New organic synthetic methods using iron carbonyl reagents

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Investigations carried out on the preparation and synthetic applications of iron carbonyl reagents are reviewed. Reaction of Na₂Fe(CO)₄, prepared by the reduction of FeCl₃ in THF with sodium naphthalenide under CO atmosphere at 25°C, with alkyl bromides gives the corresponding aldehydes, ketones and carboxylic acids under appropriate conditions. Reaction of NaR(CO)₃Fe(CO)₃ with CuCl at 25°C in THF, leads to the formation of 1,2-diketones. However, in the presence of methylacrylate in addition to the 1,2-diketones the corresponding acyloins are also formed. Mechanistic pathways and intermediates involved are discussed. Reactions of NaHFe(CO)₄/RX or [HFe(CO)₅] reagents with alkynes lead to the formation of the corresponding α,β-unsaturated carboxylic acids and/or the cyclobutanediones after CuCl₂/2H₂O oxidation. Possible intermediates and mechanistic pathways are discussed.

Introduction

In recent years, the metal carbonyls are increasingly used in organic synthesis. Many transition elements form stable neutral metal carbonyls, anionic metal carbonyls, hydrido metal carbonyls, and their derivatives. These derivatives display unique reactivities in oxidation, reduction, isomerization, oligomerization, carbonylation and polymerization processes. They have been also used extensively in C–C bond formation reactions.

Among various transition metal carbonyls, the organoiron complexes have potential in all these aspects. We have undertaken efforts to prepare readily accessible reactive iron carbonyl reagents for applications in organic synthesis. We describe the results of these investigations in this article.

Methods of preparation of Na₂Fe(CO)₄

The super nucleophile Na₂Fe(CO)₄ (Collman reagent) has been demonstrated to be a versatile reagent in several organic transformations. Numerous methods have been reported for the preparation of this reagent from readily available starting materials. The Na₂Fe(CO)₄ reagent is useful as a nucleophile in the conversion of alkyl bromides, iodides, and tosylates into aldehydes, ketones, carboxylic acid derivatives, esters and amides. It is generally prepared using Fe(CO)₅, sodium and benzophenone. However, use of polar benzophenone might pose problems during the isolation of products. Hence, we have developed a method for in situ generation of Na₂Fe(CO)₄ from Fe(CO)₅ using Na/naphthalene. Naphthalene can be readily separated from polar products. It was also observed that the Na₂Fe(CO)₄ can be prepared directly from FeCl₃ using Na/naphthalene and CO in THF (eq. 1).

Na + Naphthalene $\xrightarrow{\text{FeCl}_3}$ CO $\xrightarrow{\text{Na}_2\text{Fe(CO)}_4}$

The formation of Na₂Fe(CO)₄ has been confirmed by performing the anticipated reactions with aliphatic halides to obtain the corresponding aldehydes, carboxylic acids and ketones (Scheme 1). It has been proposed that NaRCOFe(CO)₄ is the intermediate involved in all these transformations. We have decided to investigate further applications of this intermediate species.

Reaction of NaRCO[Fe(CO)₄] with CuCl

The acylmetals such as ‘RCOCu’ are one of the most sought after intermediates in organometallic chemistry. It was anticipated that the use of CuCl in the place of H⁺ (Scheme 1) could lead to the formation of ‘RCOCu’. However, it was observed that the reaction of NaRCO[Fe(CO)₄] with CuCl gives the corresponding 1,2-diketones (70–90%) with 1,2-diketones (70–90%) (Scheme 1). This transformation is a general one and several alkyl bromides are converted into the corresponding 1,2-diketones (eq. 2).

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Besides the corresponding 1,2-diketone (32%), dialkyl ketone (8%) and 1-nonoic acid (29%) (eq. 5)\(^1\).

\[
\text{NaRCO[Fe(CO)]}_4 \xrightarrow{1. \text{I}_2/\text{THF, } 0^\circ \text{C}} \xrightarrow{2. \text{12h, } 25^\circ \text{C}} \text{RCO}_2 \text{R} + \text{RCO}_2 \text{R} + \text{RCO}_2 \text{H}
\]

(5)

32% 8% 29%

Also, the reaction of NaRCO[Fe(CO)]\(_4\) with I\(_2\) in the presence of methylacrylate produces acyloin along with other products (eq. 6)\(^1\).

