Carbon Monoxide as a Raw Material in Organic Synthesis*

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Summary: Organo transition metal $\sigma$-complexes undergo carbon monoxide insertion reactions under comparatively mild conditions. Carbylation of phenyl derivatives of transition metals known to form metal carbonyls yields benzophenone. Pentacyano benzylcobaltate is inactive towards carbon monoxide but the coordinatively unsaturated tricyano benzylnickelate absorbs carbon monoxide at 0°C in aqueous solution to give dibenzyl ketone. A variety of organolithium compounds are found to react with carbon monoxide at -70°C to give symmetrical ketones.

Amines undergo carbylation reaction with carbon monoxide in the presence of metal carbonyls or carbonyl selenide to produce 1,3-dialkyl ureas. Especially, carbonyl selenide is an excellent carbylating agent to amines and may be used as a catalyst.

The halides which contain unsaturated bond at the $\beta$-$\gamma$-position of the halides are found to be reactive towards metal carbonyls (iron or nickel) and to give unstable $\sigma$-complexes as intermediates, whose decomposition yields dimers, ketones or $\beta$-epoxy ketones. The reaction of benzyl halides or iodobenzene with metal carbonyls (nickel or iron) in the presence of certain olefins gives benzylolation or phenylation products of the olefins.

Organolithium compounds add to metal carbonyls reductively to form lithium acyl- or aroylmetal carbylates, which are found to be useful reagents for organic synthesis. The synthesis of aldehydes, 1,4-diketones and unsymmetrical ketones have been achieved by using these acyl- or aroylmetal carbylate reagents.

During the last twenty years, carbon monoxide has become one of the important starting materials for organic synthesis because of its availability and its unique reactivity. A number of synthetic reactions have been reported and furthermore some of them have found technical applications. Although carbon monoxide behaves as a nucleophilic or radicalic reagent, the use of metal complexes as catalysts has been found to be more satisfactory for the utilization of carbon monoxide in organic synthesis.

The discoveries of oxo-synthesis and Reppe's acrylic acid synthesis have prompted a number of organic chemists to study the reaction of carbon monoxide using metal complexes. This paper deals with the reactions of carbon monoxide or metal carbonyls, which have been carried out by the present authors in order to clarify the reactivity of carbon monoxide and also to establish a new synthetic reaction scheme using carbon monoxide or metal carbonyls.

1 The Reaction of Carbon Monoxide with Organometallic Compounds

Recently, it has become apparent that unstable organometallic compounds are formed as intermediates in the reaction of carbon monoxide using metal complexes as catalysts or stoichiometric reagents and that application of carbon monoxide in organic synthesis may be achieved effectively by means of metal complexes. Carbon monoxide insertion reactions into the carbon metal bond of alkyl (or aryl)-transition metal complexes are well known. Carbylation of organometallic $\pi$-complexes also gives synthetically useful results. In the case of olefin-palladium dichloride complexes in benzene, the products are $\beta$-chloro acid chlorides which were assumed to be produced by carbon monoxide insertion into the carbon-palladium bond of the intermediate $\sigma$-complexes, followed by migration of chloro atom to acyl group$^1)$. Organometallic $\sigma$-complexes seem to be reactive to carbon monoxide. The phenyl derivatives of transition metals known to form metal carbonyls, including chromium, nickel and cobalt, react with carbon monoxide at a low temperature under 1 atm. to give reaction products (benzophenone or benzoin) derived from carbon monoxide insertion$^2)$. However, diphenylcadmium and phenylcopper are unreactive to carbon monoxide under the mild conditions and no products derived from carbon monoxide insertion were obtained in significant

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amounts. So the coordination of CO to metals may be considered to be the first step in these reactions; then phenyl-acyl rearrangement occurs to form benzyol derivatives of transition metals and finally another phenyl group will migrate to the benzyol group, producing benzophenone. In this regard, when di-\(\pi\)-cyclopentadienylidiphenyltitanium is carbonylated with CO under pressure at room temperature, benzophenone is isolated in good yields\(^3\).

It has been reported that pentacyanobenzylcobaltate \(\text{[C}_6\text{H}_5\text{CH}_2\text{Co(CN)}_5]_3^-\) shows no immediate reaction with CO\(^4\) and no reports have yet appeared about such a CO insertion reaction. The organonickel complex salt (II), prepared by the reaction between potassium hexacyanodinickelate (I) and benzyl halides, is coordinatively unsaturated and so is expected to be reactive towards CO. Indeed, bubbling of CO into the yellow solution of (II) at 0°C for 3 hr. gives dibenzyl ketone (34%) as well as bibenzyl (59%)\(^1\)

\[
\begin{align*}
K_4\text{[Ni}_2\text{CO}_2\text{CN}]_6 \rightarrow & 4\text{[NiCN]}_2\text{Br_2} \\
& + \text{Co} \\
\rightarrow & \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2 \quad \text{CH}_2\text{CH}_2
\end{align*}
\]

It is well known that (I) is also coordinatively unsaturated and its aqueous solution absorbs two molecules of CO to give the yellow salt, \(\text{K}_4\text{[Ni}_2\text{CO}_2\text{CN}]_6\) (III)\(^5\). The yield of dibenzylketone, 90.4%, increased remarkably when (III) was used as a starting material. These results show a good contrast to the inactiveness of the saturated complex, pentacyanobenzylcobaltate, towards CO.

