Cobalt carbonyls: A versatile reagent and catalyst in organic synthesis

Javed Iqbal*, Beena Bhatia and Vibha Khanna
Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India.

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Abstract

Cobalt carbonyls are versatile reagents for the insertion of carbon monoxide between carbon-cobalt bond. This methodology has been utilized for the synthesis of some naturally occurring compounds. In this review, cobalt carbonyl-mediated novel reactions (2+2+1 and 2+2+2 cycloaddition reactions, Nicholas reaction, carbonylation reactions, etc.) have been discussed. Mechanisms of these reactions have also been presented.

Key words: Dicobalt octacarbonyl, cycloaddition, propargylic cobalt complex, carbonylation.

Introduction

One of the outstanding features in the growth of contemporary organic chemistry has been the emergence of transition metal-mediated organic reactions at the frontiers of organic synthesis. Its instant acceptance by synthetic chemists is primarily due to the fact that transition metal-mediated organic transformations are extremely versatile and experimentally convenient. Recent development in the catalysis of organic reaction by transition metals has paved the way for achieving a remarkable level of chemo- and stereoselectivity, and for certain reactions this achievement has reached an extent where near enzyme-like selectivity has been witnessed. This development has clearly expanded the arsenal of synthetic chemists which has eventually facilitated the intensity of assault on some of the most challenging problems of synthesis.

Transition metal carbonyls1-2, particularly from Fe, Co, Rh, Ni, Pd, play an important role in industrial chemistry3, since they allow for high selectivity and economic efficiency in such processes as hydrogenation, hydroformylation4, oxidation5, epoxidation6, etc. In addition to this, metal carbonyls7-12 derived from Mo, Cr, W have also been successfully applied to a wide range of unique organic transformations. The introduction of one carbon in organic substrates under the aegis of metal carbonyls constitutes a very important transformation in contemporary organic synthesis13. Among the various transition metal carbonyls, the carbonyls derived from Co have made outstanding contribution towards achieving a wide range of organic transformations, like hydroformylation, carbonylation, oxysilylation.

* For correspondence.
cycloaddition reaction of alkynes, Nicholas reaction, etc. Impressive advances have been made in the domain of cobalt carbonyl-mediated organic synthesis over the last one decade as clearly evident from the remarkable level of efficiency and selectivity achieved during the synthesis of complex natural products.

In view of the importance of these reactions this review covers literature on cobalt carbonyl-catalysed or mediated reactions in organic synthesis. The review has been divided into the following sections.

1. Cycloaddition reactions
   1.1 [2+2+1] Cycloaddition reactions
   1.2 [2+2+2] Cycloaddition reactions

2. Nicholas reaction

3. Carbonylation reaction

4. Miscellaneous reactions

1. Cycloaddition reactions

1.1. [2+2+1] Cycloaddition reactions

[2+2+1] Cycloaddition reactions (Pauson–Khand reaction) is a novel and useful method for the synthesis of cyclopentenone derivatives. This reaction, first reported by Pauson and Khand in 1973, involves the cocyclization of alkynes with alkene and carbon monoxide under the aegis of dicobaltoctacarbonyl. This transformation is a [2+2+1] cycloaddition which involves thermally stable hexacarbonyldicobalt complex I, obtained by co-ordination of Co$_2$(CO)$_8$ with alkynes in hydrocarbon solvents of ether. Subsequent reaction of complex I with alkene followed by insertion of carbon monoxide leads to the formation of cyclopentenone (eqn 1).

\[ RC\equiv CR' \xrightarrow{Co_2(CO)_8} \text{[Diagram]} \rightarrow \text{[Structure]} \]

This reaction is compatible with a wide range of functionalities like ether, alcohols, tertamines, thioethers, ketones, ketals, esters, tert-amides and aromatic rings including benzene, furan and thiophene.

This reaction can be divided into two categories: (a) Intermolecular reaction, and (b) Intramolecular reaction.

1.1.1. Intermolecular [2+2+1] cycloaddition reactions

Intermolecular reaction of strained alkenes with acetylene and Co$_2$(CO)$_8$ reacts with norbornene and its derivatives to generate cyclopentenone derivatives 3 (eqn 2). Similarly,
unsymmetrical alkynes react with 4 via its Co-complex 5 to provide 8-oxabicyclo[3.2.1]oct-6-ene-3-one 6 in quantitative yields (eqn 3).

\[
\text{HC} \equiv \text{CH.Co}_2(\text{CO})_6(2) \xrightarrow{\text{C}_6\text{H}_6, 60-70^\circ\text{C}, 4 \text{ h}} \text{3(56)}
\]

\[
\text{PhC} \equiv \text{CH.Co}_2(\text{CO})_6 5 \xrightarrow{\text{DMF, 60}^\circ\text{C}, 2 \text{ days}} \text{6(42)}
\]

Nitrogen-bridged bicyclic systems have also been shown to undergo Pauson-Khand cycloaddition. Thus, 7 undergoes addition to acetylenic Co-complex 2 to provide 8 in good yields (eqn 4). High regioselectivity in incorporation of the unsymmetrical alkyne in the product is a characteristic feature of this reaction. In addition, these reactions also occur with high stereoselectivity as exo-adduct is obtained as the predominant product.

\[
\text{N.CO}_2\text{Me} \xrightarrow{\text{DMF, 60}^\circ\text{C}, 2 \text{ days}} \text{8(47)}
\]

Simple unstrained alkenes are unreactive under these reaction conditions; however, alkenes containing electron-withdrawing groups 9 react to yield conjugated dienes (eqn 5). Alkenes containing one or more electron-withdrawing groups react with acetylenic cobalt complex to give conjugated diene. However, due to the low yields, this reaction cannot be used as a general synthetic route to conjugated dienes.

\[
1 + \text{YCH=CH} \xrightarrow{9} \text{RCH=CR'-CH=CHY}
\]

These reactions are believed to occur via the insertion of alkene into the cobalt-acetylene complex to give 2a which subsequently incorporates the carbon monoxide to afford 2b which on reductive elimination of cobalt leads to cyclopentenone (Scheme 1). The formation of diene may be occurring via a similar pathway involving the hydrogen migration followed by a process of reductive elimination (Scheme 2).
Styrene and substituted styrene represent the borderline cases where both modes of reaction (i.e., cyclopentenone and diene formation) are observed (eqn 6).

\[
\text{Ar} + 1 \rightarrow \text{ArC} = \text{CH} - \text{C} = \text{CHR} + \text{ArCH} = \text{CH} - \text{C} = \text{CHR} \quad (6)
\]

Usually terminal alkenes give poor yields and regioselectivity. Krafft has shown that alkenes containing groups capable of acting as soft ligands at a homoallylic position give both
enhanced yields and regioselectivity. This may be a result of coordination of heteroatom prior to insertion (Scheme 3).

\[
\begin{align*}
\text{R} & \quad \text{PhC} \equiv \text{CH} \quad \text{Co}_2(\text{CO})_8 \\
\rightarrow & \quad \text{X} & \quad \text{X} \\
\end{align*}
\]

\[
\begin{align*}
\text{R} = \text{Me}, \text{X} = \text{NMe}_2 & \quad 74 \\
\text{R} = \text{H}, \text{X} = \text{SMe} & \quad 1 & \quad 1
\end{align*}
\]

Scheme 3.

Schore\textsuperscript{26} has synthesised 4,5-disubstituted 2-cyclopentenones 11 from the cycloaddition product 10 of norbornadiene using cuprate addition followed by retro Diels–Alder reaction (Scheme 4).

\[
\begin{align*}
\text{n-C}_4\text{H}_5\text{C} \equiv \text{CH} & \quad \text{Co}_2(\text{CO})_8 \\
\rightarrow & \quad \text{10} \\
\text{a) } & \text{tBu}^\text{b} \text{PrC} \equiv \text{C} \text{CuLi} \\
\text{b) } & 600^\circ \text{C} \sim \text{C}_8\text{H}_6 \\
\rightarrow & \quad \text{11}
\end{align*}
\]

Scheme 4

This reaction is regio- and stereoselective\textsuperscript{27} as with bicyclic alkene 12; the less-hindered face of the \(\pi\)-bond preferentially reacts to give exo-ring fusion product 13 exclusively (eqn 7).

\[
\begin{align*}
\text{OMe} & \quad \text{H} \\
\text{H} & \quad \text{MeC} \equiv \text{CH} \\
\rightarrow & \quad \text{MeO} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{K} & \quad \text{K}
\end{align*}
\]

\text{13(60) only isomer}
This high selectivity has been exploited by Schore and co-workers during the synthesis of guaianolide and pseudoguaianolide. The stereochemistry of the ring fusion as present in the key intermediate 15 is remarkably achieved in the first step using the Pauson–Khand reaction on alkene 14 (Scheme 5).

