DIRECT CARBONYLATION OF AROMATIC SEMICARBAZONES AND AZINES *

by

STEWART MILLWARD

B.Sc., University of British Columbia, 1960

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in the Department

of

Chemistry

We accept this thesis as conforming to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA
June, 1963

In presenting this thesis in partial fulfilment of the requirements for an advanced degree at the University of British Columbia, I agree that the Library shall make it freely available for reference and study. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by the Head of my Department or by his representatives. It is understood that copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Department of Chemistry

The University of British Columbia,
Vancouver 8, Canada.

Date Sept 3, 1963
ABSTRACT

Benzophenone semicarbazone reacted with carbon monoxide at about 300 atmospheres and at 235-245° in the presence of preformed dicobalt octacarbonyl as catalyst to yield 3-phenylphthalimidine (XXXVII), 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine (XXXIV), \( N,N' \)-dibenzhydrylurea (XXXV), and \( N \)-benzhydrylurea (XXXVI). At 200-220° benzophenone semicarbazone gave \( N \)-benzhydrylurea (XXXVI), benzophenone azine (XXXVIII), and benzophenone 4-benzhydrylsemicarbazone (XXXIX).

When the reaction temperature was further reduced to 175-180°, benzophenone semicarbazone did not produce the carbonylation product obtained in the second experiment but only the degradation and reduction products, XXXVIII and XXXIX respectively. Carbonylation of benzophenone azine (XXXVIII) at 235-245° produced 3-phenylphthalimidine (XXXVII), whereas carbonylation of benzophenone 4-benzhydrylsemicarbazone at the same temperature yielded 3-phenylphthalimidine and 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine (XXXIV).

An independent synthesis of the latter compound and of benzophenone 4-benzhydrylsemicarbazone, both in good yield, has been carried out.

When benzaldehyde semicarbazone was carbonylated at 200-220° only the degradation product, benzaldehyde azine (XLII) was formed. Increasing the temperature to 235-245° did not alter the course of the reaction. Carbonylation of benzaldehyde azine at 235-245° yielded 2-benzylphthalimidine (XLIII), phthalimidine (L), and 2-(N-benzylcarboxamido)phthalimidine (XLVI). The significance of the presence of
phthalimidine and 2-(N-benzylcarboxamido)phthalimidine in the
carbonylation products of benzaldehyde azine is discussed in regard
to the mechanism of the cyclization reaction. A mechanism is
proposed for the cyclization reaction and evidence is presented in
support of the proposal.

The ureido group (-NHCONH₂) or its degradation products has been
shown to have an inhibitory effect on the catalytic activity of dicobalt
octacarbonyl.

An independent synthesis of 2-(N-benzylcarboxamido)phthalimidine is
also reported.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Direct Carbonylation of Aromatic Semicarbazones and Azines</td>
<td>35</td>
</tr>
<tr>
<td><strong>Experimental</strong></td>
<td></td>
</tr>
<tr>
<td>A. General Considerations</td>
<td>65</td>
</tr>
<tr>
<td>B. Carbonylation of Benzophenone Semicarbazone at 210°</td>
<td>66</td>
</tr>
<tr>
<td>C. Chromatographic Separation of the Products from B</td>
<td>66</td>
</tr>
<tr>
<td>D. Characterization of the Products from B</td>
<td>66</td>
</tr>
<tr>
<td>1. Diphenylmethane (XXXII)</td>
<td>66</td>
</tr>
<tr>
<td>2. 1,1',2,2'-Tetraphenylethane (XXXIII)</td>
<td>68</td>
</tr>
<tr>
<td>3. Reduction of Tetraphenylethylene in Sodium and Liquid Ammonia</td>
<td>68</td>
</tr>
<tr>
<td>4. 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine (XXXIV)</td>
<td>69</td>
</tr>
<tr>
<td>5. Exchange Reaction of 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine with Deuterium Oxide</td>
<td>70</td>
</tr>
<tr>
<td>6. Synthesis of 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine</td>
<td></td>
</tr>
<tr>
<td>a) Diphenylacetylchloride</td>
<td>70</td>
</tr>
<tr>
<td>b) Benzhydrylisocyanate</td>
<td>70</td>
</tr>
<tr>
<td>c) Condensation of Benzhydrylisocyanate with 3-Phenylphthalimidine</td>
<td>71</td>
</tr>
<tr>
<td>7. N,N'-dibenzhydrylurea (XXXV)</td>
<td>72</td>
</tr>
<tr>
<td>8. Synthesis of N,N'-dibenzhydrylurea</td>
<td>72</td>
</tr>
<tr>
<td>9. N-benzhydrylurea (XXXVI)</td>
<td>72</td>
</tr>
<tr>
<td>10. Synthesis of N-benzhydrylurea</td>
<td>73</td>
</tr>
<tr>
<td>E. 3-Phenylphthalimidine (XXXVII)</td>
<td>73</td>
</tr>
<tr>
<td>Section</td>
<td>Page</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>F. Blue Cobalt Complex</td>
<td>74</td>
</tr>
<tr>
<td>G. Carbonylation of Benzophenone Semicarbazone at 200-220°</td>
<td>74</td>
</tr>
<tr>
<td>H. Characterization of the Products from G</td>
<td></td>
</tr>
<tr>
<td>1. Benzophenone Azine (XXXVIII)</td>
<td>76</td>
</tr>
<tr>
<td>2. Synthesis of Benzophenone Azine</td>
<td>76</td>
</tr>
<tr>
<td>3. Benzophenone 4-benzhydrylsemicarbazone (XXXIX)</td>
<td>76</td>
</tr>
<tr>
<td>4. Synthesis of Benzophenone 4-benzhydrylsemicarbazone</td>
<td>77</td>
</tr>
<tr>
<td>a) Benzhydrylamine</td>
<td>77</td>
</tr>
<tr>
<td>b) Condensation of Benzhydrylamine with Benzophenone Semicarbazone</td>
<td>77</td>
</tr>
<tr>
<td>I. Carbonylation of Benzophenone Semicarbazone at 175-180°</td>
<td>78</td>
</tr>
<tr>
<td>J. Chromatographic Separation of the Products from I</td>
<td>78</td>
</tr>
<tr>
<td>K. Carbonylation of Benzophenone Azine at 240°</td>
<td>79</td>
</tr>
<tr>
<td>L. Carbonylation of Benzophenone 4-benzhydrylsemicarbazone</td>
<td>82</td>
</tr>
<tr>
<td>M. Carbonylation of Benzaldehyde Semicarbazone at 215-220°</td>
<td>82</td>
</tr>
<tr>
<td>N. Chromatographic Separation of the Products from M</td>
<td>84</td>
</tr>
<tr>
<td>O. Carbonylation of Benzaldehyde Semicarbazone at 240°</td>
<td>89</td>
</tr>
<tr>
<td>P. Chromatographic Separation of the Products from O</td>
<td>89</td>
</tr>
<tr>
<td>Q. Characterization of the Products from M and O</td>
<td></td>
</tr>
<tr>
<td>1. Bibenzyl (XLI)</td>
<td>91</td>
</tr>
<tr>
<td>2. Benzaldehyde Azine (XLII)</td>
<td>91</td>
</tr>
<tr>
<td>3. Synthesis of Benzaldehyde Azine</td>
<td>91</td>
</tr>
<tr>
<td>4. Compound XLIII</td>
<td>92</td>
</tr>
<tr>
<td>5. Compound XLIV</td>
<td>92</td>
</tr>
</tbody>
</table>
R. Carbonylation of Benzaldehyde Azine at 240°C 93
S. Chromatographic Separation of the Products from R 93
T. Characterization of the Products from R

1. Bibenzyl (XLI) 98
2. Compound XLIV 98
3. 2-(N-benzylcarboxamido)phthalimidine (XLVI) 98
4. Synthesis of 2-(N-benzylcarboxamido)phthalimidine
   a) Preparation and Characterization of Benzylisocyanate 98
   b) Condensation of Benzylisocyanate with Phthalimidine 99
5. Compound XLVII 99
6. 2-Benzylphthalimidine (XLVIII) 100
7. Compound XLIX 100
8. Phthalimidine (L) 101
9. Compound LI 101

Bibliography 103
ACKNOWLEDGEMENTS

Many thanks are due to Dr. Alex Rosenthal for giving me the opportunity to work under his expert guidance and for his encouragement and patience during the course of this research project.

Thanks are due also to I. A. M. for the many hours she spent in preparing this manuscript for presentation.

This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgement is hereby made to the donors of said fund.
# LIST OF CHARTS

<table>
<thead>
<tr>
<th>Chart</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>Carbonylation of Benzophenone Phenylhydrazone</td>
<td>13</td>
</tr>
<tr>
<td>II.</td>
<td>Carbonylation of Azobenzenes</td>
<td>14</td>
</tr>
<tr>
<td>III.</td>
<td>Carbonylation of 4-Methylbenzophenone Phenylhydrazone</td>
<td>15</td>
</tr>
<tr>
<td>IV.</td>
<td>Carbonylation of Aromatic Aldehyde Phenylhydrazones</td>
<td>17</td>
</tr>
<tr>
<td>V.</td>
<td>Reaction of Acetylenes with Iron and Cobalt Carbonyls</td>
<td>26</td>
</tr>
<tr>
<td>VI.</td>
<td>Studies on the Mechanism of the Cyclization Reaction</td>
<td>32</td>
</tr>
<tr>
<td>VII.</td>
<td>Mechanism of Carbonylation of Benzaldehyde 1-Phenylhydrazone-1-N15</td>
<td>33</td>
</tr>
<tr>
<td>VIII.</td>
<td>Carbonylation of Benzophenone Semicarbazone at 240°</td>
<td>37</td>
</tr>
<tr>
<td>IX.</td>
<td>Carbonylation of Benzophenone Semicarbazone at 175-180° and 200-220°</td>
<td>40</td>
</tr>
<tr>
<td>X.</td>
<td>Carbonylation of Benzophenone Azine and Benzophenone 4-benzhydrylsemicarbazone at 240°</td>
<td>42</td>
</tr>
<tr>
<td>XI.</td>
<td>Carbonylation of Benzaldehyde Semicarbazone</td>
<td>47</td>
</tr>
<tr>
<td>XII.</td>
<td>Carbonylation of Benzaldehyde Azine at 240°</td>
<td>50</td>
</tr>
<tr>
<td>XIII.</td>
<td>Proton Magnetic Resonance Spectra of Compound LI</td>
<td>52</td>
</tr>
<tr>
<td>Table</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>I.</td>
<td>Chromatographic Separation of Material B from the Carbonylation of Benzophenone Semicarbazone at 240°</td>
<td>67</td>
</tr>
<tr>
<td>II.</td>
<td>Chromatographic Separation of Material D from the Carbonylation of Benzophenone Semicarbazone at 200-220°</td>
<td>75</td>
</tr>
<tr>
<td>III.</td>
<td>Chromatographic Separation of the Products from the Carbonylation of Benzophenone Semicarbazone at 175-180°</td>
<td>80</td>
</tr>
<tr>
<td>IV.</td>
<td>Chromatographic Separation of the Products from the Carbonylation of Benzophenone 4-benzhydrylsemicarbazone at 240°</td>
<td>83</td>
</tr>
<tr>
<td>V.</td>
<td>Chromatographic Separation of Material E from the Carbonylation of Benzaldehyde Semicarbazone at 215-220°</td>
<td>85</td>
</tr>
<tr>
<td>VI.</td>
<td>Chromatographic Separation of Material F from the Carbonylation of Benzaldehyde Semicarbazone at 215-220°</td>
<td>86</td>
</tr>
<tr>
<td>VII.</td>
<td>Chromatographic Separation of Material F after Extraction with Petroleum Ether (b.p. 30-60°)</td>
<td>87</td>
</tr>
<tr>
<td>VIII.</td>
<td>Chromatographic Separation of Material H from the Carbonylation of Benzaldehyde Semicarbazone at 240°</td>
<td>90</td>
</tr>
<tr>
<td>IX.</td>
<td>Chromatographic Separation of the Material Extracted from the Black Solid (J) from the Carbonylation of Benzaldehyde Azine at 240°</td>
<td>94</td>
</tr>
<tr>
<td>X.</td>
<td>Chromatographic Separation of the Greenish-black Solid (K) from the Carbonylation of Benzaldehyde Azine at 240°</td>
<td>95</td>
</tr>
<tr>
<td>XI.</td>
<td>Rechromatography of the First Fraction from the Chromatography of Material K.</td>
<td>97</td>
</tr>
</tbody>
</table>
INTRODUCTION

Reactions involving carbon monoxide, hydrogen, organic substrates and metal carbonyl catalysts have become so extensive during the last decade that it has become necessary to classify them for purposes of discussion and to limit the discussion to the pertinent category. Further it is regrettable necessary to avoid discussion of such related topics as the chemistry of metal carbynols, their organo-metallic derivatives, and their use in polymerization reactions except where germane to the present topic.

Such terms as the oxo process, hydroformylation, carbonylation, carboxylation, disproportionation, direct carbonylation, and cyclization reactions of carbon monoxide have found frequent use in the literature.

The use of the term Oxo arose as a result of the pioneering work, in the application of metal carbynols to organic syntheses, carried out by W. Reppe and his co-workers at I. G. Farben during the Second World War (1,2). One of the main results of this work was the Oxo process for the conversion of olefins into the homologous aldehydes or alcohols by reaction with synthesis gas (a mixture of CO and H₂) and a cobalt catalyst (3,4,5,6), added as preformed dicobalt octacarbonyl, a cobalt salt or as the reduced metal. Other catalysts such as iron and nickel (7,8), rhodium and iridium have also been used. The latter two have been advocated (9) as allowing the reaction to be carried out at a lower temperature than with cobalt.
Since this reaction may be visualized as entailing the addition of the elements of formaldehyde (H-CHO) across the double bond it is also referred to as the hydroformylation reaction.

\[
RCH=CHR' + CO + H_2 \xrightarrow{100-120^\circ} RCH=CHR' + CO + H_2 \rightarrow RCH_2C(H)(R')CHO
\]

Insofar as the products of such reactions are primarily aldehydes, the term hydroformylation is preferable. The temperatures normally employed in the hydroformylation reaction are in the region 100-120° while at higher temperatures, 150-180°, subsequent reduction of the aldehyde to a primary alcohol occurs. Carbon monoxide-hydrogen pressures of 200-300 atmospheres are typical.

\[
RCH=CHR' + CO + 2H_2 \xrightarrow{150-180^\circ} RCH_2C(H)(R)CH_2OH
\]

The direction of addition seems to be governed largely by steric effects (10) the aldehyde group being attached preferentially to the less hindered end of the double bond. Additionally, the proportion of branched chain aldehyde appears to increase at higher reaction temperatures (11). There are a number of reviews of the hydroformylation of olefins, with the most recent being that of C. W. Bird (12).

The fundamental, and from a commercial point of view the most important, carboxylation reaction is typified by the exothermic conversion of acetylene to acrylic acid, in 95% yield, by the reaction of acetylene with nickel carbonyl under aqueous acidic conditions, at about 40° (13,14). In the presence of other compounds possessing active hydrogen, for example, alcohols, amines, etc., the corresponding derivatives of acrylic acid are obtained. The synthesis of ethylacrylate by this route can be represented as follows:
\( \text{H}_2\text{C}=\text{C}_2\text{H}_2 + \text{Ni(CO)}_4 + \text{EtOH} + 2\text{HCl} \rightarrow \text{H}_2\text{C}=\text{CHOEt} + \text{NiCl}_2 + \text{H}_2 \)

This reaction can be achieved by the addition of a stoichiometric amount of nickel carbonyl (stoichiometric method) or, by carrying out the conversion under an atmosphere of carbon monoxide in the presence of a catalytic amount of nickel carbonyl (catalytic method).

In both cases it appears the nickel carbonyl furnishes carbon monoxide and because the synthesis results in the formation of an acid or its derivatives (i.e. addition of the elements of formic acid, \( \text{H}-\text{COOH} \)), the synthesis has been called carboxylation.

A wide variety of solvent systems (15) has been employed successfully including primary, secondary and tertiary alcohols, acetone, methyl ethyl ketone, dioxane, tetrahydrofuran, ethylacetate, pyridine and anisole. However water must be present and in anhydrous alcoholic solvents only much reduced yields of acids are obtained. Most of the carboxylation reactions reported in the literature have been carried out in aqueous ethanol and the product is the ethyl ester, formed by subsequent esterification of the acid.

The efficiency of, and the precise conditions for, the carboxylation reaction depend on the individual acetylene and it has been possible to divide substituents into two classes: (A) those which facilitate carboxylation: alkyl; aryl; \(-\text{CH}_2\text{OH}\); \(-\text{CH}_2\text{OAc}\); \(-\text{CH}-\text{OAc}\); \(-\text{CH}_2\text{CH}_2\text{OH}\); \(-\text{CH}_2\text{CH}(_3)(\text{OH})\); \(-\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}\); and (B) those which hinder carboxylation: \(\text{H}\); \(-\text{CHROH}\); \(-\text{CR}_2\text{OH}\); \(-\text{CR}_2\text{OAc}\); \(-\text{CH}_2\text{C}(_3\text{H})_2\text{OH}\); \(-\text{Ac}\); \(-\text{COOH}\); \(-\text{CO}_2\text{Et}\).

