DIRECT CARBONYLATION OF AROMATIC NITRILES USING
DICOBALT OCTACARBONYL

by

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ABSTRACT

A new method of synthesizing \( N \)-substituted phthalimidines is described. When benzonitrile was reacted with carbon monoxide containing about 0.04 volume percent of hydrogen and in the presence of dicobalt octacarbonyl and pyridine in benzene solution at 235° and 3400 p.s.i. pressure the following compounds were produced: \( N \)-benzylphthalimidine (8%), \( N \)-phenylphthalimidine (3.7%), and benzamide (3.9%). When 40 p.s.i. hydrogen was added under the same reaction conditions, the yield of \( N \)-benzylphthalimidine increased (16%). When benzonitrile was subjected to the same reaction conditions using 240 p.s.i. hydrogen and no pyridine, \( N \)-benzylphthalimidine (15%) and sym-dibenzylurea (8%) were produced.

A study on the mechanism of the ring closure process using deuterium gas revealed, that the ortho-hydrogen of the aromatic ring is not transferred directly to the unsaturated carbon-nitrogen bond in the course of the reaction.

When phenylacetonitrile was reacted with carbon monoxide and 350 p.s.i. hydrogen at 250° in the presence of dicobalt octacarbonyl the following compounds were isolated: phenacetyl-\( \beta \)-phenethyamine (30%), di-\( \beta \)-phenylethylamine (23%), di-\( \beta \)-phenylethylurea (3.1%) and phenylacetamide (3%).

When \( m \)-tolunitrile was reacted under similar reaction conditions with 185 p.s.i. hydrogen at 240°, \( N \)-m-xylylurea (9.5%), \( N,N' \)-di-\( m \)-xylylurea (13.5%), and \( m \)-toluamide (11.5%) were produced.

Organometallic complexes were also obtained in all the reactions described above.
The infrared spectra of all the compounds obtained, and the n.m.r. spectra of N-benzylphthalimidine and N-phenylphthalimidine are described.
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# Table of Contents

I  Historical Background

(a) Introduction  
(b) Transfer of Carbon Monoxide  
(c) Transfer of Hydrogen  
(d) Transfer of Carbon Monoxide and Hydrogen  
(e) Kinetics and Mechanism  
(f) Properties and Structure of Dicobalt octacarbonyl  
(g) Oxo and related reactions of certain nitrogen containing organic compounds

II  Discussion

Reactions of Carbon Monoxide and Hydrogen with:

A. Benzonitrile  
B. Phenylacetonitrile  
C. m-Tolunitrile

III  Experimental

General considerations  
Reaction of benzonitrile with carbon monoxide in the presence of dicobalt octacarbonyl  
Reaction of benzonitrile with carbon monoxide and hydrogen in the presence of dicobalt octacarbonyl  
Reaction of benzonitrile with carbon monoxide and deuterium in the presence of dicobalt octacarbonyl  
Reaction of phenylacetonitrile with carbon monoxide in the presence of dicobalt octacarbonyl  
Reaction of phenylacetonitrile with carbon monoxide and hydrogen in the presence of dicobalt octacarbonyl
Reaction of m-tolunitrile with carbon monoxide in the presence of dicobalt octacarbonyl 46

Reaction of m-tolunitrile with carbon monoxide and hydrogen in the presence of dicobalt octacarbonyl 49

Synthesis of authentic compounds 52

IV Bibliography 54
### List of Figures

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table I.</td>
<td>Reactions of aromatic nitriles with carbon monoxide and hydrogen</td>
<td>20</td>
</tr>
<tr>
<td>Chart I.</td>
<td>Reactions of benzonitrile with carbon monoxide and hydrogen</td>
<td>21</td>
</tr>
<tr>
<td>Chart II.</td>
<td>Reaction of phenylacetonitrile and m-tolunitrile with carbon monoxide and hydrogen</td>
<td>22</td>
</tr>
</tbody>
</table>
HISTORICAL BACKGROUND

(a) Introduction

In recent years dozens of new reactions catalysed by the metal carbonyls at elevated temperatures and pressures have been discovered. There is now less mystery about the ways by which hydrogen and carbon monoxide are transferred to organic molecules by transition metals. Excellent reviews of this work have been presented by Wender, Sternberg and Orchin (1)(2). The detailed mechanism of insertion of carbon monoxide, whether directly from the gas phase or from an adjacent carbonyl group, has not yet been established. However, the fact that a carbon-metal sigma-bond can be formed and that carbon monoxide can be inserted between metal and carbon contributes greatly to the understanding of reactions catalysed by metal carbonyls. It is in fact only the last few years that the synthetic applications of metal carbonyls have attracted the attention of academic rather than industrial chemists. Much of this awakening interest seems to stem from the revival of interest in organo-metallic compounds engendered by new concepts of bonding, as typified by ferrocene.

A related reaction which sheds light on the function of metal carbonyls as catalytic intermediates is the exchange of carbonyl groups in certain organic compounds catalysed by cobalt carbonyl (3). The exchange of carbonyl groups in anhydrides has been interpreted as involving splitting of a carbon-oxygen bond with formation of a metal-oxygen and metal-carbon bond. The possibility of a carbon-nitrogen bond being split in a similar manner is supported by the fact that diphenylurea undergoes
exchange with carbon monoxide at elevated temperature, probably by splitting of a carbon-nitrogen bond to give aniline. In spite of the fact that only two types of organic carbonyl groups are known to undergo exchange, the formation of intermediates containing carbon-metal and nitrogen-metal bonds may also occur in other reactions undergoing this catalysis.

There are more than 50 such catalysed reactions known today and the number seems to be increasing rapidly. They may be classified as follows: those involving transfer of carbon monoxide, transfer of hydrogen, and transfer of carbon monoxide and either hydrogen or compounds containing labile hydrogen such as water, alcohols or amines. These reactions are carried out in the presence of metal carbonyls at pressures up to 4000 atm. and at temperatures up to 300°C. A variety of heterocyclic compounds have been prepared by reactions carried out under similar conditions.

In addition, metal carbonyls in the form of surface complexes probably play a role as catalytic intermediates in the Fischer-Tropsch synthesis, for the conversion of water gas into hydrocarbons (\textsuperscript{4}). Although this process has been known since 1925, its dependence on the in situ formation of metal carbonyls was not recognized immediately and most of the pioneering work in the application of metal carbonyls to organic synthesis was carried out by W. Reppe and his co-workers at I. G. Farben during the Second World War (\textsuperscript{5})(\textsuperscript{6}). One of the main results of this work was the "OXO" process for the conversion of olefins into homologous aldehydes or alcohols, by reaction with synthesis gas - a mixture of carbon monoxide and hydrogen - and a cobalt catalyst (\textsuperscript{7})(\textsuperscript{1})(\textsuperscript{8})(\textsuperscript{9}). Since
the 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. Insofar as the products of such reactions are primarily aldehydes the term hydroformylation is preferable.

(b) Transfer of Carbon Monoxide

Carbonylation of primary and secondary amines (10)(16) can be achieved by using stoichiometric amounts of dicobalt octacarbonyl as a source of carbon monoxide. Many of these reactions take place at room temperature and pressure, forming the N-formyl derivatives and ureas. This transfer of carbon monoxide may involve formation of nitrogen-cobalt and hydrogen cobalt bonds, e. g.

\[
\begin{align*}
\text{CH}_3\text{NH} & + \text{Co}_2(\text{CO})_8 \rightarrow \text{CH}_3\text{NCo}(\text{CO})_4 + \text{HCo}(\text{CO})_4 \\
\text{CH}_3\text{NCo}(\text{CO})_4 & \rightarrow \text{CH}_3\text{NCOCo}(\text{CO})_3 \\
\text{CH}_3\text{NCOCo}(\text{CO})_3 + \text{HCo}(\text{CO})_4 & \rightarrow \text{CH}_3\text{NCHO} + \left[\text{Co}_2(\text{CO})_7\right]
\end{align*}
\]

followed by insertion of carbon monoxide from adjacent carbonyl group:

and finally splitting of the cobalt-carbon bond by HCo(CO)$_4$:

The existence of an intermediate such as Me$_2$NCOCo(CO)$_3$ is supported by the formation of tetramethylurea. The latter could conceivably be formed by "aminolysis" of this complex at the cobalt-carbon bond. Similar
steps may be involved in the carbonylation of amines by Mn, Fe, Re, and Ru carbonyls (11)(12)(13).

The behaviour of tertiary amines on carbonylation is very interesting. Aliphatic tertiary amines are reported (14)(15) to give N,N-dialkyl formamides; the fate of the alkyl group is not reported. Aryl tertiary amines on the other hand are reported to react as shown where R is an alkyl group

\[
\begin{array}{c}
\text{N}^R_{R} \text{CO} \\
\end{array}
\]

The only two examples quoted are N,N-diethylaniline and N,N-dimethyl-β-naphthylamine.

(c) Transfer of Hydrogen

Hydrogenation of various organic compounds can be achieved with cobalt or iron carbonyl hydride. In the absence of hydrogen acceptor, cobalt carbonyl hydride decomposes with evolution of hydrogen and formation of dicobalt octacarbonyl:

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

In the presence of an acceptor, the hydrogen is transferred directly to the acceptor. There are many examples of reductions that can be carried out with stoicheiometric amounts of carbonyl hydride (17)(18). Addition
of hydrogen to organic compounds can also be carried out catalytically in the presence of dicobalt octacarbonyl at elevated carbon monoxide and hydrogen pressure and at elevated temperature \((19)(20)(21)\).

