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CARBONYLATION AND OTHER METAL-CATALYSED C-C COUPLING REACTIONS USED IN INDUSTRY

Abstract. — The formation of new carbon-carbon bonds is probably the most fundamental reaction in organic chemistry. Many of the most selective and energy efficient reactions today involve the use of metals and their complexes as promoters. Key routes to C-C bond formation involve carbonylation (using CO) and coupling reactions (of olefins, dienes, and arenes) following an activation step. The largest carbonylation reactions in volume terms are the hydrogenation of CO, to make long chain hydrocarbons for diesel fuel (over supported Fe, Co, Ru or Rh metal catalysts; the Fischer-Tropsch reaction) or, over a Cu-ZnO catalyst, to make methanol. Many of the important carbonylations are homogeneously catalysed, using soluble complexes of the late transition metals, such as Co, Rh, Ir, or Pd. The carbonylation of methanol to acetic acid, $MeOH + CO \rightarrow MeCOOH$ was originally developed using a Co/I^- catalyst; improvements in conditions (better energy use and selectivity), led by mechanistic considerations resulted in, first the Rh/I^- (Monsanto) and more recently, the Ir/I^- (BP, Cativa) processes. The hydroformylation of olefins, *e.g.*,

$$MeCH = CH_2 + H_2 + CO \rightarrow MeCH_2CH_2CHO + MeCH(CHO)CH_3$$

was also originally developed using a soluble cobalt catalyst, but again the use of rhodium catalysts (bearing phosphine ligands) has largely superseded the older processes. Even newer technologies, for example involving *supported* homogeneous catalysts, now promise still cleaner and more selective processes. Direct coupling reactions include Friedel-Crafts type processes, for example,

$$C_6H_6 + CH_2 = CHR \rightarrow C_6H_5 - C_2H_4R.$$

Zeolites are now the strong acid catalysts employed heterogeneously rather than the previously used $AlCl_3$ or HF; the new catalysts are much more environmentally friendly («greener») as they do not involve halides which cause corrosion and undesirable side reactions. Valuable highly selective reactions include the Cr-catalysed oligomerization of ethylene to 1-hexene or 1-octene, and of butadiene to cyclo-octadiene or cyclo-dodecatriene, over Ni catalysts. Palladium catalysed coupling and carbonylation reactions have made key steps much more environmentally acceptable in the syntheses of the important anti-inflammatory pharmaceuticals *ibuprofen* and *naproxen*.

Key words: Metal-catalyzed; C-C coupling; Carbonylation.

Riassunto. — *Carbonilazione ed altri accoppiamenti C-C catalizzati da metalli impiegati nell'industria*. La formazione di nuovi legami carbonio-carbonio è forse la reazione più fondamentale in chimica organica. Molte delle reazioni più selettive ed energeticamente efficienti implicano oggi l'impiego di metalli e loro complessi come promotori. Le vie chiave per la formazione di legami C-C sono la carbonilazione (mediante CO) e le reazioni di accoppiamento (di olefine, dieni ed areni) precedute da uno stadio di attivazione. Le maggiori reazioni di carbonilazione in termini di volume sono l'idrogenazione del CO per la produzione di idrocarburi a lunga catena destinati all'impiego come combustibili Diesel (su catalizzatori metallici supportati a base di Fe, Co, Ru o Rh; reazione di Fischer-Tropsch) o di metanolo su catalizzatore Cu-ZnO. Molte tra le più importanti carbonilazioni avvengono su catalizzatori in fase omogenea costituiti da complessi solubili di metalli alla fine di una serie di transizione come Co, Rh, Ir e Pd. La carbonilazione del metanolo ad acido acetico $MeOH + CO \rightarrow$

MeCOOH venne originariamente sviluppata usando un catalizzatore Co/I⁻; il miglioramento delle condizioni (miglior uso dell'energia e maggior selettività) sulla base di considerazioni meccanicistiche condusse in un primo tempo al catalizzatore Rh/I⁻ (processo Monsanto) e più recentemente al catalizzatore Ir/I⁻ (processo BP, Cativa). L'idroformilazione delle olefine, per esempio:

$$MeCH = CH_2 + H_2 + CO \rightarrow MeCH_2CH_2CHO + MeCH(CHO)CH_3$$

venne anch'essa sviluppata originariamente usando un complesso solubile del cobalto, ma di nuovo l'uso dei catalizzatori a base di rodio (contenenti leganti fosfinici) ha largamente superato i processi più vecchi. Anche le nuove tecnologie basate su catalizzatori omogenei supportati promettono ora processi ancora più puliti e selettivi. Le reazioni di accoppiamento diretto comprendono i processi di tipo Friedel-Crafts, per esempio:

$$C_6H_6 + CH_2 = CHR \rightarrow C_6H_5 - C_2H_4R.$$
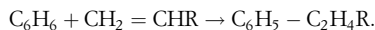
Le zeoliti rappresentano ora i catalizzatori fortemente acidi impiegati in fase eterogenea al posto di $AlCl_3$ od HF usati in precedenza; i nuovi catalizzatori sono molto più compatibili ambientalmente («più verdi») in quanto non contengono alogenuri che possono provocare corrosioni ed altre reazioni secondarie non desiderate. Pregevoli reazioni ad alta selettività comprendono l'oligomerizzazione dell'etilene ad 1-esene od 1-ottene catalizzata dal cromo o del butadiene a cicloottadiene o ciclododecatriene catalizzata dal nichel. Attraverso reazioni di accoppiamento e carbonilazione catalizzate dal palladio sono stati realizzati passaggi chiave molto più accettabili ambientalmente nella sintesi degli importanti composti farmaceutici *ibuprofen* e *naproxen.*

INTRODUCTION

The formation of new carbon-carbon bonds is probably the most fundamental reaction in organic chemistry, and an extensive methodology has been developed for that purpose. Many of the most selective and energy efficient reactions today use metals and their complexes as catalysts and promoters. The most industrially significant routes to C-C bond formation involve carbonylation (using CO) [1] or direct coupling reactions (of olefins, dienes, or arenes) [2] following an activation step.

There are many types of catalysis used in industry, but we will focus on those heterogeneously catalyzed by supported metals and those that are homogeneously catalyzed by metal complexes in solution. The latter generally involve well-characterized mono-nuclear species while the exact species that participate in heterogeneously catalyzed reactions are usually much less clearly defined. In addition there is a great deal of interest in newer catalytic systems, involving for example ionic liquids, supercritical solvents, or supported homogeneous catalysts, but these have yet to find widespread industrial applications.

