{Equation 124} \]

\[ \begin{array}{c}
2 \phi \text{C=NH} \\
\xrightarrow{[\text{O}]} \\
\phi \text{C=N-N=O}
\end{array} \]

\[ \text{XL} \quad \text{XLI} \]

\[ \text{Equation 125} \]

\[ \begin{array}{c}
\phi \text{C=NH} \\
\xrightarrow{[\text{O}]} \\
\phi \text{C=N-N=O}
\end{array} \]

\[ \text{XL} \quad \text{XLI} \]
Oxidation of N-Phenylbenzhydrylamine

N-Phenylbenzhydrylamine on oxidation with buffered permanganate (1.0 equivalent) in water:acetone (1:20) at room temperature gave N-(diphenylmethyl)-N,N',1,1-tetraphenylmethanediamine (XLII, 74%; Equations 126 - 127).

\[ \phi \text{CH-NH-} \phi + [0] \rightarrow \phi \text{C=NH-} \phi \]  
\[ \text{XLI} \text{II} \]  
\[ \phi \text{CH-NH}\phi + \text{XLI} \text{II} \rightarrow \phi \text{C-NH-} \phi \]  
\[ \phi \text{N-CH-} \phi \]  
\[ \text{XLIII} \]

The infrared spectrum of XLII exhibited strong absorption for a NH grouping at 3.05 \( \mu \); there was no absorption for the imine (Schiff base) linkage. The molecular weight determined for XLII was 498.7; theory 516.65. Oxidation of N-phenylbenzhydrylamine to N-diphenylmethylenaniline (XLIII) could only be effected in trace quantities. Even upon oxidation of N-phenylbenzhydrylamine with 1.5 to 1.75 equivalents of permanganate, XLII (40-60%) was the major product. The resistance of dissociation of XLII to N-phenylbenzhydrylamine and XLIII is of note.
It is interesting to comment on results obtained previously on reduction of nitrones. Reduction of N-benzylideneaniline-N-oxide with zinc and ammonium chloride gave N-benzylideneaniline (Equation 128); N-diphenylmethyleneaniline-N-oxide to behave similarly should give N-diphenylmethyleneaniline, XLIII, m.p. 116°. Instead of XLIII, N-diphenylmethyleneaniline-N-oxide gave a compound which melted at 83° (Equations 129 - 130).

\[
\begin{align*}
\text{O} & \quad \text{Zn} \quad \text{NH}_4\text{Cl} \\
\text{O} & \quad \text{Zn} \quad \text{NH}_4\text{Cl}
\end{align*}
\]

No structure was assigned to the product other than it appeared to be a molecular addition compound of XLIII and N-phenylbenzhydrylamine. Present work assigns it the structure, N-(diphenylmethyl)-N,N',1,1-tetraphenylmethanediame (XLII) on the basis of its molecular weight and its identical infrared spectra, melting point and mixed melting
point with a sample prepared from equimolar quantities of N-phenylbenzhydramine and XLIII in acetone and subsequent crystallization from ethanol. The isolation of XLIII on permanganate oxidation of N-phenylbenzhydramine is another example indicating that amines add nucleophilically to Schiff base (imine) linkages much faster than do they reduce permanganate.

**Oxidation of Aliphatic Amines**

**On Small Scale**

In order to determine the utility of amines as precursors for their corresponding carbonyl compounds, a number of aliphatic amines were oxidized with buffered permanganate. In general the amine was rapidly added to a stirred warm solution of potassium permanganate and calcium sulfate in water: t-butanol and the mixture distilled as rapidly as possible into 2,4-dinitrophenylhydrazine reagent to give the corresponding 2,4-dinitrophenylhydrazone. The results are summarized in Tables 1 and 2.

It was found that rapid removal of the carbonyl compound from the reaction mixture by distillation or steam distillation was essential if the carbonyl compound was susceptible to further oxidation. The yields of ketones were good; those of aldehydes were fair. In order to obtain satisfactory yields of ketones, 2.5 - 3.0
TABLE 1
OXIDATION OF AMINES