Interestingly, cyclopropane ring is tolerated in the acetylenic partner during the cycloaddition on cyclic alkenes to give 17. This methodology has been used during the synthesis of linearly fused triquinanes 18 from cyclopropyl acetylene 16 and cyclopentene (Scheme 6).

Serratosa and co-workers have synthesised angularly fused triquinanes 21 starting from 19 and 20 (eqn 8).
Smit-Caple and co-workers\textsuperscript{31} have shown that intramolecular Khand reaction could be carried out with an increased efficiency in a solvent-free system with the substrate adsorbed on the surface of chromatography adsorbent (dry state adsorption conditions). Intermolecular reaction between 22 and 23 was conducted by conventional Pauson–Khand reaction. Later, they have shown that under dry state adsorption conditions the \([2+2+1]\) cycloaddition of 24 with 5 proceeds quite smoothly in high yields (Scheme 7). These reactions have been shown to occur on strained alkene using \(\text{Al}_2\text{O}_3\) or \(\text{MgOSiO}_2\) as dry media.

\[
\text{22} + \text{PhC}≡\text{CH} \xrightarrow{\text{SiO}_2, 2\, \text{h}, 50^\circ\text{C}} \text{23} \rightarrow \begin{align*}
\text{24} & \quad \text{5} \\
\begin{array}{c}
\text{MeS} \\
\text{Ph}
\end{array} & \begin{array}{c}
\text{MeS} \\
\text{Ph}
\end{array}
\end{align*} (2:1)
\]

\[
\text{24} + \text{MeC}≡\text{CH} \xrightarrow{\text{SiO}_2, 2\, \text{h}, 70^\circ\text{C}} \rightarrow \begin{align*}
\text{22} & \quad \text{23} \\
\begin{array}{c}
\text{Me} \\
\text{Me}
\end{array} & \begin{array}{c}
\text{Me} \\
\text{Me}
\end{array}
\end{align*} (5:1) 64\%
\]

\[
\text{24} + \text{PhC}≡\text{CH} \xrightarrow{\text{SiO}_2, 2\, \text{h}, 70^\circ\text{C}} \rightarrow \begin{align*}
\text{22} & \quad \text{23} \\
\begin{array}{c}
\text{Ph} \\
\text{Ph}
\end{array} & \begin{array}{c}
\text{Ph} \\
\text{Ph}
\end{array}
\end{align*} (1:1) 89\%
\]

\textbf{Scheme 7.}

Recently, Krafft and co-workers\textsuperscript{32} have shown that the regioselectivity of co-cyclization is directed by the use of soft atoms like sulfur or nitrogen. They observed that alkene containing S or N at homoallylic position is more effective in controlling the regioselectivity as compared to alkene containing S or N at allylic or homoallylic position (Scheme 8).

\[
\text{24} + \text{MeC}≡\text{CH} \xrightarrow{\text{Co}_2\text{(CO)}_8} \rightarrow \begin{align*}
\text{22} & \quad \text{23} \\
\begin{array}{c}
\text{MeS} \\
\text{MeS}
\end{array} & \begin{array}{c}
\text{MeS} \\
\text{MeS}
\end{array}
\end{align*} (2:1)
\]

\[
\text{24} + \text{PhC}≡\text{CH} \xrightarrow{\text{Co}_2\text{(CO)}_8} \rightarrow \begin{align*}
\text{22} & \quad \text{23} \\
\begin{array}{c}
\text{MeS} \\
\text{MeS}
\end{array} & \begin{array}{c}
\text{MeS} \\
\text{MeS}
\end{array}
\end{align*} (18:1)
\]

\textbf{Scheme 8.}
Jeong and co-workers\textsuperscript{33} have devised a highly efficient one-pot strategy for the preparation of aza-bicyclic compounds via Nicholas reaction (see Section 2) with amidic nitrogen nucleophiles followed by Pauson-Khand reaction (Scheme 9).

\begin{equation}
\begin{array}{c}
\begin{array}{c}
\text{OH} \\
\text{Co}_2(\text{CO})_6
\end{array} \\
+ \\
\begin{array}{c}
\text{N} \\
\text{tos}
\end{array}
\end{array} \xrightarrow{\text{BF}_3\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2 \text{, } -70^\circ\text{C}}
\begin{array}{c}
\begin{array}{c}
\text{tos} \text{N} \\
\text{cis:trans}=2:1
\end{array} \\
\text{cis:trans}=2:1
\end{array} \xrightarrow{\text{Et}_3\text{N N-oxide/O}_2/\text{CH}_2\text{Cl}_2}
\begin{array}{c}
\begin{array}{c}
\text{cis:trans}=2:1
\end{array} \\
\text{cis:trans}=2:1
\end{array}
\end{equation}

\textit{Scheme 9}

1.1.2. Intramolecular $2+2+2$ cycloaddition reactions

Intramolecular Pauson-Khand reaction was first reported by Schore and Croudace\textsuperscript{34} in 1981. This methodology has been used during the synthesis of various natural products. Enynes cyclize, upon complexation to Co$_2$(CO)$_8$ and subsequent heating, to give bicyclic enones. The most extensively studied is the synthesis of bicyclo [3.3.0] oct-1-ene-3-one from hept-1-ene-6-yne (eqn 9). Hex-1-en-5-yne produces a mixture of products of trimerization of the alkyne functionality.

\begin{equation}
\begin{array}{c}
\text{=} \\
\text{Co}_2(\text{CO})_8
\end{array} \xrightarrow{\text{Co}_2(\text{CO})_8} \\
\text{=}
\end{equation}

(9)

The presence of bicyclic [3.3.0] octane ring system in a variety of biologically active natural products has generated considerable interest in the synthesis of its functionalized derivatives. In these cycloadditions, substitution on both the alkyne as well as the chain linking the alkyne and the alkene is often readily tolerated.

Hua and co-workers\textsuperscript{35} have prepared the key precursor 26 for the synthesis of optically active pentalene and racemic pentalenolactone E methyl ester from enyne 25 (eqn 10).

\begin{equation}
\begin{array}{c}
\text{=} \\
\text{OSi(}^{t}\text{Bu)Me}_2
\end{array} \xrightarrow{\text{heptane, } 80^\circ\text{C, } 2 \text{ days}} \\
\text{=}
\end{equation}

(10)

Later, Seto et al\textsuperscript{36} have shown that Co$_2$(CO)$_8$-mediated cyclization of an acyclic-enyne 27 provides bicyclic pentenone 28, which can be elaborated to antibiotic pentalenolactone G 29 (Scheme 10).

Magnus and co-workers\textsuperscript{37} have exploited intramolecular Pauson-Khand reaction to the total synthesis of coriolin 32, a linearly fused triquinane. The key intermediate 31 was prepared in one step from the readily available enyne 30 (Scheme 11).
Magnus has systematically examined the factors that contribute to the stereoselectivity shown in intramolecular Pauson–Khand reaction. This methodology has been used for the synthesis of hirsutic acid\(^{38}\) \(35\) from enyne \(33\) via bicyclopentenone \(34\) (Scheme 12).

Magnus\(^{39}\) has developed an elegant approach to the synthesis of quadrone \(38\) from the key precursor bicyclo [3.3.0] oct-1-ene-3-one \(37\) prepared in one step from the enyne \(36\) in a highly stereoselective manner (Scheme 13).

Magnus and co-workers have also achieved a stereoselective synthesis of a carbocyclic analogue\(^{40}\) \(41\) using the enyne \(39\) via the cyclopentenone \(40\) (Scheme 14).

The presence of alkene in a ring (e.g., \(42\)) is compatible with intramolecular cyclization as angularly fused triquinanes like bisnorisocomene\(^{41}\) can be synthesised from cyclopentenone.
43 stereoselectively. This reaction has the limitation as only trisubstituted alkenes and simple terminal alkynes can be used for the cyclopentenone formation (eqn 11).