The emphasis of this account is on procedures introduced over the recent past and which reflect current societal needs, such as minimizing pollution by using highly selective processes with minimum need for disposal of waste products, and lower energy requirements.

The largest carbonylation reactions in volume terms are the hydrogenation of CO, to make long chain hydrocarbons for diesel fuel, generally over supported Fe or Co catalysts (the Fischer-Tropsch reaction; >> 8Mt/a = million tonnes per annum) or, over a Cu-ZnO catalyst, to make methanol (*ca.* 30Mt/a). In the Fischer-Tropsch reaction the C-O bond is initially split, to give surface carbide, and water; the long chain hydrocarbons arise from the carbide via hydrogenation and polymerization steps. Methanol synthesis is generally believed to proceed via the insertion of carbon *di*oxide into metal-hydride bonds to give

surface formates which then react with more hydride to give surface methoxide and then methanol. The development of a catalyst for the Fischer-Tropsch reaction will be discussed later in the Symposium by Carlo Perego.

Methanol carbonylation

In addition to the above, heterogeneously catalyzed reactions, many important carbonylations occur homogeneously in solution, using soluble complexes of the late transition metals (especially, Co, Rh, Ir, or Pd). One such is the carbonylation of methanol to acetic acid,

$$MeOH + CO \rightarrow MeCOOH$$
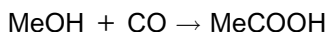
Acetic acid is a basic commodity chemical extensively used as an intermediate and as a solvent. Older routes to it include the fermentation of ethanol, pyrolysis of wood, oxidation of acetaldehyde (from acetylene or ethylene) and perhaps most important, the BP oxidation (burning) of naphtha or butane. The last is a basically simple process but in addition to acetic acid it gives carbon dioxide and a mixture of formic and propionic acids. The low selectivity of that reaction required separation by fractional distillation, a laborious, capital- and energy-intensive process.

The ready availability of carbon monoxide as a cheap feedstock prompted research into carbonylation reactions, initially by Reppe (BASF). A mixture of CO and hydrogen, known as *syngas* (or *water gas*), is produced from readily available raw materials, for example, by the partial oxidation of coal or the reforming of methane (*i.e.*, natural gas),

$$CH_4 + H_2O \longrightarrow CO + 3H_2$$
$$(\Delta H_{298K} \ 206 \ kJ \ mol^{-1} \ ; \ \Delta G_{1073K} \ -24 \ kJ \ mol^{-1})$$
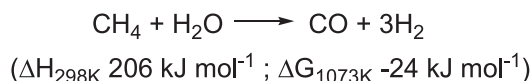
The ratio of CO to H_2 can be adjusted by the water-gas shift reaction, for which various catalysts, including supported iron or solutions of Rh/I^- can be used.

$$CO + H_2O \rightleftharpoons CO_2 + H_2$$
$$(\Delta H_{298K} \ -41 \ kJ \ mol^{-1} \ ; \ \Delta G_{298K} \ -28 \ kJ \ mol^{-1})$$
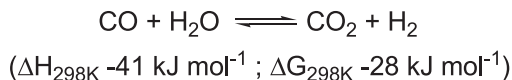
The availability of syngas allowed the development of good routes to methanol which in turn was an excellent feedstock for acetic acid. The methanol carbonylation route was invented in 1960 by BASF using a Co/I^- catalyst under quite stringent conditions (~ 230ºC, ~ 600 atm).

In 1970 Monsanto developed a lower temperature and lower pressure (~ 180ºC, ~ 35atm) carbonylation route that needed less catalyst, and also gave higher selectivity (> 99% compared to ~ 90% for the Co/I^- process). Although the Monsanto process used an extremely expensive Rh/I^- catalyst, it dominated acetic acid production for nearly 30 years. Current world production capacity is *ca.* 9Mt/a.

The mechanism of the reaction has been extensively investigated, first by Forster at Monsanto and later by our group at Sheffield University, and is well-understood. The basic features are illustrated in fig. 1,
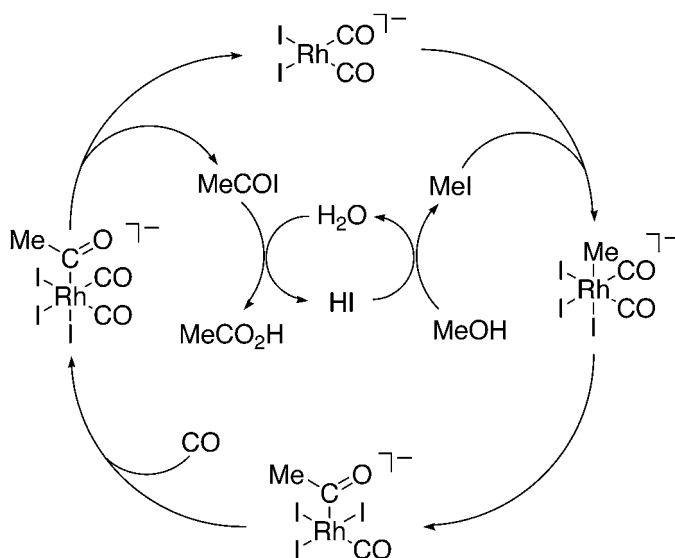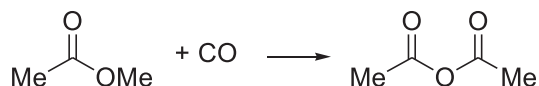
Fig. 1. – Schematic representation of the mechanism of the Rh/I⁻ catalyzed carbonylation of methanol [3].

The slowest, rate determining, step for the whole catalytic cycle is the *oxidative addition* of MeI to the square planar d^8 Rh^I anion, [Rh(CO)$_2$I$_2$]$^-$; this produces the 6-coordinate d^6 Rh^{III} anion [Rh(Me)(CO)$_2$I$_3$]$^-$ which very rapidly undergoes *methyl migration* to give the 5-coordinate acyl-Rh^{III} complex [Rh(COMe)(CO)I$_3$]$^-$. In turn this undergoes *reductive elimination* of acetyl iodide (MeCOI) to regenerate the starting Rh^I anion, [Rh(CO)$_2$I$_2$]$^-$ which allows the cycle to recommence. In addition to the organometallic cycle there is also a purely organic cycle in which the acetyl iodide is hydrolyzed to the product, acetic acid; HI is also formed that then reacts with the methanol feedstock to regenerate methyl iodide.