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<tr>
<th>Amine</th>
<th>Equivalents</th>
<th>Product of 2,4-DNPH</th>
<th>Yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
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<tr>
<td>Cyclobutylamine</td>
<td>2.5</td>
<td>Cyclobutanone</td>
<td>71</td>
</tr>
<tr>
<td>Cyclohexylamine</td>
<td>3.0</td>
<td>Cyclohexanone</td>
<td>75</td>
</tr>
<tr>
<td>Dicyclohexylamine</td>
<td>3.0</td>
<td>Cyclohexanone</td>
<td>84.6</td>
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<tr>
<td>N-Ethylidicyclohexylamine</td>
<td>3.5</td>
<td>Cyclohexanone</td>
<td>89</td>
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<tr>
<td>Isopropylamine</td>
<td>2.5</td>
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<tr>
<td>Diisopropylamine</td>
<td>2.5</td>
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<td>86</td>
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<td>79</td>
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<td>2-Butanone</td>
<td>91</td>
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<td>Di-Sec-butylamine</td>
<td>2.5</td>
<td>2-Butanone</td>
<td>96</td>
</tr>
<tr>
<td>α-Phenylethylamine</td>
<td>2.0</td>
<td>Acetophenone</td>
<td>78</td>
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<tr>
<td>Benzhydrylamine</td>
<td>1.5</td>
<td>Benzophenone</td>
<td>83</td>
</tr>
</tbody>
</table>

(a) Based on the fact that each group gives the corresponding carbonyl compound.
### Table 2

**Oxidation of Amines**

<table>
<thead>
<tr>
<th>Amine</th>
<th>Equivalents of K\textsubscript{MnO}_4 Used</th>
<th>Product, 2,4-DNPH of</th>
<th>Yield\textsuperscript{a} %</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Propylamine</td>
<td>1.25</td>
<td>Propionaldehyde</td>
<td>42</td>
</tr>
<tr>
<td>n-Butylamine</td>
<td>1.25</td>
<td>Butyraldehyde</td>
<td>46</td>
</tr>
<tr>
<td>Di-n-butylamine</td>
<td>1.25</td>
<td>Butyraldehyde</td>
<td>49.8</td>
</tr>
<tr>
<td>Tri-n-butylamine</td>
<td>1.0</td>
<td>Butyraldehyde</td>
<td>33</td>
</tr>
<tr>
<td>Isobutylamine</td>
<td>1.25</td>
<td>Isobutyraldehyde</td>
<td>50.5</td>
</tr>
<tr>
<td>Diallylbutylamine</td>
<td>1.0</td>
<td>Isobutyraldehyde</td>
<td>56</td>
</tr>
<tr>
<td>Benzylamine</td>
<td>1.25</td>
<td>Benzaldehyde</td>
<td>61</td>
</tr>
<tr>
<td>p-Methylbenzylamine</td>
<td>1.25</td>
<td>p-Methylbenzaldehyde</td>
<td>67</td>
</tr>
<tr>
<td>p-Chlorobenzylamine</td>
<td>1.25</td>
<td>p-Chlorobenzaldehyde</td>
<td>68</td>
</tr>
<tr>
<td>p-Methoxybenzylamine</td>
<td>1.25</td>
<td>p-Methoxybenzaldehyde</td>
<td>70</td>
</tr>
<tr>
<td>p-Nitrobenzylamine</td>
<td>1.25</td>
<td>p-Nitrobenzaldehyde</td>
<td>59</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Based on the fact that each group gives the corresponding carbonyl compound.
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equivalents of permanganate per group were required. When 1.0 - 1.5 equivalents of permanganate were used, the yields of ketones from oxidation of branched aliphatic amines were unsatisfactory. There were present in major amounts high boiling materials. Although these materials were not characterized it is expected that they are azines and Schiff bases. Azines are formed from oxidative coupling of intermediate imines; Schiff bases result from reaction of the parent amine with the corresponding imine or ketone.

**Oxidation of Aliphatic Amines On Large Scale**

A practical method for oxidation of amines to their corresponding ketones was developed. Cyclohexylamine (20 g.), dicyclohexylamine (15 g.), and 2-aminohexane (20 g.) were oxidized with 3.0 equivalents of neutral permanganate in water:t-butanol (1:1). The reaction mixture was heated and distilled as rapidly as possible to minimize loss of ketone due to oxidative cleavage. The distillate was extracted with petroleum ether (30 - 60°C). The products were isolated by fractionation. Cyclohexylamine gave cyclohexanone in 56% yield; cyclohexanone was obtained in 67% yield from dicyclohexylamine; 2-heptanone was realized in 59% yield from 2-aminohexane. Details as
well as complications in using this oxidation method for preparative purposes are summarized in the experimental section.