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_2\text{CO[Fe(CO)]}_4 & \xrightarrow{1. \text{I}_2, 0^\circ \text{C}, 2h} \text{CH}_3\text{CH}=\text{CHCOOCH}_3 \\
\text{CH}_3\text{CH}=\text{CHCOOCH}_3 & \xrightarrow{2. \text{CH}_2=\text{CHCOOCH}_3} \text{RCO}_2 \text{R} + \text{RCO}_2 \text{R} + \text{RCO}_2 \text{H}
\end{align*}
\]

18% 5% 7%

R = -(CH\(_2\))\(_2\)CH\(_3\)

It seems likely that, the RCO[Fe(CO)]\(_4\) species is responsible for the formation of 1,2-diketones (20–28%) and acyloins (35–52%). It may be formed through either the homolysis of I(RCO)Fe(CO)_4 and Cu(RCO)Fe(CO)_4 or more likely through one-electron oxidation by CuCl or I\(_2\) (Scheme 2).

\[
\text{RMgX} + \text{Fe(CO)}_5 \xrightarrow{\text{CuCl}} \text{RCO}_2 \text{R}
\]

(4)

The 1,2-diketone is also formed (32% yield) in the reaction of NaRCO[Fe(CO)]\(_4\) (R = n-octyl) with I\(_2\) in THF

\[
\begin{align*}
\text{NaRCO[Fe(CO)]}_4 & \xrightarrow{1. \text{I}_2/\text{THF, } 0^\circ \text{C}} \xrightarrow{2. \text{12h, } 25^\circ \text{C}} \text{RCO}_2 \text{R} + \text{RCO}_2 \text{R} + \text{RCO}_2 \text{H}
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(4)

The 1,2-diketone is also formed (32% yield) in the reaction of NaRCO[Fe(CO)]\(_4\) (R = n-octyl) with I\(_2\) in THF
We have also examined the photochemical reaction of a mixture of Fe(CO)$_5$, RCOCOR (R = n-octyl) and methylacrylate using a 450 W medium pressure mercury lamp for 5 h to examine whether the anticipated co-ordinatively unsaturated 'Fe(CO)$_4$' species could react with the 1,2-diketone and methylacrylate to give acyllactone. Indeed, the corresponding acyllactone was obtained in 28% yield (eq. 7)

\[ \text{R-C-C-R} + \text{Fe(CO)}_5 + \text{CH}_2=\text{CHCOOMe} \]
\[ \xrightarrow{\text{hv}} \text{5h} \]
\[ \text{R-C-C-R} + \text{Fe(CO)}_5 + \text{CH}_2=\text{CHCOOMe} \]
\[ \xrightarrow{\text{hv}} \text{28%} \]

This result illustrates the ability of the co-ordinatively unsaturated iron carbonyl species to react with 1,2-diketone and methylacrylate to give acyllactone (Scheme 3).

Fe(CO)$_5$ + RCOCOR →

\[ \xrightarrow{1. \text{CH}_3I / 0 \degree C} \]
\[ \xrightarrow{2. \text{R}=\text{C}=\text{C}=\text{R}} \]
\[ \xrightarrow{3. \text{Me}_2\text{C}=\text{CH}=\text{CH}_2 \text{Cl}_2 \text{H}_2\text{O}} \]

Scheme 3.

**Preparation of 'Fe(CO)$_4$'**

The co-ordinatively unsaturated species 'Fe(CO)$_4$' is isolobal with carbene and hence it is expected to have interesting reactivities. It has been previously prepared by the methods outlined in Scheme 4 (refs 17–21).

The 'Fe(CO)$_4$' forms addition complexes with CH$_3$CN, acetone, amines and phosphines. During our efforts on the synthetic applications of Na$_3$Fe(CO)$_4$, we became interested in the preparation and applications of these species.