The various metal carbonyl complexes involved and the overall mechanism have been conveniently studied, under a working pressure of CO, in a specially constructed High Pressure IR cell (HP-IR) [3]. Carbonyl groups absorb radiation strongly in a characteristic region of the infra-red spectrum and considerable structural information can be obtained from the number of bands, and their positions and intensities. Thus we were able to identify, characterize and estimate the amounts and the lifetimes, of highly reactive intermediates such as [Rh(Me)(CO)$_2$I$_3$]$^-$ in kinetic studies. Another technique that has been useful in carbonylation studies is High Pressure NMR spectroscopy (HP-NMR).

The cycle in fig. 1 also conveniently exemplifies three of the main reactions that are undergone by organo-transition metal complexes: oxidative addition, reductive elimination and migration. A further important general reaction is ß-elimination (and its reverse, the olefin hydrometallation) for example, M-CH$_2$CH$_2$R $\rightleftarrows$ M-H + CH$_2$=CHR, in which a metal alkyl is in reversible equilibrium with an olefin and a metal hydride; see later.

A variation in conditions (anhydrous medium, Rh catalyst, in the presence of extra iodide) allowed the production of acetic anhydride by carbonylation of methyl acetate,

$$\text{Me} \overset{\displaystyle O}{\underset{}{\|}} \text{OMe} \ + CO \longrightarrow \ \text{Me} \overset{\displaystyle O}{\underset{}{\|}} O \overset{\displaystyle O}{\underset{}{\|}} \text{Me}$$

Further improvements in conditions (better energy use and higher selectivity), led by mechanistic considerations, resulted more recently in the Ir/I$^-$ (BP, Cativa) process for making acetic acid. A problem with the Monsanto process was the need to retain some water to keep the Rh-I catalyst stable and in solution; if this was not done then the catalyst would decompose in the «flash tank» where the CO pressure was low (fig. 2) and be lost to the system. However the industrial requirement is for anhydrous acetic acid which is then used as a feedstock for making further chemicals or as a solvent, and thus the water has to be removed, which requires a special distillation train.

The need for appreciable water levels in the Rh-catalysed acetic acid process was circumvented by the development of an iridium-iodide catalyst. The rates and selectivity of this catalyst system were similar or better than for the Rh/I$^-$ catalyst; however the iridium catalyst was much more stable at low $p_{(CO)}$. The great advantage stemming from that was that the reaction could be run at very much lower water levels than for Rh without metal plating out. Since the object of the synthesis is to make *anhydrous* acetic acid, the Cativa process allowed the omission of some of the distillation train; this resulted in considerable energy savings, which reduced both working and construction costs.

Although the chemistry of the Cativa process is closely similar to that of the Monsanto process there are some significant and instructive differences. Thus, the first step in the cycle, the oxidative addition of MeI to the square planar Ir^I anion [Ir(CO)$_2$I$_2$]$^-$ was fast but,
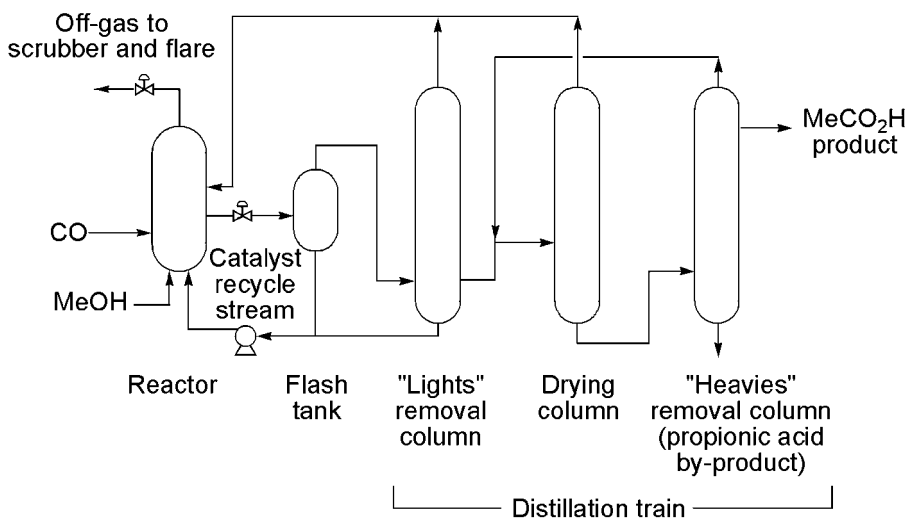

Fig. 2. – Schematic representation of a commercial scale plant for the Rh/I$^-$ catalyzed carbonylation of methanol.
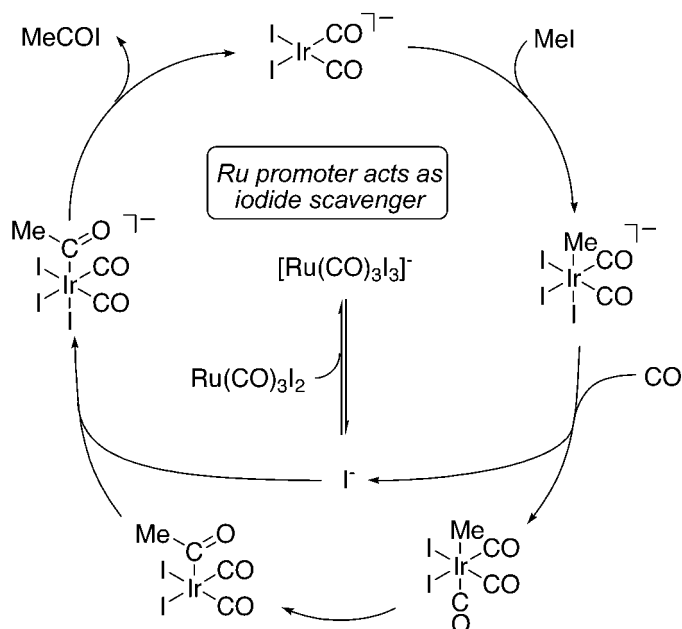
Fig. 3. – Simplified mechanism for the Ir/I⁻ catalyzed, Ru promoted carbonylation of methanol (the BP-Cativa process) [4].