**Oxidation of Cyclopropylamine**

Cyclopropylamine on oxidation with osmium tetroxide is reported\(^4^9\) to give a product similar to the hydrate of cyclopropanone, but its identity could not be proved. The product on long exposure to oxygen gave acrolein, probably by isomerization of initially formed cyclopropanone or its hydrate. Preparation of cyclopropanone from diazomethane and ketene has been attempted.\(^6^4\) Reaction of ketene and excess diazomethane gave cyclobutanone, whereas diazomethane and excess ketene in methanol gave cyclopropanone methyl hemiacetal. Cyclopropanone ethyl hemiacetal could not be obtained pure; on shaking with dilute potassium hydroxide, it isomerized to ethyl propionate. In the absence of alcohol, diazomethane and ketene gave cyclopropanone hydrate.

All attempts to prepare cyclopropanone as a monomer resulted in a polymer. Efforts to prepare cyclopropanone

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(64) P. Lipp, J. Buchkremer and H. Seeles, Ann., 499, 1(1932).
semicarbazone gave a semicarbazono-semicarbazone (XLIV).

It is of note that XLIV could not be obtained from authentic acrolein.

\[
\begin{align*}
\text{CH}_2\text{-NH-NH-} & \text{O-NH}_2 \\
\text{CH}_2\text{-CH=N-NH-} & \text{O-NH}_2 \\
& \text{XLIV}
\end{align*}
\]

In the present investigation cyclopropylamine* was rapidly added to a stirred warm solution of potassium permanganate (≈1.0 equivalent) and calcium sulfate in water: t-butanol (2:1) and the mixture distilled as rapidly as possible. The volatile product was isolated by reaction with 2,4-dinitrophenylhydrazine and p-nitrophenylhydrazine in sulfuric acid.

A yellow crude 2,4-dinitrophenylhydrazone, m.p. 83 - 88° was obtained in 7.1% yield. Its infrared spectrum (see Appendix) exhibited very weak absorption for a NH grouping (3.01 μ) but strong absorption for \( \equiv \text{C=H} \) (6.1 μ). Its ultraviolet spectrum was essentially identical with that of cyclobutanone 2,4-dinitrophenylhydrazone in 95% ethanol. Its experimental molecular weight was 233.1; the

* Cyclopropylamine was tested by gas-liquid chromatographic and nuclear magnetic resonance techniques and found to be 100% pure.
molecular weight calculated for cyclopropanone 2,4-dinitrophenylhydrazone is 236.2. (Benzene was the solvent for the molecular weight determination.)

When the crude 2,4-dinitrophenylhydrazone was crystallized from hot ethanol, acrolein 2,4-dinitrophenylhydrazone (XLVI, ~ 44% of the initial 2,4-dinitrophenylhydrazone) remained as an insoluble residue and an orange yellow micro-crystalline solid (m.p. 114 - 120°) was obtained from solution. The yellow crude 2,4-dinitrophenylhydrazone when chromatographed on neutral alumina using benzene as an eluent, turned deep red and melted over a very wide range (~ 75 - 145°).

The nuclear magnetic resonance spectrum* of the crystallized 2,4-dinitrophenylhydrazone showed the presence of XLVI as an impurity, the n.m.r. spectrum of the initially precipitated 2,4-dinitrophenylhydrazone indicated the absence of XLVI.

Although proof of the identity of the product is incomplete, the results tentatively indicate that the crude product may be cyclopropanone 2,4-dinitrophenylhydrazone (XLV), which partially isomerizes to XLVI during crystallization from ethanol.

* The n.m.r. spectra were gratefully run and interpreted by Mr. T. F. Page of the Battelle Memorial Institute, Dr. G. Fraenkel and Mr. T. Cantrell of this department.
It is also possible that XLV exists in hydrazone, azo or enamine (cyclopropene) tautomeric forms.