The presence of carbon monoxide is necessary to prevent decomposition of dicobalt octacarbonyl:

\[
\text{Co}_2(\text{CO})_8 \rightarrow 8\text{CO} + 2\text{Co}
\]

As in the reductions with stoichiometric amounts of carbonyl hydride, the immediate source of hydrogen in these reactions is probably cobalt carbonyl hydride formed reversibly from dicobalt octacarbonyl and hydrogen. The reduction of aldehydes, for example, may be pictured occurring in the following manner. Cobalt carbonyl hydride adds to the aldehyde to give one of the two complexes shown:

\[
\begin{align*}
\text{CH}_3\text{CHO} + \text{HCo(CO)}_4 & \rightarrow \text{CH}-\text{C}-\text{Co(CO)}_4 \\
& \rightarrow \text{CH}-\text{C}-\text{O}-\text{Co(CO)}_4
\end{align*}
\]

Hydrogenolysis of the cobalt-carbon or cobalt-oxygen bond then yields the alcohol. It is also possible to carry out reductions with water as the source of hydrogen \((22)(23)\). In some instances, however, such as in the cobalt catalyzed reactions of carbon monoxide and olefins with alcohols and amines, products containing added hydrogen are formed \((24)\). In the absence of gaseous hydrogen, the hydrogen is furnished by the reactants e.g. water from the dehydrogenation of alcohol or amine, via the formation and decomposition of cobalt hydrocarbonyl.
(d) Transfer of Carbon Monoxide and Hydrogen

The transfer of carbon monoxide and hydrogen to organic substrates may be explained by the concepts outlined before. First, an intermediate with a carbon-metal bond is formed; carbon monoxide is then inserted between the atoms forming this bond, and the sequence is terminated by reaction with hydrogen or with another compound containing labile hydrogen.

The hydroformylation or oxo reaction i.e. the synthesis of next higher aldehyde from an olefin is an example of transfer of carbon monoxide and hydrogen to an olefin catalysed by a metal carbonyl. As customarily performed a cobalt catalyst is employed and is added either as preformed dicobalt octacarbonyl, a cobalt salt or as the reduced metal. Iron and nickel catalyst also have been indicated for the hydroformylation reaction in the patent literature (25)(26), but both in fact appear to be inactive under the usual conditions. The use of rhodium or iridium catalysts also has been advocated (27). This seems perfectly feasible since both are known to form carbonyl hydrides analogous to cobalt hydrocarbonyl, which is now recognized to be the true intermediate in the hydroformylation reaction (28). The temperatures normally employed are in the region 100-120°C, as at higher temperatures 150-180°C, subsequent reduction of the aldehyde to a primary alcohol occurs. Carbon monoxide-hydrogen pressures of 200-300 atmospheres are typical.

Conjugated dienes are converted to the saturated aldehyde (29). This may proceed via the unsaturated aldehyde which is known to be reduced under hydroformylation conditions (30)(21). Unsaturated acids and esters, however, are generally hydroformylated at the $\beta$-carbon atom.
Alcohols may be used in place of olefins, under hydroformylation conditions. Where feasible the reaction appears to proceed via olefin formation (31). Products frequently encountered are formate esters and hydrocarbons; such hydrogenolyses occur particularly frequently with benzyl alcohols (32)(33)(34), and in some cases may be the predominant reaction. It has been shown (32) that both the rate of reaction and the extent of hydrogenolysis are increased by the introduction of nuclear para or meta electron releasing substituents. Nitro groups are reduced to amino groups under these conditions (32). Acetylenes react very sluggishly under hydroformylation conditions (35).

The mechanism of the above reactions can be examined in the light of recent findings.

(e) Kinetics and Mechanism

A variety of mechanisms have been proposed from time to time for the carbonylation reactions discussed so far in the literature. While a complex postulated in the reaction has not been isolated, there is good evidence that a carbonyl group may be replaced by an olefinic double bond (36), with formation of a metal-olefin bond, if the primary complex is formed from cobalt carbonyl hydride and an olefin. A logical intermediate derived from the olefin and dicobalt octacarbonyl has also been reported recently by Kirch and Orchin (37).

The process of carbonyl insertion is now better understood, and was found to be a reversible process, largely as a result of the study of alkyl and acyl manganese pentacarbonyls (38). The reactions are currently envisioned as proceeding via three distinct stages. Initial reaction of
the substrate with the metal carbonyl leads to the eventual formation of a carbon-metal sigma bond. A carbonyl insertion between the carbon and metal atoms then occurs and this is followed by cleavage of the carbon-metal bond. The observations indicate a mechanism in which the carbon monoxide residue inserted is one originally bonded to manganese and the over-all reaction may be envisioned as occurring via a metal to carbon migration of the alkyl group. Whether or not the insertion of the carbonyl group and the coordination of another carbon monoxide molecule to the manganese atom are concerted process is uncertain.

Most carbonylations proceed by insertion of carbon monoxide between carbon-metal and nitrogen metal bonds, and there is a strong feeling that hydroformylation proceeds through similar intermediates. A variety of reaction sequences have been proposed by individual investigators to account for the observed interdependencies of the reactants. The main evidence is the now proven intermediacy of cobalt hydrocarbonyl in the reaction. Under normal hydroformylation conditions dicobalt octacarbonyl is converted rapidly to cobalt hydrocarbonyl (39). However, in the presence of an olefin, no free cobalt hydrocarbonyl is detectable until hydroformylation is complete. Furthermore it is found (28) 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 supplied by the observation that the rate of this reaction with various olefins parallels the relative rates at which the same olefins undergo hydroformylation (40).
The formation of hydrocarbons in the hydroformylation reaction is readily envisioned in terms of the reaction
\[
\text{RCo(CO)}_4 + \text{HCo(CO)}_4 \rightarrow \text{RH} + \text{Co}_2(\text{CO})_8
\]
competing with prior carbonyl insertion. This is very well illustrated by the hydroformylation of nuclear substituted benzyl alcohols, where electron-withdrawing substituents favoured hydrocarbon formation (32). In this connection the reluctance of trifluoromethylpentacarbonylmanganese to undergo carbonyl insertion may be mentioned (38), it was converted to the trifluoromethyl compound on heating but the reverse process could not be achieved.

The reaction rate is reported (41) to be increased by the presence of small amounts of organic bases, and decreased by large amounts. Pyridine and its homologs are particularly effective, whereas primary and secondary amines are much less efficient and tertiary amines almost inhibit the reaction. Variations in solvent medium have little effect on the reaction rate (40).

The mechanism of the hydroformylation reaction is not yet clear, since much uncertainty still surrounds the precise mode of formation of most of the observed products, but there can be little doubt that the reaction proceeds along the lines outlined for the carbonylation reactions in general.

(f) Properties and structure of Dicobalt octacarbonyl (1)

Under a slight pressure of carbon monoxide the octacarbonyl is stable indefinitely at room temperatures. In the absence of carbon monoxide
decomposition takes place according to the following equation

\[ 2\text{Co}_2(\text{CO})_8 \rightarrow \text{Co}_4(\text{CO})_{12} + \text{CO} \]

The octacarbonyl is readily soluble in hydrocarbon solvents but reacts more or less readily with polar solvents such as alcohols, ketones, amides and amines.

The tetramer \((\text{Co}_4(\text{CO})_{12})\), is pyrophoric but indefinitely stable in an inert solvent.

Cobalt hydrocarbonyl \((\text{HCo(CO})_4)\), forms pale yellow crystals stable below their melting point \((-26^\circ\text{C})\). Above this temperature it decomposes rapidly:

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

It is a stable strong acid on oxygen free aqueous solution at \(25^\circ\text{C}\) and may be titrated using phenolphthalein as an indicator. The accepted electronic structures for these compounds are shown below:

\[
\begin{align*}
\text{O} \equiv \text{C} - & \text{Co} - \text{Co} - \text{C} \equiv \text{O} \\
\text{O} \equiv \text{C} - & \text{Co} - \text{C} \equiv \text{O} \\
\text{H} - & \text{Co} - \text{C} \equiv \text{O} \\
\text{C} & \equiv \text{O}
\end{align*}
\]

Communications show that the cobalt hydrocarbonyl, in the presence of carbon monoxide and hydrogen, reacts with certain substrates which may be considered as a homomolecular disproportionation, at room temperature and atmospheric pressure to give products that are also secured from the same substrates under hydroformylation conditions. The substrate must be a base in the Lewis sense and fulfill geometric requirements. Hieber
and Wiesboeck (42) examined the products when many nitrogen bases reacted with dicobalt octacarbonyl. This work shows that cobalt carbonyls react with benzonitrile to form a definite complex compound of polar structure as follows:

\[ 3 \left[ \text{Co(CO)}_4 \right]_2 + 12\text{PhCN} \rightarrow 2 \left[ \text{Co(PhCN)}_6 \right] \left[ \text{Co(CO)}_4 \right]_2 \]

This complex has a black crystalline structure and is very sensitive to air, and loses benzonitrile above -5°C to give

\[ \left[ \text{Co(PhCN)}_{1.9} \right] \left[ \text{Co(CO)}_4 \right]_2 \]

this is soluble in methanol and acetone due to the solvation of the nitriles. They also used picoline, quinoline, pyridine, aniline and others, and concluded that the equation above is general for these nitrogen bases. When B is a primary or secondary aliphatic amine, dicobalt octacarbonyl reacts with this base to form a salt according to the equation

\[ B + \text{Co}_2(\text{CO})_8 \rightarrow \left[ \text{BCo(CO)}_4 \right] + \left[ \text{Co(CO)}_4 \right]^- \]

When B is a weak base such as pyridine, this salt is not stable.

Isonitriles, the RS group of mercaptans, and acetylene have been shown to replace one or more carbonyl groups in dicobalt octacarbonyl. Acetylene for example replaces the two bridge carbonyl groups according to the equation

\[ \text{Co}_2(\text{CO})_8 + \text{HC}≡\text{CH} \rightarrow \text{Co}_2(\text{CO})_6\text{C}_2\text{H}_2 + 2\text{CO} \]

Some light has been thrown on the way in which more than one carbon monoxide unit may be introduced. It has been found that the acetylene-dicobalt hexacarbonyl complex (43) reacts with carbon monoxide at 200
atmospheres and 70°C, three moles of carbon monoxide are taken up and a new complex (\( \text{hh} \)) is formed as shown in the following scheme:

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{C} & \quad \text{C} \\
\text{(CO)}_3 & \quad \text{Co} - \text{Co} - (\text{CO})_3 \\
\end{align*}
\]

\[
\text{CH} - \text{CO} \quad \text{CH} \\
\text{(CO)}_3 \\
\text{Co} - \text{Co} - (\text{CO})_3
\]

The conversion of this new intermediary complex to the observed products is readily conceivable, (h5,h6) as is also its conversion to succinic acid.