Organolithium compounds are also reactive towards CO and the reaction at -10°C yields various products, such as benzhydryl phenyl ketone, benzoin, benzophenone and triphenylmethane\(^6\). The formation of these products could be interpreted in terms of an ionic reaction mechanism involving a benzoyl anion intermediate. The formation of benzyol leads to the conclusion that benzyollithium, the anion of which is carbene in one of its limiting resonance structures, can dimerize to give dilithium salt of enedio\(^7\)

\[
\text{PhLi} + \text{CO} \rightarrow \text{PhCOLi}
\]

The reaction of an organolithium compound with CO occurs violently, so it seems desirable to control the reaction when applying the reaction to a synthesis. In this regard, we have undertaken a study of the reaction of CO with organolithium compounds in ether solution at \(-70°C\). This reaction gave symmetrical ketones in good yields instead of acyloin which was expected on the basis of the previous results. The reaction mechanism is not clear, but the reaction seems to proceed according to the following equation:

\[
2\text{RLi} + 3\text{CO} \rightarrow \text{R-C-R} + (\text{LiCO})_2
\]

The ethereal solution of vinylithium, which was obtained by the reaction between tetravinyltin and phenylithium in ether, reacted with CO at various temperatures. At \(-70°C\), a small amount of divinyl ketone was obtained as well as a polymer, and the amount of polymer increased with rising temperature\(^10\). The polymer obtained was light yellow in color, and the I.R. spectrum showed the strong characteristic absorption band of carbonyl group at 1,680 cm\(^{-1}\). Elementary analysis showed that the ratio of carbon to hydrogen was 5:6.24.

This new method is simple and can be extended to similar reactions. The authors applied this method to the reaction of CO with polymethylene dilithiums to synthesize cyclic ketones (by intramolecular ketonization) and poly-ketones (by intermolecular ketonization)\(^11\). The polymethylene dilithiums were prepared by the reaction of the corresponding polymethylene dibromides with metallic lithium in an ether solution at \(-10\sim-5°C\). Then CO was bubbled into the solution at \(-70°C\). Thus cyclic ketones (cyclopentanone, cyclohexanone and cycloheptanone) and several poly-ketones were synthesized.

\[
\text{Li(}\text{CH}_2\text{)}_2\text{Li} + 3\text{CO} \rightarrow (\text{CH}_2)_3\text{C}=\text{O} + (\text{LiCO})_2
\]

We have also undertaken a study of the effect of dilution with a solvent (diethyl ether) on the yields of cyclic ketones; it has been found that the yields of cyclic ketones are considerably increased by the high dilution of the ethereal solution of polymethylene dilithiums with the solvent.

2 The Reaction of Carbon Monoxide with Amines

Carbon monoxide is inactive towards amines.
but, in the presence of certain catalysts, carbo-
ylation of amines occurs easily.

Carbonylation of amines at 65\textdegree{}\textdegree{}–85\textdegree{}\textdegree{} under
1.4 atm. of CO using an equimolar amount of
Palladium dichloride gives good yield of isocya-
nates\textsuperscript{12}.

\begin{align*}
\text{RNH}_2 + \text{CO} + \text{PdCl}_2 \rightarrow \text{RNCO} + \text{Pd} + 2\text{HCl}
\end{align*}

R = \text{C}_4\text{H}_9, 49\% \quad \text{R = C}_6\text{H}_5, 68\%.

Under more vigorous conditions (180\textdegree{}\textdegree{}, 100 atm.
of CO), \text{n-decylamine yields 1,3-didecylurea and}
N,N-didecyloxadime\textsuperscript{19)}. Metal carbonyls also
carbonylate aniline forming diphenylurea and
lesser amount of formanilide. Aliphatic amines
give N-formyl derivatives as the main products.
However, 1,3-dialkylureas are the major products
in the reaction of primary aliphatic amines with
dimanganese decacarbonyl\textsuperscript{14}). In the carbo-
ylation of diethylamine with Nickel carbonyl,
both the formamide and urea derivative are pro-
duced, larger amounts of nickel carbonyl favoring
the formation of urea\textsuperscript{15}).