The \( p \)-nitrophenylhydrazone, an orange red microcrystalline solid, was obtained in 6.7% yield. This material analyzed properly for cyclopropanone \( p \)-nitrophenylhydrazone. Its infrared spectrum exhibited absorption bands at 3.05 \( \mu \) for the NH grouping and at 6.12 \( \mu \) for \( \geq C=N \) linkage. Its N.M.R. spectrum (in chloroform) showed absorption only in the region around 7.7\( \tau \) and in the aromatic region. There was no evidence for an olefinic proton. The complexity of the spectrum in the 7.7\( \tau \) region indicates that the hydrogens on the ring are
not equivalent and that there is a chemical shift between the CH cis and trans to NH. According to Dr. G. Fraenkel of this department, the n.m.r. spectrum corresponded to cyclopropanone p-nitrophenylhydrazone.
The Mechanisms of Oxidation by Permanganate

Permanganate\(^{65}\) oxidizes various functional groups by distinctive reaction paths. Ions derived from every valence state of manganese from +7 to +2, as well as hydroxyl radicals, have been proposed as the active species responsible for oxidation by permanganate. It is not in the scope of this dissertation to review the mechanism of oxidation by permanganate of all the various groups. Since permanganate oxidation of alcohols bears some similarity to that of amines and since carbonyl compounds are produced in the present work, the mechanisms of permanganate oxidation of alcohols, ketones and aldehydes are of interest here.

The mechanism of permanganate oxidation of benzhydrol\(^{66}\)


has been studied. The reaction is strongly base catalyzed. When equivalent quantities of benzhydrol and permanganate were used and when hydroxyl ion was in excess, the reaction
was second order and in agreement with the rate law

\[
-\frac{d[MnO_4^-]}{dt} = k_2[MnO_4^-] [(C_6H_5)_2CHOH]
\]

The reaction kinetics, the hydroxide ion catalysis, the presence of a positive salt effect and the sign and magnitude of the entropy of activation all indicate that the rate controlling step consists of a reaction between benzhydrolate ion and permanganate ion. The isotope effect (6.6:1) in oxidation of benzhydrol-α-d, and the fact that when potassium permanganate -O\textsuperscript{18} was the oxidant, no excess oxygen-18 appeared in the product, suggest that the reaction occurred by hydride ion transfer from benzhydrolate ion to permanganate ion. The following mechanism for the base catalyzed permanganate oxidation of benzhydrol and of alcohols in general was suggested (Equations 131-132).

\[
(C_6H_5)_2CHO^- + MnO_4^- \xrightarrow{\text{slow}} (C_6H_5)_2CO = 0 + HMnO_4^{2-} \quad (131)
\]

\[
HMnO_4^{2-} + MnO_4^- \xrightarrow{\text{fast}} 2MnO_4^{2-} + H^+ \quad (132)
\]
A possible valence change of Mn$^{4+}$ to Mn$^{2+}$ in oxidation of alcohols by permanganate in the presence of ferrous sulfate or hydrogen peroxide has been pointed out. It is believed that ferrous sulfate or hydrogen peroxide reduces the permanganate to Mn$^{4+}$ and the ion then undergoes a two-electron transfer from the alcohol to give manganous ions. That two electrons are involved is suggested by the inability to detect free radicals during the reaction (Equations 133 - 136).

$$\text{MnO}_4^- + \text{H}_2\text{O}_2 \rightarrow \text{Mn}^{4+}$$

(133)

$$\text{C} - \text{O} : + \text{Mn}^{4+} \rightarrow \text{C} - \overset{+}{\text{O}} \rightarrow \text{Mn}^{3+}$$

(134)

$$\text{C} - \overset{+}{\text{O}} - \text{Mn}^{3+} \rightarrow \text{C} - \overset{+}{\text{O}} - \text{Mn}^{3+} + \text{H}^+$$

(135)

$$\text{C} \overset{3+}{\underset{\text{H}}{\text{O}}} \rightarrow \text{C} = \overset{3+}{\text{O}} \rightarrow \text{C} = \overset{3+}{\text{O}} + \text{H}^+ + \text{Mn}^{2+}$$

(136)
Aliphatic aldehydes and ketones \(^{68, 69}\) undergo permanganate oxidation after enolization (Equation 137).

\[
\begin{align*}
R-\overset{\circ}{\text{O}}-\text{CH}_2-\text{CH}_2-R' & \quad \xrightarrow{\text{OH}} \quad R-C=\text{CH}-\text{CH}_2-R' \\
& \quad \xrightarrow{\text{MnO}_4^-} \\
R-\overset{\circ}{\text{O}}-\text{CH}_2R'
\end{align*}
\]

\(^{137}\)

\(R = \text{radical or hydrogen.}\)

Control of the rate of oxidation by enolization has also been suggested for oxidation of acetophenone \(^{70}\) by acid permanganate.

Permanganate oxidation of benzaldehyde and of substituted benzaldehydes to the corresponding benzoic acids has been investigated \(^{71}\) in the pH range of 5 to 13. With