Sly (h7) reports a detailed X-ray crystallographic study of diphenyl acetylenedicobalt hexacarbonyl and he found that each carbon was bonded to each cobalt, and that the plane of the carbon-carbon bond was roughly at 90° to the plane of the cobalt-cobalt bond. Sly stated that this structure represents one of the first molecules to be studied which exhibits a multipoint attachment of a single organic molecule to more than one metal atom. He feels this is possibly analogous to the postulated attachment of an organic substrate to a metal surface during heterogeneous catalytic reactions.

It has been found that the two bridged carbonyls in dicobalt octacarbonyl can be replaced at room temperature on standing (h8), and a reaction mechanism has been proposed by Tirpak (h9) for the system where disubstituted acetylene is allowed to react with carbon monoxide and dicobalt octacarbonyl in the absence of hydrogen. A possible explanation for the fact that acetylene is less reactive than the olefins is that the catalyst is removed to form acetylenic dicobalt hexacarbonyls.
If this complex is not catalyst no reaction occurs until it becomes active. This is in contrast with the mechanism suggested by Aldridge et al (50), who suggests that the hydroformylation reaction may be heterogeneously catalysed. They report data from which it can be deduced that the rate of hydroformylation of an olefin is not directly dependent upon the amounts of soluble cobalt present under reaction conditions. The insoluble cobalt may provide a fresh highly active metal surface which is constantly being consumed and deposited by carbonyl formation and breakdown. These authors conclude that it appears likely that any direct role in hydroformylation catalysis the cobalt carbonyls or cobalt hydrocarbonyls may play must be carried out in conjunction with a solid cobalt surface.

(g) Oxo and related reactions of certain nitrogen containing organic compounds

Many workers (51)(52)(53)(54)(55)(56) have investigated the reactions of organic compounds containing the N=N, the N=O, and the C≡N groupings. The formation of urea derivatives observed in all cases, and especially the fact that a formation of symmetrically substituted urea derivatives were found from asymmetrically substituted azo compounds is of special note.

Azobenzenes are converted, in part, to N,N'-diarylureas when reacting with dicobalt octacarbonyl and carbon monoxide and hydrogen (1:1). Under the same conditions both nitrobenzene and hydrazobenzene also were converted to N,N'-diphenylurea. In the case of unsymmetrically substituted azobenzenes all three possible N,N'-diarylureas are formed, although the one containing two different aryl nuclei predominates (53)(54).
Ureas also have been obtained from oximes, arylhyrazones and of aniline. Thus, benzaldoxime gave N,N'-dibenzylurea and N-benzylurea (55), and analogous products were obtained from the oxime of 2-acetylnaphthalene (57), together with heterocyclic products.

Acetone phenylhydrazone in benzene, when reacted with carbon monoxide at about 250°C in the presence of preformed dicobalt octacarbonyl yielded sym-diphenylurea, monophenylurea, and diphenyl (58). The fact that diphenyl was present in the reaction product suggests strongly that during the reaction phenyl free radicals were produced, and these subsequently combined. Aniline also gave sym-diphenylurea although in much lower yield.

In 1958 Nakamura (59) reported reduction of Schiff bases under hydroformylation conditions to secondary amines. The authors noted those Schiff bases which are the most unsaturated are most easily reduced, and form the lowest amounts of resinous byproducts. They also noted that amines, especially aliphatics, lower the yield considerably. This is possibly connected with the type of reaction mentioned by Hieber (42). Murahashi also reduced C=N linkages in the reaction of Schiff bases with synthetic gas (54).

Several routes to heterocyclic compounds have started with compounds containing carbon-nitrogen double bonds as in Schiff bases or oximes, and nitrogen-nitrogen double bonds as in azobenzenes. Anils, such as benzalaniline, are converted by reaction with dicobalt octacarbonyl in benzene at 200-230°C and carbon monoxide pressures in the range 100 to 200 atmospheres into 2-phenylphthalimidines as shown:
Murahashi in 1955 (60) reported this reaction, and also that it failed with nickel catalysts but ring closure occurred with dicobalt octacarbonyl present. The reaction also failed when water or alcohol was present as the solvent. He claims that this is the first example of a dicobalt octacarbonyl catalysed reaction in which carbon monoxide becomes attached to an aromatic nucleus. 1-Naphthaldehyde anil produced an analogous compound. It is noteworthy that this case ring closure occurred in the 3-position, since most ring closure reactions of 2-substituted naphthalene derivatives take place in the 1-position.

A wide variety of Schiff bases have been employed in this type of reaction (60)(53)(61)(56). Iron pentacarbonyl also catalyses this reaction, but less effectively. In the presence of hydrogen the anils are reduced to the corresponding amines. The factors controlling the direction of cyclization are not obvious; only a few m-substituted benzaldehyde anils have been employed, and ring closure was reported to give the 2,5-substituted phthalimidines.

The effect of substituents on the rates of reaction of a series of anils $RN=CR^1,R^2$ have been observed (53). When $R=R^1 = C_6H_5$, the nature of $R^2 = H, CH_3$ or $C_6H_5$ had no appreciable effect on the rate. Ortho
substituents on $R=C_6H_5$ lowered the rate, but no steric effect from the ortho substituents was observed for the reduction of the anils. In the cases when $R = p$-nitrophenyl, $R^1 = H$, $R^2 = C_6H_5$, and $R = C_6H_5$, $R^1 = H$, $R^2 = o$-nitrophenyl no reaction occurred.

The application of the oxo reaction to several aromatic aldoximes and ketoximes has been thoroughly investigated recently. Attempts to prepare 2-hydroxyphthalimidines have been unsuccessful. Benzophenone oxime (62) and its O-methyl ether (63) gave 3-phenylphthalimidine and phenyl-benzylketoxime produced 3-benzylphthalimidine. An extension of previous studies of the reaction of carbon monoxide with aromatic ketoximes led to a new benzoquinoline synthesis. 2-Acetonaphthoxime (A) gave mono- and di-substituted ureas analogous to that of benzaldoxime (55) together with 10% of B and 41% of C, compound B was formed probably as a result of hydrogenolysis of the N-hydroxy derivative of compound B (64).

Cyclization of the oxime A with carbon monoxide took place when the ratio of carbon monoxide to hydrogen (98.5:1.5).

Azobenzene reacts with dicobalt octacarbonyl at 170-190° under carbon monoxide pressure of 150 atm. forming 2-phenylindazolone (D) and a small amount of 3-phenyl-2,3-dioxo-1,2,3,4-tetrahydroquinazoline (E) and diphenylurea (65)(52).
That the formation of E probably proceeds through D was shown by the fact that D reacts with carbon monoxide to give E in quantitative yield at 230°C. In the case of substituted azobenzenes ring closure occurred on the ring containing the substituent. Identical observations have been made as regards catalysts and solvents as for conversion of anils to phthalimidines.

In 1962 Rosenthal and Weir (66) reported on the reaction of carbon monoxide with benzophenone phenylhydrazone and 1-methyl-benzophenone phenyl-hydrazone. The products, depending on the temperature applied, were 3-phenylphthalimidine-N-carboxyanilide (F) and 3-phenylphthalimidine.

Here the exocyclic carbonyl group is situated between the two nitrogen atoms forming an N-carboxyanilide side chain. 1-Methylbenzophenone phenylhydrazone when reacted with carbon monoxide gave a mixture of two isomers, 3-phenyl-6-methyl- and 3-(p-tolyl)-phthalimidine-N-carboxyanilide. Their results differ from previous observations on the effect of substituents on carbon monoxide ring closure reactions of
substituted azobenzenes (65), where the cyclization always occurred on the substituted ring, and the second molecule of carbon monoxide was incorporated between the two nitrogen atoms via the reaction in the formation of quinazolons from indazolone (52).

Most recent findings on carbonylation reactions were obtained in this department as a result of a study of the carbonylation of aromatic imino compounds, containing the ureido (-N-C-NH₂), ureylene (-N-C-N-) and imino groups attached to the nitrogen of the C=N group (67). In particular benzophenone semicarbazone and benzophenone azine were reacted with carbon monoxide using dicobalt octacarbonyl catalyst at 235-245°C, to yield substituted ureas, substituted phthalimidines, and 3-phenylphthalimidine, respectively.

In 1960 Horiie and Murahashi reported (68) on the mechanism of phthalimidine and indazolone formation, from Schiff bases and azo compounds. From their results it appeared that the primary step would be the addition of cobalt-carbonyl to the lone pair of nitrogen, which is hindered by o-substituent of large steric requirement. The experiment with p-methyl substituted anil has shown that the methyl group had rather promoting effect when free from steric effect. Hence a steric effect was operative in the complex formation. The N-CO bond is then stabilized with the formation of a five membered ring with the carbon atom of benzene, with the transfer of the hydrogen atom of ortho position of benzene to the unsaturated bond of C=N or N=N. The presence of such hydrogen atom acceptor is essential, and would assist the ring formation.
Where there is lacking such an accepting group, the complex would stabilize by converting to the N-formyl compound.

Aromatic nitriles e.g. benzonitrile trimerize readily at high pressures 35-50,000 atm. and high temperatures 350-500°C to the corresponding triazines (69). Cairns and Larchar (70) trimerized benzonitrile to the corresponding triazine under the influence of methanol or weak bases at pressures of 7000-8500 atm.