\begin{align*}
\text{Et}_2\text{NH} + \text{Ni(CO)}_4 + \text{CO} \rightarrow \quad \text{Et}_2\text{NCHO} + \text{Et}_2\text{NCONEt}_2
\end{align*}

Carbonyl sulfide or carbonyl selenide also
carbonylates amines to produce ureas. It has
been reported that the reaction of primary amines
with sulfur and carbon monoxide at temperatures
of about 100\textdegree{}\textdegree{} gives the corresponding ureas in
high yields\textsuperscript{16}). This reaction is widely applicable
to aliphatic amines and high yields of 1,3-disub-
stituted ureas are obtained. Aromatic amines
react only slightly under the conditions employed
for the formation of dialkyl ureas. However,
high yields of several diaryl ureas have been
achieved by applying a tertiary amine as the
catalyst without any solvent. In this reaction,
carbonyl sulfide was found to be the active species
for the carbonylation. More recently, it has been
found that 1,3-disubstituted ureas are produced
in excellent yields under milder reaction condi-
tions by carbonylation of amines using carbonyl
selenide\textsuperscript{17}).

\begin{align*}
\text{SeCO} + 2\text{RNH}_2 \rightarrow \text{(RNH)}_2\text{CO} + \text{H}_2\text{Se}
\text{H}_2\text{Se} + 1/2\text{O}_2 \rightarrow \text{Se} + \text{H}_2\text{O}
\end{align*}

Selenohydride is decomposed by oxygen to produce
metallic selen. Futhermore, amines are carbo-
ynlated in the presence of catalytic amount of
metallic selen instead of carbonyl selenide to
give quantitative yields of 1,3-dialkyl ureas.

3 The Reaction of Metal Carbonyls with
Organo Monohalides

The chemistry of metal carbonyls can be divided
into two main parts. The first comprises the
structural studies of metal carbonyls and the
various organotransition metal complexes from
metal carbonyls. The second deals with the
organic synthesis via metal carbonyls as catalysts
or stoichiometric reagents. Versatile behavior of
metal carbonyls in organic reactions have been
revealed during these ten years and now metal
carbonyls have become important reagents in
organic synthesis.

This section deals with the reactions of metal
carbonyls with organohalides, which offer the
simplest method for the formation of transition
metal-carbon \(\sigma\)-bond complexes, and also with
the reaction between unsaturated compounds
and the unstable \(\sigma\)-bond complexes.

Monohalides tend to add oxidatively to metal
carbonyls to form unstable alkyl- or acyl-metal
halides.

The reactivity of monohalides towards metal
carbonyls is remarkably affected by the organic
moeities of halides. That is, the halides which
contain unsaturated bonds (e.g. C=C, C=O, \(-\text{C} = \text{N}\))
at the \(\beta\gamma\) -position are reactive towards nickel
carbonyl or iron carbonyls.

Allyl halides are the most thoroughly studied as
the reactants with Nickel carbonyl. Represen-
tative allylic chlorides are coupled in excellent
yields by nickel carbonyl in methanol as solvent\textsuperscript{18}).
Recently, it was confirmed that the true inter-
mediate of the coupling reaction was \(\pi\)-allynnickel
chloride\textsuperscript{18}).

\begin{align*}
2\text{CH}_2=\text{CHCH}_2\text{Cl} + \text{Ni(CO)}_4 \rightarrow \quad \text{Ni}\left(\text{Cl}\right)\text{CCH}_2\text{CH}_2
\end{align*}

Organic synthesis by means of \(\pi\)-allynnickel com-
plex has been extensively studied by Chiusoli and
his coworkers and the results have been described
in detail in his review\textsuperscript{21}).

Corey and his coworkers have established an
interesting synthetic reaction using \(\pi\)-allynnickel

\begin{align*}
\text{R} = \text{H, CH}_3\text{COOC}_2\text{H}_5
\end{align*}

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complexes. Reaction of π-allylnickel(II) bromides with a variety of halides in polar coordinating media gives high yields of cross-coupling products.

Instead of allyl halides, aryl iodides or benzyl halides can be used as a partner for the reaction with metal carbonyls. Iodobenzene reacts with nickel carbonyl at 50~60°C to form benzylnickel carbonyl iodide as an intermediate complex, and its thermal decomposition or alcoholysis gives benzil or ester of benzoic acid, respectively. Triiron dodecacarbonyl also reacts with iodobenzene in refluxing toluene to give benzenophene and with benzyl halides to give dibenzyl ketone, but, contrary to the case of nickel carbonyl, the formation of α-diketone is not observed. Similar to the above case, the formation of benzyl- or phenyliron carbonyl halides, which contain carbon-iron σ-bond, is assumed to precede ketone formation.