Thus in an acetylene \(\text{X}C\equiv\text{CY}\) if both \(\text{X}\) and \(\text{Y}\) belong to class A the reaction is smooth. Similarly if \(\text{X}\) comes from A and \(\text{Y}\) from B the reaction proceeds
smoothly with the formation of \( YCH=\text{C}X\text{CO}_2\text{H} \), but if both \( X \) and \( Y \) come from group B the reaction is not exothermic and gives only a low yield of unsaturated acid after prolonged heating (12). Of course, acetylene reacts smoothly, where \( X = Y = H \).

In general, the addition of the elements of formic acid is always cis and obeys the Markownikoff rule (16). The following equations illustrate these rules:

\[
\text{H-C}^\equiv\text{C-C}_2\text{H}_5 + \text{CO} \xrightarrow{\text{H}_2\text{O}^+} \text{H}_2\text{C}^\equiv\text{C-C}_2\text{H}_5\text{COOH}
\]

\[
\text{R-C}^\equiv\text{C-C}_2\text{H}_5 + \text{CO} \xrightarrow{\text{H}_2\text{O}^+} \text{R}_2\text{C}^\equiv\text{C-C}_2\text{H}_5\text{COOH}
\]

The carboxylation reaction particularly lends itself to the synthesis of \( \alpha \)-methylenic acids as illustrated by the synthesis of the antibiotic, \( \alpha \)-methylenebutyrolactone (17).

\[
\text{HOCH}_2\text{CH}_2\text{C}^\equiv\text{CH} \rightarrow \text{CH}_2\text{C}^\equiv\text{CH} \text{CH}_2\text{C}^\equiv\text{O}
\]

Vinylacetylenes are not very readily carboxylated but the reaction appears to be catalyzed by pyridine (18). The products of these reactions are the subject of considerable controversy (12, 14, 18, 19, 20).

Attempts to carboxylate diacetylenes were unsuccessful (16).

Acetylene can be carboxylated with dicobalt octacarbonyl in methanol at 95° and a carbon monoxide pressure of 250 atmospheres to give as the major product, dimethyl succinate (21), or in the presence of aniline the
dianilide (22). The reaction is complicated however by the formation of at least nine side products (23,24).

\[
\text{HC≡CH} + \text{MeOH} + \text{CO} \xrightarrow{\text{Co}_2(\text{CO})_8} 95^\circ \rightarrow \text{MeOOC(CH}_2)_2\text{COOMe}
\]

When olefins are reacted with nickel carbonyl under aqueous acid conditions the products are saturated acids. The conditions for the olefins are in general more stringent than for acetylenes (12). Thus for the stoichiometric method, temperatures around 160° at pressures of about 50 atmospheres of carbon monoxide are normally employed, while catalytically, temperatures in the region of 250° and carbon monoxide pressures of around 200 atmospheres are used (25,26,27). Cobalt and iron carbonyls have also been employed but the latter particularly appears to be less effective and cobalt tends to cause more side reactions (25).

The direction of addition of the elements of formic acid to olefins does not appear to be as selective as with acetylenes.

Alcohols may be used in place of olefins but a higher temperature and the addition of a nickel halide are necessary. Secondary and tertiary alcohols react at 275° and primary at 300° (28). The reaction generally appears to proceed via the olefin. Phenyl substituted alcohols appear to undergo preferential hydrogenolysis to the parent hydrocarbon.

Carboxylic acid derivatives such as, esters (26,29,30), thioesters (26,30), amides (26,29,30,31), or anhydrides (26,32,33) are obtained by conducting the reaction in the presence of the appropriate alcohol, thiol, amine or carboxylic acid.
Treatment of an aryl halide with nickel carbonyl, aqueous acid, and carbon monoxide at temperatures around $300^\circ$ and pressures of about 600 atmospheres gives the corresponding benzoic acid (34). Apart from nickel carbonyl the use of iron (35) and cobalt carbonyls (34,35) also have been reported.

A number of modifications to the general procedure have been employed. Thus, the corresponding esters are obtained if an anhydrous alcohol (36,37), or lower ester (36,38), such as methylformate is used as reaction medium. Amides or nitriles are the products in the presence of formamide, urea, or oxamide (39). The aroyl fluoride is formed by the use of sodium fluoride under anhydrous conditions (40).

The disproportionation of benzoic anhydrides to phthalic anhydrides and benzene occurs when the former is heated with nickel carbonyl at $325^\circ$, and a carbon monoxide pressure of 100 atmospheres (41,42).

\[
\begin{align*}
\text{benzoic anhydride} + \text{Ni(CO)}_4 & \rightarrow \text{phthalic anhydride} + \text{benzene} \\
\text{N,N-dibenzoylaniline} + \text{Ni(CO)}_4 & \rightarrow \text{N-phenylphthalimide} + \text{benzene}
\end{align*}
\]

Similarly, N,N-dibenzoylaniline disproportionates into N-phenylphthalimide and benzene (41).
When phthalic anhydride is treated with hydrogen and dicobalt octacarbonyl it is converted quantitatively to benzoic acid (I,3).

Primary or secondary amines undergo carbonylation by reaction with a wide variety of metal carbynols forming the N-formyl derivatives and ureas (I,4,6,26). Many of these reactions take place at room temperature and atmospheric pressure.

\[
\text{Ni(CO)}_4 + \text{PhNH}_2 \rightarrow \text{PhNHCHO} + \text{PhNHCONHPH}
\]

\[
(\text{CH}_3)_2\text{NH} + \text{Co}_2(\text{CO})_8 \rightarrow (\text{CH}_3)_2\text{NCHO} + \left[(\text{CH}_3)_2\text{N}\right]_2\text{CO}
\]

Alkyl tertiary amines are reported (I,4,6,26) to give N,N-dialkylformamides; the fate of the alkyl group is not reported. Aryl tertiary amines on the other hand react as shown, where R is an alkyl group.

\[
(\text{CH}_3)_3\text{N} + \left[\text{Co(CO)}_4\right]_2 \rightarrow (\text{CH}_3)_2\text{NCHO}
\]

The reversible nature of urea formation has been shown by the conversion of urea to hydrazine using iron, cobalt, nickel, molybdenum, or tungsten metal at temperatures from 40 to 150° depending on the metal (I,6). When iron is used, semicarbazine is formed as a major by-product. Conversely, hydrazine hydrate reacts with iron pentacarbonyl at 45° under 900 atmospheres of carbon monoxide to give semicarbazone while at 100° and 500 atmospheres of carbon monoxide, both urea and semicarbazone are formed (I,7).
The reversible nature of this reaction is further demonstrated by the exchange of $^{14} \text{CO}$ with $N,N'$-diphenylurea at $230^\circ$ in the presence of dicobalt octacarbonyl (43).

Murahashi and Horiie (48,49,50,51) have shown that azobenzenes are converted in part to diarylureas when reacted with dicobalt octacarbonyl, carbon monoxide and hydrogen.

$$\text{Ph-N=Ph} \rightarrow \text{(PhNH)$_2$CO}$$

Rosenthal and co-workers (52) reacted benzaldoxime to give $N,N'$-dibenzylurea (35%) and $N$-benzylurea (10%). Analogous products were obtained from the oxime of 2-acetylnaphthalene (53). Ureas have also been obtained in low yields from aniline (11,54), aliphatic phenylhydrazones (54), aromatic semicarbazones (55), ketazines (56) and nitriles (57) using cobalt carbonyl and high purity carbon monoxide (containing 0.01% hydrogen).

Carbonylation reactions with metal carbonyls and carbon monoxide have afforded a variety of heterocyclic compounds from substrates containing carbon-nitrogen double bonds as in Schiff bases, oximes, hydrazones, ketazines and semicarbazones; nitrogen-nitrogen double bonds as in azobenzenes, and carbon-nitrogen triple bonds as in nitriles.
When anils, such as benzalaniline are reacted with dicobalt octacarbonyl in benzene at 200-230° and carbon monoxide pressures in the range 100 to 200 atmospheres, the products are 2-phenylphthalimidines (50,58,59,60,61). A wide variety of Schiff bases have been employed in this reaction. Iron pentacarbonyl also catalyzes the reaction although less effectively while no reaction occurred with nickel carbonyl (50,62), although its use is claimed in a patent (61). The reaction is inhibited by polar solvents, such as ethanol, tetrahydrofuran and water (50,62). In the presence of hydrogen, the anils are reduced to the corresponding amines (50,51). The latter reference (51) also reports the reaction of benzonitrile and benzylcyanide with synthesis gas and cobalt carbonyl to give a small quantity of amines (mixtures of primary and secondary ones) revealing that reduction of nitriles would be difficult to realize and no reaction product was obtained in which carbon monoxide had been involved. More recently, however, Rosenthal and co-workers (57) have reacted the nitriles at a higher temperature (about 250°) with carbon monoxide and a carefully controlled amount of hydrogen in the presence of cobalt carbonyl to yield phthalimidines, amides and ureas. Thus when benzonitrile was reacted with carbon monoxide at 235° in the presence of catalytic amounts of dicobalt octacarbonyl and pyridine, the product
was N-benzylphthalimidine. The use of organic bases, such as pyridine, was reported to be effective in increasing the rate of the hydroformylation reaction (63) and was also used to catalyze the carboxylation of vinylacetylenes (18). When small amounts of hydrogen were added to the reaction system, the yield of N-benzylphthalimidine was increased and sym-dibenzylurea was also produced.

![Chemical structure](image)

Benzylcyanide, under similar conditions gave the corresponding disubstituted urea, secondary amine and mono-substituted amide.

\[
\text{PhCH}_2\text{CN} \xrightarrow{235^\circ} (\text{PhCH}_2\text{CH}_2\text{NH})_2\text{CO} + [\text{Ph(CH}_2\text{)}_2]_2\text{NH} + \text{PhCH}_2\text{O-NHCH}_2\text{CH}_2\text{Ph}
\]

Aromatic ketoximes gave 3-substituted phthalimidines when reacted with carbon monoxide - hydrogen [98:1.5] pressures of 300 atmospheres and temperatures around 250\(^\circ\), in the presence of preformed dicobalt octacarbonyl (64).

![Chemical structure](image)

\( R = \text{CH}_3^-, \text{C}_6\text{H}_5^-, \text{C}_6\text{H}_5\text{CH}_2^- \).
The oxime of 2-acetylnaphthalene gave a small amount of 3-methylbenzophthalimidine (I) and a large amount of benzoquinoline (II) plus ureas.

\[
\text{Ph} - \text{C} - \text{C} - \text{Ph} \quad \rightarrow \quad \text{Ph} - \text{N} = \text{N} - \text{Ph} - \text{N} - \text{N} - \text{Ph} - \text{N} - \text{N} - \text{Ph}
\]

Formation of II was later shown to be independent of the presence of carbon monoxide, hydrogen and dicobalt octacarbonyl (65). Reaction of the 0- and N-methyl derivatives of aromatic ketoximes with carbon monoxide and hydrogen at 220° in the presence of cobalt carbonyl similarly gave 3-substituted phthalimidines (66). Under similar conditions 2-benzil-N,N'-dimethyldioxime gave tetraphenylpyrazine - a remarkable transformation (66).

Thus the attempts to prepare 2-hydroxyphthalimidines via this route were unsuccessful.

As mentioned earlier, the aromatic aldoximes are reported to give mono and disubstituted ureas under the above conditions (52). At about the same time however, Murahashi (59) reported that benzaldoxime gave benzamidine when reacted at 220-230° with carbon monoxide and cobalt catalyst.
Murahashi (51) also reported that benzaldehyde phenylhydrazone did not give any definite products when reacted with synthesis gas at 200 atmospheres and temperatures of 120-130°. Rosenthal and Weir later showed that both aromatic ketone (67) and aromatic aldehyde phenylhydrazones (68) undergo cyclization with high purity carbon monoxide, in the presence of preformed dicobalt octacarbonyl at temperatures of 190 to 250°.

Thus when benzophenone phenylhydrazone was reacted with carbon monoxide at 275 atmospheres and at 230 - 240° (Chart I), 3-phenylphthalimidine-N-carboxyanilide (III) was obtained in 70% yield. When the reaction temperature was reduced to 210-220°, a mixture of 3-phenylphthalimidine (IV) and 3-phenylphthalimidine-N-carboxyanilide (III) was obtained. When the temperature was reduced to 190-200°, only 3-phenylphthalimidine (IV) was obtained. The same temperature dependence of the number of carbon monoxide entities incorporated into the product was observed by Murahashi and co-workers (49,69) wherein they showed that azobenzene reacts under 150 atmospheres of carbon monoxide to form indazolone (V) at 190°, and 3-phenyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (VI) at 230° (Chart II).

When 4-methylbenzophenone phenylhydrazone was treated with carbon monoxide at 230° under the same conditions, a mixture of 3-(p-tolyl)-phthalimidine-N-carboxyanilide (VII) and 3-phenyl,6-methylphthalimidine-N-carboxyanilide (VIII) were obtained in approximately equal yield (Chart III) (67). These results differed from the observations of Murahashi and co-workers (69) on the effect of substituents on carbon monoxide ring-closure reactions in substituted azobenzenes; here the
CHART I: CARBONYLATION OF BENZOPHENONE PHENYLHYDRAZONE
CHART II
CARBONYLATION OF AZOBENZENES
CHART III: CARBONYLATION OF 4-METHYLBENZOPHENONE PHENYLHYDRAZONE
cyclization always occurred on the substituted ring (Chart II).

In general, the aromatic aldehyde phenylhydrazones gave more complex product mixtures, with lower yields of cyclic products, than the aromatic ketone phenylhydrazones (68).

When aromatic aldehyde phenylhydrazones were reacted under similar conditions to the ketone phenylhydrazones, the major product was N-phenylphthalimidine (IX) in 50% yield (Chart IV) (68). The m-tolylhydrazone of benzaldehyde under similar conditions, yielded N-(m-tolyl), phthalimidine (X), while the 1-naphthaldehyde phenylhydrazone afforded a mixture of 2-phenylbenz[e]isoindolin-1-one (XI), sym-diphenylurea, and naphthonitrile (Chart IV).

The attempts to form a six-membered heterocyclic system by carbonylation have failed. Thus phenylbenzylketoxime gave only 3-benzylphthalimidine (64),

\[
\begin{align*}
\text{PhCH}_2\text{CPh} & \quad \text{Ph} \\
\text{NOH} & \quad \text{250°} \\
\text{CO} & \quad \text{CO} \\
\end{align*}
\]

while dibenzylketoxime (70) gave 35% yield of N-formyl derivative and 60% of the secondary amine as shown:

\[
(\text{PhCH}_2)_2\text{C} = \text{NOH} \xrightarrow{\text{CO:H}_2, [19:1]} \begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\end{array} \quad (\text{PhCH}_2)_2\text{C-NCHO} + (\text{PhCH}_2)_2\text{NH}
\]

Methyl-\(\beta\)-phenylethyl ketoxime (70) gave similar products.
**Chart IV: Carbonylation of Aromatic Aldehyde Phenyldrazones**

1. \( \text{H} \text{-N=N-Ph} \xrightarrow{230^\circ\text{C}} \text{Ph} \text{-N=N-Ph} \)

2. \( \text{H} \text{-N=N-Ph} \xrightarrow{230^\circ\text{C}} \text{Ph} \text{-N=N-Ph} \)

3. \( \text{H} \text{-N=N-Ph} \xrightarrow{230^\circ\text{C}} \text{Ph} \text{-N=N-Ph} \)
When the phenylhydrazone of dibenzylketone (70) was reacted with carbon monoxide at 235°, no six-membered ring was formed but 2-benzyl-3-phenylindole was isolated in about 50% yield along with a small amount of diphenylurea.

\[
\text{PhCH}_2\text{CCH}_2\text{Ph} \quad \text{CO} \quad \text{235°} \rightarrow \quad \begin{array}{c}
\text{Ph} \\
\text{Bz} \\
\text{NNHPh}
\end{array}
\]

When phenylacetaldehyde phenylhydrazone (68) was reacted under similar conditions, the only isolable products were mono- and sym-diphenylurea (68). Murahashi and co-workers (59) also reported that the anil of phenylacetaldehyde failed to cyclize.

In review then, we have seen that both alcohols and aldehydes can be produced under the oxo conditions and that, when aldehydes are the principle product, the term hydroformylation is preferred. The latter involves the addition of the elements of formaldehyde (CO + H₂ = HCHO) across an acetylenic or olefinic linkage. Similarly, in carboxylations, the elements of formic acid (CO + H₂O = HCOOH) are pictured as adding across the unsaturated linkage giving rise to carboxylic acids and hence the name, carboxylation.

When amines are carbonylated with metal carbonyls the synthesis is referred to as formylation in view of the product formed, namely N-formyl compounds.