All previous attempts to carry out carbonyl insertions in aromatic nitriles were unsuccessful. Murahashi attempted (54) to obtain amino acids or a polypeptide directly from nitriles under oxo condition. The experiments gave only a small quantity of amines (primary and secondary) and no reaction product was obtained in which carbon monoxide had been involved, and he concluded that reduction of nitrile would be very difficult to be realized.
<table>
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<tr>
<th>Expt. No.</th>
<th>Substrate</th>
<th>Substr. mole</th>
<th>Catalyst mole</th>
<th>Solvent ml</th>
<th>CO p.s.i.</th>
<th>H₂ mole</th>
<th>Reaction Temp.°C</th>
<th>Reaction Time (hr)</th>
<th>Product(s)</th>
<th>Yield %</th>
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<tr>
<td>1</td>
<td>Benzonitrile</td>
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<td>2030</td>
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<td>225</td>
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a) 0.0063 mole of pyridine was added
Preformed dicobalt octacarbonyl catalyst, and benzene solvent was used in all experiments
All yields should be considered 10-15% higher than reported, due to experimental losses in
the superpressure reaction vessel. The void of the vessel was 180 ml when 50 ml solvent was used.
REACTIONS OF BENZONITRILE WITH CARBON MONOXIDE AND HYDROGEN

**CHART I**

(a) PhCN:CO:H₂(1:7.5:1)
(b) PhCN:CO:H₂(1:58:1)
CHART II  Reaction of Phenylacetonitrile and m-Tolunitrile with Carbon Monoxide and Hydrogen
DISCUSSION

The object of this investigation was to obtain fundamental information concerning the carbonylation of aromatic nitriles and related reactions under oxo conditions. This arose as a consequence of previous studies on the high pressure carbonylation and oxo reaction of certain other nitrogen-containing organic compounds.

It is well known that nitriles are reduced to amines via the Schiff base, and that cobalt carbonyl is able to catalyze the oxo-reaction and hydrogenations in the presence of carbon monoxide and hydrogen. There have been previous examples of dicobalt octacarbonyl catalysed reactions at elevated pressure and temperature, in which carbon monoxide readily cyclized nitrogen (in the trivalent state) to the aromatic ring \((52)(56)(60)(62)(63)(64)(65)(66)\). From chemical considerations it might be conceivable that if an addition of carbon monoxide to the double bond of a Schiff base could occur, it is possible that the nitrogen in an aromatic nitrile might undergo a similar type of reaction.

The reaction of nitriles under oxo-conditions had not been previously explored and so that of benzonitrile, phenylacetonitrile and m-tolunitrile was examined in the present research.

A. Benzonitrile (See Chart I, page 21, and Table I, page 20)

When a benzene solution of benzonitrile (I) (0.029 mole) and pyridine (0.0063 mole) was reacted with 2220 p.s.i. carbon monoxide (containing 0.04% hydrogen) at 235° in the presence of preformed dicobalt
octacarbonyl for eight hours, N-benzylphthalimidine (IV) (8%), N-phenylphthalimidine (II) (3.7%) and benzamide (III) (3.9%) were formed. The reaction products were separated on an alumina column, and their structures were established by direct comparison (mixed m.p. and infrared) with authentic samples.

Since about 10% of the substrate escaped through the hole of the liner (the material outside of the liner was not recovered because of possible contamination), the reported yields of products are correspondingly lower than they actually were.

By varying the reaction conditions, it became clear that certain parameters play an important role in the course of these reactions. With reference to this Markó reported recently (83) that the upper limit for the stability of cobalt carbonyls is 206° and that maximum conditions for the oxo reaction can be obtained around 210°.

Increasing the reaction time and addition of an organic base, such as pyridine was found to be very important. The pyridine, according to Wender (86), facilitates the disproportionation of the catalyst, which then under the reaction conditions forms the reactive intermediary complex leading to the observed products. The relative stability of the complex may depend upon the basicity and geometry of the entering group. One might assume that stronger complexing had occurred between benzonitrile and the catalyst than between pyridine and the catalyst thus facilitating the cyclization reaction.

It is not clear whether the activation of the organometallic complex entails, thermal decomposition, a reaction of the complex with carbon
monoxide or a reaction of the complex with the organic substrate. An intermediary labile complex between the benzonitrile and the catalyst, in contrast to the fully characterized organometallic complexes readily formed from nitriles and cobalt carbonyls (42), has never been isolated.

The indications are that the low yield at higher temperatures was due to the absence of dicobalt octacarbonyl catalyst. The presence of Co metal in the reaction product suggests that the catalyst readily decomposes above 230°, and therefore the absence of this carrier is the cause of the low yield.

The fact that both N-benzyl- and N-phenylphthalimidines were present in the reaction product suggested that there might be at least two reactive intermediates in the direct ring closure reaction. A free radical mechanism is possible. The products also indicate that the high purity carbon monoxide (containing about 0.01% hydrogen according to the manufacturer) acted as a reducing agent (84) and the benzonitrile was reduced by some type of hydrogen transfer process, as envisaged by Natta and co-workers (24), and the cobalt carbonyl acted as a hydrogen transfer agent. It is likely that all three reactants, i.e., the benzonitrile, carbon monoxide, and hydrogen are united in one complex at some stage of the reaction.

It is interesting that neither toluene, benzylamine, nor biphenyl could be detected in the reaction product. The presence of methylamine would indicate the elimination of the cyanide group from benzonitrile, producing benzene which readily forms at 250° in the vapour phase catalytic hydrogenation of aromatic nitriles (85). The presence of benzamide indicates
that a small amount of moisture was present in the reactor. No phthalimidine could be detected in the reaction mixture.

In each run a brown solid was found in the reaction mixture which appeared to be an organometallic complex (m.p. over 360°). Reduced cobalt metal was also found in all cases where the experiment was carried out above 240°. No complete characterization work was done on the complexes. They showed absorption in their infrared spectra in the carbonyl and N-H stretching region, but failed to show absorption in the Co-H stretching region of cobalt carbonyl hydride near 1950 cm⁻¹.

In one case 0.12 mole of hydrogen gas was added to a mixture of 0.132 mole of benzonitrile, 50 ml of dry benzene, 0.0175 mole of dicobalt octacarbonyl and 1800 p.s.i. carbon monoxide. The reactants were heated with rocking at 250° for 10 hours. The products, identified by comparison with authentic samples were N-benzylphthalimidine (IV) (15%) and sym-dibenzylurea (V) (8%). The presence of the latter compound in the reaction product indicated that it must have been formed by some type of condensation reaction in two steps:

(a) Hydrogenation of benzonitrile to benzylamine

(b) Condensation of two moles of primary amine with one mole of carbon monoxide to yield sym-dibenzylurea.

Such dehydrogenation has been shown in the presence of dicobalt octacarbonyl (24h) probably by the formation and decomposition of cobalt hydrocarbonyl. For step (a) to occur readily the amount of hydrogen present must be critical.
The complete mechanism for the ring closure reaction giving N-substituted phthalimidines is unknown, however it was of interest to determine if hydrogen was directly transferred from the aromatic ring to the carbon of C-N group. As a consequence, an experiment was set up in which 40 p.s.i. deuterium was used instead of hydrogen gas. If the hydrogen is transferred, the ratio should be 1:2 for the deuteration of the methylene group of the fused five membered ring to the methylene in -N-CH₂-C₆H₅ in the only major cyclized product N-benzylphthalimidine. However this was not realised. By n.m.r. the methylene group of the fused five membered ring in N-benzylphthalimidine was found to be deuterated to the same extent as the methylene group of -N-CH₂-C₆H₅.

In a second experiment, when 50 p.s.i. deuterium was added to the reaction mixture the former was deuterated 10% more, and also the deuteration of the two non equivalent methylenes both increased about 10%.

The only reasonable conclusion which can be drawn from the above experiment is that the ortho-hydrogen atom on the benzene ring is not transferred directly to the unsaturated carbon-nitrogen bond during the ring closure process, but to some other suitable hydrogen acceptor probably dicobalt octacarbonyl to form cobalt hydrocarbonyl. The latter might then exchange its hydrogen with the deuterium to yield cobalt deuterocarbonyl and this in turn could transfer its deuterium to the nitrile.

In addition to the N-benzylphthalimidine, a liquid fraction was isolated from the product mixture by adsorption chromatography on alumina.
This fraction was tentatively assigned the structure of N-formyl piperidine on the following bases; 1) absorption at 1735 cm⁻¹ in the infrared indicating a carbonyl; 2) a strong signal at 1.2 (δ) and at about 8.0 (δ) in the n.m.r. which might arise from methylene groups and from the formyl hydrogen respectively. Other workers have reacted pyridine with carbon monoxide and hydrogen to yield N-formyl and N-methyl piperidine (82).

B. Phenylacetonitrile (See Chart II, page 22, and Table I, page 20).

In an attempt to extend the above ring closure reactions of aromatic nitriles to the six membered ring, phenylacetonitrile was subjected to the carbonylation reaction conditions to produce N-substituted derivatives of isoquinolin-1-one. (Expt. No. 6). That the reaction did not take place was indicated first by the fact that no absorption of carbon monoxide was observed after the completion of the experiment. The only isolated product in a minor amount was phenylacetamide (X) (3%) due to hydrolysis.

It was hoped that by increasing the reaction time and adding excess hydrogen (substrate: H₂, 1:2), the reduction of the carbon-nitrogen bond in the nitrile which is believed to be the first step in these type of reactions, would be facilitated. When 11.7 g of phenylacetonitrile (0.1 mole) and 2.5 g (0.0073 mole) of dicobalt octacarbonyl were reacted in 50 ml benzene with 350 p.s.i. (0.2 mole) of hydrogen and 1740 p.s.i. of carbon monoxide at 250° for eight hours (Expt. No. 7) the following products were observed: phenacetyl-β-phenethylamine (VII) (30%), di-β-phenylethylamine (VIII) (23%), N,N'-di-β-phenylethylurea
(IX) (3.1%) and phenylacetamide (X) (1.3%). The only product obtained from this condensation reaction is the urea in which carbon monoxide had been involved, since the other compounds can be produced independently under the reaction conditions. The formation of the urea can be postulated via the primary amine produced by the reduction of phenylacetonitrile, and then condensing with carbon monoxide to give the observed product.