Whitmire et al. previously reported the formation of Fe(CO)$_4$(CH$_2$CN) and CH$_4$ in the reaction of [Et$_3$N]HFe(CO)$_4$ with CH$_3$I in CH$_3$CN (eq. 8).

\[ [\text{Et}_3\text{N}]\text{HFe(CO)}_4 + \text{CH}_3\text{I} \xrightarrow{\text{CH}_3\text{CN}} \text{Fe(CO)}_4(\text{CH}_2\text{CN}) + \text{CH}_4 \]

Since HFe(CO)$_4$ can be readily prepared through the reaction of Na$_3$Fe(CO)$_4$ with CH$_3$COOH, we have examined this method of generation of 'Fe(CO)$_4$' as it would serve as a simple alternative procedure.

**Double carbonylation of alkynes**

It was observed that the NaHFe(CO)$_4$/CH$_3$I reagent combination reacts with alkynes at 60°C followed by CuCl$_2$, H$_2$O oxidation giving the corresponding cyclobutenediones (27–42%) and the α,β-unsaturated carboxylic acids (10–22%) (eq. 9).

\[ \text{NaHFe(CO)}_4 \xrightarrow{1. \text{CH}_3\text{I / 0 \degree C}} \xrightarrow{2. \text{R}=\text{C}=\text{C}=\text{R}} \xrightarrow{3. \text{Me}_2\text{C}=\text{CH}=\text{CH}_2 \text{Cl}_2 \text{H}_2\text{O}} \]

**Reaction of NaHFe(CO)$_4$/CH$_2$Cl$_2$ system with alkynes**

It has been reported by Whitmire and Lee that the HFe(CO)$_2$ slowly decomposes to [HFe$_x$(CO)$_{11}$] in CH$_2$Cl$_2$ through the 'Fe(CO)$_4$' intermediate (eq. 10).

\[ \text{Fe(CO)}_5 \xrightarrow{\text{hv}} \text{Fe}_{2+} \]
\[ \text{Fe}_2\text{+} \]
\[ \text{Fe}_3\text{+} \]
\[ \text{Fe}_4\text{+} \]

Scheme 4.
the methyl ester besides the corresponding cyclobutenedione. The corresponding amide (50%) was obtained when diethylamine was used instead of CH₂OH. Similar transformations were also observed with 1-heptyne.

**Reaction of NaIIFe(CO)₄/Me₃SiCl system with alkynes**

We have also examined the reactivity of the species generated using NaIIFe(CO)₄/Me₃SiCl combination to compare the results obtained using alkyl halides. It was observed that the intermediate complex, generated *in situ* by treating NaIIFe(CO)₄ (3 equiv.) with Me₃SiCl (3 equiv.) reacts with terminal and internal alkynes (1 equiv.) at 25°C to yield α,β-unsaturated carboxylic acids (45-54%) with excellent regio- and stereoselectivities (eq. 13).²⁶

\[
\text{NaIIFe(CO)}_4 \xrightarrow{25^\circ C} \text{Me}_3\text{SiCl} \xrightarrow{1. \text{R} \equiv \text{C} \equiv \text{C} \equiv \text{R'}} \text{HOOC} \xrightarrow{2. \text{CuCl}_2 \cdot 2\text{H}_2\text{O}} \text{R} = \text{R'} = 3
\]

- a) -Ph   -Ph   60%
- b) -C₆H₁₁ -SiMe₃ 41%
- c) -C₄H₁₇ -SiMe₃ 37%
- d) C₆H₁₁ -H    50%
- e) C₄H₁₇ -H    42%

The reaction was found to be general and various alkynes were converted to (E)-alkenonic acids. This reactivity pattern is similar to that realized using the NaIIFe(CO)₄/CH₂Cl₂ reagent system. In all these cases, the corresponding cyclobutenediones were obtained in very low yields (<5%).