by contrast, carbonylation of the anionic methyl species $[Ir(Me)(CO)_2I_3]^-$ to give the acetyl was now very slow, and was rate determining for the cycle. To achieve a working catalyst system it was therefore necessary to accelerate this step. This was done by adding an iodide acceptor to the catalyst; that had the effect of converting the methyl-iridium anion into a neutral species, $[Ir(Me)(CO)_3I_2]$, where migration occurred very much more rapidly than in the anion. [Methyl migration is faster in the neutral tricarbonyl $[Ir(Me)(CO)_3I_2]$ than in the dicarbonyl anion $[Ir(Me)(CO)_2I_3]^-$ because of a lower energy LUMO arising from more competition for π-back-bonding (to 3 CO's *vs* 2 CO's)]. Several iodide acceptors were tried and the most useful was found to be the ruthenium species $[Ru(CO)_3I_2]$ which acts as a scavenger of iodide in a separate sub-cycle. The overall mechanism is illustrated in fig. 3 [4].

To illustrate the continual striving for better processes in the chemicals industry, that is by no means the «last word» in the story of acetic acid manufacture today. A new Acetica process has recently been developed by Chiyoda using a «supported homogeneous catalyst», this uses the conventional Rh-based catalyst $[Rh(CO)_2I_2]^-$ but the counter ion is not a proton (H^+) as in the Monsanto process but a quaternary ammonium cation on an ion exchange resin. The catalyst is thus «immobilised» and can easily be recovered from the reaction solution by filtration.

As in many other aspects of progress, the production of acetic acid may still go full circle, returning to alkane oxidation. In this case a new process based on ethane (which is currently plentiful) is being developed to make acetic acid directly and with high selectivity.

Closely related reactions have been used in the synthesis of the important pharmaceuticals *ibuprofen* and *naproxen*. The ibuprofen synthesis now relies on a key palladium catalysed carbonylation reaction (fig. 4). By this means the previous lengthy six-step classical organic synthesis (fig. 5) with significant waste by-products (MeCO$_2$H,
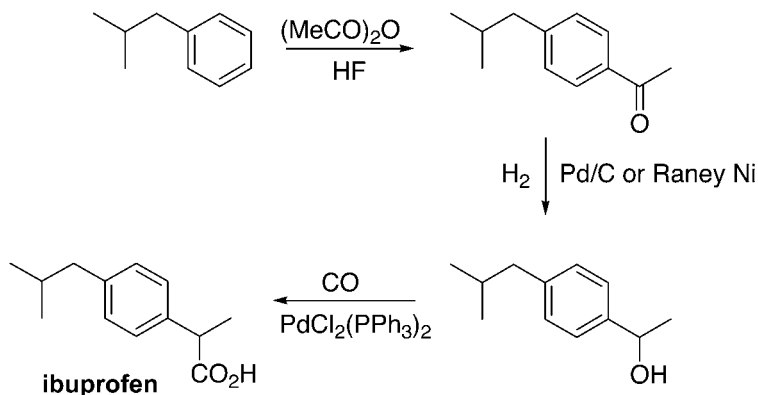

Fig. 4. – Modern low waste and economical 3-step synthesis of ibuprofen involving a palladium catalyzed carbonylation.
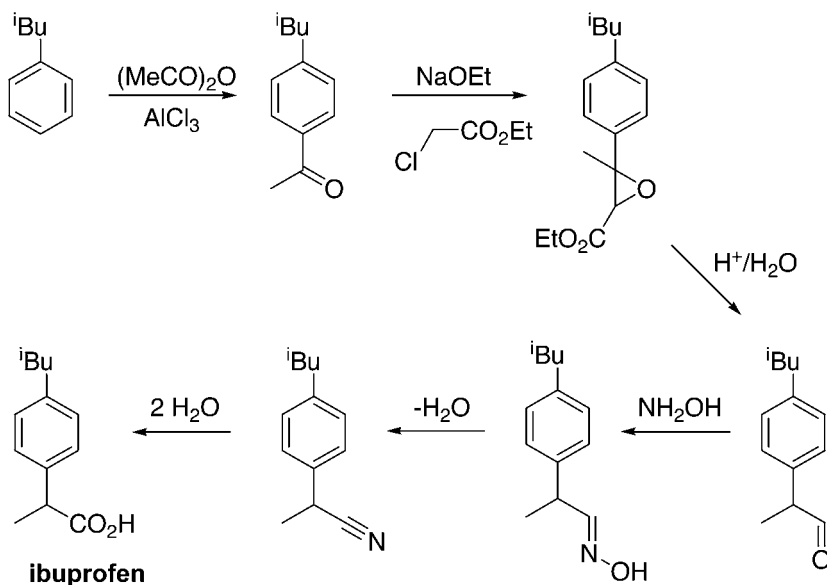

Fig. 5. – The older, classical, six-step synthesis of ibuprofen *not* involving metal-catalyzed carbonylation.

EtOH, NaCl, $EtOCO_2H$, $2H_2O$ and NH_3) has been shortened to a three step procedure, with virtually no waste materials, making it much more economical and environmentally acceptable.

Many C-C forming reactions rely on the alkylation of aromatics. One example is in the synthesis of ibuprofen, another is ethylbenzene, the intermediate in the synthesis of the key polymerization monomer, styrene, which is made from ethylene and benzene

$$C_6H_6 + CH_2\!=\!CH_2 \rightarrow C_6H_5CH_2CH_3$$
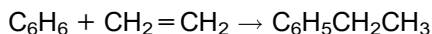
Typical catalysts used for the reaction were usually aluminium chloride or HF, both heavily polluting materials by virtue of their contained halide; the halide is also responsible for forming unwanted by-products.

Those catalysts are now being replaced by acidic zeolites such as ZSM-5, which act as Brønsted acids but are insoluble and can easily be filtered off at the end of the process. Active sites in zeolites are located in a regular network of channels of uniform dimensions, whose shapes and sizes are characteristic of the individual zeolites [5]. The diameter of the pore ports are of similar magnitude to the molecular dimensions of smaller organic compounds. *Shape selectivity* is the first and best known consequence of this. It can be defined as the capacity of zeolites to discriminate reactants, products and intermediates on the basis of their sizes and shapes. Thus for example in acid catalyzed cracking, only linear paraffins that are able to diffuse and are adsorbed inside the pores can undergo the chemical transformation.