Reactions involving the insertion of carbon monoxide between two N atoms, or between a ring carbon and a side chain N (as in the oximes) with subsequent ring formation, are called carbonylation reactions or insertion reactions. The term cyclization is, of course, self-explanatory.
Mechanism of Carbonyl Insertion Reactions

The first mechanisms proposed for the carbonylation reactions which accounted for many of the observed results involved a cyclopropanone or cyclopropenone intermediate. It has however, become increasingly obvious that such an explanation is untenable. The final disproof was provided by a study of the reactions of the recently prepared diphenylcyclopropenone under carboxylation conditions (71). Thus, in the absence of nickel carbonyl it was found to be perfectly stable under the acidic conditions used for carboxylating diphenylacetylene, even when nickel chloride was present. In the presence of nickel carbonyl, conversion to trans \( \alpha \)-phenylcinnamic acid occurred. That this took place via diphenylacetylene was demonstrated by the ready decarbonylation of diphenylcyclopropenone with nickel carbonyl in benzene.

\[
\begin{align*}
\text{PhC} &= \text{CPh} & \text{Ni(CO)}_4 & \xrightarrow{} \text{H} & \text{PhC} &= \text{C} \text{COOH} \\
& & \text{PhC} &= \text{CPh} & \text{PhC} &= \text{C} \text{COOH}
\end{align*}
\]

There is now less mystery about the ways by which hydrogen and carbon monoxide are transferred to organic molecules by transition metals. An appropriate starting point for a discussion of metal carbonyls and related complexes as catalytic intermediates in organic syntheses is the reaction between \( \text{MeMn(CO)}_5 \) and carbon monoxide (72). When \( \text{MeMn(CO)}_5 \) is treated with carbon monoxide at room temperature and elevated pressure, carbon monoxide is inserted between methyl and manganese and the corresponding acetyl complex \( \text{Me\cdotCO\cdotMn(CO)}_5 \), is formed. On heating, carbon monoxide is given off and \( \text{MeMn(CO)}_5 \) formed again:
The fact that a carbon metal σ bond can be formed, and that carbon monoxide can be inserted between metal and carbon, contributes greatly to our understanding of reactions catalysed by metal carbynols.

Further interesting information came from the carbonylation of methylmanganese pentacarbonyl with \( ^{14} \text{CO} \) when the carbonyl group inserted was found not to contain any carbon \( ^{14} \). Additionally, \( \text{CH}_3^{14} \text{CO} \cdot \text{Mn} \text{(CO)}_5 \) gave after decarbonylation, methylmanganese pentacarbonyl still retaining all of the original carbon \( ^{14} \). These observations indicate a mechanism in which the carbon monoxide residue inserted is one originally bonded to manganese and the overall reaction may be envisioned as occurring via a metal to carbon migration of the methyl group. Whether or not the insertion of the carbonyl group and the coordination of another carbon monoxide molecule to the manganese atom are concerted processes is uncertain.

The generality of this reaction was demonstrated (72) by the conversion of \( \pi \)-cyclopentadienylmethylidicarbonyliron to the corresponding acetyl compound by treatment with carbon monoxide at \( 140 \) atmospheres and \( 125^\circ \):

\[
\begin{align*}
\text{Me} \cdot \text{Fe} \text{(CO)}_2 + \text{CO} & \rightarrow \text{Me} \cdot \text{CO} \cdot \text{Fe} \text{(CO)}_2 \\
\text{CH}_3 \cdot \text{Mo} \text{(CO)}_3 + \text{CO} & \rightarrow \text{Me} \cdot \text{CO} \cdot \text{Mo} \text{(CO)}_3
\end{align*}
\]
It was subsequently shown that methyl, ethyl, benzyl (73) and allyl (74) tetracarbonylcobalt compounds also undergo reversible carbonylation to the corresponding acyltetracarbonyl cobalt compounds.

\[
R \cdot \text{Co(CO)}_4 + \text{CO} \xrightleftharpoons[-\text{CO}]{\text{CO}} R\text{COCo(CO)}_4
\]

A related reaction which sheds some light on the function of metal carbynls as catalytic intermediates is the exchange of carbonyl groups with certain organic compounds catalysed by cobalt carbonyl (75). Thus when phthalic anhydride is treated with carbon monoxide in the presence of \(\text{Co}_2(\text{CO})_8\) at elevated pressure and temperature the carbonyl groups in the anhydride exchange with carbon monoxide in the gas phase. This exchange may be explained by the annexed sequence of reactions (75).

This elimination and insertion is plausible in view of the reaction:

\[
\text{Me Mn(CO)}_5 + \text{CO} \xrightleftharpoons{} \text{MeCOMn(CO)}_5
\]
Although it is unnecessary to explain the exchange of carbon monoxide by elimination of carbon monoxide to form XIII, the latter seems likely in view of the fact that when hydrogen is present in this system, benzoic acid is formed quantitatively according to:

\[
\begin{align*}
\text{benzoic acid} & \xrightarrow{\text{H}_2} \text{XIII} \\
\text{XIII} & \xrightarrow{\text{H}_2} \text{benzoic acid}
\end{align*}
\]

The formation of benzoic acid may be accounted for by hydrogenolysis of the intermediate XIII.

A variety of mechanisms have been proposed over the years to account for the products of the hydroformylation reaction; most however ignore the now-proven intermediacy of cobalt hydrocarbonyl in the reaction. Under normal hydroformylation conditions dicobalt octacarbonyl is converted rapidly to cobalt hydrocarbonyl (76). However in the presence of an olefin, no cobalt hydrocarbonyl is detectable until hydroformylation is complete. Furthermore it is found (77) that cobalt hydrocarbonyl reacts rapidly with olefins at room temperature and pressure absorbing carbon monoxide and giving as products an aldehyde and dicobalt octacarbonyl in accordance with the equation:

\[
2\text{HCo(CO)}_4 + \text{CO} + \text{olefin} \rightarrow \text{Co}_2(\text{CO})_8 + \text{aldehyde}
\]

Additional circumstantial evidence is provided by the observation that the rate of this reaction with various olefins (77) parallels the
relative rates at which the same olefins undergo hydroformylation (10). On the basis of these observations the sequence of equations (a) – (d) fairly accurately summarizes the pathway of hydroformylation (12).

\[(a) \quad \text{Co}_2(\text{CO})_4 + \text{H}_2 \rightarrow 2\text{HCo(CO)}_4\]

\[(b) \quad \text{HCo(CO)}_4 + \text{RCH} = \text{CH}_2 \rightarrow \text{RCH}_2\text{CH}_2\text{Co(CO)}_4\]

\[(c) \quad \text{RCH}_2\text{CH}_2\text{Co(CO)}_4 + \text{CO} \rightarrow \text{RCH}_2\text{CH}_2\text{COCO(CO)}_4\]

\[(d) \quad \text{RCH}_2\text{CH}_2\text{COCO(CO)}_4 + \text{HCo(CO)}_4 \rightarrow \text{RCH}_2\text{CH}_2\text{CHO} + \text{Co}_2(\text{CO})_8\]

Step (b) is probably a multi-step process,

e.g.

\[
\begin{align*}
\text{RCH} & \quad + \quad \text{HCo(CO)}_4 \quad \rightarrow \quad \text{RCH} \quad + \quad \text{Co(CO)}_3 + \text{CO} \\
\text{CH}_2 & \\
\text{H} & \\
\text{RCH} & \quad \rightarrow \quad \text{Co(CO)}_3 + \text{CO} \quad \rightarrow \quad \text{RCH}_2\text{CH}_2\text{Co(CO)}_4 \\
\text{CH}_2 & \\
\text{or} & \\
\text{RCH} & \quad \rightarrow \quad \text{Co(CO)}_3 \quad \rightarrow \quad [\text{RCH}_2\text{CH}_2\text{Co(CO)}_3]
\end{align*}
\]

The carbonyl insertion reaction has also been formulated (73) as proceeding

\[\text{RCH}_2\text{CH}_2\text{Co(CO)}_4 \rightarrow \text{RCH}_2\text{CH}_2\text{COCO(CO)}_3\]

with the latter acyltricarbonylcobalt complex being reduced to products by hydrogen. However the evidence for this process is based on the successful reduction of an acyltetracarbonylcobalt compound by hydrogen at 25°; a process which was completely inhibited by a high pressure of
carbon monoxide. It was suggested that the entity actually reduced is the acyltricarbonylcobalt complex and the reported observations are explained on the basis of the equilibria:

\[
\begin{align*}
\text{RCOC} &= \text{Co} \\
\text{RCOC} &= \text{Co} \\
\text{RCOC} &= \text{Co}
\end{align*}
\]

The formation of hydrocarbons in the hydroformylation reaction is readily envisioned in terms of the reaction,

\[
\text{RCO} + \text{HCo} \rightarrow \text{RH} + \text{Co}_2(\text{CO})_8
\]

competing with prior carbonyl insertion. This is very well illustrated by the hydroformylation of nuclear substituted benzyl alcohols where electron-withdrawing substituents favored hydrocarbon formation (78). We recall here also, the reluctance of trifluoromethylpentacarbonylmanganese to undergo carbonyl insertion reactions (72).

The kinetics of the carboxylation of olefins (72) roughly parallels those of the hydroformylation reaction (79). Hydrolysis of an acyltetracarbonylcobalt complex is a likely proposal, e.g.,

\[
\begin{align*}
\text{RCOC} + \text{H}_2\text{O} &\rightarrow \text{RCOOH} + \text{HCo} \\
\end{align*}
\]

Acetylene reacts with nickel carbonyl in benzene at 80° forming indan-1-one, presumably via formation of the cyclopentadienone dimer (80).
Diphenylacetylene, under similar conditions is converted to
tetraphenylcyclopentadienone together with hexaphenylbenzene (71).

\[
\text{PhC}≡\text{CPh} + \text{Ni(CO)}_4 \rightarrow \text{PhC}=\text{CPh}
\]

The most extensively investigated reaction of this type is that
of iron carbonyls with diphenylacetylene under non-aqueous conditions
(81, 82, 83). The reaction is carried out in benzene either by
irradiating the refluxing solution and iron pentacarbonyl, heating
with iron dodecacarbonyl, or stirring with iron enneacarbonyl at
room temperature. Some tetraphenylcyclopentadienone is formed directly
and isolated as its iron tricarbonyl complex (XIV) (Chart V). Other
complexes are also formed, including XV and XVI, which are readily
converted to tetraphenylcyclopentadienone or its iron tricarbonyl
complex by irradiation, heating with carbon monoxide, reaction with
bromine in acetic acid, or reduction with lithium aluminum hydride.

The cyclopentadienone ring is also formed when diphenyl- or
dimethyl- acetylene is irradiated with \( \text{Cp}^\ast \) -cyclopentadienylocobalt dicarbonyl,
the product being the complex XVII (Chart V) (84).

The primary step in these reactions seems to occur via an initial
dissociation of the metal carbonyl to a coordinatively unsaturated
species which then coordinates with the substrate. Dissociation of

\[
\text{M(CO)}_n \xrightarrow{} \text{M(CO)}_{n-1} + \text{CO}
\]
$\text{PhC} = \text{CPh} + \text{Fe(CO)}_5 \xrightarrow{\text{C}_6\text{H}_6, 80^\circ, \text{hv}} \begin{align*}
\text{XIV} & \quad \begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph}
\end{array} \\
\text{Fe(CO)}_3 \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Fe(CO)}_3
\end{align*} \\
\text{XV} & \quad \begin{align*}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Fe(CO)}_3
\end{align*} \\
\text{Fe(CO)}_3 \\
\text{XVI} & \quad \begin{align*}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Fe(CO)}_3
\end{align*} \\
\text{Fe(CO)}_3
\begin{align*}
\text{RC} = \text{CR} + \text{C}_5\text{H}_5
\xrightarrow{\text{hv}} \begin{align*}
\text{RC} = \text{CR} \\
\text{C}_5\text{H}_5
\end{align*}
\xrightarrow{\text{hv}} \begin{align*}
\text{R} = \text{CH}_3, \text{Ph} \\
\text{Co(CO)}_2 \\
\text{R} \\
\text{R} \\
\text{R}
\end{align*} \\
\text{XVII} & \quad \begin{align*}
\text{R} = \text{CH}_3, \text{Ph} \\
\text{R} \\
\text{R} \\
\text{R}
\end{align*} \\
\text{O} \\
\text{CH}_3 \\
\text{CH}_3
\end{align*}$

CHART V: REACTION OF ACETYLENES WITH IRON AND COBALT CARBONYLS
metal carbonyls is known to occur under irradiation by ultraviolet light and as already noted, some reactions show a marked temperature dependence or are aided by irradiation.

The subsequent reaction of the substrate metal carbonyl complex then may be

\[
\begin{align*}
\text{M(CO)}_{n-1} \quad \text{RCH}_2 \text{CH} + X^+ \quad \text{RCHCH}_2X
\end{align*}
\]

where \(X\) may be a proton or an incipient allylic carbonium ion as in a modification of the carboxylation of acetylenes. This accounts for the observed over-all cis-addition of formic acid in the carboxylation of acetylenes (16).

Alternatively the complex may react in an analogous way with another olefin or acetylene molecule, e.g.

\[
\begin{align*}
\text{M(CO)}_{n-1} \quad \text{RCH}_2 \text{CH} + \text{RCH} = \text{CH}_2 \quad \text{RCH} \text{CHR}
\end{align*}
\]

Such a scheme entailing essentially carbanionic addition would account for the apparent absence of skeletal rearrangements in the carbonylation reactions of bicyclo[2.2.1]heptadiene (85, 12). Carbonyl insertion then can be envisioned as occurring in the normal way.
In consideration of the products of these reactions, the cleavage of the acyl metal carbonyl complexes may be generalized as:

\[
\text{RCOM(CO)}_{n-1} + Y^- \rightarrow \text{RCOY} + \text{M(CO)}_{n-1}
\]

where \( Y^- \), for example, may be a hydride ion as in hydroformylation, hydroxide ion in carboxylation, or fluoride ion as in formation of aroyl fluorides. The metal subcarbonyl thus produced is then available, for further reaction with another molecule of substrate, thus providing a chain reaction or, for combination with a carbon monoxide molecule.

The first mechanism proposed for the cyclization reactions of azo compounds and Schiff bases was that proposed by Horiie and Murahashi in 1960 (86). These workers showed that the more electronegative the C=N or N=N bond was, the easier the reaction proceeded and reasonably conceived two alternative methods for the attachment of the catalyst on the reactive centre of the substrate. The first was the attachment of cobalt carbonyl across the \( \pi \) -bond of C=N or N=N in much the same manner as Wender and co-workers (87) had postulated for the oxo reaction when olefins and cobalt carbonyl were reacted (XVIII) and which had been isolated from cobalt carbonyl and acetylene (XIX).

\[
\begin{align*}
\text{R} & \quad \text{R} \\
\text{HC} & \quad \text{CH} \\
(CO)_3\text{Co} & \quad \text{Co(CO)}_3 \\
\text{C} & \quad \text{O} \\
\text{XVIII} & \\
\text{HC} & \quad \text{CH} \\
(CO)_3\text{Co} & \quad \text{Co(CO)}_3 \\
\text{XIX} &
\end{align*}
\]

In this case a steric requirement should necessarily be considered as was used to explain the observed differences in reaction velocity for
various olefins. Such a complex is shown in XX and XXI, for Schiff bases and azo compounds respectively.

These workers demonstrated that the reaction of benzaldehyde anil, acetophenone and benzophenone-anils showed no difference in the velocity and no sterically hindered effect of the phenyl group was discernible. Hence the formation of this type of complex (XX) could hardly be acceptable.

Their alternative method was the attachment of cobalt carbonyl to the lone pair of nitrogen giving rise to a complex which could act as an intermediate for the reaction. To test this hypothesis they reacted several benzal anils with ortho-substituents in the aniline ring in the belief that a steric factor might be observed (see asterisks in XXII)

Using benzal anil as the standard, the reaction velocity was increased when a methyl group was substituted in the para-position and decreased when a methyl group was substituted in the ortho-position. In the ortho,
ortho-disubstituted reactions the diethyl was more effective than
dimethyl in decreasing the reaction velocity. Thus in spite of having
a methyl group of promoting action the fact is that in the case of
ortho-substituted anils there was a marked lower conversion. On the
other hand the reduction of the anil double bond with synthesis gas and
cobalt carbonyl goes smoothly even where the substituents in the ortho
position showed greatest resistance to the formation of phthalimidines
and no distinct steric effect was observed. They concluded from this
that the clear distinction of both reactions indicated a fundamental
difference in catalytic behaviour and explained the formation of
indazolone and phthalimidine as follows:

1) Some kind of complex formation occurred at first between a lone
pair of the nitrogen atom of the anil or of azo-double bond, and
here a steric effect was operative.

2) The formation of the N-CO bond was then stabilized by formation of
a five-membered ring with the carbon atoms of the benzene nucleus
and simultaneous transfer of a hydrogen atom from the ortho position of
benzene to the unsaturated bond of C=N or N=N.

The nature of the complex and the mode of addition of $[\text{Co(CO)}_4]_2$,
as well as the overall electronics of the complex remained in obscurity.
It was apparent from the products of the carbonylation of the aromatic aldehyde phenylhydrazones (Chart IV) that a nitrogen atom had been split out of the substrate sometime during the reaction (68). The fact that the meta-tolyl hydrazone of benzaldehyde afforded only N-(m-tolyl)phthalimidine (X), suggested that the substituent on the phthalimidine nitrogen was derived from the substrate and not from the solvent (benzene). Furthermore, the meta-tolyl group must not come free during the rearrangement, otherwise the structural integrity of the N-substituent would not have been retained. Elimination of the imino nitrogen was confirmed when benzaldehyde 1-phenylhydrazone-1-N\textsuperscript{15} (XXIII) reacted under similar condition to give N-phenyl-phthalimidine-N\textsuperscript{15} (XXIV) containing 97.5\% enriched nitrogen (Chart VI).