A stereocontrolled approach to pentalenes[42] has been shown by using the above methodology (eqn 12).

Serratosa and co-workers have developed an exceptionally efficient approach to triquinacenes[45] making use of similar intramolecular cycloadditions of cyclic alkenes 44 containing alkynyl substitution (eqn 13).

Billington and co-workers[44] have cyclized substituted allyl-propargyl ethers 46 to give 3-oxa bicyclo [3.3.0] oct-5-en-7-ones 48 via hexacarbonyl dicobalt complexes 47. Hydrogenation
of 48 followed by deprotection afforded the key intermediate\(^\text{49}\) for the synthesis of tetrahydro anhydroaucubigenone 50 (Scheme 15).

Schreiber\(^\text{45}\) and Smit\(^\text{46}\) have synthesised polyheterocycles 52 and 54 by combining Nicholas and Pauson–Khand cycloaddition reactions using enyne ether 51 and 53, respectively (Scheme 16).
Later, Smit and co-workers have shown unusual effect on the efficiency of Co-mediated conversion of an enyne-ether 55 into the corresponding bicyclo[3.3.0] octenone 56 by adsorption of Co-complexed enyne-ether on to silica gel under O₂ or air (Scheme 17).

Veretenov and co-workers have developed a simple route for the synthesis of polycyclic linearly and/or angularly fused compounds 58 from 57. This cycloaddition occurs with participation of double bond, having an electron-withdrawing group (eqn 14).

Schreiber and co-workers have developed an efficient method which provides a milder and more stereoselective alternative to the corresponding thermal reactions. Tertiary amine oxide (e.g., N-methylmorpholine-N-oxide, NMO) readily promotes intramolecular Pauson-Khand cyclization at room temperature on 59 under an inert atmosphere. Due to the milder condition required, this reaction tolerates various functional groups like alcohols, silyl ethers, acetals, remote olefins, etc., and leads to the formation of 60 and 61. One of the outstanding features of this reaction is the high level of stereoselectivity as compared with ultrasonic or thermal reaction (Scheme 18).
A novel route to the precursor 63 of (±) Loganine 64 has been developed by Jeong and co-workers\(^6\) from homoallyl-propargyl acetal 62 (Scheme 19).

Recently, Hoye and Suriano\(^5\) have shown that electron-deficient alkynes can be inter- or intramolecularly cyclized to give bicyclic enediones in good yields. They have observed that there is a remarkable effect on the reactivity by changing the solvent. The effect of solvent is evident from the reaction of 65 in acetonitrile with norbornene which gives 66 by intermolecular addition whereas the enyne 67 on intramolecular cyclization affords 68 in high yields. A similar transformation in methanol was quite sluggish (Scheme 20).

Interestingly, the highly functionalized alkyne 69 undergoes intramolecular cyclization in the presence of NMO to afford 70 in high yields and good stereoselectivity\(^9\) (eqn 15).
Smit and co-workers\cite{Smit} have synthesised several fenestrane derivatives 72 based on intramolecular Pauson–Khand reaction followed by [2+2] photocycloaddition on intermediate 71 (eqn 16).

\[
\text{Me} \quad \overset{\text{M}}{\text{Me}} \quad \overset{\text{O}}{\text{Me}} \quad \overset{\text{Co}_2(\text{CO})_6}{\text{Me}} \quad \overset{\text{SiO}_2, 40^\circ \text{C}, 2 \text{ h}}{\text{Me}} \quad \overset{\lambda > 300 \text{ nm}}{\text{Me}} \quad \overset{\text{Toluene, 71^\circ \text{C}}}{\text{Me}} \quad \overset{\text{71}}{\text{Me}} \quad \overset{\text{72}}{\text{Me}}
\]

Krafft and co-workers\cite{Krafft} have shown the rate of the thermal intramolecular Pauson–Khand cycloaddition can be enhanced by 1,6-enyne-bearing co-ordinating ligands (sulfur or oxygen atom) in the homo and bishomopropargylic position. They have shown that sulfur provides more acceleration than oxygen (Scheme 21).

\[
\text{Co}_2(\text{CO})_6 \quad \overset{\text{Toluene, 71^\circ \text{C}}}{\text{L}} \quad \overset{\text{time (h)}}{\text{L}} \quad \overset{\% \text{ yield}}{7.5 \quad 67 \quad 2 \quad 60 \quad 1.25 \quad 75}
\]

Scheme 21.

1.2. [2+2+2] Cycloaddition reactions

The discovery of new synthetic methods has already made possible to construct the most complex natural products and the most 'unnatural' assemblies. Despite these advancements
there remains much room for improvement of synthetic strategies to get the chemo-, regio-
and stereoselectivity of the compounds. A simple analysis showed that a more powerful
strategy would be based upon the [2+2+2] cycloadditions of the unsaturated moieties.
CpCo(CO)₂ as a catalyst was found to promote the successful execution of [2+2+2]
cycloadditions⁵⁴. The many previously unattainable molecules generated in this way have
been used as a starting material for the preparation of several unnatural and natural products
of theoretical, medicinal and synthetic interest. Two decades earlier, it was found that
CpCo(CO)₂ catalyses a variety of [2+2+2] cycloadditions involving α,ω-diynes to give
annelated benzenes⁵⁵. In order to get chemoselectivity, bulky alkynes such as trimethylsilyl-
alkynes were employed⁵⁶,⁵⁷ (eqn 17). Cobalt-catalysed cocyclization reaction was used in
silicon-directed intermolecular regioselective Friedel–Crafts acylation⁵⁷ (eqn 18).

\[
\begin{align*}
\text{Si(CH₃)₃} & \quad \text{Si(CH₃)₃} \\
\text{CH}_2 & \quad \text{CO}_2\text{CH}_2\text{CH}_3 \\
\text{BF}_3\cdot\text{Et}_2\text{O} & \quad \text{CpCo(CO)}_2
\end{align*}
\]

To understand the mechanism of these reactions⁵⁸–⁶⁰ many studies have been carried out
which resulted in the isolation of two intermediates 73 and 74. Cyclobutadiene complexes
derived from both 73 and 74 are obtained as byproducts in catalytic reactions employing α,ω-
diynes⁵⁷ and are responsible for some of the catalyst depletion since they appear to be
unsuitable as precursors for any catalytic intermediates⁶¹.

The trimethylsilyl group which is used extensively for controlling the chemo- and
regioselectivity has a pronounced tendency to promote α-selectivity in the metallacycle. This
effect was synthetically demonstrated in the formation of 77 as the sole isomer on
cocyclization of 1-trimethylsilyl 1-1, 5-hexadiyne 75 and trimethylsilylacetylene⁵⁵ 76 (Scheme
22). On the other hand, if more Me₃Si groups are present, i.e., 78 then the reaction proceeds
via $o$-xylylene formation and intramolecular ring closure to give benzhydridane nucleus $79$ (Scheme 23).

The $\text{CpCo(CO)}_2$- catalysed [2+2+2] cycloaddition of three alkyne units was applied to total synthesis of a variety of natural products such as antitumor anthracyclene aglycones $^{62}$ (Scheme 24) and the protoberberine alkaloids $^{63}$. The protoberberine $81$ is readily prepared by cocyclization of $80$ with bis(trimethylsilyl) acetylene $^{65}$ (Scheme 25).
1,2-Dihydrocyclobutabenzenes are used in the construction of a host of theoretically interesting benzenoid hydrocarbons\textsuperscript{56-58}. Initially, 1,5-hexadiyne undergoes one-step trimerization which on oxidative photocyclization gives the two isomeric dicyclobutaphenantrenes showing the tandem cyclization–cycloaddition reaction\textsuperscript{59} (Scheme 26). A novel series of compounds called as multiphenylenes have been prepared using cobalt complexes as catalyst\textsuperscript{70,71} (Scheme 27). Apart from their use in the synthesis of different strained ring systems, the 1,2-dihydrocyclobutabenzenes have been used in producing polycyclic systems\textsuperscript{72,73}.