The hydroformylation of olefins, *e.g.*, [3]

$$MeCH\!=\!CH_2 + H_2 + CO \rightarrow MeCH_2CH_2CHO + MeCH(CHO)CH_3$$

was also originally developed (by Roelen) using a soluble cobalt catalyst; here again rhodium catalysts (in this case bearing tertiary phosphine ligands) have, at least to some degree, superseded the older cobalt based processes.

A high regiospecificity, usually to make the linear *n*-aldehyde in preference to the branched *iso*-aldehyde, is a chief objective of the synthesis. The largest volume process involves the hydroformylation of propylene to *n*-butanal, which is used to make 1-*n*-butanol (an important solvent; ~ 2Mt/a) and also 2-ethylhexanol (used as a plasticizer). Prior to the introduction of the propylene carbonylation route, butanol and butanal were made from acetaldehyde (derived from palladium catalyzed oxidation of ethylene) which underwent aldol condensation to crotonaldehyde, followed by hydrogenation.

In hydroformylation the reactivity and regiospecificity is controlled by added ligands, usually tertiary phosphines, R_3P. A simplified scheme illustrating the «unpromoted» (*i.e.*
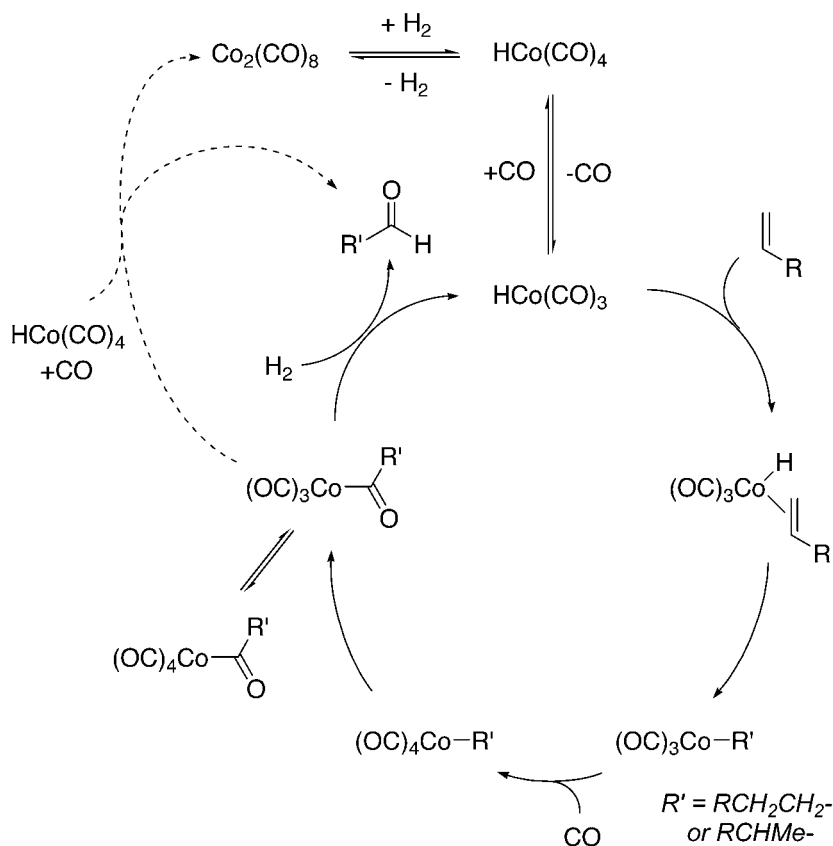
Fig. 6. – Scheme representing reactions proposed to occur during the unpromoted-cobalt catalyzed hydro-formylation of α-olefins.

no extra ligands added; typical conditions, 110-180 °C; $p_{(H2+CO)}$ ~ 200-300 bar) cobalt catalyzed reaction is shown in fig. 6. The catalyst, generally regarded as the cobalt carbonyl hydride, $CoH(CO)_4$, is derived from the precursor (often a soluble cobalt carboxylate) under the conditions of the reaction. Study of the kinetics reveals that the rate is proportional to catalyst, alkene, and hydrogen concentrations, but is inversely dependent on the CO pressure. This suggests that CO has to dissociate from the catalyst to free a coordination site on the metal in a rate determining step; as indicated by the equilibrium,

$$CoH(CO)_4 \rightleftarrows CO + CoH(CO)_3$$

Coordination of the alkene, $RCH = CH_2$, to the *coordinatively unsaturated* intermediate, $CoH(CO)_3$. is followed by Co-H addition to the alkene. That can occur in two ways, giving either the cobalt *n*-alkyl, $Co(CH_2CH_2R)(CO)_3$, or the *iso*-alkyl tricarbonyl, $Co(CHRCH_3)(CO)_3$; both of these undergo carbonylation («alkyl migration») to give

the *n*-acyl and the *iso*-acyl cobalt tricarbonyl complexes, which are then hydrogenated to give the *n*- and the *iso*-aldehyde respectively. In practice, since the catalyst decomposes readily on heating to inactive cobalt metal, a minimum pressure of CO is needed to maintain activity.

In the absence of a directing ligand on the metal there is often little discrimination and similar amounts of the two aldehydes are produced; however a strongly bound and bulky ligand on the metal will favour the formation of the *n*-alkyl in the Co-H addition step, thereby increasing the *n*-/*iso*- ratio of the final products. Thus the *n*-/*iso*- ratio is around 2-3:1 for $CoH(CO)_4$ and some 7-8:1 for $CoH(CO)_3(PR_3)$.

Not only does addition of a tertiary phosphine change the regioselectivity of the reaction, it also improves the rate. Thus, a major advance was brought about by Shell in the 1970's by the addition of a trialkylphosphine (usually a substituted bicyclic *phobane*) to the reaction mixture. The phosphine-based catalyst allowed the use of lower CO pressures and also higher reaction temperatures. In addition, as the presence of the phosphine increases the hydridic nature of the catalyst, the hydroformylation can be combined with hydrogenation to make the alcohol (often the desired end product) directly from the alkene.