Confirmation that these reactions proceeded via an intramolecular mechanism was provided by a cross-over experiment involving 1-naphthaldehyde phenylhydrazone and benzaldehyde-meta-tolylphenylhydrazone in which the only cyclized products were XI and X (Chart VI).

To explain these observations, Rosenthal and Weir (68) proposed a mechanism which involved the splitting out of ammonia after cyclization had occurred (Chart VII). The first step involves the formation of a sigma bond between cobalt carbonyl and the lone pair on nitrogen (XXVI) when the substrate is in the tautomeric form (XXV). The latter was based on the observations of Connor (88) who showed that the phenylhydrazones of aldehydes and ketones rapidly tautomerize to benzene azoalkanes. After carbon monoxide from the metal carbonyl is inserted between the nitrogen and the cobalt atom (89) to give the intermediate
CHART VI: STUDIES ON THE MECHANISM OF THE CYCLIZATION REACTION
CHART VII
MECHANISM OF CARBONYLATION OF
BENZALDEHYDE 1-PHENYLHYDRAZONE-1-N

XXX
XXVII, cyclization of the carbon monoxide to the aromatic ring occurs to yield the intermediate XXVIII. Alternatively the assumption that the attack of dicobalt octacarbonyl on the phenylhydrazone gives the N-formyl compound (XXIX), which then undergoes cyclization to yield labelled N-phenylphthalimidine (XXX), is based on the fact that amines gave formamides with dicobalt octacarbonyl (90) and aniline yields formanilide and N,N'-diphenylurea with nickel carbonyl (114). It is then suggested that hydrogenolysis of the C-N bond in XXVIII would take place easily because of the activating effect of the benzylic group.
Direct Carbonylation of Aromatic Semicarbazones and Azines

The synthesis of phthalimidines and N-carboxyanilide derivatives of phthalimidines by the direct incorporation of one and two carbon monoxide units into aromatic ketoximes and phenylhydrazones, respectively, have been previously reported (64, 67). Because the kind of products obtained was dependent on temperature we hoped to obtain information on the mechanism of the cyclization reaction by a further study of the direct carbonylation of other substrates containing the imino group (but containing different substituents on the nitrogen).

This thesis is a report of the results of a study of the carbonylation of aromatic imino compounds containing the ureido (-NHCONH₂), ureylene (-NHCONH−), and imino (-N=Ĉ) groups attached to the nitrogen of the C=N group. In particular, benzophenone semicarbazone, benzaldehyde semicarbazone, benzophenone 4-benzhydrylsemicarbazone, benzophenone azine and benzaldehyde azine were carbonylated under a variety of reaction conditions. The azines were included in this study since it is known that benzophenone semicarbazone decomposes above its melting point to yield benzophenone azine (91).

It was also desirable to establish the generality of the rearrangement with subsequent loss of the imino nitrogen as was observed for the aromatic aldehyde phenylhydrazones (68).

The ureido and ureylene groups were chosen as it was believed that these might have a greater tendency to coordinate with the catalyst than the aniline group of the phenylhydrazones studied previously (67, 68).
Benzophenone semicarbazone reacted with carbon monoxide at about 300 atmospheres and at 235–245° in the presence of preformed dicobalt octacarbonyl to give a mixture of reduction and carbonylation products (these are shown in Chart VIII) which were separated by chromatography on alumina. Most of the product crystallized directly out of the reaction mixture as a blue crystalline material (designated as A in the experimental). This material was extracted with ethanol to give a mixture of ethanol soluble compounds which were then chromatographed to yield \( N,N' \)-dibenzhydrylurea (XXXV) and 3-phenylphthalimidine (XXXVII). The structures of both of these substances were established by direct comparison with authentic samples of \( N,N' \)-dibenzhydrylurea (92) and 3-phenylphthalimidine (93) respectively.

The filtrate remaining after the removal of the blue material A was evaporated to dryness and the residue (material B in the experimental) then fractionated by alumina chromatography (see Table I in the experimental). Diphenylmethane (XXXII, 9% yield), was characterised by direct comparison (mixed melting point and infrared) with an authentic sample of diphenylmethane obtained from the Eastman Kodak Co. 1,1,2,2-Tetraphenylethane (XXXIII, 2% yield) was characterised first by comparison of the infrared spectrum of XXXIII with that of 1,1,2,2-tetraphenylethane listed in the Sadtler Standard Spectra (94) then by direct comparison (mixed melting point and infrared) with an authentic sample of 1,1,2,2-tetraphenylethane, prepared by reducing tetraphenylethylene with sodium metal in liquid ammonia solution (95).
CHART VII:
CARBONYLATION OF BENZOPHENONE SEMICARBAZONE AT 240°
Compound XXXIV was unequivocally assigned the structure of 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine on the following basis: 

(1) infrared analysis showed the presence of carbonyls at 1681 and 1700 cm$^{-1}$ and a secondary N-H (st) at 3260 cm$^{-1}$ in excellent agreement with the spectrum of the previously reported N-carboxyanilide of 3-phenylphthalimidine (Compound III - Chart I) (67); (2) refluxing compound XXXIV in 99% deuterium oxide gave a substance, the infrared spectrum of which indicated the presence of an N-D group (see experimental section). Furthermore, the carbonyl absorption at 1700 cm$^{-1}$ in compound XXXIV was lowered to 1695 cm$^{-1}$ in the deuterated product, presumably due to secondary isotope effects. The latter observation strongly suggested that the carbonyl was juxtaposed with the secondary N-H; (3) proton magnetic resonance analyses of the compound suggested a structure similar to that of 3-phenylphthalimidine-N-carboxyanilide (absorption at $\delta$ equal to 6.09 and 6.20 indicated the presence of the two benzylic hydrogens; comparison of the n. m. r. spectrum of XXXIV with that of 3-phenylphthalimidine-N-carboxyanilide established that the peak at 6.20 was due to the $\text{C}_{\text{Ph}}^{\text{H}}$ at the 3-position of the phthalimidine structure). The structure of XXXIV was then confirmed by direct comparison with an authentic sample of 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine, prepared by the condensation of 3-phenylphthalimidine with benzhydrylisocyanate according to previously described procedures (67, 96, 97).

Compound XXXVI was compared with an authentic sample of N-benzhydrylurea (98), prepared by the condensation of benzhydrylisocyanate with ammonia, and shown to be the same.
When the reaction temperature was reduced to 175-180°, benzophenone semicarbazone did not cyclize with carbon monoxide but pyrolyzed and was reduced to yield two major products (see Chart IX), one of which was readily characterized as benzophenone azine (XXXVIII). This assignment of structure is in accord with that of Borsche and Merkwitz (91) who first reported that the thermal decomposition of benzophenone semicarbazone yielded benzophenone azine (also called diphenylketazine). Comparison with an authentic sample prepared according to the method of Borsche and Merkwitz confirmed the structure.

On the basis of elemental, infrared and proton magnetic resonance studies, it appeared that the second product (compound XXXIX in the experimental) was benzophenone 4-benzhydrylsemicarbazone. As expected, hydrolysis of the latter in dilute sulfuric acid yielded benzophenone (isolated as the 2,4-dinitrophenylhydrazone). Vindication of the assigned structure was obtained by condensing benzhydrylamine with benzophenone semicarbazone to yield ammonia and benzophenone 4-benzhydrylsemicarbazone (identical in melting point and infrared to compound XXXIX).

At an intermediate temperature of 200-220°, benzophenone semicarbazone afforded the same reduction products as was obtained at 175-180°, and in addition N-benzhydrylurea (see Chart IX). It is noteworthy that these reactions therefore indicate that carbonylation of the semicarbazone to yield a urea takes place between 180-220°.

The fact that benzophenone azine and benzophenone 4-benzhydrylsemicarbazone were present in the product of the 200-220° experiment
CHART IX
CARBONYLATION OF BENZOPHENONE SEMICARBAZONE AT 175-180° & 200-220°
but were not in that of the higher temperature one, suggested that one or both of these substances might be the reactive intermediates in the direct ring closure reactions to yield the phthalimidines. In order to test this hypothesis, both of these substances were carbonylated at 235-245° (see Chart X). Benzophenone azine yielded only 3-phenylphthalimidine, whereas benzophenone 4-benzhydrylsemicarbazone afforded both 3-phenylphthalimidine and 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine.

Since some unreacted benzophenone azine remained after it had been treated with carbon monoxide at 235-245°, but none was present when benzophenone semicarbazone or benzophenone 4-benzhydrylsemicarbazone was carbonylated at the same temperature for the same time it appeared that stronger complexing had occurred between the semicarbazones and the catalyst than between benzophenone azine and the catalyst, which facilitated the cyclization reaction to yield the phthalimidines. That strong complexing had occurred between the ureido and ureylene groups and the catalyst is undoubtedly true, particularly in view of the experiments with the benzaldehyde semicarbazones (to be discussed later). However, benzophenone azine gave a much larger yield of cyclized product than the ketone semicarbazones. Hence the presence of unreacted azine may just be the manifestation of fewer side reactions.

The fact that diphenylmethane and 1,1,2,2-tetraphenylethane were present in the reaction products strongly suggests that benzhydryl free radicals were produced probably by thermal decomposition of benzophenone azine. Pyrolysis of the latter might be expected to yield molecular
Chart X:
Carbonylation of Benzophenone Azine and Benzophenone 4-Benzhydrylsemicarbazone at 240°
nitrogen and benzhydryl free radicals. Combination of two benzhydryl free radicals, followed by reduction, would then yield 1,1,2,2-tetraphenylethane. Abstraction of hydrogen from the substrate or reaction with cobalt hydrocarbonyl could give diphenylmethane. On the other hand, reduction of benzophenone azine to benzhydrylamine, followed by hydrogenolysis of the latter would also give diphenylmethane. It can be noted here that the normal product of decomposition of azobis-diphenylmethane, when warmed in benzene at 75°C, is tetraphenylethane (99).

\[
\text{Ph}_2\text{C}=\text{N}-\text{N}=:\text{CPh}_2 \xrightarrow{\Delta} \text{N}_2 + 2\text{PhC}_2
\]

The presence of ammonia in the high pressure reaction system is manifest from the studies of Borsche and Merkwitz (91) on the pyrolysis of benzophenone semicarbazone and it is well known that metal carbynyls undergo characteristic and quite general reactions with nucleophilic reagents. Thus, the direct addition of water to dicobalt octacarbynyl demonstrates the readiness with which cobalt carbynylhydride is formed (100);

\[
3\text{Co}_2(\text{CO})_8 + 4\text{H}_2\text{O} \rightarrow 4\text{HCo}(\text{CO})_4 + \text{Co(OH)}_2 + 4\text{CO}
\]

and a similar mode of reaction is followed when ammonia is used for hydrolysis. Further, dilute solutions obtained by these hydrolytic reactions have strong reducing properties (101). In the light of these considerations, it is not surprising that reduction products were isolated from the carbonylation of benzophenone semicarbazone (m.p. 164°C)
at temperatures above its melting point and in the presence of dicobalt octacarbonyl.

Thus, although the mechanism of formation of benzophenone 4-benzhydrylsemicarbazone is obscure, it is probable that benzophenone azine was reduced by the carbonyl hydride via some type of hydrogen transfer process similar to that envisaged by Natta, Pino and Ercoli (102), to yield benzhydrylamine, which subsequently condensed with a molecule of benzophenone semicarbazone to yield benzophenone 4-benzhydrylsemicarbazone (XXXIX). The ammonia released in the condensation reaction would then be available for reaction with dicobalt octacarbonyl to provide more carbonyl hydride. The credibility of the condensation reaction was demonstrated when an authentic sample of benzophenone 4-benzhydrylsemicarbazone was prepared in good yield (74%), by heating benzhydrylamine in the presence of benzophenone semicarbazone.

The possibility of inserting a carbonyl between nitrogen and cobalt is supported by the fact that diphenylurea undergoes exchange with carbon monoxide at elevated temperatures (143). When hydrogen

\[
(\text{PhNH}_2)_2\text{CO} + \text{Co}_2(\text{CO})_8 \leftrightarrow \text{PhNHCo(CO)}_4^* + \text{PhNHCOCO(CO)}_4^*
\]

\[
(\text{PhNHCo(CO)}_4^* + \text{CO} \leftrightarrow \text{PhNHCOCO(CO)}_4^*
\]

is added to this system, diphenylurea gives aniline and in view of the fact that cobalt carbonylhydride is formed from dicobalt octacarbonyl
and hydrogen, the following reaction seems likely:

\[ \text{PhNHCo(CO)}_4 + \text{HCo(CO)}_4 \underset{\text{PhNH}}{\overset{\text{PhNH} + \text{Co}_2(\text{CO})_8}{\rightleftharpoons}} \]

In view of these considerations, the last step in the reduction of benzophenone azine might be considered to be:

\[ \text{Ph}_2\text{CHNHC(O)}_4 + \text{HCo(CO)}_4 \underset{\text{Ph}_2\text{CHNH}_2 + \text{Co}_2(\text{CO})_8}{\rightleftharpoons} \]

or, alternatively, the aminotetracarbonylcobalt complex could undergo rearrangement to the acyl derivative.

\[ \text{Ph}_2\text{CHNHC(O)}_4 + \text{CO} \underset{\text{Ph}_2\text{CHNHCOCO(O)}_4}{\rightleftharpoons} \]

Nucleophilic attack by ammonia or dibenzhydrylamine will now give rise to the mono- and di-substituted ureas respectively. It should be

\[ \text{Ph}_2\text{CHNHCOCO(O)}_4 + \text{NH}_3 \underset{\text{Ph}_2\text{CHNHCONH}_2 + \text{HCo(CO)}_4}{\rightleftharpoons} \]

\[ \text{Ph}_2\text{CHNHCOCO(O)}_4 + \text{Ph}_2\text{CHNH}_2 \underset{\text{Ph}_2\text{CHNHCONHPh}_2 + \text{HCo(CO)}_4}{\rightleftharpoons} \]

pointed out that the formation of tetramethyl urea has been observed when dicobalt octacarbonyl was treated with an excess of dimethylamine (90) and it has been suggested that tetramethylurea was formed by "aminolysis" of the acyl complex according to (75):

\[ \text{(CH}_3\text{)}_2\text{NH} + \text{Co}_2(\text{CO})_8 \underset{\text{(CH}_3\text{)}_2\text{NCo(CO)}_4 + \text{HCo(CO)}_4}{\rightleftharpoons} \]

\[ \text{(CH}_3\text{)}_2\text{NCo(CO)}_4 \underset{\text{(CH}_3\text{)}_2\text{NCOCO(CO)}_3}{\rightleftharpoons} \]

\[ \text{(CH}_3\text{)}_2\text{NCOCO(CO)}_3 + \text{HN(CH}_3\text{)}_2 \underset{\text{(CH}_3\text{)}_2\text{NCON(CH}_3\text{)}_2 + \text{HCo(CO)}_3}{\rightleftharpoons} \]
The ease with which the carbonyl becomes inserted between nitrogen and cobalt (once the nitrogen-metal sigma bond is formed) is evidenced by the fact that the above reaction occurs at room temperature.

The genesis of benzophenone azine (XXXVIII) is readily envisioned as a rupture of the pyrolytic N-N bond with subsequent recombination of homologous radicals.

\[
2\text{Ph}_2\text{C}=\text{N}+\text{NHCONH}_2 \xrightarrow{\text{[2\text{Ph}_2\text{C}=\text{N}.]}} \text{Ph}_2\text{C}=\text{N}=\text{N}=\text{CPh}_2
\]

XXXVIII

Benzaldehyde semicarbazone reacted under 300 atmospheres of carbon monoxide and at 200-220° in the presence of preformed dicobalt octacarbonyl (see Chart XII) to give a product which consisted largely of a blue solid (designated as E in the experimental). The blue solid was removed by filtration, then washed exhaustively with absolute ethanol. Removal of the ethanol under reduced pressure afforded a crystalline substance which was chromatographed on alumina to yield a small amount (less than 1% yield) of bibenzyl (XLII), a large amount (40% yield) of benzaldehyde azine (XLII) and a mixture of syrups (6% by weight).

The filtrate remaining after removal of the blue solid (E) was evaporated to dryness (the odor of benzaldehyde was detected) and the residue (material F in the experimental) then fractionated by alumina chromatography (see Table VI) to yield bibenzyl (XLII) (6% yield) benzaldehyde azine (XLII) (40% yield) and a mixture of unidentified substances (5% by weight).
PhCH=NNHCONH₂

200-220° Co₂(CO)₈

→ XLII (54%)

\[
\begin{align*}
\text{CH} & \text{H} \\
\text{N} & \text{Z} \\
\text{N} & \text{C} \\
\text{H} & \text{H}
\end{align*}
\]

+ PhCH₂CH₂Ph + blue complex

XLII (6%) 39%

XLII (3%) 40%

→ XLIII (63%)

235-245° Co₂(CO)₈

PhCH=NNHCONH₂

CHART XI
CARBONYLATION OF
BENZALDEHYDE SEMICARBAZONE
Bibenzyl was expected as a product in this reaction by analogy with the experiments with the ketone semicarbazones and was readily characterized by direct comparison with an authentic sample.