**Scheme 26**

**Scheme 27.**

Enediyne 82 undergoes intramolecular cyclization to yield stereospecific cyclohexadiene complex 83 in the presence of stoichiometric amount of CpCo(CO)\textsubscript{2}\textsuperscript{74,75} (eqn 19). A sequence of 2D NMR experiments in conjunction with labelling experiments has shown the presence of intermediates which on rearrangement gives the product.
In the same way, enediynes 84 with internal double bonds undergo intramolecular cyclization to give 85. This cyclization procedure proceeds efficiently and with remarkable stereoselectivity, both with respect to the stereochemistry of the original double bond and of cobalt (eqn 20).

\[
\begin{align*}
\text{84} & \xrightarrow{\text{CpCo(CO)}_2,\Delta, \text{hv}} \text{85} \\
& \text{74\%}
\end{align*}
\]

This reaction showed that the steric encumbrance of the double bond has little influence on the success of the reaction. This advantage was utilized in the preparation of tricyclic diene 87 from a substrate containing tetrasubstituted double bond (eqn 21).

\[
\begin{align*}
\text{86} & \xrightarrow{\text{CpCo(CO)}_2,\Delta, \text{hv}, 60\%} \text{87} \\
& \text{60\%}
\end{align*}
\]

Intermolecular [2+2+2] cycloadditions of enynes 88 on co-oligomerization with BTMSA gave mainly cyclobutadiene 89 rather than expected bicycle (Scheme 28).

Scheme 28.
Based on the 'Tandem principle' described earlier, CpCo(CO)$_2$-catalysed synthesis of steroids was achieved starting from 1,5 hexadiyne. Alkylated 1,5-hexadiyne 91 underwent tandem co-catalysed cyclization followed by intramolecular ring closure via o-xylene formation to give key precursor 92 of (±) estrone$^{80}$ (Scheme 29).

Another way$^{81}$ of synthesising steroids is using CpCo(CO)$_2$ in which the -BCD portion of their framework would be fused to a pre-existing aromatic A-ring$^{82,83}$ (Scheme 30). A diastereoselective synthesis of steriod$^{84}$ has been achieved using the enediyne 93. Cyclization followed by demetallation under acidic conditions gave the known estrapentaneol$^{85}$ 94 (Scheme 31). Another approach to the steroid synthesis employing CpCo(CO)$_2$ as a matrix is O->ABCD, i.e., all four rings are assembled in one step from enetriyne 95 to give B-ring aromatic derivatives with the complete control of the crucial stereochemistry of the C,D-ring juncture$^{86}$ (Scheme 32).
Highly crowded steroids were prepared using the enediyne 96a to give 97 whereas the corresponding silylated derivative 96b afforded a highly stereoselective formation of 98 (Scheme 33). The outcome of this reaction demonstrates once again the unique ability of the catalyst to make highly hindered compounds.
In the early 1970s, several groups independently discovered that cobalt complexes could cocyclize alkynes with nitriles to furnish pyridine in stoichiometric and catalytic reactions\(^{88,89}\) (eqn 22).

\[
R^1\text{C}≡\text{N} + 2R^2\text{C}≡\text{CH} \xrightarrow{\text{CpCo(CO)}_2} \text{R}^1\text{N} = \text{N} = \text{R}^2 + \text{R}^1\text{N} = \text{N} = \text{R}^2
\]  

This reaction can be used in producing some very rare isoquinol[2,1-b]-2,6-naphthyridine nucleus\(^{64}\) 99. Similarly, the 2-azaanthracene 100 framework can be obtained efficiently (Scheme 34).

Scheme 33.

Scheme 34.
Cocyclization of bis (trimethylsilyl) 101a or bis (trimethylstannyl) di-2-propynyl ether 101b with acetonitrile provides a synthetic route to 1,3-dihydro-6-methyl-4,7 bis (trimethylsilyl) 102a or bis (trimethylstannyl)-furo[3,4-c] pyridines 102b. This methodology has been used for the total synthesis of Vitamin B₆ 103⁹⁰ (Scheme 35).

Employment of isocyanates⁹¹,⁹² in place of nitrile on cocyclization with alkynes afforded polyheterocyclic systems (eqn 23). In simple cocyclizations leading to substituted pyridone, regioselectivity was not observed, whereas when bulky substituent at the α-position of ω-alkynyl isocyanates was present (e.g., trimethylsilyl) good chemo- and regioselectivity were observed. Application of the above methodology has led to formal synthesis of the antitumor alkaloid camptothecin⁹³,⁹⁴ 104 (Scheme 36). Similarly, incorporation of the 6-heptynenitrile 105 unit into the indole gives the basic skeleton of the ergot alkaloids⁹⁵ (eqn 24).

Scheme 35.

Scheme 36.
It has been found that trimethylsilylalkynes undergo [2+2+2] cycloadditions under low-temperature photolytic conditions in the presence of stoichiometric amount of CpCo(CO)₂ to afford complexed cyclopentadienones regioselectively\(^9\) (eqn 25). Metallocyclopentadienes\(^{10a}\) and metalloyclobutenones\(^{97}\) have been used in the formation of cyclopentadienones from alkynes and carbonylmetal compounds regioselectively.

\[
\text{(CH}_3\text{)}_3\text{SiC}≡\text{CH} \xrightarrow{\text{hv, } -20^\circ\text{C}, 70\%} \begin{array}{c}
\begin{array}{c}
\text{major product}
\end{array} \\
\begin{array}{c}
\text{minor product}
\end{array}
\end{array}
\]

Sesquiterpene illudol\(^{98}\) 108 was obtained from 107 via intramolecular [2+2+2] cyclization of 106 (Scheme 37). It is interesting to note that [5.6.4] ring system is constructed during cyclization from an acyclic precursor.

Vollhardt and co-workers have shown that intramolecular cyclization of enedyene 109 (prepared by Nicholas reaction), containing a tetrasubstituted double bond, provides a diastereomeric mixture of spirocyclic diene 110a and 110b which can be converted via routine functional group manipulation to the antimicrobial diterpene stemodine\(^{99}\) 111 (Scheme 38).
Vollhardt has demonstrated that the precursor 114a and 114b for daunomycinone can be synthesised by reacting diyne 112 with alkene 113 in the presence of CpCo(CO)$_2$ (Scheme 39).
Interestingly, enamides 115 and bis(trimethylsilyl) acetylene (BTMSA) were cocyclized in the presence of CpCo(CO)$_2$ to form diastereomeric complexes 116a and 116b, providing galanthan ring systems. These intermediates were transformed to γ-lycorane$^{101}$ 117 by routine synthetic operations (Scheme 40).

Further exploration of this reaction by Vollhardt and co-workers has shown that one aromatic double bond of many heterocyclic ring systems is capable of incorporation into cyclohexadiene ring. Reaction with N-substituted heterocycles, imidazole, pyrrole, indole and uracil derivatives has shown that aromatic double bond can function as the alkene component in the cyclization. A [2+2+2] cycloaddition of pyrrole$^{102}$ 118 was carried out to afford fused dihydro indole 119 (eqn 26).

N-substituted imidazole$^{103}$ 120 was reacted with BTMSA to give cycloadduct 121 in high yields (Scheme 41).
N-substituted indole 122 also reacts with BTMSA to provide CpCo-complex. This reaction provides an entry to 4a, 9a-dihydro 9H carbazole 123 (eqn 27).

Indole derivative 124 on cocyclization with 125 gives cobalt complex 126 which on treatment with MnO₂ furnishes propellane 127, and the latter rearranges to spirofused compound 128 on oxidative removal of the metal (Scheme 42).

Substituted uranil 129 undergoes cycloaddition to give Co-complexes 130 which can lead to various nucleoside derivatives (eqn 28).

A novel synthesis of fused 2H-pyrans 132 has been achieved via η₅-cyclopentadienylcobalt complex-induced [2+2+2] cycloadditions of the alkynes 131 with ketones both inter as well as intramolecularly (eqn 29).