C. m-Tolunitrile (See Chart II, page 22, and Table I, page 20)

In order to activate the ortho positions in benzonitrile by the introduction of an m-methyl group, m-tolunitrile was subjected first to carbonylation reaction conditions. By analogy with the above described and established cyclization reactions of benzonitrile by direct carbonylation, it was hoped that N-substituted derivatives of 5-methyl phthalimidines will be obtained as the product of these reactions under similar conditions. However this has not yet been realized.

When m-tolunitrile was reacted with carbon monoxide in the presence of dicobalt octacarbonyl at 250°C for eight hours the only product obtained was m-toluamide. In a second experiment which was carried out at 235°C under similar conditions, m-toluamide (XIV) (2%) and another crystalline compound was separated in low yield (5% by weight). No structure has been assigned to this compound which melts at 67-68°C, but the strong absorption in the infrared in the carbonyl region 1670 cm⁻¹ and the n.m.r. spectra (δ units): singlet centered at 4.2 and 4.73, and multiplet centered at 7.2 strongly indicated that a cyclic product was obtained. The analysis fits C₁₇H₁₇NO.
When m-tolunitrile 6.12 g (0.052 mole) and 2 g (0.0058 mole) of dicobalt octacarbonyl in 50 ml dry benzene were reacted with 1900 p.s.i. of carbon monoxide and an excess of hydrogen 185 p.s.i. (0.103 mole) at 240° for 8.5 hours in the high pressure bomb (pressures given at room temperature) the following products were obtained: N,N'-di-m-xylylurea (XII) (13.5%), N-m-xylylurea (XIII) (9.5%) and m-toluamide (XIV) (11.5%). N,N'-Di-m-xylylurea and N-m-xylylurea were identified by mixed melting point using authentic samples (79). These compounds also possessed infrared spectra identical with those of the authentic samples. The infrared spectrum of m-toluamide was identical with that of the Sadtler Standard Spectra (80). Ammonia has been also detected in the reaction mixture.

The formation of the N-m-xylylurea can be explained by the reduction of m-tolunitrile to the primary amine, which then condensed with carbon monoxide and ammonia to give the observed product. The N,N'-m-di-xylylurea can be obtained from the mono-urea by heating, and would be expected under the reaction conditions if N-m-xylylurea were present.
EXPERIMENTAL

General considerations:

All infrared spectra reported were obtained using a Perkin-Elmer Model 21 Double beam spectrometer in this department. The vapor phase chromatography was carried out on an Aerograph Gas Chromatographic Instrument (Wilkents Instrument & Research Inc.) equipped with a Varian Associates G-10 Graphic Recorder. The n.m.r. reported were obtained using a Varian Associates A-60 analytical n.m.r. spectrometer. All alumina used for chromatography was British Drug Houses Chromatographic grade calcined alumina. Elemental microanalyses were carried out by Mrs. A. E. Aldridge of this Department and by Dr. A. Bernhardt of the Max Planck Institute, Mulheim, Ruhr, Germany. Melting points were determined using a polarising microscope on an electrically heated hot stage. Corrected melting points were read directly. The infrared and n.m.r. determinations were done by Mrs. M. Zell and Mrs. E. Brieron of this Department respectively.

Dicobalt octacarbonyl catalyst was prepared from cobalt (II) carbonate according to a previously described method (71). The carbon monoxide used contained 0.04% by volume of hydrogen (analysis supplied by the Matheson Company from whom the carbon monoxide was purchased). The hydrogen used was obtained from the Canadian Liquid Air Co. Ltd. of Vancouver, B. C. in 99.7% purity. The deuterium gas was supplied by the Liquid Carbonic Division of General Dynamics, San Carlos, Calif. in 99.7% isotopic purity. Specially dried and purified thiophene-free benzene (72) was used as solvent. Technical benzonitrile was first
dried over anhydrous magnesium sulphate as dessicant and filtered, then
distilled through a fractionating column under partially reduced pressure.
A constant boiling fraction was collected at 130°C. Reagent grade
phenylacetonitrile and m-Tolunitrile were purified by distilling under
reduced pressure. The physical constants of these compounds all
corresponded to the values found in the literature (73).

The reactions were carried out in a glass lined Aminco superpressure
reaction vessel, which was equipped with a rocker mechanism and has a
void of 180 ml. Temperature control was achieved through a Brown
pyrometer using a thermocouple which had been calibrated against a
standard thermometer.

The carbon monoxide and hydrogen were treated as
ideal gases through the temperature and pressure range involved.

Reaction of Benzonitrile with Carbon Monoxide in the presence of Dicobalt
Octacarbonyl (Expt. No. 3, Table I, page 20)

A mixture of 3 g (0.029 mole) of benzonitrile, 5 g (0.0115 mole) of
dicobalt octacarbonyl, 0.5 g (0.0063 mole) of pyridine, 25 ml of dry
benzene and carbon monoxide containing 0.04% by volume of hydrogen
(2220 p.s.i. at 22°C) was placed in the high pressure bomb. The
reactants were heated with rocking at 235°C for 8 hours. An observed
pressure drop of 50 p.s.i. at 15°C was obtained. The bomb was then
cooled overnight and vented.

The reaction product consisted of a dark brown benzene solution
and 2.07 g of blue solid. The solid was extracted with hot benzene,
chloroform and ethyl alcohol, and the extract combined with the residue, obtained by evaporation of the benzene solution under vacuum, yielded 1.0 g of organic reaction product (brown oil).

The organic material (1.0 g) was added to the top of an alumina column (11 x 3.5 cm diam.) by dissolving it in a mixture of 10 ml benzene-ethanol (3:1). The column was then developed as follows:

1. 95 ml of benzene eluted 0.8 g of brown oil.
2. 80 ml of benzene removed no material.
3. 450 ml of benzene gave 0.05 g of oil which contained traces of residual crystals melting at 230° on recrystallization from chloroform-petroleum ether (30-60°).
4. 100 ml of benzene-ethanol (92:8) yielded nothing.
5. 260 ml of benzene-ethanol (92:8) yielded 0.135 g (3.9%) of a crystalline compound. This compound which was recrystallized from ethanol gave no depression in a mixed melting point determination with an authentic sample of benzamide (m.p. 129°) prepared according to Vogel.

The Compound also had an identical spectrum to that of authentic benzamide. Infrared spectrum of benzamide in KBr disc: 3375 (s), 3160 (w), 1655 (s), 1620 (s), 1575 (s), 1450 (m), 1405 (s), 1296 (w), 1120 (m), 1025 (w), 790 (m), 684 (m) cm\(^{-1}\).

Further washing of the column with benzene-ethanol (90:10) solution produced nothing. The percent recovery was 99%.
The first fraction (0.8 g) from the chromatogram was dissolved in a mixture of 10 ml benzene-chloroform (10:1) and rechromatographed on an alumina column (10 x 3.5 cm diam.). The development of the chromatogram was as follows:

(1) 90 ml of benzene eluted 0.02 g of yellowish oil.
(2) 90 ml of benzene gave 0.05 g of fluorescent oil with some crystals which melted at 105-109°.
(3) 180 ml of benzene yielded nothing.
(4) 180 ml of benzene gave 0.198 g of crystals (3.7%) (compound A).
(5) 270 ml of benzene gave nothing.
(6) 600 ml of benzene eluted 0.247 g of oil (8%) which crystallized out on standing at room temperature (compound B).
(7) 90 ml of benzene removed no material.
(8) 270 ml of benzene-ethanol (98:2) gave 0.14 g of oily yellowish material.

Further washing of the column with benzene-ethanol (90:10) eluted nothing.
The recovery of organic material from the column was 82%.

Characterization of N-phenylphthalimidine (fraction 4):

Compound A from fraction 4 was recrystallized twice from ether-petroleum-ether (30-60°) and melted at 166°. Mixed melting point with an authentic sample of N-phenylphthalimidine (74) was 166°. Compound A in a KBr disc showed the following major absorptions in the infrared spectrum: 3450 (s), 1685 (s), 1680 (s), 1505 (w), 1308 (w), 1150 (w), 752 (s), cm⁻¹. The spectrum showed peaks at 1680 and 1685 cm⁻¹ which were attributed to the fact that a cyclic compound was obtained (C=O stretching mode). Anal. Found: N, 6.42%. Calc. for C₁₄H₁₁NO:
N, 6.7%. Compound A proved to have an identical infrared spectrum with an authentic sample of N-phenylphthalimidine. n.m.r. signals, given in δ units, spectra obtained in carbon tetrachloride: singlet centered at 4.78 (methylene of fused five membered ring, area = 2 H), multiplet centered at 7.46 (aromatic H, area = 5 H), multiplet centered at 7.78 (aromatic H of fused benzene ring, area 4 H).

Characterization of N-benzylphthalimidine (fraction 6):

Compound B from fraction (6) gave a sharp melting point of 91° on recrystallization from ether-petroleum-ether (30-60°). The mixed melting point of compound B and an authentic sample of N-benzylphthalimidine was 91°. The authentic sample of N-benzylphthalimidine was prepared from benzalbenzylamine (77) according to Murahashi (60). Compound B also had an infrared spectrum identical with that of the authentic sample. Infrared spectrum of compound B (KBr): 3040 (w), 2920 (w), 1673 (s), 1496 (w), 1470 (s), 1455 (s), 1415 (s), 1360 (m), 1326 (s), 1206 (s), 1134 (m), 1072 (m), 972 (m), 929 (m), 792 (m), 766 (s), 700 (s), cm⁻¹. n.m.r. signals: given in δ units obtained in carbon tetrachloride: singlet centered at 4.14 (methylene of -N-CH₂C₆H₅, area = 2 H), singlet centered at 4.65 (methylene of fused five membered ring, area 2 H), multiplet centered at 7.2 (aromatic H, area = 9 H). Because of the low yield, no further work was done on the rest of the fractions from the chromatogram.