Elemental and infrared analysis, and the ease of hydrolysis in dilute acid to yield benzaldehyde, indicated that compound XLII was benzaldehyde azine. Final proof of structure was provided by the preparation of authentic benzaldehyde azine according to the method of Thiele (103).

The fact that no product was identified in which carbon monoxide had been incorporated suggested that the ureido group of benzaldehyde semicarbazone had complexed so effectively with the catalyst as to inhibit its ability to bring about either carbonylation or cyclization. In support of this is the fact that benzaldoxime underwent reaction under similar condition to yield the carbonylation products, sym- and monobenzylureas in 35% and 10% yield respectively (52). Further, the aromatic aldehyde phenylhydrazones underwent reaction with carbon monoxide under similar conditions to afford the cyclization product, N-phenylphthalimidine (See Chart IV) (68).

Additional support for this hypothesis was provided when benzaldehyde semicarbazone was reacted under similar conditions, but at a temperature of 240°, to yield benzaldehyde azine in 63% yield. Thus there was no change in the course of the reaction and the yield of the major product, benzaldehyde azine (XLII) was increased by about 10%.
There can be little doubt that the formation of benzaldehyde azine came about by rupture of the pyrolytic N-N bond of the substrate. Thermal decomposition of benzaldehyde azine would then be expected to give rise to molecular nitrogen and benzylidene free radicals. Combination of two benzylidene free radicals followed by reduction would account for the formation of bibenzyl.

It seemed advisable at this stage, to carbonylate the benzaldehyde azine, particularly in view of the large yield of cyclized product afforded by the carbonylation of benzophenone azine. It was also desirable to carbonylate an aldimine substrate which could not tautomerize to the azo form as it was thought that the products from such a reaction might shed some light on the mechanism of the cyclization process. Thus, benzaldehyde azine was carbonylated at 240° yielding largely cyclization and possibly some carbonylation products accompanied by a small amount of bibenzyl (Chart XII).

The reaction product consisted of a black solid (designated as J in the experimental) which was removed by filtration and extracted with methanol in a Soxhlet apparatus. Removal of the methanol by evaporation under reduced pressure, afforded a green solid which was subsequently chromatographed on alumina (See Table IX) to yield a white solid (Compound LI), which melted at 255-256° with decomposition. Elemental analysis showed that compound LI had an empirical formula \( \text{C}_9\text{H}_6\text{N}_2\text{O}_2 \) (see experimental) and a singular molecular weight (Rast)
240°

\[ \text{Co}_2(\text{CO})_8 \]

PhCH\(_2\)CH\(_2\)Ph + XLV(1%) + XLVI(5%)

\[ \text{NCONHCH}_2\text{Ph} \]

Effl (5%) + XLIX + XLVIII(16%) + XLIX(6%) + Li(13%)

+ black solid + \[ \text{II} \]

14% 5%

CHART XII:
CARBONYLATION OF BENZALDEHYDE AZINE AT 240°
determination afforded a value of 587. The molecular weight was inconsistent with the rest of the data on compound LI. When heated with either concentrated sulfuric acid or concentrated sodium hydroxide, carbon dioxide and ammonia respectively, was evolved. Preliminary evidence suggested the tentative formulation of the following structure for compound LI:

Benzodia[2,4]epine-dione-1,3

Proton magnetic resonance analyses (see experimental) were consistent with the above structure (the n.m.r. spectra are reproduced in Chart XIII). Infrared absorptions at 3380 and 3220 cm\(^{-1}\) indicated the presence of two different mono-substituted amide functions; the one at 3380 cm\(^{-1}\) being a non-bonded NH and the one at 3220 cm\(^{-1}\), a bonded NH absorption. The CO-NH-CO group shows a single bonded amide NH absorption in the 3200 cm\(^{-1}\) region similar to cyclic lactams (104). Although not very much work has been done on the six or more membered ring systems, evidence indicates that the carbonyl absorptions of amide groups included in large ring systems are essentially similar to normal amides (104). Further, in six membered ring systems, Edwards and Singh (105) found that secondary lactams absorb at 1665 cm\(^{-1}\) and the fusion of an additional ring did not alter the frequency appreciably. They made the additional observation that \(\alpha\beta\) unsaturation
a.) Dimethylsulfoxide

b.) Deuterio-chloroform

c.) Trifluoroacetic anhydride
does not lower the carbonyl frequency. Also, the carbonyl absorptions at 1730 and 1650 cm\(^{-1}\) for 3-phenyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (Compound VI, Chart II) are consistent with the formulation of LI (70).

The tentative structure suggested for compound LI might be expected in view of the dihydrophthalazinone intermediate (Compound XXVIII, Chart VII) proposed by Rosenthal and Weir as a result of their studies on the mechanism of the cyclization reaction (68). Thus, rupture of the N-N bond, insertion of carbon monoxide (as observed by Murahashi and co-workers (69) and by Rosenthal and co-workers (67)), and hydrogenolysis of the benzyl group either before or after carbon monoxide insertion, would give rise to the structure tentatively assigned to compound LI.

A survey of the literature soon revealed that the benzodiaz[2,4]epine-dione-1,3 series of compounds were not known and consideration of possible routes for synthesizing an authentic sample were complicated with experimental difficulties.

The filtrate remaining after removal of the black solid J was evaporated to dryness and the residue (material K in the experimental) fractionated by alumina chromatography (see Tables X and XI in the experimental) to yield bibenzyl (XLI, 1% yield), a white solid designated as compound XLV (1% by weight), 2-(N-benzylcarboxamido) phthalimidine (XLVI, 5% yield), 2-benzylphthalimidine (XLVIII, 16% yield), a green solid (XLIX, 6% by weight), phthalimidine (L, 13% yield), and a grey solid (12% by weight), which was not investigated.
As compounds XLIV and XLVII showed no carbonyl absorptions in the infrared, no further work was done on them, while attempts to elucidate the structure of Compound XLIX were unsuccessful.

The structure of 2-(N-benzylcarboxamido)phthalimidine (XLVI) was suggested by virtue of the similarity between the infrared spectrum of XLVI and that of 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine isolated from the carbonylation of the benzophenone semicarbazones. Unequivocal proof was supplied by direct comparison of compound XLVI with an authentic sample of 2(N-benzylcarboxamido)phthalimidine, prepared by condensing benzylisocyanate with phthalimidine (55, 67, 96, 106). It can be pointed out here that this is the first time a carboxamide derivative of phthalimidine has been isolated from the carbonylation of the aromatic aldimine type of substrate. The significance of this find will be discussed when the mechanism of the cyclization process is considered in more detail.

On the basis of the work of Rosenthal and Weir (68) on the aromatic aldehyde phenylhydrazones, the expected product from the carbonylation of benzaldehyde azine would be 2-benzylphthalimidine (XLVIII). The melting point of XLVIII was identical to that reported in the literature for 2-benzylphthalimidine (59). Elemental, infrared and proton magnetic resonance analyses were also consistent with the assigned structure (see experimental). The infrared spectrum of XLVIII and that of an authentic sample of 2-benzylphthalimidine (57), prepared according to the method described by Murahashi and co-workers (59), were identical.
Assignment of the phthalimidine structure to compound L was suggested by infrared and elemental analyses. Absorptions, in the infrared region at 3190 cm\(^{-1}\) and 1670 cm\(^{-1}\) were consistent with the observed absorptions at 3180 and 1668 cm\(^{-1}\) for the N-H and carbonyl respectively, of 3-phenylphthalimidine isolated from the carbonylation of benzophenone azine. Further, as the reaction proceeded in part, in a manner analogous to the ketone semicarbazones (as evidenced by the isolation of 2-(N-benzylcarboxamido)phthalimidine) it seemed probable that some phthalimidine might be produced here also. Final proof was provided by direct comparison with an authentic sample of phthalimidine (118).

Before applying the mechanism deduced by Rosenthal and Weir (see Chart VII) (68) to the carbonylation reactions carried out by the author, there are a few points about their mechanism which require further clarification. The first criticism is the assumption made by these workers that the phenylhydrazones tautomerize to the azo form prior to complexing with the catalyst. This assumption was admittedly based on the observations of O'Connor (88) who showed that the phenylhydrazones of aldehydes and ketones rapidly tautomerize, in solution, to benzene azoalkanes. It should be pointed out however that O'Connor worked with alkyl phenylhydrazones and that one could argue fairly convincingly in favor of the azo tautomer, even in the absence of O'Connor's observations.

Thus the azo tautomer can extend the conjugation of the benzene ring with a concomitant increase in resonance energy for the system as a whole.
This argument, however, falls flat when applied to aromatic aldehyde phenylhydrazones, and particularly when applied to the phenylhydrazone of benzophenone. Further, if it was the azotautomer that underwent complexing with the metal carbonyl then one needs to ask himself why the indazolones and quinazolones (see Chart II) did not appear in the product, as demonstrated by Murahashi and co-workers (49) when azobenzenes were reacted under similar conditions. Additional evidence against the proposed azo tautomer was supplied from the results of the carbonylation of benzaldehyde azine (XXXII, see Chart XII) which afforded N-benzylphthalimidine (XLVIII), analogous to the N-phenylphthalimidine (XXX, Chart VII) produced under similar conditions from benzaldehyde phenylhydrazone (68). Since benzaldehyde azine cannot tautomerize it seemed unlikely that the azo tautomer was the complexing species.

Considering the fact that dimethylformamide and tetramethylurea are formed merely by dissolving Co₂(CO)₈ in dimethylamine at room temperature, a reasonable proposal for the first step in the cyclization process is the reaction of dicobalt octacarbonyl with the aniline NH to form a sigma bond between nitrogen and cobalt, maintaining the "inert" gas configuration on cobalt.

\[ \text{H} \quad \text{NNHPh} \quad \text{Co}_2\text{(CO)}_8 \quad \rightarrow \quad \text{H} \quad \text{NNHPh} \quad \text{Co(CO)}_4 \]

Rearrangement of the latter complex to the acyl form is a well established process and in view of the reaction with amines at room
temperature, probably occurs very easily once the nitrogen-metal sigma bond is formed.

What happens next is the interesting "organic part" and is somewhat obscure. However, in view of the products formed it is difficult to propose an alternative to attack by the carbonyl carbon atom at the ortho position of the benzene nucleus. An electromeric effect may be operative here which would explain why, in the absence of conjugation with the aromatic nucleus, cyclization does not occur.

The stoichiometry to this point is,

\[
\text{CNHPh} \quad \text{Co(CO)}_3^+ \quad \text{CO} \\
\text{HC}o(CO)_4 + \text{-NPh} \quad \rightarrow \ \text{-NPh} + \text{[Co(CO)]}_4^-
\]

The presence of carbonylhydride at this stage of the reaction provides a clue as to what happens next but before proceeding it is necessary to make an historical digression to review the work of Rowe (107) and Vaughan (108, 109) as corroborating evidence for subsequent proposals.

The \( \Psi \) -phthalazone-phthalazone or Rowe rearrangement (107) involves the transformation of a \( \Psi \)-phthalazone (LII) into a phthalazone (LIII) in
acid solution at 180°. Rowe discarded a mechanism involving ring contraction to an isoindolone structure (LIV) even though he isolated such a compound in some of his studies because, he argued,

\[
\text{LII} \quad \xrightarrow{H^+ \ 150^\circ} \quad \text{LIV} \quad \xrightarrow{H^+ \ 180^\circ} \quad \text{LIII}
\]

when \( R \) of LII = H, the intermediate LIV could not form.

An alternative course of rearrangement proposed by Vaughan (108) was closely related to Rowe's discarded mechanism but obviated the difficulty of the intermediate LIV, when \( R=H \), by postulating a carbonium ion derived from isoindalone. The alternative mechanism proceeded through the intermediate formation of a five membered ring, followed by a second rearrangement enlarging the ring to six members again. The formulation of Vaughan's proposals are outline below. He later validated his proposals with experimental proof using \( N^{15} \) isotopes (109).
The driving force initiating the formation of the intermediate LV may be considered an attack of a proton on the nitrogen carrying the aryl group, thus displacing the C\(^+\), which subsequently ejects the original proton.

\[
\text{LV} \quad \xrightarrow{\text{H}^+} \quad \text{LVVI}
\]

\[
\text{LV} \quad \xrightarrow{\text{R = CH}_3} \quad \text{LVIII}
\]

The isotopic studies carried out by Vaughan and co-workers (109) involved in part, the heating of 3-aryl-4-methyl-\(\psi\)-phthalazone (LVII), with excess \(N^{15}\) in the two position, at 180\(^\circ\) in acid solution to form 2-aryl-4-methylphthalazone (LVIII) enriched with \(N^{15}\) at the three position.

\[
\text{LVII} \quad \xrightarrow{180^\circ \text{H}^+} \quad \text{LVIII}
\]

The chemical method used by Vaughan to determine the position of the enriched nitrogen was based on the fact that, on reduction, both \(\psi\)-phthalazones and phthalazones afford chiefly \(N\)-substituted
isoindolones (otherwise known as phthalimidines) (LIX).

\[
\text{II or III} \xrightarrow{\text{Zn, HCl}} \text{LIX}
\]

We now return to the stoichiometric equation,

\[
\text{RNNHPh} + \text{Co}_2(\text{CO})_8 + \text{CO} \rightarrow \text{RNNHPh}^+ + 2\text{HCo(CO)}_4
\]

and consider the attack of a proton on the nitrogen carrying the aryl group, with subsequent displacement of the carbonyl carbon followed by attack of the carbonium ion on the imino nitrogen giving rise to the carbonium ion intermediate LXI:

\[
\text{LX} \xrightarrow{\text{H}^+} \begin{pmatrix} \text{R} & \text{NNHPh} \\ \text{C}^+ & \end{pmatrix} \xrightarrow{\text{LXI}} \text{RNNHPh}^+ + [\text{Co(CO)}_4]^-
\]

This is reasonable in view of the fact that cobalt hydrocarbonyl is a strong acid (110) and the experimental evidence for the acidic properties were demonstrated by Murahashi and co-workers (59) when they reacted benzaldoxime at 220-230° to give benzamide, presumably
by a Beckmann rearrangement. Transfer of a hydride ion, as suggested by Gaetz and Orchin (111) and as envisaged by Natta and co-workers (102), will result in the formation of the intermediate IXII.

Hydrogenolysis of IXII affords the 3-substituted phthalimidines (IXIII) while at higher temperatures (required to rupture the N-N bond) carbonylation occurs to form the carboxamide derivatives (IXIV).

![Diagram of chemical reactions]

In the opinion of the author, the course of the reaction will be governed primarily by the position of the equilibrium between IX and IXI. R groups which can stabilize the formation of the carbonium ion IXI (such as a phenyl group) will shift the equilibrium in favor of IXI, while those which cannot (such as H) will favor the formation of IX. In the latter case, reduction of the phthalazone (IX) to the N-substituted phthalimidine is the expected course of the reaction in

\[
\text{[PhN=NC}H_2\text{]} + 4\text{HCo(CO)}_4 \rightarrow \text{[PhN=NC}H_2\text{]} + [2\text{Co}_2(\text{CO})_8 + \text{NH}_3]
\]
view of the chemistry of phthalazones (106) and particularly in view of the fact that dilute solutions of cobalt hydrocarbonyl show strong reducing properties (101). Further, the ammonia produced here can perpetuate the reaction by production of more hydrocarbonyl (101). Thus the experiments of Rosenthal and Weir (see Chart VII) (68), and Vaughan and co-workers (109) using $^{15}$ isotopes, are complimentary. When R of IX has intermediate stabilizing ability both IX and IXI are present in the reaction medium and the products observed for the carbonylation of acetophenone phenylhydrazone are in agreement with this postulation (67).

![Chemical Reaction](image)

Additional support for the proposed equilibrium between IX and IXI is provided by the results of the carbonylation of benzaldehyde azine (see Chart XII). The initial step in this reaction may be considered the addition of cobalt hydrocarbonyl across one of the C=N linkages to form IXV.

![Chemical Reaction](image)

IXV
Cyclization follows the proposed pathway to yield LXVI, which exists in equilibrium with the carbonium ion LXVII.

LXV \rightarrow \text{Reduction} \rightarrow \text{Hydrogenolysis} \rightarrow \text{Carbonylation}

LXVI

\text{LXVII}

XLVIII (16%)
To the extent that this research was directed toward determining the tendency of various substituents on the imino group to coordinate with the catalyst, the following statement can be made:

When substrates containing the ureido group on the imino nitrogen of aromatic imino compounds are subjected to carbonylation conditions, they undergo thermal decomposition and the products of the latter process inhibit the catalytic action of cobalt carbonyl. The blue complex isolated from the carbonylation of ureido-substituted imino substrates, but not from substrates substituted with ureylene or imino groups (see experimental), suggests a relationship between the cobalt carbonyl and the ureido substituent or its degradation products.