Vollhardt and co-workers 108 have synthesised enantiomerically pure cyclopentadienyl cobalt complexes from chiral ligands obtained from naturally occurring terpenes and acids. The chiral cobalt complexes 133a-c were efficient catalysts in providing high diastereomeric excess. They have used these complexes for the photolytic cyclization of unsymmetrical α,ω-diynes 134 to metal-complexed cyclopentadienones 135 (eqn 30).
Later, these complexes were also exploited for diastereoselective enedine cyclization to complexed cyclohexadienes. Prochiral $\alpha,\delta,\omega$-enediynes 136 cyclize to chiral tricyclidiene complex 137 in the presence of 133a as diastereomeric complexes in 58:42 ratio (eqn 31).

\[ \text{Scheme 42.} \]

(35%, syn/anti=10)

(73%, anti)
2. Nicholas reaction

A phenomenon of long-standing interest in organometallic chemistry is the tremendously enhanced stability of carbonium ion flanked by organometallic metal moieties. While considerable attention has been focussed on the various possible modes of these stabilizations, the potential applications of these cations in organic synthesis have largely remained an uncharted area. The use of dicobalt octacarbonyl for the protection of a triple bond is well known and the realisation that triple bond-coordinated Co$_2$(CO)$_6^+$ moiety dramatically enhances stability of propargylic carbocations has led to the growth of the synthetic transformations now known as Nicholas reaction (Scheme 43). This methodology has found numerous applications in organic synthesis and some of the salient features of its utility are discussed.
2.1. Reaction with nucleophiles

The enhanced stability of (propargyl)\( \text{Co}_2(\text{CO})_6^+ \) cations has made them an attractive intermediate for a new bond formation on reaction with a wide range of nucleophiles. In all cases, attack by nucleophile occurs exclusively at the propargylic carbon, resulting in a versatile propargylation method subsequent to mild oxidative demetallation.

2.2. Aromatics

Electron-rich aromatic compounds\(^{113} \) including anisole, phenol, N, N-dimethylaniline, etc., react at room temperature or even below with the (propargyl)\( \text{Co}_2(\text{CO})_6^+ \) complexes to afford C-propargylated aromatic compounds (Scheme 44).

### Scheme 43.

<p>| | |</p>
<table>
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<tbody>
<tr>
<td>[Image: CO_2(CO)_6.png]</td>
<td>[Image: Scheme_43.png]</td>
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### Scheme 44.

<p>| | |</p>
<table>
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<tr>
<td>[Image: CO_2(CO)_6.png]</td>
<td>[Image: Scheme_44.png]</td>
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</table>
2.3. Reaction with X-dicarbonyls

Propargylated cobalt complexes as salts with HBF₄ or TiCl₄ react easily with β-diketones and β-ketoesters affording mono C-propargylated products in good yields (Scheme 45). This selective reaction reflects the reversibility of coupling reaction and the steric bulk of the (propargyl) Co₂(CO)₆⁺ group. Reactions of chiral cobalt complexes with the prochiral β-diketones were found to proceed with diastereoselectivities of 2:1 to 15:1.

\[
\begin{align*}
\text{HC}≡\text{C}−\text{C}−\text{OH} & \quad \text{HBF}_4 \quad \text{Et}_2\text{O} \quad \text{CH}_2\text{Cl}_2, \quad -78^\circ \text{C} \rightarrow 0^\circ \text{C} \\
\text{Co}_2(\text{CO})_6 & \quad \text{Fe(NO}_3)_3 \cdot 9\text{H}_2\text{O} \\
\text{EtOH}, 0^\circ \text{C} & \quad \text{Co}_2(\text{CO})_6
\end{align*}
\]

Scheme 45.

2.4. Reaction with allyl and enol silanes

Propargyl dicobalt hexacarbonyl cations couple with allylsilanes to give complexes of 1,5-enynes in satisfactory yields (Scheme 46). In the presence of BF₃ etherate a cobalt-complexed propargylic ether can undergo an intramolecular alkylation with an allylic silane to provide six-, seven- and eight-membered complexed cycloalkynes (eqn 32).

\[
\begin{align*}
\text{HC}≡\text{C}−\text{CH} & \quad \text{BF}_3 \quad \text{CH}_2\text{Cl}_2, 0^\circ \text{C} \\
\text{Co}_2(\text{CO})_6 & \quad \text{Fe(NO}_3)_3 \cdot 9\text{H}_2\text{O} \\
& \quad \text{Co}_2(\text{CO})_6
\end{align*}
\]

Scheme 46.

\[
\begin{align*}
\text{TMS} & \quad \text{OMe} \quad \text{BF}_3 \quad \text{Et}_2\text{O} \quad \text{n=1,2,3} \\
& \quad \text{n=1,2,3}
\end{align*}
\]

Schreiber and co-workers have performed an exocyclic intramolecular alkylation of allylic silane to afford six-membered ring with complete stereocontrol. Oxidative decomplexation of extra-annular cobalt complex provided the acetylene (eqn 33). The intermolecular version of the reaction provides high levels of diastereoselection for syn-alkylated products provided certain stereocontrol elements are maintained. The intramolecular alkylation reaction with allylic silanes affords either intra or extra-annular cobalt alkyne complexes.
Caple and Smit\textsuperscript{120} have reported the trapping of the cation formed by electrophilic addition to 1,3-enyne complexes with trimethylsilyl enol ethers or allylsilanes (eqn 34).

\[
\begin{align*}
\text{(CO)}_3\text{Co} & \quad \text{1. R}^1\text{CO}^+ \\
\text{1,3-enyne} & \quad \text{2. } \text{OSiMe}_3 \\
\text{Co} & \quad \text{3. Ce}^{4+}
\end{align*}
\]

The alkylation of silyl enol ether\textsuperscript{45} with the cobalt complex of propargylic methyl ether affords alkylated ketone. Cobalt complex can be removed from the products using trimethylamine-N-oxide or ferric nitrate while the stereochemical nature of the product is being preserved (eqn 35).

Cobalt-mediated cyclopentanone annulation was used as a new methodology to give the guaiane sesquiterpene skeleton 142 as in cyclocolorenone\textsuperscript{121} which was synthesised from the intermediate 141 derived by the reaction of enol silane 140 with cobalt complex 139. Magnus and co-workers have carried out\textsuperscript{122} an intramolecular Nicholas reaction on cobalt-complexed propargylic methyl ether to provide an access to calicheamicinone model systems (Scheme 47).

In the same way, \(\alpha\)-alkoxy cations derived from acetylenic acetals\textsuperscript{123} have been found to combine effectively with the enol derivatives, allyl silanes and enol silanes in the presence of BF\textsubscript{3}Et\textsubscript{2}O to afford the \(\beta\)-alkoxyacetylenic ketone derivatives in excellent yield and modest to excellent \(\text{syn}\) stereoselectivity (eqn 36). The uncomplexed acetals do not undergo reaction at \(-78^\circ\text{C}\) but between \(-20\) and \(0^\circ\text{C}\) reaction did occur affording the corresponding acetylenic ketone as a 1:1 mixture of \(\text{syn}\) and \(\text{anti}\) diastereomers. It is clear therefore that the metal fragment not only facilitates coupling but also has categorical effect on diastereoselectivity.
Although highly diastereoselective products have been achieved from complexed aldehyde or acetal precursors with enol and allyl nucleophiles\textsuperscript{124} as mentioned above, facile racemization of these cations has previously thwarted attempts to develop general, enantioselective route to the diastereomers. In order to get enantioselective propargylation, Nicholas and co-workers\textsuperscript{125} have used enantiomERICally pure propargylic alcohol and converted them to diastereomeric dicobalt propargylium \textit{Co}$_2$(CO)$_5$L complexes, where \textit{L} may be \textit{PPh}_3 or \textit{P}[OCH(CF$_3$)$_2$]$_3$. After demetallation of the resulting alkylated complex, enantiomERICally pure compounds were obtained (Scheme 48).

\textit{2.5. Reaction with amines}

The Nicholas reaction with carbon nucleophiles\textsuperscript{111} has been explored to a great extent and apart from this, the oxygen-centered nucleophiles\textsuperscript{126} were also used frequently. However, only little is known about Nicholas reaction with nitrogen nucleophiles. The earliest example, an unoptimized reaction of propargylic cobalt salt of HBF$_4$ with acetonitrile in the presence of sulfuric acid, dates from 1981\textsuperscript{127} (eqn 37).
In 1990, Japanese group\(^{138}\) reported the N-propargylation of indole and a few other heterocycles. Indole reacted with propargylic alcohol-Co\(_2\)(CO)\(_6\) complexes to give 3-(1,1-dimethylpropargyl) indole 143 (Scheme 49) whereas N-methoxycarbonyl-tryptamine 145 gave the corresponding N- and C-substituted derivative 146a,b with (propargyl acetate) Co\(_2\)(CO)\(_6\) complex 144 (Scheme 50).