Reaction of Benzonitrile with Carbon Monoxide and Hydrogen in the presence of Dicobalt Octacarbonyl (Expt. No. 4, Table I, page 20)

The reaction was carried out essentially in the same manner as in
the previous section. To a glass liner 13.57 g (0.132 mole) of benzonitrile, 50 ml benzene and 6 g (0.0175 mole) of dicobalt octacarbonyl catalyst were added. The liner was placed in the autoclave and hydrogen was run in up to 230 p.s.i. (0.116 mole), followed by 1800 p.s.i. carbon monoxide up to a total pressure of 2030 p.s.i. Final reading was made after pressure equilibrium was obtained in the bomb. Total heating and rocking time was 10 hours at an average of 250°, where the maximum pressure was 3600 p.s.i.

After cooling the reaction vessel to room temperature overnight, the total pressure drop (380 p.s.i. at 25°) corresponded to the absorption of 150 p.s.i. (0.088 mole) of carbon monoxide, which is 0.66 mole per mole of substrate or 5.03 mole per mole of catalyst, and 230 p.s.i. (0.116 mole) of hydrogen if we assume that all the hydrogen was used up. This would correspond approximately to one mole of hydrogen per mole of substrate.

The material from the bomb was placed in a 250 ml erlenmeyer flask, and heated on a hot plate with constant stirring for 60 minutes in the hood, at the temperature of refluxing benzene in order to decompose the catalyst and its complexes. After filtering, the solid insoluble material was washed several times with benzene and ethyl alcohol to remove all the organic material. Since further washing dissolved nothing, and left behind a black insoluble solid, the filtrate was then evaporated under reduced pressure to leave white plate-like crystals covered with a large amount of yellowish oily material. The total apparent organic yield from the reaction was 5.231 g.
As flame test showed that the insoluble black solid contained organic material, it was extracted by using a Soxhlet extraction apparatus. Benzene, chloroform and ethanol were used for extraction, each for 24 hours, respectively. Nothing appreciable was contained in the benzene and chloroform extract, although the solvents developed a pink colour during the extraction. The ethanol extracted 0.1 g of greenish blue material (compound C) which after redissolving in ethanol was precipitated out by adding low boiling petroleum ether (30-60°) in small portions. Anal. Found: N, 25.11%, C, 33.11%, H, 4.2%, O, 24.71%, and by difference Co, 12.87%. This compound C, supposedly a cobalt complex melted above 360° and was soluble in hot ethanol and methanol.

The black insoluble material was analyzed (compound D). Found; N, 8.29%, C, 16.09% and H, 1.86%. Infrared spectrum of this compound D (1.14 g) in a KBr disc gave the following major absorptions: 2120 (s), 1637 (s), 1395 (m), cm\(^{-1}\). No structure has been assigned to compound C and D, which were obtained under the reactions conditions, and are assumed to be organometallic complexes of cobalt.

An amount of 0.31 g from the organic product was weighed out for chromatographic separation on alumina (basic). All attempts to dissolve it in a small amount of benzene resulted in a cloudy (milky) solution, from which a dark-brown precipitate came down. The mixture was dissolved in 5 ml acetone and introduced into the column (size 10 x 3.5 cm diameter). The following fractions were obtained consecutively:

1. 70 ml of benzene-chloroform (70:30) gave nothing.
2. 90 ml of benzene-chloroform (70:30) yielded 0.09 g of yellow oil.
3. 700 ml of benzene-chloroform (70:30) eluted 0.13 g of oily material.
(4) 300 ml of benzene-chloroform (70:30) gave nothing.

(5) 450 ml of benzene-chloroform (70:30) removed 0.06 g of crystalline material.

(6) 90 ml of benzene-chloroform (70:30) yielded 0.01 g of brown oil.

(7) 190 ml of benzene-chloroform (70:30) gave nothing.

(8) 200 ml of benzene-ethanol (90:10) eluted 0.015 g of dark brown oil. Further washing with a mixture of benzene-ethanol eluted no more material.

Total recovery of organic material from the chromatography, 0.305 g (98%).

Characterization of N-benzylphthalimidine (fraction 3).

The oil from fraction (3) crystallized out on standing in about an hour, and was recrystallized from a mixture of ether-low boiling petroleum ether (30-60°). m.p. 91°. This compound was N-benzylphthalimidine established by comparing it (infrared spectrum and mixed melting point) with an authentic sample (60) (yield 15%).

Characterization of sym-dibenzylurea (fraction 5).

Fraction (5) was recrystallized twice from chloroform-petroleum-ether (30-60°), m.p. 169-170°C. Infrared spectrum of the crystals (needles) showed the following major absorptions in a KBr pellet cm⁻¹:

3320 (s), 3030 (w), 1625 (s), 1570 (s), 1495 (w), 1244 (s), 1074 (w), 1025 (w), 750 (w), cm⁻¹. Anal. Found: N, 11.6%. Calculated for C_{15}H_{16}N_{2}O: N, 11.6%. This compound proved to be sym-dibenzylurea (yield 8%), gave a melting point 169° undepressed on admixture with an authentic sample of sym-dibenzylurea (75). It also had the same infrared spectrum as that of the authentic sample.
n.m.r. signals (given in \( \delta \) units: spectra obtained in deuterochloroform); singlet centered at 4.28 (methylene of \( \text{C}_6\text{H}_5\text{CH}_2-\text{N} \), area = 4 H), singlet centered at 7.24 (aromatic H, area = 10 H).

The oils obtained in several fractions during the development of the chromatogram were soluble in organic solvents. Further work was abandoned because of the low yield.

Reaction of Benzonitrile with Carbon Monoxide and Deuterium in the presence of Dicobalt Octacarbonyl

(A) In one experiment 3 g (0.029 mole) of benzonitrile, 30 ml of dry benzene, 0.5 g (0.0063 mole) of pyridine, 4.5 g (0.013 mole) of dicobalt octacarbonyl catalyst, 2200 p.s.i. of carbon monoxide (containing 0.012% by volume of hydrogen) and 50 p.s.i. of deuterium gas were placed in the high pressure bomb. The reactants were heated with rocking at 230° for 11 hours. An observed pressure drop of 100 p.s.i. at room temperature was obtained. After decomposition of the catalyst and removal of the benzene and benzonitrile under vacuum, the residue was extracted with 90 ml of dry carbon tetrachloride and purified with charcoal.

The residual oil (0.57 g) was subjected to column chromatography, by introducing it to the column (alumina, size 10 x 3 cm diam.) in 10 ml of dry benzene. On elution the following fractions were then obtained consecutively:

(1) 100 ml of benzene eluted 0.04 g of oily crystals.
(2) 100 ml of benzene gave 0.15 g of yellow oil.
(3) 200 ml of benzene yielded nothing.
(4) 100 ml of benzene gave 0.01 g of crystalline oil.
(5) 300 ml of benzene eluted 0.09 g of oily crystals.
(6) 900 ml of benzene gave 0.18 g of a colorless oil which crystallized out on standing at room temperature in a few minutes.
(7) 300 ml of benzene yielded nothing.
(8) 100 ml of benzene-ethanol (5%) gave nothing.
(9) 100 ml of benzene-ethanol (5%) eluted 0.09 g oil.

Further washing with a mixture of benzene-ethanol (10%) removed nothing from the column. The total recovery of organic material was 0.47 g (98%).

Characterization of N-benzylphthalimidine (fraction 6).

The crystals obtained from fraction (6) were recrystallized from ether-pet-ether (30-60°), m.p. 91° (yield 6%). The mixed melting point of this compound and an authentic sample of N-benzylphthalimidine (60) was 91°. The infrared spectra of both compounds were identical in most absorptions. Infrared spectrum in KBr disc (the number in parentheses indicates the value for the non-deuterated authentic sample of N-benzylphthalimidine): 3040 (w), 2900 (w) (2920), 1670 (s), 1496 (m), 1470 (m), 1455 (w), 1390 (s) (1415), 1290 (w), 1286 (w), 1227 (m), 1150 (w), 1103 (w), 1025 (w), 993 (w), 935 (w), 790 (m), 718 (s) (738), 698 (s), cm⁻¹.

n.m.r. signals; given in δ units, spectra obtained in carbon tetrachloride: singlet centered at 4.14 (methylene of -N-CH₂-C₆H₅, area = 0.5 H, 1.5 D), singlet centered at 4.66 (methylene of fused five membered ring, area = 0.4 H, 1.6 D), multiplet centered at 7.2 (aromatic H, area 9 H). No correction was made for deuterium exchange.
n.m.r. signals for the non deuterated authentic sample of N-benzylphthalimidine, given in \( \int \) units and obtained in carbon tetrachloride: singlet centered at 4.14 (methylene of \(-\text{N-CH}_2\text{C}_6\text{H}_5\), area = 2 H), singlet centered at 4.65 (methylene of fused five membered ring, area = 2 H), multiplet centered at 7.2 (aromatic H, area = 9 H).

Fraction (2). Infrared (film NaCl): 2925 (s), 2860 (s), 1735 (s), 1525 (s), 1455 (s), 1370 (s), 1027 (w), 780 (w), 742 (w), and 695 (w), cm\(^{-1}\).

n.m.r. signals; in \( \int \) units obtained in carbon tetrachloride: singlet centered at 1.24 (area = 23), and a broad signal centered at 7.25 (area = 10.5). On the basis of the work of Pino (21) it is assumed that fraction (2) is contaminated N-formyl piperidine.

No characterization work was done on further fractions from this experiment.