The move from a cobalt- to a rhodium-based process that occurred the late 1960's in methanol carbonylation was echoed in hydroformylation [3, 6]. Wilkinson and his colleagues found that $RhH(CO)(PPh_3)_2$ was an outstanding catalyst as it was very selective to aldehyde products (no alcohol formation, no alkene hydrogenation or isomerization occurred) and that very high *n*-/*iso*- aldehyde selectivities of 20:1 for a variety of 1alkenes could be obtained under mild conditions (25 °C, 1 bar; 1:1 H_2/CO). As was found for the methanol carbonylation, the milder conditions and the better selectivity more than made up for the cost of using the more expensive rhodium-based catalyst. However, by contrast to the acetic acid process, halide is not necessary and indeed it inhibits the reaction. The technology was developed by Union Carbide in conjunction with Davy Powergas and Johnson Matthey. Currently some three-quarters of industrial hydroformylation processes are based on rhodium triarylphosphine catalysts, especially for the lower alkenes where high regioselectivity to linear aldehydes is critical.

Mechanistic investigations of the rhodium-triphenylphosphine catalyzed process have elicited the mechanism illustrated in fig. 7. The active catalyst here is the coordinatively unsaturated 4-coordinate Rh^I complex $RhH(CO)(PPh_3)_2$ derived from the commercially available 5-coordinated, $RhH(CO)(PPh_3)_3$.

The first step is loss of a PPh_3 ligand from $RhH(CO)(PPh_3)_3$ and its replacement by the olefin; hydride migration then occurs to give either the *n*- or the *iso*-alkyl-rhodium intermediate. This then takes up CO and undergoes migratory insertion to give a Rh-acyl, which then oxidatively adds hydrogen to regenerate $RhH(CO)(PPh_3)_2$ and releases the aldehyde product. While the basic form of the cycle is generally agreed, there is still dispute about the rate determining step, and it has been suggested that several of the fundamental steps have similar rate constants, making it difficult to specify one that is overall rate determining.
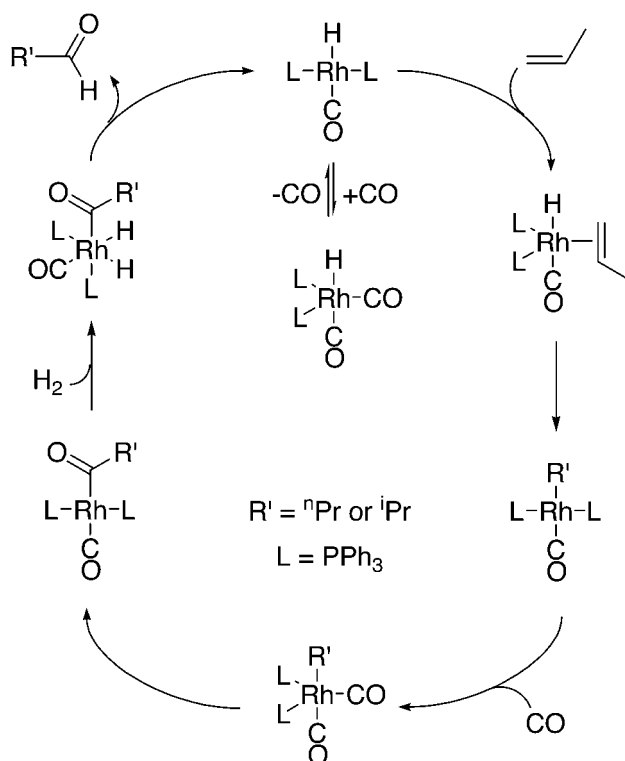
Fig. 7. – Representation of the chief steps during the Rh/PPh$_3$ catalyzed hydroformylation of propylene [6].

One important variant of Rh/PPh$_3$ catalysis is the two-phase catalyst system developed by Kuntz at Rhône-Poulenc in 1981, using a sulfonated triphenylphosphine ligand, P(C$_6$H$_4$-*m*-SO$_3$Na)$_3$ (TPPTS) to generate the water soluble catalyst: RhH(CO)[P(C$_6$H$_4$-*m*-SO$_3$Na)$_3$]$_3$.

Since the catalyst has a very high (9-) formal charge it is totally insoluble in all but the most polar solvents. The resultant two-phase catalyst system has the advantage over the completely homogeneous system in that all the organic product, butyraldehyde, is essentially in the organic phase and can easily be separated. Similarly, recovery of the catalyst is straightforward as it all stays in the aqueous phase. An excess of the phosphine ligand is required for good n-/iso- selectivities, as with the Rh/PPh$_3$ catalysts, but lower concentrations are required because the TPPTS phosphine dissociation equilibrium in water is shifted towards the Rh-TPPTS coordinated complexes. Shorter chain alkenes (C$_2$-C$_4$) are water soluble enough that sufficient migrates into the aqueous catalyst phase to allow hydroformylation. Rather high linear to branched regioselectivities of 16-18:1 for propylene can be obtained using this water soluble catalyst, but rates are slower than with conventional Rh/PPh$_3$ catalysts due to lower alkene concentrations in the water phase. Alkenes higher than 1-pentene are not soluble enough in water, and the process is limited to shorter chain

alkenes that have some degree of water solubility. Celanese-Ruhrchemie currently operates several hydroformylation plants based on this water soluble rhodium catalyst technology.

Although there has been a great deal of research activity to find good hydroformylation procedures to make aldehydes and alcohols enantioselectively, none seems as yet to have been commercialized. Nevertheless the potential is so high that it will certainly not be long before this methodology is applied to problems in the pharmaceutical and agrochemical industry. Much of the interest has focussed on Pt^{II} complexes containing chiral diphosphines, which have been used elsewhere for enantioselective hydrogenations. However, it has been suggested that as the coordination requirements for the critical hydroformylation intermediates are likely to be 5-coordinate they may well be different from those for hydrogenation. Rhodium complexes based on very bulky chiral mixed phosphine-phosphite BINAPHOS, for example, the complex $Rh(H)(CO)_2$(R,S-BINAPHOS) can hydroformylate styrene to an 88:12 mixture of $PhCHMe(CHO)$ and $PhCH_2CH_2CHO$ at 99% conversion, the former having an ee of 94%, in 43h at 60 °C with $CO + H_2$ (100 bar; 1:1).

Direct C-C Coupling: Oligomerization reactions.