Scheme 49.
The reactions of the \([(\text{HC}=\text{CCH})\text{Co}_2(\text{CO})_6]\) \(\text{BF}_4\) have been carried out with a wide range of amines to give the corresponding propargylic amines\(^{129,130}\) (Scheme 51). The primary amines were simultaneously C-alkylated by protecting the \(-\text{NH}_2\) group.

\[
\text{R-NH}_2 + H_2\text{C}^+\text{C}=\text{CCH}, \text{BF}_4^- \xrightarrow{\text{CH}_2\text{Cl}_2, 20^\circ\text{C}} \begin{cases} \text{R-NCH}_2\text{C}=\text{CCH} \\
\text{R-NHCH}_2\text{C}=\text{CCH} \\
\text{R-NHCOCH}_3 \end{cases}
\]

\(\text{R} = \begin{cases} \text{H}_3\text{CO} \\
\text{H}_3\text{CO} \end{cases}\)

Scheme 51.
Recently, tertiary amines\textsuperscript{131} have been synthesised by a selective reaction from cobalt-complexed propargyl cation using primary and secondary amines as nucleophiles (eqn 38).

\[ \text{HC} \equiv \text{C}-\text{CH}_2 \text{BF}_4^- + \text{Co}_2(\text{CO})_6 \rightarrow \text{HC} \equiv \text{C}-\text{CH}_2 \text{NH}_2 \]
\[ \text{DME} \rightarrow -20^\circ\text{C} \]
\[ 66\% \]

\[ \text{eqn 38} \]

2.6. Reaction with other organometallic nucleophiles

The reaction of several methyl-metallic compounds (CH\textsubscript{3})\textsubscript{3} ML\textsubscript{n} with the propargylated cobalt complexes had been tried to produce the methylated derivatives of propargyl group containing compounds\textsuperscript{132,133} (eqn 39). The most efficient method of coupling of propargyl cations with acetylenic group was via the reaction (alkyne)\textsubscript{2}Al with complexed propargyl acetates to form 1,4-diyn complex\textsuperscript{134} (Scheme 52).

\[ \text{HC} \equiv \text{C}-\text{CH}_2 \text{Co}_2(\text{CO})_6 \]
\[ + \]
\[ \frac{(\text{CH}_3)_3\text{Al}}{\text{CH}_2\text{Cl}_2} \]
\[ -78^\circ\text{C} \]
\[ \text{HC} \equiv \text{C}-\text{CH}_2\text{CH}_3 \text{Co}_2(\text{CO})_6 \]
\[ 91\% \]

\[ \text{eqn 39} \]

\[ \text{HC} \equiv \text{C}-\text{CH}_2\text{OAC} + (\text{n-C} \equiv \text{C})_3\text{Al} \]
\[ \frac{\text{CH}_2\text{Cl}_2}{-78^\circ\text{C} \rightarrow 0^\circ\text{C}} \]
\[ \text{HC} \equiv \text{C}-\text{CH}_2 \text{C} \equiv \text{C} \rightarrow \text{n-Bu} \text{Co}_2(\text{CO})_6 \]
\[ -78^\circ\text{C} \]
\[ (\text{NH}_4)_2\text{Ce(NO}_2)_6 \text{acetone} \]
\[ \text{HC} \equiv \text{C}-\text{CH}_2 \text{C} \equiv \text{C} \rightarrow \text{n-Bu} \text{66\%} \]

Scheme 52.
2.7 Miscellaneous nucleophiles

Although not much work has been done on the reaction of propargyl \( \text{Co}_2(\text{CO})_6^+ \) cation with non-carbon-centered nucleophiles, Siegel et al.\(^{34,35} \) found that secondary alkyl acetylenes can be prepared through the reduction of the corresponding cobalt-complexed \( \alpha \)-acetylenic alcohols with \( \text{NaBH}_4/\text{CF}_3\text{COOH} \) in dichloromethane (Scheme 53). Deuterium-labelled diisopropylacetylene prepared by this method has been used in the synthesis of (hexaisopropyl-d\(_6\)) benzene.

![Scheme 53](image)

2.8 \( \alpha \)-Alkoxy cations

The highly reactive (1,2-epoxy alkyne) dicobalt hexacarbonyl complexes 147 had been generated \textit{in situ} by treatment of 1,2 epoxy-3-alkyne (from 1-octene-3-yn/MCPBA) and with a slight deficiency of \( \text{Co}_2(\text{CO})_6 \) in benzene solution at 5°C. The epoxide reacts with several nucleophiles (\textit{i.e.}, \( \text{CH}_3\text{OH}, \text{H}_2\text{O}, \text{Cl}_3\text{COOH} \)) under acidic conditions to produce the 1-substituted 2-hydroxy products\(^{136,137} \) in good yields (Scheme 54).

![Scheme 54](image)
2.9. α-Vinyl cations

In order to further elucidate the steric and electronic properties of the propargylic carbonium ion stabilized with Co₂(CO)₆, the reactions of various nucleophiles with the vinylogous cations were examined. Accordingly, it was demonstrated that anisole reacts regio- and stereoselectively with 148 to give (E)-1,3-ene 149 derivative in good yields (eqn 40).

\[
\text{HBF}_4\cdot\text{Et}_2\text{O} \quad \text{CH}_2\text{Cl}_2 \quad -78^\circ\text{C}
\]

2.10. α-Cyclopropyl cations

Descoins and Samain have shown the contrast between the stereoselectivities of the reaction with the free and complexed cyclopropyl carbinols. It shows that attachment of complex not only facilitates the reaction but also provides a highly stereoselective (E)-1,3-ene formation. Saha has extended this reaction to carbon nucleophiles (i.e., allylsilanes, anisole, vinylacetate, etc.) which reacted without cleavage of cyclopropane ring (Scheme 55).

Scheme 55.
3. Carbonylation reaction

Carbonylation\textsuperscript{113}, as the name suggests here, involves the process of introducing CO into the molecule. Transition metal-promoted carbonylation\textsuperscript{142,143} of olefins, acetylenes, halides, alcohols, amides, nitro compounds, etc., are very important in both industrial and academic research. Cobalt carbonyls have been widely used and most extensively studied among the metal carbonyls. It catalyses the hydroformylation of olefin, and was first discovered by Roslen in 1937 (eqn 41). Olefins react with Co\textsubscript{2}(CO)\textsubscript{8} in the presence of CO/H\textsubscript{2} to provide aldehydes\textsuperscript{144} in very high yields. These reactions were later on developed into an useful industrial process\textsuperscript{145} for the synthesis of aldehydes from alkenes (Scheme 56).

\begin{equation}
\begin{array}{c}
\text{C}=\text{C} \quad \text{Co}_2(\text{CO})_8 \\
\text{H} \quad \text{C} \quad \text{C} \quad \text{CHO}
\end{array}
\end{equation}

\textbf{Scheme 56.}

The carbonylation process using Co\textsubscript{2}(CO)\textsubscript{8} is more useful with vinyl ethers\textsuperscript{146} or vinyl acetates which leads to the formation of mainly one regioisomer (eqn 42). These reactions have found widespread application on carbohydrate substrates owing to their high regioselectivity and mild conditions (eqn 43).

\begin{equation}
\begin{array}{c}
\text{CH}_2\text{OAc} \\
\text{AcO}
\end{array}
\quad \text{Co}_2(\text{CO})_8 \\
\text{CO} + \text{H}_2
\quad \begin{array}{c}
\text{CH}_2\text{OAc} \\
\text{AcO}
\end{array}
\quad 100\%
\end{equation}
Heck and co-workers have developed a novel route to alkyl-Co(CO)$_4$ complex$^{147}$ from the reaction between alkyl halide or sulphonates and Co$_2$(CO)$_8$. The alkyl cobalt complex thus prepared underwent CO insertion to give acyl cobalt complex which was converted to aldehydes, amides or esters on reaction with hydrogen, amine or alcohols, respectively (Scheme 57).