RX + Fe₃(CO)₁₂ → R-Fe(CO)₆ + RC-Fe(CO)₆⁻₁
X

The unstable organometallic σ-complexes, which were assumed as intermediates in the oxidative addition reaction of monohalides to metal carbonyls, were expected to be reactive towards olefins, and so the reaction of benzyl halides or iodobenzene with metal carbonyls (nickel or iron) in the presence of olefins were studied. When benzyl halides or iodobenzene are used as the partners for the reaction with triiron dodecacarbonyl, benzylation or phenylation of olefins occurs.

RX + CH₂=CH-Y + Fe₃(CO)₁₂ → R-CH-C=CH-Y + R-CH₂CH₂-Y
R = C₄H₉CH₃, C₄H₅, X = Cl, Br, I.
Y = C₃H₅CN, COOEt.

Similarly, arylnickel carbonyl iodide, prepared from aryllodide and nickel carbonyl, reacts with several olefins to give benzoyl-adducts of olefins or γ-lactones.

ArI + Ni(CO)₄ → (ArCNi(CO)₂)I

In connection with the benzylation or phenylation reaction of olefins, the substitution reaction of olefinic hydrogen by carbomethoxyl group was carried out.

Although various reactions of olefins with carbon monoxide have been reported, the synthesis of α,β-unsaturated carboxylic acids or esters from olefins and CO is not so easy. The first direct synthesis of methyl esters of α,β-unsaturated carboxylic acids from olefins and CO was carried out by a unique electrochemical method in the presence of a platinum carbonyl complex.

C₅H₅CR-C≡CH + CO + CH₃O⁻ →

In these electrochemical reactions, it may be assumed that the formation of unsaturated esters proceeds by the addition of the Pt-COOCH₃ group in the platinum-carbonyl complex to the olefinic double bond via anodic process.

A remarkable solvent effect was observed in the reaction of α-bromoketones with nickel carbonyl. When dimethylformamide is used as the solvent, the reaction between phenacyl bromide and nickel carbonyl proceeds at 30°C to yield 2,4-diphenylfuran, but in tetrahydrofuran the reaction occurs at 50~60°C giving 1,4-di-phenylbutane-1,4-dione. This furan producing reaction has been successfully extended to the other aryl or alkyl α-bromoketones.

In the reaction between α-bromoketone and nickel carbonyl, the isolated intermediates, precursors to the unsymmetrically substituted furans, are shown to be β-epoxyketones. For example, a reaction with bromomethyl t-butylketone in dimethylformamide gives 2-t-butyl-5,5-dimethyl-1,2-epoxyhexane-4-one in a yield of 61%.

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4 The Reaction of Metal Carbonyls with Organolithium Compounds

As mentioned above, organomonohalides add
oxidatively to metal carbonyls to form unstable organometallic intermediates, whose decomposition gives dimers, ketones and \(\beta\)-epoxyketones. However, general monohalides which contain none of unsaturated bond at \(\beta,\gamma\)-position are less reactive towards neutral mononuclear metal carbonyls. The preparation of alkyl transition metal carbonyls seems to be possible only by using the reaction of halides with metal carboxylate anions\(^1\).

On the other hand, organolithium compounds are very reactive towards metal carbonyls and add reductively to the metals even at low temperature to form rather stable anionic complexes. Two different aspects of such reactions with alkyl- or aryllithiums have received recent attention: (1) the synthesis of carbene-transition metal complexes using chromium, molybdenum and tungsten hexacarbonyls, (2) the organic synthesis by means of iron pentacarbonyl and nickel carbonyl.

Nickel carbonyl or iron pentacarbonyl is the most reactive towards organolithium compounds. The reaction of alkyl or aryllithiums with nickel carbonyl proceeds exothermically even at \(-70°C\) to form anionic nickel carbonylate complexes. The term "lithium acyl or aroylmetal carbonylate" will be used for the anionic complex formed by the reductive addition of organolithium compounds to iron pentacarbonyl or nickel carbonyl\(^2\).

\[
\text{RLi + Fe(CO)}_\text{5} \rightarrow \text{Li[RC-Fe(CO)}_\text{5} + \text{H}^+ \\
\text{RC(O)}_\text{n} \rightarrow \text{R-C-H} \\
\text{R-C-R'} \rightarrow \text{R-C-CH}_\text{2} \text{C}_\text{2} \text{H}_\text{4} \\
2\text{Li[RC-Ni(CO)}_\text{3} + \text{R'C=CH} \rightarrow \text{R-C=CH}_\text{2} \text{C}_\text{2} \text{H}_\text{4} \\
\text{RLi + Ni(CO)}_\text{5} + \gamma-C-C-\text{C} \rightarrow \text{R-C=CH}_\text{2} \text{C}_\text{2} \text{H}_\text{4}
\]

References

16) Hashimoto, I., Ryang, M., Tsutsumi, S., unpublished work.

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