That the catalyst was inhibited, as mentioned above, was shown by subsequent carbonylation of the thermal decomposition products. Thus, while benzaldehyde semicarbazone did not afford a product in which carbon monoxide had been directly incorporated, benzaldehyde azine did undergo reaction to form products in which carbon monoxide had played a role. Under the conditions of the cyclization reaction, benzophenone semicarbazone afforded a low yield (33%) of cyclized products while the thermal decomposition and reduction products (benzophenone azine and benzophenone 4-benzhydrylsemicarbazone respectively) afforded, under similar conditions, 80% and 76% yields, respectively, of cyclized product.
Experimental

A. General Considerations

a) The high pressure equipment has been described previously (64).

b) In every carbonylation experiment, preformed dicobalt octacarbonyl (112) was used, and high purity carbon monoxide containing 0.01% hydrogen, supplied by the Matheson Co., East Rutherford, N. J., was added to an initial pressure of about 2100 p.s.i. at room temperature.

c) The aluminum oxide (calcined) "Analar" was procured from the British Drug Houses (Canada) Ltd., Toronto 1,.

d) All melting points were obtained on a Leitz heating stage and are uncorrected.

e) The infrared analyses were done by Mrs. Zell of this Department, on a Perkin Elmer spectrophotometer, Model 21, using a sodium chloride crystal.

f) The nuclear magnetic resonance (n. m. r.) analyses were done by Mrs. E. Brion of this Department on a Varian Associates' A60 instrument. Tetramethysilane (TMS) was used as an internal standard.

g) Microanalyses were performed by Dr. A. Bernhardt, Mikroanalytisches Laboratorium, im Max-Planck Institut fur Kohlenforschung, Mulheim (Ruhr), Germany and by Mrs. A. Aldridge of this Department.
B. Carbonylation of Benzophenone Semicarbazone at 240°

To a mixture of 10.0 g (0.012 mole) of benzophenone semicarbazone in 45 ml of dry, purified benzene, was added 3.0 g (0.01 mole) of preformed dicobalt octacarbonyl and 2100 p.s.i. of carbon monoxide. The mixture was heated at 235-245° for 150 minutes. The bomb was then cooled overnight (pressure drop at room temperature was 40 p.s.i., equal to 0.02 mole of carbon monoxide) and vented. The vented gas contained no basic material (shown by bubbling a portion (700 p.s.i.) of the vented gases through ethanolic hydrogen chloride). The reaction product consisted of 7.4 g of a blue solid (A) and a brown liquid (essentially free of catalyst), which on evaporation under reduced pressure, yielded 4.6 g of a brown solid (B). The latter material was shown to contain five substances by thin layer chromatography (113) on silica gel using chloroform as a developer and concentrated sulfuric-nitric acid (95:5) as a detector.

C. Chromatographic Separation of the Products from B

A 2.17 g portion of material B, dissolved in a minimum of warm benzene, was chromatographed on an alumina column (133 x 5/4 mm diam.). The results are shown in Table I.

D. Characterization of the Products from B

1. Diphenylmethane (XXXII)

Compound XXXII, a liquid at room temperature, was purified by vapor phase chromatography using a silicone column at 270°. Scratching of the
Table 1

Chromatographic Separation of Material B from the Carbonylation of Benzophenone Semicarbazone at 240°C

<table>
<thead>
<tr>
<th>Developer</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene:petroleum ether (b.p. 30-60°C) (50:50)</td>
<td>600</td>
<td>0.283 clear liquid</td>
<td>9</td>
<td>Diphenylmethane (XXXII)</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>0.050 white solid</td>
<td>2</td>
<td>1,1,2,2-Tetraphenylethane (XXXIII)</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>800</td>
<td>0.328 white solid</td>
<td>8</td>
<td>3-Phenyl-2-(N-benzhydrylcarboxamido)-phthalimidine (XXXIV)</td>
</tr>
<tr>
<td>Benzene:Ethanol (99:1)</td>
<td>1200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(98:2)</td>
<td>500</td>
<td>0.595 yellow solid</td>
<td>15</td>
<td>N,N'-dibenzhydrylurea (XXXV)</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(85:15)</td>
<td>400</td>
<td>0.312 brown syrup</td>
<td>7</td>
<td>N-benzhydrylurea (XXXVI)</td>
</tr>
</tbody>
</table>

a. Developers were added consecutively

b. Yields are calculated in mole percent
effluent liquid induced crystallization, m.p. 25°; mixed m.p. with an authentic sample of diphenylmethane was 24°-25°. n.m.r. signals (given in δ units; spectrum obtained in carbon tetrachloride): 3.80 (H₂C-Ph₂, area = 2 H), 7.01 (aromatic H, area = 10 H).

Infrared spectrum (film): 3060 (w), 3030 (w), 2900 (w), 1720 (w), 1596 (w), 1493 (m), 1451 (m), 1074 (w), 1028 (w), 735 (s), 695 (s).

Comparison of this spectrum with that of authentic diphenylmethane showed them to be identical.

2. 1,1,2,2-Tetraphenylethane (XXXIII)

Compound XXXIII was recrystallized from ligroin, m.p. 210-212°. Elemental analysis showed this compound to be a hydrocarbon while the n.m.r. spectrum showed only aromatic and benzylic protons. Infrared spectrum (KBr): 3060 (w), 3020 (w), 2880 (w), 1593 (w), 1577 (w), 1493 (m), 1450 (m), 1206 (w), 1180 (w), 1157 (w), 1070 (m), 1029 (m), 744 (s), 695 (s).

n.m.r. signals (given in δ units; spectrum obtained in carbon tetrachloride): 4.65 (HC-Ph₂, area = 2 H), 6.99 (C₆H₅⁻, area = 20 H).

Calc. for C₂₆H₂₂: C, 93.50; H, 6.64. Mol. wt. 334.

Comparison of Compound XXXIII with an authentic sample of tetraphenylethane (infrared and mixed melting point) showed them to be identical.

3. Reduction of Tetraphenylethylenne in Sodium and Liquid Ammonia (95)

To a 150 ml cylindrical vessel equipped with a gas inlet tube and containing 3.12 g (0.01 mole) of tetraphenylethylenne (Aldrich Chem. Co.), and 0.50 g (0.27 mole) of clean, finely cut sodium metal, was added
40 ml of freshly distilled ammonia at -70°. The blue solution was magnetically stirred, without further cooling, for thirty minutes. The original volume of liquid ammonia was then replenished and an excess of ammonium chloride added directly until the blue color had disappeared. The ammonia was allowed to evaporate at room temperature and the remaining white residue extracted with 3 x 25 ml of benzene. The combined benzene extracts were filtered and the filtrate evaporated to dryness (in vacuo). The product (3.0 g - 98% yield) was recrystallized from carbon tetrachloride, m. p. 210-212°.

4. 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine (XXXIV)

Compound XXXIV was recrystallized from benzene-petroleum ether (b.p. 30-60°) to give white fluffy crystals, m.p. 200-201°. Mixed melting point of compound XXXIV with an authentic sample of 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine, 200-201°.

Infrared spectrum (KBr): 3260 (w), 3050 (w), 3020 (w), 2930 (w), 1700 (s), 1684 (s), 1607 (w), 1593 (w), 1582 (w), 1528 (s), 1493 (m), 1465 (w), 1453 (w), 1359 (m), 1340 (m), 1324 (m), 1295 (w), 1236 (w), 1201 (w), 1185 (m), 1158 (w), 1137 (m), 1090 (w), 1083 (m), 1024 (w), 894 (w), 849 (w), 770 (m), 762 (m), 750 (s), 738 (s), 727 (s), 697 (s).

n.m.r. signals (given in 6 units; spectrum obtained in deuteriochloroform): 6.09 (HC-Ph₂, area = 1H), 6.20 (HC=Ph, area = 1 H), 7.20 (aromatic H, area = 15 H), 7.48 (phenylphthalimidine aromatic H, area about 4 H), 9.45 (N-H, doublet, area = 1 H).

Anal. Found: C, 80.80; H, 5.29; N, 6.58.

Calc. for C₂₈H₂₂N₂O₂: C, 80.35; H, 5.30; N, 6.70.
5. **Exchange Reaction of 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine with Deuterium Oxide**

A few milligrams of 3-phenyl-2-(N-benzhydrylcarboxamido)phthalimidine were refluxed for 17 hours in 10 ml of D₂O containing a pinch of K₂CO₃. The deuterated product was obtained by extraction with warm benzene. Mixed melting point of the white crystalline product with the starting material, 198-200°. The infrared spectrum showed a strong N-D band at 2130 cm⁻¹ (10µ) and a lowering of the exocyclic carbonyl band to 1695 cm⁻¹.

6. **Synthesis of 3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine**

a) **Diphenylacetylchloride (97)**

Diphenylacetic acid (20.0 g) was dissolved in 50 ml of dry, freshly distilled carbon tetrachloride containing 30.0 g of thionyl chloride (BDH reagent grade) and the mixture refluxed gently during 2 hours while a stream of nitrogen was passed through the reaction mixture. The cooled solution was suction filtered and the filtrate evaporated under reduced pressure yielding a yellow solid mass. The latter was taken up in dry ethyl ether (25 ml) and cooled in a dry ice - acetone bath giving a white crystalline solid from which the yellow supernatant was decanted. The product (18.2 g - 84% yield) was washed with 10 ml of cold dry ethyl ether, m.p. 56-58°. Literature m.p. 57° (114).

b) **Benzhydrylisocyanate (115)**

Sodium azide (2.9 g, 0.014 mole), dissolved in 10 ml of water was added to a 100 ml flask equipped with a dropping funnel containing
diphenylacetylchloride (5.0 g, 0.02 mole) in 35 ml of acetone. The latter was added to the well stirred azide solution at such a rate that the temperature remained between 10-15° (20 minutes). Stirring was continued for a further 75 minutes; then 20 ml of cold aqueous sodium bicarbonate solution (10%) was added. The reaction mixture was transferred to a separatory funnel containing 50 ml of ice-cold water and extracted with 3 x 40 ml portions of cold ethyl ether. The combined ethereal extract was washed with 20 ml of cold aqueous sodium bicarbonated (10%) then with 2 x 20 ml of cold water and filtered on anhydrous magnesium sulfate. The dried ethereal extract was filtered into 100 ml of sodium-dried benzene and warmed to 65° for 90 minutes with simultaneous distillation of the ether. Removal of the benzene (in vacuo) yielded 3.32 g (73% yield) of the crude isocyanate which was subsequently distilled yielding 2.0 g (45% of theoretical, based on diphenylacetylchloride), b.p. 110-113°, 0.08 mm Hg, nD 1.5765. The infrared spectrum (film) showed the characteristic strong absorption band at 2270 cm⁻¹ (116) and a medium absorption band at 2130 cm⁻¹.

c) Condensation of Benzhydrylisocyanate with 3-Phenylphthalimidine

(67, 96)

Benzhydrylisocyanate (0.48 g, 2.3 x 10⁻³ mole) and 3-phenylphthalimidine (0.48 g, 2.3 x 10⁻³ mole), in 30 ml of anhydrous toluene was refluxed for 24 hours. Upon cooling, a white solid (0.89 g, 93% yield) was removed by filtration and dried, m.p. 197-199°. Mixed melting point with compound XXXIV, 197.5—199.5°. The infrared spectra of the condensation product and 3-phenyl-2-(N-benzhydrylcarboxamido)-
phthalimidine (XXXIV), were identical.

Anal. Found: C, 80.37; H, 5.41.
Calc. for C_{28}H_{22}N_{2}O_{2}: C, 80.35; H, 5.30.

7. **N,N'-dibenzhydrylurea (XXXV)**

Compound XXXV was rechromatographed on alumina using benzene: chloroform (4:1). The first fraction was decolorized with Norite and recrystallized from ethyl acetate, m.p. 289-290° (needles).

Infrared spectrum (KBr) of purified XXXV: 3290 (m), 3050 (w), 3020 (w), 2890 (w), 1623 (s), 1583 (sh-s), 1568-1560 (broad-s), 1490 (m), 1451 (m), 1340 (w), 1305 (w), 1270 (m), 1234 (w), 1188 (w), 1082 (w), 1057 (w), 1026 (w), 982 (w), 920 (w), 910 (w), 880 (w), 840 (w), 767 (m), 743 (m), 727 (w), 702 (s), 693 (s).

The strong absorption at 1623 cm\(^{-1}\) was indicative of the sym-disubstituted ureas (52).

8. **Synthesis of N,N'-dibenzhydrylurea (117)**

An authentic sample of XXXV was prepared by allowing the benzhydryl-isocyanate to react with the moisture in the air. The product, after recrystallization from acetone, had a melting point of 291-291.5° (needles); mixed melting point with XXXV, 290-291°. The literature melting point for this compound is 269-270° (92).

Anal. Found: C, 82.81; H, 6.47; N, 6.95.
Calc. for C_{27}H_{24}N_{2}O: C, 82.62; H, 6.16; N, 7.14.

9. **N-benzhydrylurea (XXXVI)**

Compound XXXVI was recrystallized from benzene then from hot water, m.p. 118-119° (Long needles). The infrared spectrum was similar to that
of monobenzylurea formed under similar conditions using benzaldehyde oxime (118).

Anal. Found: C, 73.89; H, 6.45; N, 12.33
Calc. for C_{14}H_{14}N_{2}O: C, 71.30; H, 6.23; N, 12.38.

10. **Synthesis of N-benzhydrylurea**

Concentrated ammonia (3 drops) was added to 3 drops of benzhydrylisocyanate dissolved in 2 ml of dry benzene. Dry acetone was added to effect a single phase and the mixture refluxed for one hour; then a further 3 drops of concentrated ammonia was added and refluxing continued for another hour. The solvent was then removed under reduced pressure and the resulting white solid recrystallized from hot water, m.p. 117.5-119.5° (needles). Mixed melting point with XXXVI, 117.5-119°. Literature melting point of N-benzhydrylurea, 113° (98).

E. **3-Phenylphthalimidine (XXXVII)**

The blue solid (A) was extracted with ethanol for 24 hours in a Soxhlet apparatus yielding 4.3 g of crystalline material. Chromatography of 0.105 g of the latter material on alumina using benzene:chloroform (5:1) as developer, yielded 0.019 g (10%) of N,N'-dibenzhydrylurea (XXXV). Further elution with chloroform afforded 0.054 g (25%) of a white solid which, on recrystallization from ethanol, had a melting point of 222-224°. The mixed melting point of the latter substance and authentic 3-phenylphthalimidine (93) was 222-224°. The infrared spectra of the two compounds were identical.
F. Blue Cobalt Complex

The blue solid (3.1 g) remaining after the ethanol extraction in E, did not melt below 360° and evolved ammonia (litmus reaction) when heated with concentrated sodium hydroxide. Attempts to dissolve the complex in a variety of organic solvents, including carbon disulfide, dimethylsulfoxide and N,N-dimethylformamide, were unsuccessful. Treatment with 2N HCl afforded CO₂ (precipitate with Ba(OH)₂). The latter acid solution was basified with NaOH and extracted with ethyl ether but yielded nothing.


G. Carbonylation of Benzophenone Semicarbazone at 200-220°

Benzophenone semicarbazone (8.0 g) was carbonylated at 200-220° under conditions similar to those used under section B. The reaction product consisted of 1.10 g of a blue solid (C) and a brown liquid, which on evaporation under reduced pressure, yielded 7.16 g of a brown solid (D). A 2.2 g aliquot of the latter was chromatographed on alumina, the results of which are shown in Table II. The blue solid (C) was extracted in a Soxhlet apparatus with acetone for 3 hours yielding 0.207 g of a yellow crystalline solid (XXXVIII), m.p. 90-91°. The remaining blue complex was insoluble in all the common organic solvents.

Analysis of the blue complex. Found: C, 22.45; H, 3.30; N, 21.61.
### Table II
Chromatographic Separation of Material B from the Carbonylation of Benzophenone Semicarbazone at 200-220°

<table>
<thead>
<tr>
<th>Developer a)</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield b)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>0.07 clear liquid</td>
<td>4</td>
<td>Diphenylmethane (XXXII)</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>0.28 yellow solid</td>
<td>10</td>
<td>Benzophenone azine (XXXVIII)</td>
</tr>
<tr>
<td></td>
<td>2300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Benzene:chloroform (75:25)</td>
<td>1200</td>
<td>0.45 white solid</td>
<td>11</td>
<td>Benzophenone 4-benzhydrylsemicarbazone (XXXIX)</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>0.10 brown solid</td>
<td>35</td>
<td>Benzophenone semicarbazone (XXXI)</td>
</tr>
<tr>
<td>(50:50)</td>
<td>700</td>
<td>0.75 yellow syrup</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chloroform</td>
<td>200</td>
<td>0.10 brown solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Benzene:ethanol (98:2)</td>
<td>1000</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(90:10)</td>
<td>400</td>
<td>0.09 brown solid</td>
<td>4</td>
<td>N-benzhydrylurea (XXXVI)</td>
</tr>
<tr>
<td>(50:50)</td>
<td>600</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

a. Developers were added consecutively

b. Yields are calculated in mole percent based on moles of substrate consumed.
H. Characterization of the Products from G

1. Benzophenone Azine (XXXVIII)

Compound XXXVIII was recrystallized from benzene-petroleum ether (b.p. 30-60°), m.p. 159-160°.