![Scheme 57.](attachment:Scheme57.png)

Conjugated dienes undergo reductive hydroformylation to yield saturated monoaldehyde$^{148}$ whereas non-conjugated dienes are prone to form ketones as byproduct (eqn 44).

$$\text{CH}_2=\text{CH}-\text{CH}=	ext{CH}_2+\text{CO} + \text{H}_2 \xrightarrow{\text{Co}_2(\text{CO})_8} \text{CH}_3(\text{CH}_2)_{3}\text{CHO} + \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CHO}$$  \hspace{1cm} (44)

Secondary and tertiary alcohols readily undergo hydroformylation presumably via the corresponding olefins (eqn 45).

$$\text{PhCH}_2\text{OH} + \text{H}_2 + \text{CO} \xrightarrow{\text{Co}_2(\text{CO})_8} \text{PhCH}_2\text{CH}_2\text{OH} + \text{PhCH}_3$$  \hspace{1cm} (45)
Dilactone\textsuperscript{149} can be synthesised by Co-catalysed carbynylation of acetylenes via the isolable complexes Co\textsubscript{2}(CO)\textsubscript{6}C\textsubscript{2}H\textsubscript{2} and Co\textsubscript{2}(CO)\textsubscript{9}C\textsubscript{2}H\textsubscript{2} as intermediates (eqn 46).

\[
\text{HC}={\text{CH}} + \text{CO} \xrightarrow{\text{Co}_2(\text{CO})_8} \text{O}=\text{O} \\
70\%
\]

Alper and co-workers\textsuperscript{150} have synthesised γ-hydroxy lactone using acyl-Co-complexes derived from the reaction of Co\textsubscript{2}(CO)\textsubscript{8} with CH\textsubscript{3}I and CO. Co-complex reacts with alkyne to give 4-keto-3-alkenoyl cobalt intermediate, using phase transfer catalyst. This complex gives unsaturated keto acid that cyclised to give γ-hydroxy lactone (eqn 47).

\[
\text{PhC}={\text{CH}} \xrightarrow{\text{cat.} \text{Co}_2(\text{CO})_8, \text{Me}1} \text{Me} \xrightarrow{5\text{N NaOH, CTAB, C}_6\text{H}_6, \text{CO, r.t.}} \text{Me} \xrightarrow{44\%} \]

One of the outstanding developments in the area of carbynylation using Co\textsubscript{2}(CO)\textsubscript{8} is the contribution from Murai and co-workers\textsuperscript{151}. They have developed a direct method for the synthesis of enolsilyl ether from cyclic olefins in the presence of CO and diethyl (methyl) silane (eqn 48). They have suggested a catalytic pathway for siloxymethylation.

\[
\text{+ CO + HSiEt}_2\text{Me} \xrightarrow{\text{Co}_2(\text{CO})_8} \text{OSiEt}_2\text{Me} \quad (48)
\]

High affinity of silicon towards oxygen in the key intermediate R\textsubscript{5}SiCo(CO)\textsubscript{4} is\textsuperscript{152} the driving force for the cleavage of C–O bond in oxygenated compound 148 to give intermediate 149 having carbon–cobalt bond. Insertion of CO gives acyl cobalt complex 150 which reacts with HSiR\textsubscript{3} to give Co-complex 151 and the latter on reductive elimination of R\textsubscript{5}SiCo(CO)\textsubscript{3} provides aldehyde. Subsequently the reductive addition of HSiR\textsubscript{3} gives Co-complex 152, which on elimination of HSiCo(CO)\textsubscript{3} provides enolsilane 153 (Scheme 58).

Reaction of epoxides with Co\textsubscript{2}(CO)\textsubscript{8}/CO depends upon the solvent used in the reaction as 3-hydroxy esters\textsuperscript{146} were obtained by using MeOH as solvent whereas in aprotic solvent α,β-unsaturated acids were found to be the major products (Scheme 59). This methodology has been used for the synthesis of 2-(6-methoxycarbonylhexyl)-cyclopent-2-ene-1-one 154. This is a simple and short route for the synthesis of 154 via Co-catalysed carbynylation of intermediate epoxide. The reaction does not occur in the absence of base and ethanol was used for achieving the highest selectivity (Scheme 60). When reaction of epoxides was carried out in the presence of H\textsubscript{2}, aldehydes or alcohols\textsuperscript{153} were obtained as major products (Scheme 61).
COBALT CARBONYLS

Scheme 58.

Scheme 59.
Later, Murai and co-workers have reported hydroformylation of cyclic ethers\textsuperscript{154} in the presence of hydrosilanes. It has been shown that direct hydroformylation of these molecules suffers from undesirable side reactions.

Tetrahydrofuran, oxetane and 1,2-epoxycyclohexane undergo cleavage with diethyl (methyl) silane and CO to give silyl-protected hydroxy aldehydes\textsuperscript{155} (Scheme 62). In the absence of CO, epoxides are rearranged to ketone\textsuperscript{1} by $\text{Co}_2(\text{CO})_8$ (Scheme 63).

\textbf{Scheme 62.}
Oxetanes react with $\text{Co}_2(\text{CO})_8$ and CO to give 4-hydroxy acyl cobalt tetracarbonyls which decompose to give $\gamma$-lactone\(^{156}\). Large ring lactones can also be prepared by using chloroalcohol (Scheme 64). Allyl alcohols on intramolecular cyclization give lactones (eqn 49).

Alkyl and acyl Co-complexes react with 1,3-dienes to provide $\eta^3$-allyl derivatives\(^{150}\) which decompose to give 1-acyl, 1,3-dienes (eqn 50).

1,2-Bis(siloxy) olefin\(^{157}\) can be prepared from Co-catalysed reaction of aldehydes with HSiR\(_3\) in the presence of PPh\(_3\). The PPh\(_3\) as co-catalyst is necessary to avoid undesired hydrosilylation of aldehydes (eqn 51). In these reactions, 3-fold excess of HSiEt\(_2\)Me was used.
Later, these authors reported conversion of aldehydes to their higher α-siloxy aldehydes\(^{158}\) by hydrosilane and CO. Here the use of an excess of starting aldehyde is essential to avoid formation of 1,2-bis(sil oxy) alkenes (eqn 52).

\[
\begin{align*}
\text{RCHO} & \quad \text{[MeEt}_2\text{SiCo(CO)}_3\text{L]} \quad \rightarrow \quad \text{OSiEt}_2\text{Me} \\
\text{R} & \quad \text{C} \quad \text{H} \quad \text{Co(CO)}_3\text{L} \\
\end{align*}
\]

These reactions may be proceeding via silyl cobalt complex 155 formed \textit{in situ} from Co\(_2\)(CO)\(_8\) with hydrosilane. The intermediate is α-siloxy alkyl cobalt compound 156 formed \textit{in situ} from 155 with aldehyde. The high affinity of silyl group for oxygen may force C-Co bond formation (eqn 53). Murai and co-workers\(^{159}\) have described transformation of alkyl acetates to (trialkylsiloxy)methylenealkanes (Scheme 65).

This methodology is also applicable to lactone which is converted to the corresponding silyl enol ethers obtained by reductive opening of the ring (Scheme 66).

Later, these workers have reported a cobalt carbonyl-catalysed ring enlargement of cyclobutanones\(^{160}\) with hydrosilanes and CO. This was the first example reported for the catalytic incorporation of CO into a ketonic carbon (Scheme 67). This reaction provides a
novel method for the formation of five-membered rings containing disiloxo alkene which can be useful in the synthesis of polycyclopentanoids.

The authors have also reported that $[R_3SiCo(CO)_4]$ is efficient catalyst for nucleophilic oxymethylation\textsuperscript{161} of oxiranes to give 1,3-diol derivatives (Scheme 68). It was observed that functional groups present in oxiranes are not affected under these reaction conditions.
Murai and co-workers have reported a novel route for the synthesis of C-glycosyl compounds from glycosyl acetates via glyoxymethylation\(^\text{162}\) (Scheme 69). C-Glycosyl compounds are valuable as multipurpose building blocks and also as intermediate for methylene phosphonate and homo-C-nucleosides. This method is useful for one carbon chain extension at the anomeric centre of glycosides.

\[
\begin{align*}
\text{OAc} & \quad \text{OAc} & \quad \text{OAc} \\
\text{OAc} & \quad \text{OAc} & \quad \text{OSiMe}_3
\end{align*}
\]

\[\text{HSiMe}_3, \text{CO} \quad \text{Co}_2(\text{CO})_8 \quad 78\%
\]

\[
\begin{align*}
\text{YO} & \quad \text{OAc} & \quad \text{YO} & \quad \text{OSiMe}_3 \\
\text{YO} & \quad \text{OAc} & \quad \text{YO} & \quad 70\% \\
& & \quad \text{75}\%
\end{align*}
\]

\[\text{YO} = \text{Ac} \quad \text{YO} = \text{COPh}
\]