(B) In a second experiment 40 p.s.i. deuterium gas was added to the reaction mixture, otherwise everything else was the same as above.

n.m.r. signals for N-benzylphthalimidine, given in \( \int \) units and obtained in carbon tetrachloride: singlet centered at 4.14 (methylene of \(-\text{N-CH}_2\text{C}_6\text{H}_5\), area = 0.76 H, 1.24 D), singlet centered at 4.66 (methylene of fused five membered ring, area = 0.76 H, 1.24 D), multiplet centered at 7.2 (aromatic H, area = 9 H).

Reaction of Phenylacetonitrile with Carbon Monoxide in the presence of Dicobalt Octacarbonyl (Expt. No. 6, Table I, page 20).

A mixture of 11.7 g (0.1 mole) of phenylacetonitrile, 1.5 g (0.0014 mole) of dicobalt octacarbonyl, 50 ml of dry benzene and carbon monoxide
containing 0.04% by volume of hydrogen (2100 p.s.i. at 22°) was placed in the high pressure bomb. The reactants were heated with rocking at 250° for 6 hours. No absorption of gas was observed after the completion of the reaction. After the catalyst was decomposed at 70°, the benzene was removed under reduced pressure to yield 11.5 g of oil, and 0.34 g of cobalt metal corresponding to 0.99 g of decomposed dicobalt octacarbonyl catalyst.

About one half of the product (5.6 g) was weighed out for separation on an alumina column (size 20 x 4.5 cm diam.). On elution the following fractions were obtained consecutively:

1. 350 ml of benzene-petroleum ether (30-60°) (1:1) gave 3.31 g of yellow liquid.
2. 125 ml of benzene-ethyl ether (5:1) eluted 1.15 g of yellow liquid.
3. 150 ml of benzene-chloroform (1:1) yielded 0.013 g of brown oil.
4. 100 ml of benzene-chloroform (1:1) gave nothing.
5. 250 ml of benzene-chloroform (1:10) eluted 0.18 g of oil. No characterization work was done on this fraction since its infrared showed no absorption in the carbonyl stretching region, and the principal interest lay in the carbonylated compounds.
6. 160 ml of chloroform gave nothing.
7. 300 ml of benzene-isopropyl alcohol (98:2) eluted nothing.
8. 250 ml of benzene-ethanol (9:1) yielded 0.2 g of oil.

Further washing removed nothing. The total recovery of organic material was 4.8 g (86%).
Characterization of fraction (1) and (2):

Fractions (1) and (2) were identified as phenylacetonitrile, by comparing their infrared spectra with that of the starting material.

Characterization of Phenylacetamide:

From fraction (8) 0.2 g oil, crystals were obtained on the addition of a mixture of chloroform-petroleum ether (30-60°) when the mixture was left stand in the refrigerator. After recrystallization the m.p. was 158°. Anal. Found: C, 70.68%; H, 6.16%; N, 10.23%. Calc. for C₉H₇NO: C, 71.01%; H, 6.66%; N, 10.36%. Infrared in KBr pellet:

3350 (s), 3165 (s), 2800 (w), 1660 (s), 1635 (s), 1495 (m), 1451 (m), 1415 (s), 1287 (m), 1203 (m), 1183 (m), 1158 (m), 1132 (m), 1070 (m), 1028 (m), 1000 (w), 915 (w), 884 (m), 825 (m), 745 (m), 696 (s), cm⁻¹. This compound proved to be phenylacetamide (3%) on comparison (mixed m.p. and infrared) with an authentic sample prepared according to Vogel (72) literature m.p. 156°.

Reaction of Phenylacetonitrile with Carbon Monoxide and Hydrogen in the presence of Dicobalt Octacarbonyl (Expt. No. 7, Table I, page 20)

To a solution of phenylacetonitrile (11.7 g, 0.1 mole) and dicobalt octacarbonyl (2.5 g, 0.0073 mole) in 50 ml of dry benzene contained in a glass liner in the bomb was added 1740 p.s.i. of carbon monoxide (containing 0.04% by volume of hydrogen) and 350 p.s.i. (0.2 mole) of hydrogen at 18°. The bomb was rocked and heated at 250° for 8 hours. The over-all pressure drop was 410 p.s.i. measured at 11°. When the bomb was opened the characteristic smell of ammonia was observed and also detected by litmus paper.
After the dicobalt octacarbonyl was decomposed at 70-80° C, the benzene was removed under reduced pressure. The oily solid residue was extracted three times each with benzene, chloroform and ethyl alcohol. The combined extract was evaporated under reduced pressure yielding 12.4 g organic reaction product (dark oil). The solid residue from the extraction probably an organometallic complex (0.52 g) contained 0.9 g of Co metal.

After the preliminary work on separation was completed, 1.15 g from the organic product was weighed out for separation on an alumina column (8.5 x 5.5 cm diam.). The material was added to the top of the column by dissolving it in 10 ml of benzene, and the following mixtures of developer were then added consecutively with the results indicated.

1) 375 ml of petroleum-ether (65-110°)(1:1) eluted nothing.
2) 750 ml of benzene-petroleum-ether (65-110°)(2:1) gave a yellow liquid (0.23 g) which had a strong smell of nitrile, and proved to be phenylacetonitrile by comparing its infrared spectrum with an authentic sample.
3) 1000 ml of benzene-petroleum-ether (65-110°)(2:1) eluted 0.658 g of brown fluorescent syrup.
4) 310 ml of benzene-petroleum-ether gave nothing
5) 625 ml of benzene-chloroform (1:1) yielded 0.04 g of oil with traces of crystals.
6) 250 ml of benzene-chloroform eluted nothing.
7) 875 ml of benzene-chloroform (1:1) gave 0.02 g of crystals.
8) 250 ml of benzene-chloroform gave nothing.
(9) 175 ml of benzene-ethanol (92:8) eluted some traces of oil
(10) 500 ml of benzene-ethanol yielded 0.051 g of colorless crystals.
(11) 300 ml of benzene-ethanol eluted nothing.

The total recovery of organic material was 1.0 g (87%).

Characterization of phenacetyl-β-phenethylamine (fraction 3):

On addition of benzene-pet-ether (30-60°C) to colorless crystals precipitated out overnight at room temperature; m.p. 93-94°C. The compound was recrystallized twice more from same solvent pair, and the melting point remained unchanged. Infrared spectrum showed the following absorptions in a KBr disc: 3260 (s), 3040 (w), 2900 (w), 2840 (w), 1636 (s), 1535 (s), 1495 (w), 1452 (m), 1413 (m), 1345 (w), 1250 (w), 1192 (s), 1030 (m), 1025 (w), 749 (s), 698 (s), cm⁻¹.

Anal. Found: C, 80.45%; H, 7.38%; N, 6.03%. Calc. for C₁₆H₁₇NO:
C, 80.4%; H, 7.12%; N, 5.86%. Compound (3) had identical physical properties, infrared, solubility, mixed m.p. as that of an authentic sample of phenacetyl-β-phenethylamine prepared according to the literature (78) (Yield, 30%).

Characterization of di-β-phenylethylamine:

The filtrate from fraction (3) was evaporated under reduced pressure, and HCl gas was bubbled into an ethereal solution of this residue, which was found to be basic. The bulky precipitate (flakes) had a melting point of 260-262°C, and on addition of AgNO₃ in 5% ethanol gave AgCl. These crystals were identified as the HCl salt of di-β-phenylethylamine. Anal. Found: N, 5.61%. Calc. for C₁₆H₂₀NCl: N, 5.36%.
Characterization of sym-di-$\beta$-phenylethylurea (fraction 5):

The eluted crystals were recrystallized from chloroform-pet-ether (30-60°), and identified on the bases of infrared spectrum and melting point as sym-di-$\beta$-phenylethylurea. M.p. 136-137°, Lit. m.p. 137° (81). Infrared spectrum in KBr dis: 3305 (s), N-H, 3020 (w), 2900 (w), 1615 (s) C=O, 1575 (s) amide II, 1475 (w) CH$_2$, 1453 (w) CH$_2$, 1302 (w) C-N, 1235 (m), 745 (s), 699 (s), cm$^{-1}$.

Fraction (7). The oil eluted in this fraction crystallized out in a mixture of chloroform-benzene and melted at 266-270°. About 10 mg was obtained, and further attempts to identify this product was unsuccessful.

Characterization of phenylacetamide (fraction 10):

The crystals obtained in this fraction were recrystallised twice from chloroform-pet-ether (30-60°). It gave no depression on a mixed melting point determination, and had an identical infrared spectrum with that of an authentic sample of phenylacetamide m.p. 159° (72).

Reaction of m-Tolunitrile with Carbon Monoxide in the presence of Dicobalt Octacarbonyl (Expt. No. 8, Table I, page 20).

(A) A mixture of 6.55 g (0.056 mole) of m-tolunitrile, 50 ml of dry benzene 2 g (0.0058 Mole) of dicobalt octacarbonyl and carbon monoxide 2100 p.s.i. was placed in the high pressure bomb. The reactants were
heated with rocking at 250° for 8 hours. The bomb was then cooled overnight and a pressure drop of 70 p.s.i. was observed at 18° (room temperature). The reaction product was a dark brown oil which after decomposition of the catalyst at 60° and the removal of benzene under vacuum gave 7 g of oil. This oil was then distilled under reduced pressure to remove the unreacted m-tolunitrile. The distillate contained 4.5 g of m-tolunitrile. The residue was extracted with ethyl-ether and ethyl-alcohol, and after evaporation gave 0.28 g of oil. The remaining solid (0.07 g) melted above 350° and probably is an organometallic complex.

The product oil (0.28 g) was subjected to column chromatography (alumina size 10 x 3 cm diameter). The following fractions were obtained:

1. 625 ml of benzene-petroleum ether (30-60°)(1:1) eluted nothing.
2. 750 ml of benzene-chloroform (1:1) gave an oil 0.06 g identified as m-tolunitrile by infrared.
3. 500 ml of benzene-chloroform eluted an oil 0.05 g.
4. 350 ml of benzene-chloroform yielded nothing.
5. 750 ml of benzene-chloroform (1:1) eluted 0.03 g of oil.
6. 150 ml of benzene-chloroform gave nothing.
7. 380 ml of benzene-ethanol (93:7) eluted 0.09 g of yellow oil.