An interesting temperature effect was noted for this reaction. It was found that the reagent, prepared using NaIIFe(CO)₄/Me₃SiCl at 60°C, on reaction with diphenylacetylene followed by CuCl₂/2H₂O oxidation produced cyclobutenedione (51-63%) as the only product (eq. 14).²⁶

\[
\text{NaIIFe(CO)}_4 \xrightarrow{60^\circ C} \text{Me}_3\text{SiCl} \xrightarrow{1. \text{R} \equiv \text{C} \equiv \text{C} \equiv \text{R'} \ \text{2. } 60^\circ \text{C} \ \text{3. CuCl}_2 \cdot 2\text{H}_2\text{O}} \text{R} = \text{R'} = 4
\]

- a) -Ph   -Ph   63%
- b) -C₆H₁₁ -SiMe₃ 51%
- c) -C₄H₁₇ -SiMe₃ 53%
- d) -C₆H₁₁ -CH=CH=CH₂ 60%
- e) -C₆H₁₁ -H    56%
- f) -C₄H₁₇ -H    57%

The presence of CH₂Cl₂ as a co-reactant is required for this transformation. It was observed that the reaction leads to low yield of carboxylic acid (<10%) without CH₂Cl₂. As mentioned earlier, the reaction of [Et₃N]ΗFe(CO)₄ with CH₂Cl₂ affords [ΗFe₂(CO)₁₁]⁺. Presumably, the reactive species responsible for the formation of both cyclobutenediones and carboxylic acids may be derived from these species.

It is well-known that acylferrous anion [RCOFε(CO)₄]⁻ reacts with I₂ in the presence of nucleophiles such as CH₂OH and R₂NH to give the corresponding carboxylic acid derivatives.²⁰ A similar type of reactivity may be anticipated for the intermediate formed here. Regio- and stereoselective synthesis of α,β-unsaturated carboxylic acid derivatives could be achieved if such generalizations could be made. Indeed, this has been observed (eq. 12).²⁶

\[
\text{NaIIFe(CO)}_4 \xrightarrow{\text{I}_2/\text{MeOH}} \text{MeOOCC} \xrightarrow{1. \text{PhC} \equiv \text{CPh} \ \text{2. PhC} \equiv \text{CPh} \ \text{3. I}_2/\text{MeOH}} \text{R} \xrightarrow{55\%} \text{R} \xrightarrow{20\%}
\]

The intermediate generated *in situ* in the reaction (eq. 11) upon I₂ treatment in the presence of methanol, gives...
SPECIAL SECTION: ORGANOMETALLIC CHEMISTRY

The reaction was found to be general. The corresponding cyclobutenediones were obtained in relatively good yields using representative terminal, internal and substituted alkynes. It has been reported that the R₂Si(H) Fe(CO)₄ on heating gives 'Fe(CO)₄' species which readily undergoes trimerization to Fe₃(CO)₁₂ (refs 27–29).

Reaction of the [HFe₃(CO)₁₁]⁻ reagent with alkynes

Since the reaction of CH₂Cl₂ with NaHFe(CO)₄ was reported to give HFe₃(CO)₁₁, we decided to investigate the reactivity of these species with alkynes. The [HFe₃(CO)₁₁]⁻ species has been previously prepared using Fe(CO)₅, NaBH₄/CH₃OH/CH₃COOH in THF and isolated as PPN salt in 73% yield (eq. 15)⁴⁰.

\[
\text{NaBH}_4 + \text{Fe(CO)}_5 \xrightarrow{1. \text{CH}_3\text{OH}} \xrightarrow{2. \text{CH}_3\text{COOH}} \text{HFe}_3\text{(CO)}_{11} \quad (15)
\]

It was observed that the [HFe₃(CO)₁₁]⁻ species, prepared in situ using Fe(CO)₅/NaBH₄/CH₃COOH reacts with alkynes to give the corresponding cyclobutenediones in good yield (60–73%) after CuCl₂,2H₂O oxidation (eq. 16)³¹. Several alkynes were converted to the corresponding cyclobutenediones.

\[
\begin{align*}
\text{Fe(CO)}_5 & \xrightarrow{1. \text{NaBH}_4} \xrightarrow{2. \text{CH}_3\text{COOH}} \xrightarrow{3. \text{RC} \equiv \text{CR'}} \text{CuCl}_2 \text{2H}_2\text{O} \\
\end{align*}
\]