In addition to the above carbon-carbon bond forming reactions and those discussed by Hans Brintzinger (olefin polymerization) and by Jean-Marie Basset (olefin metathesis), a number of highly selective olefin and diene oligomerization reactions have been commercialized. These include the Cr-catalyzed oligomerization of ethylene to 1-hexene or 1-octene, and of butadiene to 1,5-cyclo-octadiene or 1,5,9-cyclo-dodecatriene, over Ni catalysts.

These reactions are quite distinct from the polymerization reactions, and occur by quite different mechanisms, via metallacycle intermediates rather than by the more usual linear addition/insertion reactions.

NICKEL CATALYZED BUTADIENE DI-AND TRI-MERIZATION: CYCLO-OCTA-1,5-DIENE (COD) AND CYCLO-DODECA-1,5,9-TRIENE (CDT)

One of the first such reactions to be defined was the nickel catalyzed di- and tri-merizations of butadiene discovered by Wilke's group at the Max-Planck Institut für Kohlenforschung in Mülheim [7-9]. Cyclo-octadiene (COD) is conveniently made using the very bulky tris-o-tolylphosphite as a ligand,

>93% yield
TOF ca. 780
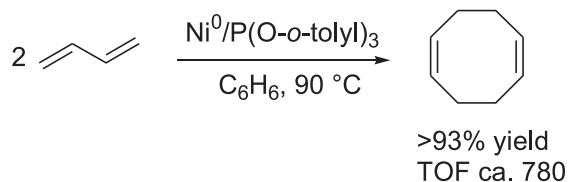
while cyclo-dodecatriene is the major product when «naked nickel» is employed,

i.e., no added phosphine or phosphite ligands. By suitably adjusting the ligands on nickel the reaction can be further modified to give either vinylcyclohexene or 1,2-divinylcyclobutane.

91% yield
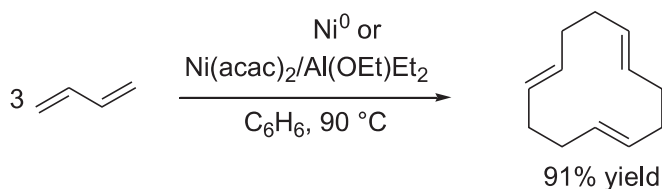
A characteristic of this chemistry is the reaction of zerovalent nickel complexes with the diene to give intermediate nickelacycles and allylic complexes, formally of Ni^{II}, illustrated in fig. 8. This formation of Ni^{II}-metallacycles and bis-allylic complexes from the Ni^0 ligand complex is formally a type of oxidative addition.

Related chemistry occurs in the duPont synthesis of adiponitrile by the double addition of HCN to butadiene, and also in the dimerization of butadiene in the presence of water and a palladium catalyst, to give octadienol.

Shell manufactures mixed α-olefins (used as monomers and to make detergents and other surfactants) from ethylene by oligomerization with a nickel catalyst in a polar solvent such as ethylene glycol. This forms part of the SHOP (Shell Higher Olefin Process); the world production is estimated to be over 1 Mt/a.
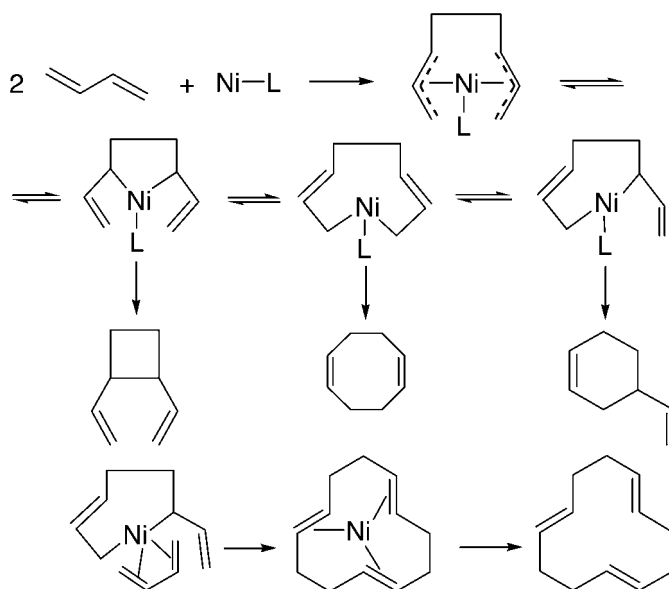

Fig. 8. – Proposed mechanism of the di- and tri-merization of butadiene on nickel(0) to give bis-allylic intermediates and cyclic olefins [7-9].

CHROMIUM CATALYZED OLIGOMERIZATION OF ETHYLENE TO 1-HEXENE AND TO 1-OCTENE:
COMPARISON OF LINEAR AND CYCLIC MECHANISMS

The classic olefin polymerization systems developed by Ziegler and Natta uses as catalyst a transition metal chloride, frequently $TiCl_3$, and an alkyl-aluminium promoter on a magnesium chloride support [10]. These polymerization reactions were commonly understood on the basis of the Arlman-Cossee mechanism, where reaction occurs at a Ti^{III} on the edge of a catalyst particle; the alkyl-aluminium transfers an alkyl (a methyl when the promoter is MAO, methylalumoxane) to the Ti. If the octahedrally coordinated edge-Ti also has a vacant site then an ethylene (or other olefin) can coordinate; migration of the alkyl onto the olefin gives the next higher homologous alkyl and creates a new vacant site where the coordination and migration process can be repeated. The polymers obtained show typical Schulz-Flory distributions of molecular masses; single oligomers are not obtained.

An interesting development has been the selective trimerization of ethylene to 1-hexene, using a Phillips chromium catalyst [11]. Chevron-Phillips now operate a plant in Qatar, based on the trimerization with a chromium catalyst prepared from Cr^{III}-2-ethylhexanoate, 2,5-dimethylpyrrole, diethylaluminium chloride and triethylamine in toluene (115 °C / 100 bar). The main product (*ca.* 94%) is 1-hexene, formed with a TOF *ca.* 156 kg/g Cr/h. The aromatic solvent presumably stabilizes a chromium intermediate complex through coordination.