Infrared spectrum (KBr): 3050 (w), 3020 (w), 1584 (m), 1560 (m), 1486 (m), 1444 (m), 1319 (s), 1294 (w), 1270 (w), 1175 (w), 1157 (w), 1075 (w), 1025 (w), 999 (w), 983 (w), 973 (w), 956 (s), 917 (w), 909 (w), 774 (s), 764 (s), 724 (w), 690 (s), 666 (w), 655 (s).

Anal. Found: C, 87.13; H, 5.69; N, 7.30; mol. wt. (Rast) 360.
Calc. for C26H20N2: C, 86.63; H, 5.60; N, 7.78; mol. wt. 360.

2. Synthesis of Benzophenone Azine (91)

Benzophenone semicarbazone (4.65 g) was heated at 210° and atmospheric pressure for 90 minutes. The yellow melt was extracted with boiling ethyl ether until the ether was colorless. Concentration of the combined ethereal extracts afforded light yellow prisms (3.32 g, 95% yield), m.p. 163-165°. Mixed melting point with XXXVIII, 163-165°.

3. Benzophenone 4-benzhydrylsemicarbazone (XXXIX)

Compound XXXIX was recrystallized from benzene-petroleum ether (b.p. 30-60°), m.p. 179-181°.

Infrared spectrum (KBr): 3110 (m), 3150 (w), 3060 (w), 1668 (s), 1580 (m), 1495 (s), 1445 (m), 1365 (w), 1325 (w), 1230 (w), 1180 (m), 1105 (s), 1065 (m), 1025 (m), 945 (w), 910 (w), 862 (w), 835 (w), 782 (m), 753 (s), 735 (m), 695 (s).

n.m.r. signals (given in ° units; spectrum obtained in deuteriochloroform): 6.25 (HCPH2, doublet, area = 1 H), 6.95 (NH, area = 1 H),
7.32 (aromatic H, area = 20 H), 7.72 (NH, area = 1 H).

Anal. Found: C, 79.60; H, 5.67; N, 10.58; O, 4.11; mol. wt. (Rast) 369.
Calc. for C27H23N3O: C, 79.97; H, 5.72; N, 10.13; O, 3.95; mol. wt. 405.

Hydrolysis of XXXIX with dilute sulfuric acid yielded benzophenone (isolated as benzophenone 2,4-dinitrophenylhydrazone).

4. Synthesis of Benzophenone 4-benzhydrylsemicarbazone

a) Benzhydrylamine (92)

Benzophenone oxime (2.50 g, 0.013 mole), prepared in the usual manner (117), in 40 ml of absolute ethanol was poured down a reflux condenser on a freshly cut piece of sodium metal (4.30 g, 0.187 mole). The oxime dissolved and sufficient heat was generated to dissolve the sodium. After 50 minutes (time required to completely dissolve the sodium), the excess ethanol was removed under reduced pressure and water (50 ml) was added to the remaining residue. After partial neutralization with dilute sulfuric acid, the solution was extracted with 2 x 100 ml portions of ethyl ether and the combined ethereal extracts dried over potassium hydroxide pellets and filtered. Gaseous hydrogen chloride precipitated the benzhydrylamine as the hydrochloride which was subsequently removed by filtration and dried to yield 2.70 g (97% of theoretical) of product.

b) Condensation of Benzhydrylamine with Benzophenone Semicarbazone

Benzhydrylamine (0.47 g, 2.5 m moles), was added to powdered benzophenone semicarbazone (0.38 g, 1.6 m moles) and heated at 120° for
4 hours. The reaction was followed by the evolution of ammonia. A white precipitate formed after about 2 hours. The white solid was taken up in boiling ethanol (25 ml) which, upon cooling, afforded 0.47 g (74% yield) of white crystals, m.p. 179.5-180.5°. Mixed melting point with benzopheone 4-benzhydrylsemicarbazone (XXXIX), 179-180°.

I. Carbonylation of Benzophenone Semicarbazone at 175-180°

A mixture of 15.3 g (0.06 mole) of benzophenone semicarbazone, 4.6 g (0.01 mole) of preformed dicobalt octacarbonyl in 60 ml of purified chlorobenzene was placed in the glass liner of the bomb. To the air freed bomb was added 3280 p.s.i. (1.4 moles) of carbon monoxide at 20°. In one hour the temperature had reached 175° (5100 p.s.i.). Rocking was continued at 175° for a further one and one-half hours. The venting pressure was 3010 p.s.i. at 15°, which corresponds to 0.09 mole of carbon monoxide used. The catalyst was decomposed at 80° under an atmosphere of nitrogen. The solution was suction filtered and the blue residue (3.0 g) that remained was washed with acetone. The filtrate and washings were then evaporated to dryness under reduced pressure yielding 13 g of solid material.

J. Chromatographic Separation of the Products from I

The mixture was analyzed by chromatography using the gradient elution technique (119) on an alumina column (330 mm x 50 mm diam.) which had been washed with 300 ml petroleum ether (b.p. 30-60°). An amount of 3.64 g was dissolved in boiling chloroform (50 ml) and applied to part of the solid phase (alumina) contained in a beaker. The chloroform
was evaporated by passing warm air over the contents and the alumina was then added to the top of the column. The results are shown in Table III.

**Carbonylation of Benzophenone Azine at 240°C**

Benzophenone azine (1.50 g) was carbonylated at 235-245°C under conditions similar to those used in the first experiment (see Section B). Removal of the solvent under reduced pressure yielded 2.0 g of crude reaction product. A 0.830 g sample of the latter was extracted with petroleum ether (b.p. 30-60°C) in a Soxhlet apparatus yielding 0.17 g of solid. Further extraction using benzene afforded 0.63 g of solid leaving 0.03 g of insoluble residue. The petroleum ether-soluble fraction was redissolved in a minimum of refluxing petroleum ether (b.p. 30-60°C) and stored at 0°C overnight to yield 0.06 g of 3-phenylphthalimidine (XXXVII), identified by comparison (mixed melting point and infrared) with authentic 3-phenylphthalimidine (93). The supernatant was evaporated to dryness yielding 0.118 g of solid. A 0.06 g sample of the latter was chromatographed on alumina, as previously described, yielding 0.03 g of light yellow solid, m.p. 168-170°C, which was shown to be benzophenone azine (XXXVIII) by comparison (mixed melting point and infrared) with the starting material. A portion of the benzene-soluble fraction (0.110 g) was chromatographed on alumina yielding 0.011 g of benzophenone azine (XXXVIII) using benzene as a developer. Further elution with benzene:chloroform (1:1) afforded 0.076 g of 3-phenylphthalimidine (XXXVIII), m.p. 224-226°C.
Table III
Chromatographic Separation of the Products from the Carbonylation of Benzophenone Semicarbazone at 175-180°

<table>
<thead>
<tr>
<th>Developer</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield a (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether (b.p. 30-60°)</td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Petroleum ether (b.p. 30-60°):benzene (75:25)</td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>100</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(25:75)</td>
<td>150</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>200</td>
<td>0.106 clear liquid</td>
<td>6</td>
<td>Diphenylmethane (XXXII)</td>
</tr>
<tr>
<td>200</td>
<td>200</td>
<td>0.050 white solid</td>
<td>1</td>
<td>1,1,2,2-Tetraphenylethane (XXXIII)</td>
</tr>
<tr>
<td>600</td>
<td>600</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>200</td>
<td>0.0114 brown syrup</td>
<td></td>
<td></td>
</tr>
<tr>
<td>450</td>
<td>450</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>750</td>
<td>750</td>
<td>0.970 yellow solid</td>
<td>24</td>
<td>Benzophenone azine (XXXVIII)</td>
</tr>
<tr>
<td>200</td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:chloroform (75:25)</td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>600</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(25:75)</td>
<td>400</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>1200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>400</td>
<td>0.740 yellow solid</td>
<td>16</td>
<td>Benzophenone 4-benzhydrylesemicarbazone (XXXIX)</td>
</tr>
</tbody>
</table>

...contd.
<table>
<thead>
<tr>
<th></th>
<th>1100</th>
<th>1.400 yellow solid</th>
<th>35</th>
<th>Benzophenone semicarbazone (XXXI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene:ethanol (98:2)</td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95:5)</td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(90:10)</td>
<td>800</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(75:25)</td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol (100%)</td>
<td>700</td>
<td>0.080 green oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Yields are calculated in mole percent.
L. Carbonylation of Benzophenone 4-benzhydrylsemicarbazone at 240°

Benzophenone 4-benzhydrylsemicarbazone (0.47 g, 1.16 m moles) and preformed dicobalt octacarbonyl (0.8 g, 0.23 m mole) in 10 ml of anhydrous, thiophene-free benzene was carbonylated at 240-245° for 150 minutes. The reaction mixture was then refluxed to decompose the catalyst, filtered hot and the solvent removed under reduced pressure yielding 0.34 g of solid. The latter was taken up in a minimum of warm benzene and chromatographed on an alumina column (124 x 35 mm diam.). The results are shown in Table IV.

Identities of each component were confirmed by mixed melting points and comparison of the infrared spectra with those compounds previously identified with the exception of benzophenone (XL), which was identified as its 2,4-dinitrophenylhydrazone, again by comparison (infrared and mixed melting point) with an authentic sample of benzophenone 2,4-dinitrophenylhydrazone.

M. Carbonylation of Benzaldehyde Semicarbazone at 215-220°

To a solution of 10.0 g (0.06 mole) of benzaldehyde semicarbazone in 50 ml of anhydrous thiophene-free benzene, was added 3.0 g (0.01 mole) of preformed dicobalt octacarbonyl and 2050 p.s.i. of carbon monoxide. The mixture was heated with rocking, for three hours at 215-220°. The reaction product consisted of 5.47 g of blue solid (E) and a brown liquid which, on evaporation under reduced pressure, afforded 4.32 g of a solid green-colored material (F).
Table IV
Chromatographic Separation of the Products from the Carbonylation of Benzophenone \( \mu \)-benzhydrylsemicarbazone at \( 240^\circ \)

<table>
<thead>
<tr>
<th>Developer ( ^a )</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield ( ^b )</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>100</td>
<td>0.014 liquid</td>
<td>23</td>
<td>Diphenylmethane (XXXII)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.015 oil</td>
<td>7</td>
<td>Benzophenone (XL)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.029 white solid</td>
<td>6</td>
<td>3-Phenyl-2-(N-benzhydrylcarboxamido)phthalimidine (XXXIV)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>900</td>
<td>0.010 white solid</td>
<td>21</td>
<td>( N,N' )-dibenzhydrylurea (XXXV)</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:chloroform (67:33)</td>
<td>600</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1300</td>
<td>0.170 white solid</td>
<td>70.0</td>
<td>3-Phenylphthalimidine (XXXVII)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:ethanol (90:10)</td>
<td>800</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>400</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol:H(_2)O (50:50) (^2)</td>
<td>100</td>
<td>Trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>0.011 white solid</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( ^a \) Developers were added consecutively

\( ^b \) Yields are calculated in mole percent
The blue solid (E) was washed exhaustively with warm, absolute ethanol which yielded, on evaporation under reduced pressure, 1.66 g of crystalline solid. A 1.20 g portion of the latter, dissolved in a minimum of warm benzene, was chromatographed on an alumina column (133 x 54 mm diam.). The results are shown in Table V. The blue solid, having been exhaustively extracted, remained insoluble in the common organic solvents.

Anal. Found: C, 19.38; H, 3.09; N, 28.43.
Infrared spectrum (KBr disc): 3500-3200 (s-broad), 1625 (s-broad), 1450 (w), 1400 (w), 820 (w).

A 0.81 g sample of the green solid (F) dissolved in a minimum of benzene, was chromatographed on an alumina column (96 x 35 mm diam.). The results are shown in Table VI.

A portion of Material F was extracted with 2 x 20 ml portions of petroleum ether (b.p. 30-60°) to remove benzaldehyde azine. A 0.86 g sample of the petroleum ether - insoluble portion was dissolved in 10 ml of benzene and chromatographed on an alumina column (112 x 54 mm diam.). The results are shown in Table VII.
Table V

Chromatographic Separation of Material E from the Carbonylation of
Benzaldehyde Semicarbazone at 215-220°

<table>
<thead>
<tr>
<th>Developer a</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether (b.p. 30-60°)</td>
<td>100</td>
<td>0.011 clear liquid</td>
<td>1 b</td>
<td>Bibenzyl (XLI)</td>
</tr>
<tr>
<td></td>
<td>800</td>
<td>0.628 yellow solid</td>
<td>1 b</td>
<td>Benzaldehyde azine (XLII)</td>
</tr>
<tr>
<td>Benzene</td>
<td>600</td>
<td>0.179 clear syrup</td>
<td>3 c</td>
<td></td>
</tr>
<tr>
<td>Benzene:ethanol (98:2)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>0.138 syrup</td>
<td>2 c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.084 white solid</td>
<td>1 c</td>
<td></td>
</tr>
<tr>
<td>Ethanol (100%)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

a. Developers were added consecutively
b. Yields calculated in mole percent
c. Yields calculated in weight percent
Table VI

Chromatographic Separation of Material F from the Carbonylation of Benzaldehyde Semicarbazone at 215-220°

<table>
<thead>
<tr>
<th>Developer</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether (b.p. 30-60°)</td>
<td>200</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Benzene:Petroleum ether (b.p. 30-60°)(50:50)</td>
<td>175</td>
<td>0.061 white solid</td>
<td>6</td>
<td>Bibenzyl (XLI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>225</td>
<td>0.160 yellow solid</td>
<td>40</td>
<td>Benzaldehyde azine (XLII)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Benzene:Ethanol (99:1)</td>
<td>425</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.098 orange syrup</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(85:15) 150</td>
<td>trace syrup</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(50:50) 100</td>
<td>trace brown oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>200</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

a. Developers were added consecutively

b. Yields calculated in mole percent

c. Yield calculated in weight percent
Table VII
Chromatographic Separation of Material F after Extraction with Petroleum Ether (b. p. 30 - 60°)

<table>
<thead>
<tr>
<th>Developer a</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether (b.p. 65-110°)</td>
<td>250</td>
<td>0.006 clear liquid</td>
<td>Bibenzyl (XLI)</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Petroleum ether (b.p. 65-110°):benzene (75:25)</td>
<td>250</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>250</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>0.78 yellow solid</td>
<td>Benzaldehyde azine (XLII)</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>0.051 green oil</td>
<td></td>
</tr>
<tr>
<td>Benzene:chloroform (80:20)</td>
<td>500</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>500</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(25:75)</td>
<td>400</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>trace yellow oil</td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>200</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Benzene:ethanol (99:1)</td>
<td>200</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(96:4)</td>
<td>200</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>0.031 yellow oil</td>
<td></td>
</tr>
<tr>
<td>(90:10)</td>
<td>1200</td>
<td>0.075 grey solid</td>
<td>XLIII</td>
</tr>
</tbody>
</table>

...contd...
<table>
<thead>
<tr>
<th></th>
<th>250</th>
<th>250</th>
<th>500</th>
<th>250</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(80:20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>(50:50)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Ethanol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Ethanol:water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(75:25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>trace red oil</td>
</tr>
<tr>
<td>(25:75)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.036 yellow-white solid</td>
</tr>
</tbody>
</table>

a. Developers were added consecutively.
O. Carbonylation of Benzaldehyde Semicarbazone at 240°

To 5.90 g (0.036 mole) of benzaldehyde semicarbazone in 45 ml anhydrous, thiophene-free benzene, was added 1.8 g (5.3 m mole) preformed dicobalt octacarbonyl and 2000 p.s.i. of carbon monoxide. The mixture was heated for 150 minutes at 235-245°. The reaction product consisted of 2.76 g of blue solid (G) and a brown liquid, which on evaporation under reduced pressure afforded 3.50 g of a brown solid material (H).

The blue solid (G) was placed in a Soxhlet apparatus and extracted for 48 hours with 150 ml of ethyl ether. The latter, on evaporation, yielded 0.19 g of yellow solid. Further extraction with chloroform for 24 hours yielded only a trace of yellow solid and the remaining blue solid was insoluble in the common organic solvents. The 0.19 g of yellow solid was extracted with petroleum ether (b.p. 65-110°) to yield 0.06 g of yellow needles (m.p. 90-92°), the infrared spectrum of which, was identical to that of benzaldehyde azine obtained previously.

P. Chromatographic Separation of the Products from O

A 0.87 g sample of material H was dissolved in a minimum of benzene and chromatographed on an alumina column (125 x 35 mm diam.). The results are shown in Table VIII.
Table VIII
Chromatographic Separation of Material H from the Carbonylation of Benzaldehyde Semicarbazone at 240°

<table>
<thead>
<tr>
<th>Developer a</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>50</td>
<td>0.019 white solid</td>
<td>2 b</td>
<td>Bibenzyl (XLI)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.569 yellow solid</td>
<td>61 b</td>
<td>Benzaldehyde azine (XLII)</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>trace yellow solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1650</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:chloroform (50:50)</td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.045 brown solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:Ethanol (98:2)</td>
<td>250</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>200</td>
<td>0.040 white solid</td>
<td>3 c</td>
<td>XLIV</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol (100%)</td>
<td>250</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Developers were added consecutively
b. Yields are calculated in mole percent
c. Yield of XLIV calculated in weight percent
Q. Characterization of the Products from M and O

1. Bibenzyl (XLI)

This fraction was suspected as being bibenzyl by analogy with the previous experiments with the ketone semicarbazones and comparison of the infrared spectrum (film) of compound XLI with that of an authentic sample of bibenzyl (Eastman Kodak Chem. Co.) showed the two to be identical.