\text{Scheme 69}

Ito\(^\text{163}\) has utilised this methodology for the synthesis of 2-deoxy-C-nucleoside skeletons (Scheme 70). It was noted that siloxymethyl group has been introduced \textit{trans} to the adjacent (C-3) acetate group which is in consonance with Murai's result.

\[
\begin{align*}
\text{YO} & \quad \text{OAc} & \quad \text{YO} & \quad \text{OSiMe}_3 \\
\text{YO} & \quad \text{OAc} & \quad \text{YO} & \quad 70\% \\
& & \quad \text{75}\%
\end{align*}
\]

\[\text{YO} = \text{Ac} \quad \text{YO} = \text{COPh}
\]

\text{Scheme 70.}

Foa and co-workers\(^\text{164}\) have shown that in the presence of appropriate base alkyl tetracarbonyl cobalt complexes catalyse the carboxylation of aryl halides in aliphatic alcohols to provide ester. In contrast, Murai and co-workers have shown that the reaction of aryl halides under phase transfer conditions in the presence of MeI and NaOH have a mixture of aryl methyl ketones and aromatic carboxylic acid (eqn 54). This reaction proceeds via methyl tetra carbonyl cobalt complex\(^\text{165}\) which can be generated \textit{in situ} from \text{Co}_2(\text{CO})_8 with MeI. Product composition is highly dependent on base and solvent used.

\[\text{Ar}_x \xrightarrow{\text{Co}_2(\text{CO})_8/\text{CO}/\text{MeI}/\text{NaOH}} \xrightarrow{\text{C}_6\text{H}_6-\text{H}_2\text{O}/\text{CTAB}} \text{ArCOMe} + \text{ArCO}_2\text{H} \quad (54)
\]
Later, Miura and co-workers\textsuperscript{166} have demonstrated the carbonylation of vinyl halides on the corresponding carboxylic acid under these conditions (eqn 55).

\[
\begin{array}{c}
\text{Ph} \quad \text{Br} \\
\text{H} - \text{CH} = \text{CH} - \text{Br}
\end{array}
\xrightarrow{\text{CO/Co$_2$(CO)$_8$}}
\begin{array}{c}
\text{Ph} \quad \text{COOH} \\
\text{H} - \text{CH} = \text{CH} - \text{COOH}
\end{array}
\]
\[
\text{Dioxane-water/Ca(OH)$_2$}
\]

\[
\text{H} - \text{CH} = \text{CH} - \text{COOH} \quad 92\%, E
\]

This methodology can be employed for the synthesis of Furan-2(5H)-ones\textsuperscript{167} by carbonylation of 3-chloroprop 2-enols. When carbonylation was carried out in the presence of benzaldehyde using NaOH, an adduct was formed in 70\% and furanone in 13\% yield. These products were further converted into \(\gamma\)-alkyldenebutenolides on treatment with thionyl chloride in pyridine (Scheme 71).

\[
\begin{array}{c}
\text{Cl} \quad \text{CH} = \text{CH} - \text{OH} \\
\text{Ph} \quad \text{CHO} \\
\end{array}
\xrightarrow{\text{CO/Co$_2$(CO)$_8$, Mel/Ca(OH)$_2$}}
\begin{array}{c}
\text{O} \quad \text{CH} = \text{CH} - \text{Ar} \\
\text{Ph} \quad \text{O} = \text{CH} - \text{Ar} \\
\end{array}
\xrightarrow{\text{SOCl$_2$/C$_5$H$_5$N}}
\]

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scheme 71</td>
<td>Adduct</td>
<td>73%</td>
</tr>
<tr>
<td>Scheme 71</td>
<td>Furanone</td>
<td>33%</td>
</tr>
</tbody>
</table>

Alper and co-workers\textsuperscript{168} have developed an efficient method for regiospecific acylation of fulvenes by using phase transfer agent (eqn 56). Later, these workers\textsuperscript{169} have shown the hydroxyacylation of allenes under similar conditions (eqn 57).

\[
\begin{array}{c}
\text{Ph} \quad \text{Ph} \\
\text{Ph} \quad \text{Ph} \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, PhCH$_2$N(C$_2$H$_5$)$_4$Cl$^-$}}
\begin{array}{c}
\text{Ph} \quad \text{Ph} \quad \text{COOMe} \\
\text{H}_7\text{C}_8\text{Br} \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{OH} \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{OH} \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\xrightarrow{\text{Co$_2$(CO)$_8$/ Mel/ CO, 5N NaOH, n-C$_{16}$H$_{33}$N(CH$_3$)$_3$Br$^-$}}
\begin{array}{c}
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\text{H}_7\text{C}_8\text{C} = \text{CH}_2 \\
\end{array}
\]
Cobalt carbonyl is an efficient catalyst for carbonyl insertion reactions between C–N and N–N double or triple bond. Unsaturated amines and amides give lactams and imides, respectively, under the aegis of cobalt carbonyl and CO (Scheme 72). Schiff bases and azo compounds provide phthalimides and 2-phenyl indazolone, respectively, by cyclocarbonylation reaction with Co$_2$(CO)$_8$/CO (Scheme 73). Phenyl hydrazones and oximes also undergo cyclocarbonylation reactions to give cyclic amides (Scheme 74).
Aldehydes and amides in the presence of Co_2(CO)_8/CO provide N-acyl amino acids\(^{172}\) (eqn 58). Trifluorovaline and trifluoronovaline are synthesised via cobalt-catalysed amidocarbonylation\(^{142}\) of 2-TFMPA and 3-TFMPA, respectively, which are further hydrolysed to give free amino acid (Scheme 75).

\[
\text{PhCH}_2\text{CHO} + \text{CH}_3\text{CONH}_2 \xrightarrow{\text{Co}_2(\text{CO})_8/\text{CO}} \text{PhCH}_2\text{CH}-\text{CO}_2\text{H}
\]

(58)

Ketones can be prepared by the reaction of organomercury compounds\(^{173}\) in the presence of Co_2(CO)_8/CO (eqn 59).

\[
\text{PhC} = \text{N} \xrightarrow{\text{HSiMe}_3, \text{cat. Co}_2(\text{CO})_8/\text{CO}} \text{PhC} - \text{N}\text{SiMe}_3
\]

(59)

4. Miscellaneous reactions

Murai and co-workers\(^{174}\) have developed a novel and efficient method for the synthesis of N, N-disilylamines by reduction of aromatic nitriles using cobalt carbonyl-catalysed addition of two molecules of HSiMe_3.

Aliphatic nitriles did not react with HSiMe_3 whereas in p-(cyanomethyl)-benzonitriles, the cyano group adjacent to benzene ring, selectively reacts with HSiMe_3. The rate of conversion of aromatic nitriles having electron-withdrawing group or sterically hindered nitriles is rather low (Scheme 76).
Chatani and co-workers\textsuperscript{175} have developed a method for the formation of pyrrole ring from alkynes and cyanotrimethyl silane in the presence of CO\textsubscript{2}(CO)\textsubscript{8} (Scheme 77).

\begin{equation}
\text{BuC}≡\text{CMe} \xrightarrow{\text{Co}_2(\text{CO})_8} \text{BuC}≡\text{CMe} + \text{Me}_3\text{SiCN} \quad \text{(36 : 64) 95%}
\end{equation}

Isobe and co-workers\textsuperscript{176} have recently shown the epimerization of C-1 alkynyl group on pyranose ring through cobalt complexes under acidic conditions. Thus, 157 on complexation with Co\textsubscript{2}(Co)\textsubscript{8} provides Co-complex 158 which was equilibrated under acidic conditions by using TfoH to give the opposite isomer in very high yields. This reaction was carried out under various conditions and best results were obtained at higher temperatures with catalytic amount of iodine which afforded the isomer in very high yields. A similar transformation is also achieved on pyranose ring 159 containing substituent with two triple bonds by epimerisation of bis-cobalt complex 160 (Scheme 78).

5. Conclusion

The foregoing sections have clearly established the versatility of cobalt carbonyl in contemporary synthesis and this development has a very strong bearing on the future attempts towards pursuit of selectivity during the construction of sensitive and complex organic structures. Pauson–Khand, Nicholas and Vollhardt reactions are the outstanding features of these endeavours which will go a long way in achieving the desired efficiency and selectivity which has now become a hallmark of modern synthesis.
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