Further washing with benzene-ethanol (90:10) yielded nothing. The total recovery of organic material was 0.23 g (82%).
Characterization of m-toluamidine:

Fraction (7) was purified by column chromatography (alumina, size 7 x 2 cm diam.). Benzene-ethanol (98:2) was used as eluent and the crystals which were obtained melted at 94-95°. After recrystallizing twice, this compound was identified as m-toluamidine (2%) by comparing its infrared spectra with that of the Sadtler Standard Spectra (80). Literature m.p. 94°.

No further work was done on the remaining fractions, because of the low yield.

(B) In a second experiment a solution of 23.7 g (0.2 mole) of m-tolunitrile and 3 g (0.008 mole) of dicobalt octacarbonyl was reacted with carbon monoxide (1850 p.s.i.) in the autoclave at 230° for nine hours. The reaction product after evaporating the benzene and the unreacted nitrile was 5 g of oily material (organic), and 1.7 g of complex. Separation was carried out the same way as in part (A) above.

Benzene-chloroform eluted colorless crystals from the column. The latter compound was recrystallized from chloroform-light petroleum ether m.p. 67-68°. Infrared spectrum in KBr: 3030 (w), 2977 (w), 1670 (s), 1623 (s), 1485 (m), 1460 (s), 1415 (s), 1350 (m), 1290 (m), 1267 (m), 1225 (s), 1150 (w), 1123 (w), 970 (w), 916 (w), 885 (w), 830 (s), 790 (s), 763 (s), 735 (m), 700 (s), and 680 (m) cm⁻¹.

n.m.r. signals obtained in deuterochloroform (δ units): doublet centered at 2.36 (area = 8.5), singlet centered at 4.2 (area = 2.6), singlet centered at 4.73 (area = 2.3), multiplet centered at 7.12 (area = 9.5), doublet centered at 7.8 (area = 2). No structure has been assigned to this compound.
Benzene-ethanol (20:1) eluted m-toluamide, which was identified the same way as in part (A) above.

Reaction of m-Tolunitrile with carbon Monoxide and Hydrogen in the presence of Dicobalt Octacarbonyl (Expt. No. 9, Table I, page 20).

To a solution of m-tolunitrile (6.11 g, 0.052 mole) and dicobalt octacarbonyl (2 g, 0.0058 mole) in 50 ml of dry benzene contained in a glass liner in the bomb was added 1900 p.s.i. of carbon monoxide (containing 0.01% by volume of hydrogen) and 185 p.s.i. (0.103 mole) of hydrogen at 21°C. The bomb was rocked and heated at 210°C for 8.5 hours. The over-all pressure drop was 250 p.s.i. measured at 20°C.

The reaction product consisted of a dark brown oil (4.75 g), 0.02 g of complex material and 0.45 g of Co metal after filtering and evaporating the solvent under vacuum.

A fraction of the product oil 1.21 g was subjected to exhaustive chromatographic fractionation on alumina (size of column 15 x 3.2 cm diameter), and developed as follows:

1. 750 ml of petroleum-ether (30-60°C) (1:1) eluted 0.19 g of fluorescent oil which had a strong smell of nitrile, and the infrared spectrum of which had a strong band at 2200 cm⁻¹.

2. 800 ml of benzene-petroleum ether (65-110°C) gave nothing.

3. 500 ml of benzene gave nothing.

4. 900 ml of benzene-chloroform (4:1) gave 0.1 g of oil. The separation of this very complex mixture was unsuccessful.

5. 120 ml of benzene-chloroform (4:1) eluted nothing.
(6) 800 ml of benzene-chloroform gave 0.21 g of crystals.
(7) 300 ml of benzene-chloroform eluted nothing.
(8) 750 ml of benzene-chloroform (1:1) eluted 0.25 g of oil with some residual crystals.
(9) 250 ml of benzene-chloroform yielded nothing.
(10) 200 ml of benzene-ethanol (97:5:2.5) yielded nothing.
(11) 125 ml of benzene-ethanol eluted 0.006 g of oil.
(12) 250 ml of benzene-ethanol eluted 0.20 g of crystals.
(13) 400 ml of benzene-ethanol gave nothing.
(14) 500 ml of benzene-ethanol (90:10) eluted 0.20 g of oil.
(15) 300 ml of benzene-ethanol gave nothing.

Total recovery of organic material was 1.1 g (92%).

Characterization of N,N'-di-m-xylylurea (fraction 6):

The crystals obtained from fraction (6) 0.21 g were recrystallised from chloroform-petroleum ether (30-60°) twice m.p. 137-138°. Infrared spectrum in KBr disc. cm⁻¹: 3295 (s), 3010 (w), 2890 (w), 2842 (m), 1615 (s), 1563 (s), 1465 (m), 1375 (w), 1336 (w), 1287 (w), 1210 (w), 1190 (w), 1057 (w), 970 (w), 887 (w), 790 (m), 770 (m), 743 (m), 699 (s), cm⁻¹. Anal. Found: N, 10.49%. Calc. for C₁₇H₂₀N₂O: N, 10.44%. This compound was found to be N,N'-Di-m-xylylurea yield 13.5%, by comparing it (mixed melting point and infrared) with an authentic sample prepared according to Bromme (79).
Characterization of m-toluamide (fraction 12):

From the oil in fraction (12) 0.20 g, plate like crystals precipitated out overnight in the fridge on addition of a mixture of chloroform-petroleum ether (30-60°). M.p. 94°. Infrared spectrum in KBr disc cm⁻¹: 3370 (s), 3180 (s), 1643 (s), 1610 (s), 1578 (s), 1432 (m), 1364 (s), 1308 (w), 1285 (w), 1135 (w), 1112 (m), 1037 (w), 914 (w), 883 (m), 812 (m), 770 (w), 730 (m), 682 (s) cm⁻¹. The infrared spectrum of this compound was identical with that of m-toluamide in Sadter Standard Spectra (80). Anal. Found: C, 70.6%; H, 6.7%; N, 10.5%. Calc. for C₈H₉NO: C, 71.1%; H, 6.62%; N, 10.36%. On the bases of infrared, melting point and analysis this compound was identified as m-toluamide (yield 11.5%).

Characterization of N-m-xylylurea (fraction 11+):

By adding a mixture of chloroform-petroleum ether (30-60°) to the oil eluted in fraction (11+), colorless crystals precipitated in five minutes. It was recrystallized twice more. M.P. 150°. Infrared spectrum in a KBr pellet: 3420 (s), 3318 (s), 3030 (w), 2900 (w), 2860 (w), 1644 (s), 1595 (s), 1550 (s), 1467 (s), 1380 (s), 1315 (s), 1210 (w), 1140 (m), 1175 (w), 890 (w), 785 (s), 750 (m), and 697 (s) cm⁻¹. Anal. Found: N, 17.02%. Calc. for C₉H₁₂N₂O: N, 17.05%. It was established that this compound is N-m-xylylurea (yield 9.5%), since it gave no depression in melting point by admixing it, and had an identical infrared spectrum with an authentic sample of N-m-xylylurea (79).
Synthesis of authentic compounds

Benzamide

The benzamide was prepared by the addition of benzoyl chloride to a concentrated solution of ammonia, as described by Vogel (72), and recrystallized from hot water m.p. 129°. Literature m.p. 129°.

Phenylacetamide

Phenylacetonitrile was hydrolysed to phenylacetamide according to the method of Vogel (72) using concentrated hydrochloric acid m.p. 156°. Literature m.p. 156°.

Phenacetyl-β-phenylethylamine

a) β-Phenylethylamine was prepared by the reduction of phenylacetonitrile with hydrogen and Raney-nickel according to Vogel (72). B.p. 95°/20 mm, and the hydrochloride m.p. 220° was in accord with the value found in the literature.

b) Phenacetyl-β-phenethylylamine was synthesised by condensing phenylacetic acid with β-phenylethylamine as described by Decker (78) m.p. 94°. Literature m.p. 95°.

sym-Dibenzylurea

sym-Dibenzylurea was prepared from benzylamine and urea, as described by Davis and Blanchard (75), m.p. 169°. Literature m.p. 169°.

m-Xylylamine

Reagent grade m-tolunitrile (10 g) was dissolved in a solution (150 ml) of methyl alcohol and then saturated with ammonia (from a cylinder). The solution was placed in a high pressure hydrogenation bomb, and 20 ml of settled Raney-nickel catalyst was added. Then hydrogen was introduced into the bomb, up to a pressure of 1000 p.s.i. and heated with stirring
for four hours at 120°. After the reaction was completed, the liquid from the bomb was filtered to remove the catalyst. The solvent and ammonia were removed by distillation, and the residue fractionated through a short column. The amine was collected at 205-206°/760 mm. Hydrochloride m.p. 208 from ethanol. Literature m.p. 209°.

N-m-Xylylurea

m-Xylylamine was reacted with an equimolar quantity of potassium cyanate as described by Bromme (79) to yield N-m-xylylurea m.p. 149°. Literature m.p. 148°.

N,N'-Di-m-xylylurea

An ethereal solution of m-xylylamine was treated with phosgene (from a cylinder) according to the method of Bromme (79) and the product worked up from absolute alcohol m.p. 137°. Literature m.p. 137°.

N-Phenylphthalimidine

This compound was prepared previously by Dr. Mary Weir, by the reduction of phthalanil, obtained by fusion of aniline and phthalic anhydride, with Zn-dust and hydrochloric acid according to the method of Graebe (74) in acetic acid solution m.p. 165°.

N-Benzylphthalimidine

The preparation was carried out by reacting benzalbenzylamine (77) with carbon monoxide (2200 p.s.i.) in the presence of dicobalt octacarbonyl catalyst at 230° for six hours as described by Murahashi and Horiie (60) m.p. 91°.
BIBLIOGRAPHY