2. Benzaldehyde Azine (XLII)

Compound XLII was recrystallized from absolute ethanol to give yellow needles, m.p. 92-93°.

Infrared spectrum (KBr): 3000 (w), 2920 (w), 1619 (m), 1570 (w), 1492 (w), 1446 (m), 1320 (w), 1305 (w), 1288 (w), 1210 (m), 1170 (w), 1070 (w), 1020 (w), 999 (w), 955 (m), 912 (w), 857 (m), 751 (s), 691 (s), 675 (m).

Calc. for C\textsubscript{11}H\textsubscript{12}N\textsubscript{2}: N, 13.45.

When XLII was warmed in 15% sulfuric acid, the odor of benzaldehyde was detected almost immediately. The addition of 2,4-dinitrophenylhydrazine reagent resulted in an immediate orange precipitate, m.p. 250-251°. The infrared spectrum of the 2,4-dinitrophenylhydrazone of hydrolyzed XLII was identical to the infrared spectrum of authentic benzaldehyde 2,4-dinitrophenylhydrazone. Mixed melting point, 250-251°. Literature m.p. 250° (117).

3. Synthesis of Benzaldehyde Azine (103)

To 9.1 g (0.07 mole) of hydrazine sulfate dissolved in 150 ml of water, was added 4.7 ml of concentrated ammonia. This was followed by
the slow addition of 15.0 g (0.14 mole) of benzaldehyde under rapid stirring. The stirring was continued for thirty minutes after the addition was completed, whereupon the yellow crystalline solid was removed by filtration, washed with water and recrystallized from hot ethanol yielding 22.5 g (78% of theoretical) of yellow needles, m. p. 93.5-94°. Literature value, 92° (103). The infrared spectrum of the authentic benzaldehyde azine was identical to the infrared spectrum of XLII and an admixture showed no depression on melting.

4. **Compound XLIII**

This fraction was treated with Norite which removed the slight discoloration then recrystallized, first from carbon tetrachloride containing trace amounts of ethanol, then from benzene-petroleum ether yielding a white solid of m.p. 250.5-251.5°.

Infrared spectrum (KBr): 3380 (s), 3170 (s), 3060 (w), 1652 (s), 1620 (s), 1575 (s), 1450 (m), 1400 (s), 1295 (w), 1270 (w), 1179 (w), 1140 (m), 1118 (m), 1068 (w), 1019 (m), 916 (w), 845 (w), 807 (m), 787 (m), 768 (m), 700 (s), 681 (s).

n.m.r. signals (given in ° units; spectrum obtained in deuteriochloroform), 7.5 ± 0.5 (area = 5 H), 6.2 ± 0.2 (area about 1 H).

5. **Compound XLIV**

This fraction was recrystallized from hot benzene to yield a white solid, m. p. 214-215.5°.

Infrared spectrum (KBr): 3460 (m), 3380 (m), 3180 (m), 3070 (m), 3000 (m), 2980 (m), 2920 (m), 1685 (s), 1645 (s), 1595 (s), 1517 (w), 1489 (w) 1452 (m), 1430 (m), 1353 (m), 1325 (w), 1311 (w), 1294 (w), 1230 (w),
1140 (m), 1087 (m), 1069 (w), 1025 (w), 986 (w), 962 (w), 942 (m),
855 (w), 759 (s), 690 (s), 665 (w).

R. Carbonylation of Benzaldehyde Azine at 210°

To 8.20 g (0.04 mole) of benzaldehyde azine in 50 ml of anhydrous, thiophene-free benzene, was added 3.0 g (0.01 mole) of preformed dicobalt octacarbonyl and 1900 p.s.i. of carbon monoxide. The mixture was heated for 2.5 hours at 210°. The pressure drop was 110 p.s.i. at 18°. The reaction vessel contained 2.28 g of a black solid (J) and a dark green solution which upon evaporation under reduced pressure, afforded 7.15 g of greenish black solid (K).

S. Chromatographic Separation of the Products from R

The black solid J was extracted using methanol in a Soxhlet apparatus for 24 hours yielding 0.83 g of a green solid after removal of the methanol under reduced pressure. A 0.22 g sample of the latter green solid was dissolved in 4 ml of hot benzene and chromatographed on an alumina column (125 x 28 mm diam.). The results are shown in Table IX.

A 2.28 g sample of the greenish-black solid (K) was chromatographed on an alumina column (130 x 60 mm diam.). The results are shown in Table X. The first fraction from the chromatography of the greenish-black solid K (see Table X) was dried in vacuo, dissolved in hot benzene and petroleum ether (b.p. 30-60°) added to turbidity. The resulting white solid (0.130 g) was removed by filtration and dried (Compound XLVII). The filtrate was evaporated to dryness under reduced pressure, redissolved in a minimum of benzene and rechromatographed on alumina. The results are shown in Table XI.
Chromatographic Separation of the Material Extracted from the Black Solid (J) from the Carbonylation of Benzaldehyde Azine at 240°

<table>
<thead>
<tr>
<th>Developer (a)</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (b)</th>
<th>Compound Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>300</td>
<td>trace liquid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>trace solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>350</td>
<td>0.006 white solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:chloroform (75:25)</td>
<td>900</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>trace solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>trace oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>800</td>
<td>0.113 white solid</td>
<td>5</td>
<td>LI</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>400</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>trace blue solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>600</td>
<td>0.021 blue solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene:Ethanol (98:2)</td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol:H(_2)O (50:50)</td>
<td>500</td>
<td>black solid</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(a\). Developers were added consecutively

\(b\). Yield of LI calculated in weight percent
Table X
Chromatographic Separation of the Greenish-black Solid (K) from the Carbonylation of Benzaldehyde Azine at 240°

<table>
<thead>
<tr>
<th>Developer a</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>75</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1100</td>
<td>0.372 oily solid</td>
<td></td>
<td>(See Table XI)</td>
</tr>
<tr>
<td></td>
<td>1300</td>
<td>trace oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>0.449 white solid</td>
<td>16 b</td>
<td>2-Benzylphthalimidine (XLVIII)</td>
</tr>
<tr>
<td>Benzene:chloroform (75:25)</td>
<td>800</td>
<td>0.077 brown solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>800</td>
<td>0.057 white solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>550</td>
<td>0.187 green solid</td>
<td>6 c</td>
<td>XLIX</td>
</tr>
<tr>
<td></td>
<td>350</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50:50)</td>
<td>600</td>
<td>0.094 white solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>125</td>
<td>0.028 red solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>100</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>green solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>0.021 green solid</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>0.211 white solid</td>
<td>13 b</td>
<td>Phthalimidine (L)</td>
</tr>
<tr>
<td>Benzene:ethanol (8:2)</td>
<td>750</td>
<td>0.243 white solid</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

.....contd.
<table>
<thead>
<tr>
<th></th>
<th>50</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol (100%)</td>
<td>250</td>
<td>green oil</td>
</tr>
<tr>
<td>Ethanol:water (50:50)</td>
<td>500</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>0.369 grey solid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12° C</td>
</tr>
</tbody>
</table>

a. Developers were added consecutively  
b. Yields calculated in mole percent  
c. Yield of XLIX calculated in weight percent
Table XI
Rechromatography of the First Fraction from the Chromatography of Material K (See Table X)

<table>
<thead>
<tr>
<th>Developer a</th>
<th>Volume (ml)</th>
<th>Weight (g)</th>
<th>Yield (%)</th>
<th>Compound (Symbol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether (b.p. 30-60°)</td>
<td>100</td>
<td>0.023 clear liquid</td>
<td>1 b</td>
<td>Bibenzyl (XLI)</td>
</tr>
<tr>
<td>Benzene:petroleum ether (b.p. 30-60°) (50:50)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Benzene</td>
<td>100</td>
<td>green solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Benzene:chloroform (75:25)</td>
<td>100</td>
<td>0.033 white solid</td>
<td>1 c</td>
<td>XLIV</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>green solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>0.043 grey solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>0.127 white solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chloroform</td>
<td>100</td>
<td>trace yellow solid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

a. Developers were added consecutively.
b. Yields calculated in mole percent.
c. Yield of XLV calculated in weight percent.
T. Characterization of the Products from R

1. Bibenzyl (XLI)

This compound was readily identified by comparison with the bibenzyl previously isolated.

2. Compound XLIV

Compound XLIV was twice recrystallized from ethyl ether-petroleum ether (b.p. 30-60°) to yield colorless needles, m.p. 242-242.5°.

Infrared spectrum (KBr): 3400 (broad-w), 1585 (w), 1520 (s), 1444 (w), 1366 (s), 1296 (w), 1171 (w), 1064 (w), 1025 (w), 840 (w), 743 (m), 682 (m), 645 (w).

3. 2-(N-benzylcarboxamido)phthalimidine (XLVI)

Compound XLVI was recrystallized from benzene-petroleum ether (b.p. 30-60°), decolorized with charcoal, and recrystallized from ethyl ether-petroleum ether (b.p. 30-60°) to yield colorless needles, m.p. 127-128°.

Infrared spectrum (KBr): 3290 (m), 3030 (w), 2940-2920 (w), 1710 (s), 1675 (m), 1613 (w), 1590 (w), 1533 (s), 1494 (w), 1470 (w), 1442 (m), 1355 (sh), 1369 (s), 1343 (w), 1342 (m), 1302 (m), 1258 (m), 1237 (w), 1216 (w), 1193 (w), 1162 (sh), 1155 (m), 1104 (w), 1078 (w), 754 (m), 737 (s), 693 (s), 682 (m), 650 (m).

4. Synthesis of 2-(N-benzylcarboxamido)phthalimidine

a.) Preparation and Characterization of Benzylisocyanate (10h)

To 15.0 g of freshly distilled benzyl chloride (B & A reagent) was added 21.6 g of silver cyanate (Eastman Kodak) contained in a 100 ml flask equipped with a reflux condenser. The flask was warmed
with a bunsen flame to initiate the reaction after which the reaction proceeded on its own and appeared complete in about ten minutes. The apparatus was arranged directly for downward distillation and 6.4 g (40% of the theoretical) of a light yellow liquid was distilled over at the water aspirator. A few drops of concentrated ammonia was added to a few drops of the yellow liquid product above and set aside. Long white needles were subsequently filtered off, m.p. 150-152°. Literature melting point for monobenzyl urea, 147-149° (52).

b. Condensation of Benzylisocyanate with Phthalimidine (55, 67, 96)

To 70 mg of phthalimidine (0.52 mmole) dissolved in dry toluene, was added 70 mg (0.52 mmole) of the freshly distilled benzylisocyanate. The mixture was refluxed gently over 12 hours and the toluene subsequently removed in vacuo, to afford a white solid. The latter was chromatographed on alumina using benzene as developer to give 95 mg (68% of theoretical) of a white solid which, after recrystallization from carbon tetrachloride-petroleum ether (b.p. 30-60°), gave white needles, m.p. 126-127°. Mixed melting point with compound XLVI, 126.5-127.5°. The infrared spectra were identical.

Anal. Found: C, 72.28; H, 5.13; N, 10.17.
Calc. for C_{16}H_{14}N_{2}O_{2}: C, 72.16; H, 5.30; N, 10.52.

5. Compound XLVII

Compound XLVII was recrystallized from hot benzene to yield colorless needles, m.p. 288-288.5°.

Infrared spectrum (KBr): 3020 (m), 1593 (m), 1581 (m), 1500 (m), 1485 (m), 1480 (sh), 1459 (s), 1445 (w), 1441 (w), 1407 (w), 1395 (w), 1320 (w),
1200 (w), 1173 (w), 1155 (w), 1125 (m), 1068 (m), 1025 (w), 1000 (w),
980 (w), 965 (m), 915 (m), 851 (w), 837 (w), 775 (m), 765 (s), 734 (s),
712 (s), 705 (s), 696 (s), 689 (s), 649 (m).
Anal. Found: C, 84.90; H, 6.66; N, 8.17.
Calc. for C₁₂H₂₃N₂: C, 84.92; H, 6.87; N, 8.26.

6. 2-Benzylphthalimidine (XLVIII)

Compound XLVIII was rechromatographed on alumina using benzene as
developer, then recrystallized from boiling petroleum ether (b.p.
30-60°), yielding white fluffy needles, m.p. 90-91°. Literature melting
point of 2-benzylphthalimidine 91° (59). The infrared spectrum of
compound XLVIII, and that of an authentic sample of 2-benzylphthalimidine
(57), prepared by the method of Murahashi and co-workers (59), were
identical.

Infrared spectrum (KBr): 3020 (w), 2900 (w), 1667 (s), 1492 (w),
1466 (m), 1450 (m), 1436 (w), 1411 (m), 1354 (m), 1324 (w), 1315 (w),
1298 (w), 1284 (w), 1264 (m), 1219 (w), 1203 (m), 1180 (w), 1140 (w),
1086 (w), 1070 (w), 968 (w), 926 (w), 900 (w), 855 (w), 809 (w),
792 (w), 764 (w), 747 (sh-s), 735 (s), 697 (m), 680 (w).

n.m.r. signals (given in δ units; spectrum obtained in deuterio-
chloroform), 7.5 ± 0.5 (area = 9 H), 4.77 (area = 2 H), 4.20 (area = 2 H).
Anal. Found: C, 80.61; H, 5.97; N, 6.25.
Calc. for C₁₅H₁₃NO: C, 80.67; H, 5.87; N, 6.27.

7. Compound XLIX

Compound XLIX was rechromatographed on alumina using benzene:
chloroform (9:1) as developer yielding 0.119 g of white solid.
The latter was recrystallized from hot benzene, m.p. 295-297°.

Infrared spectrum (KBr): 3100 (broad-s), 3010 (w), 2900 (w), 1715 (s), 1680 (s), 1655 (sh), 1615 (m), 1566 (m), 1539 (m), 1370 (m), 1304 (m), 1297 (m), 1210 (m), 1195 (sh), 1159 (m), 1150 (w), 1100 (m), 1070 (w), 1014 (w), 995 (w), 950-957 (broad-w), 846 (w), 795 (w), 790 (sh), 762 (w), 745 (m), 758 (s), 708 (m), 679 (m).

8. Phthalimidine (L)

Compound L was dissolved in a benzene-ethanol mixture, treated with charcoal, filtered and the filtrate evaporated to dryness under reduced pressure and recrystallized from benzene-petroleum ether (b.p. 30-60°) yielding colorless needles, m.p. 151°-151.5°. Literature melting point for phthalimidine (120), 119° (needles). Comparison of compound L (infrared and mixed melting point) to an authentic sample of phthalimidine (118), prepared by the method of Graebe (121) showed them to be identical.

Infrared spectrum (KBr): 3190 (m), 3060 (w), 2900 (w), 1670 (s), 1616 (w), 1585 (w), 1469 (m), 1448 (m), 1350 (m), 1316 (w), 1300 (w), 1210 (w), 1184 (w), 1136 (w), 1051 (w), 1011 (w), 939 (w), 841 (w), 796 (w), 771 (w), 726 (s), 710 (m), 680 (w).

9. Compound LI

Compound LI was recrystallized from hot benzene, m.p. 255-256°. Purified LI was only slightly soluble in benzene, carbon tetrachloride, chloroform, dioxane and ethanol but dissolved readily in dimethylsulfoxide, trifluoroacetic acid and trifluoroacetic anhydride.

Infrared spectrum (KBr): 3380 (s), 3220 (m), 3030 (w), 2900 (w), 1715 (s), 1664 (s), 1597 (sh-s), 1580 (s), 1555 (sh-m), 1470 (m), 1455 (m), 1391 (m),
1363 (s), 1320 (m), 1300 (m), 1219 (m), 1183 (w), 1154 (m), 1145 (m),
1082 (w), 922 (w), 820 (w), 800 (w), 761 (m), 730 (m), 677 (w), 668 (w),
651 (w), 643 (w).

n.m.r. signals (given in $\delta$ units): 1) spectrum obtained in
trifluoroacetic anhydride, 4.96 (area = 2 H), 7.55, 7.60, 7.79
(area = 4 H), 7.90, 8.01 (area = 2 H); 2) spectrum obtained in dimethyl-
sulfoxide, 4.80 (area = 2 H), 7.72 \pm 0.30 (area = 6 H). When compound
LI was heated in concentrated sulfuric acid, carbon dioxide was
evolved (precipitate with Ba(OH)$_2$); when heated in concentrated sodium
hydroxide, a basic (to litmus) gas was evolved.

Anal. Found: C, 61.65; H, 4.82; N, 15.78; O, 18.13. Mol. wt. (Rast) 587.
Calc. for C$_9$H$_8$N$_2$O$_2$: C, 61.35; H, 4.58; N, 15.91; O, 18.16. Mol. wt. 176.
Bibliography


89. I. Wender. Private communication to A. Rosenthal.

100. W. Hieber. Z. Elektrochem. 40, 158 (1934).