More recently Sasol has developed a homogeneous catalyst system that will, depending on the ligands used, selectively give either 1-hexene or 1-octene [12, 13]. In these oligomerization reactions there is good evidence for the intermediacy of chromacyclic species, for example as shown in fig. 9, rather than for an Arlman-Cossee linear polymerization mechanism, though there are now systems where, depending on the ligands
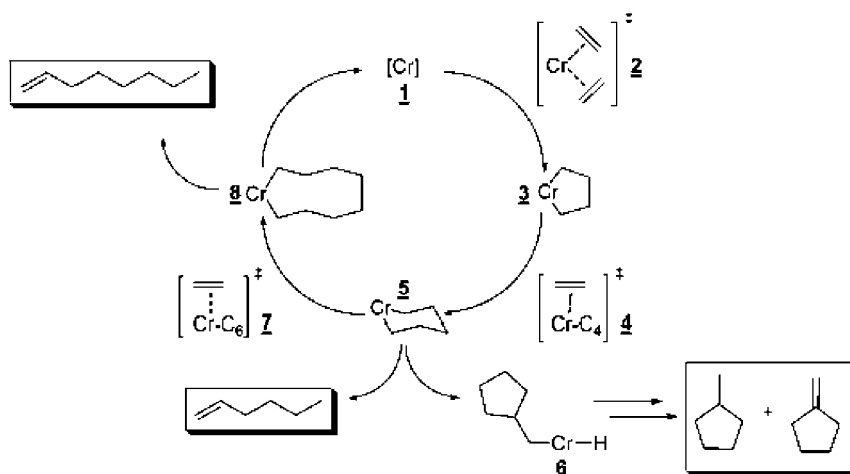

Fig. 9. – Representation of the Sasol metallacycle mechanism for the oligomerization of ethylene, especially to give 1-hexene or 1-octene [12, 13].

and the metal used, either selective oligomerization or polymerization can occur [14, 15]. A key feature appears to be the use of ligands that are *hemi-labile* to control the reactions.

These new reactions offer outstanding routes to individual 1-alkenes which would require either expensive separation and isolation techniques, for example from the mixtures obtained from Fischer-Tropsch reactions, or else long and complex syntheses by standard organic syntheses. It seems likely that they will become key feedstocks for a variety of new and useful products, especially as monomers and co-monomers.

These discoveries are but the latest examples of how metal catalysts extend the range of new products while at the same time provide new, commercially viable, *and* ecologically acceptable, synthetic routes for the chemical industry.

Summary

All enterprises are now under pressure to be environmentally more friendly: to be less polluting, more efficient and more selective, and to use less energy. This is particularly true of the chemicals industry. Historically our industries have not put environmental worries at the top of the agenda: they have been mostly concerned with cost-effectiveness. Recently, however it has become apparent that cost-effectiveness and care for the environment can go hand in hand: we can develop processes that are both more eco-friendly *and* cost-effective.

Catalysis is at the heart of the new approach and the lecture concentrates on the key reactions of the chemicals industry: making C-C bonds. Two types of metal-catalyzed reaction to form C-C bonds are reviewed: those involving carbon monoxide as a prime feedstock and those in which C-C bond formation occurs by the coupling of organic species such as olefins. The account is selective rather than comprehensive and reflects personal views on which of today's industrial processes are most interesting and which best illustrate how mechanistic understanding influences the development of better processes.

The topics considered include aspects of: methanol carbonylation: hydroformylation; Ni catalyzed butadiene reactions; di-, tri-, and tetra-merizations of ethylene compared to polymerization; Arlman-Cossee vs metallacycle mechanisms; and zeolites in Friedel-Crafts. Current views on mechanisms and some directions for potential improvements are presented.

References

[1] P.M. Maitlis - A. Haynes, in: G.P. Chiusoli, P.M. Maitlis (eds.), *Metal-catalysis in industrial organic processes*. RSC Publishing, Cambridge, UK, 2006, chapter 4.

[2] F. Calderazzo - M. Catellani - G.P. Chiusoli, in: G.P. Chiusoli, P.M. Maitlis (eds.), *Metal-catalysis in industrial organic processes*. RSC Publishing, Cambridge, UK, 2006, chapter 5.

[3] P.M. Maitlis - A. Haynes - G.J. Sunley - M.J. Howard, *Methanol Carbonylation Revisited: 30 Years On*. J. Chem. Soc., Dalton Trans., 1996, 2187-2196.

[4] A. Haynes - P.M. Maitlis - G.E. Morris - G.J. Sunley - H. Adams - P.W. Badger - C.M. Bowers - D. B. Cook - P.I.P. Elliott - T. Ghaffar - H. Green - T.R. Griffin - M. Payne - J.M. Pearson - M.J. Taylor - P.W. Vickers - R.J. Watt, J. Am. Chem. Soc., 125, 2004, 2847-2861.

[5] M. Clerici - P.M. Maitlis, in: G.P. Chiusoli, P.M. Maitlis (eds.), *Metal-catalysis in industrial organic processes*. RSC Publishing, Cambridge, UK, 2006, Appendix 2, Section A2.9.

[6] P.W.N.M. van Leeuwen - C. Claver, *Rhodium catalyzed hydroformylation*. Kluwer Academic Publishers, Dordrecht 2002.

[7] B. Bogdanovic - B. Spliethoff - G. Wilke, Angew. Chem., Int. Ed. Engl., 19, 1980, 622-623.

[8] P.W. Jolly - G. Wilke, *The Organic Chemistry of Nickel.* Vol. 1. *Organonickel complexes*. Academic Press, New York 1974.

[9] P.W. Jolly - G. Wilke, *The Organic Chemistry of Nickel.* Vol. 2. *Organic synthesis*. Academic Press, New York 1975.

[10] G. Fink - H.-H. Brintzinger, in: G.P. Chiusoli, P.M. Maitlis (eds.), *Metal-catalysis in industrial organic processes*. RSC Publishing, Cambridge, UK, 2006, Chapter 7.

[11] M.M. Lashier (Phillips Petroleum Co.), EPO 780353 A1, 1997.

[12] M.J. Overett *et al.*, Chem. Commun., 2005, 622-624.

[13] S. Kuhlmann *et al.*, J. Catal., 245, 2007, 279-284.

[14] P.J.W. Deckers - B. Hessen - J.H. Teuben, Angew. Chem. Int. Ed., 40, 2001, 2516-2519.

[15] B. Hessen, J. Mol. Catal. A, 213, 2004, 129-135.

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