R R' 4
a) -C₅H₁₁ -H 72%  
b) -C₅H₁₃ -H 69%  
c) -C₆H₁₇ -H 70%  
d) -C₁₀H₂₁ -H 68%  
e) -Ph -H 65%  
f) -C₆H₁₁ -CH₂=CH₂ 60%  
g) -C₆H₁₁ -CH(C₆H₅)(OH) 61%  
h) C₅H₁₁ -CPh(CH₃)(OH) 63%  

The UV-spectra recorded for the reaction mixture in all these reagent combinations described above exhibit characteristic absorptions reported for [HFe₃(CO)₁₁]⁻ in solution³². If the reactive species is derived from this reagent, then the reactivity difference between the species generated using Fe(CO)₅/NaBH₄/CH₃COOH in THF and the reagent prepared using NaHFe(CO)₅/CH₂Cl₂ in THF is difficult to rationalize. The reaction of the former combination with alkynes leads to cyclobutenediones (eq. 16) and the latter results in the formation of α,β-unsaturated carboxylic acid (eq. 11). Presumably, the CH₃COOH used to destroy the excess NaBH₄ may play a role in the formation of the reactive species from [HFe₃(CO)₁₁]⁻ (eq. 17).

\[
\text{HFe}_3\text{(CO)}_{11} + \text{CH}_3\text{COOH} \rightarrow \text{H}_2\text{Fe}_3\text{(CO)}_{11} \rightarrow \text{Fe}_3\text{(CO)}_{11}' + \text{H}_2 \quad (17)
\]

If this is the case, use of an additional amounts of CH₃COOH in the reaction using NaHFe(CO)₅/CH₂Cl₂ should also give similar results. Indeed, this was observed. The corresponding cyclobutenedione was obtained in 33% yield and the α,β-unsaturated carboxylic acid was not formed under these conditions (eq. 18)³².

\[
\begin{align*}
\text{NaHFe(CO)}_4 & \xrightarrow{1.\text{CH}_2\text{Cl}_2} \xrightarrow{2.\text{CH}_3\text{COOH} \text{(4 equiv.)}} \xrightarrow{3. \text{RC} \equiv \text{CH}} \xrightarrow{4. \text{CuCl}_2\text{2H}_2\text{O}} \\
\end{align*}
\]

An interesting acylation-cyclization was observed when RCO[Fe(CO)₅]⁻ was treated with CuCl in the presence of alkynes and CH₃CN in THF at room temperature. The corresponding benzenediones (26–32%) besides cyclobutenediones (10–13%) were formed. Control reactions indicated that the CuCl is necessary for this transformation (eq. 19)³³.

\[
\begin{align*}
\text{RMgBr} & \xrightarrow{\text{Fe(CO)}_5} \xrightarrow{\text{THF}, \text{rt}} \text{RCO[Fe(CO)}_5]_- \xrightarrow{\text{PhC} \equiv \text{CPh}} \text{CuCl} \\
\end{align*}
\]

Mechanism and intermediates

The reactive species formed in all these seems to be co-ordinatively unsaturated, fluxional, polymeric iron carboxyl species. A tentative mechanistic pathway for the formation of cyclobutenediones can be visualized as shown in Scheme 5.
The intermediates involved may be of the type I or II. The species II has been reported to give cyclobutenediones on oxidation using FeCl₃ (ref. 34).

The formation of α,β-unsaturated carboxylic acids may take place through hydrometallation of the alkynes by [HFe₃(CO)₁₁]⁺ produced under the reaction conditions (Scheme 6).

Conclusion

The Na₂Fe(CO)₄ reagent prepared using Fe(CO)₅/Na/naphtalene and FeCl₃/Na/naphtalene and CO was used for the synthesis of Na₅RCOFe(CO)₄. The reaction of Na₅RCOFe(CO)₄ with CuCl or I₂ leads to the formation of 1,2-diketones RCOCOR, RCOR and RCOOH. It was found that the reaction of Na₅RCOFe(CO)₄ with CuCl or I₂ in the presence of methyl acrylate leads to the formation of acrylactone besides RCOCOR, RCOR and RCOOH. It appears that the RCOFe(CO)₄ species formed, either from Cu(RCO)Fe(CO)₄ and I₅RCOFe(CO)₄ through homolysis of Fe–Cu and Fe–I bonds or through one-electron oxida-

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