Catalytic Formation of Carbon–Carbon Bonds by Activation of Carbon–Hydrogen Bonds

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Keywords: Homogeneous catalysis / C–H activation / Carbon–carbon coupling

The direct functionalization of C–H bonds by formation of a C–C bond is an interesting and important alternative to coupling reactions involving halide derivatives. These reactions are complex but during the past few years a number of new systems have been developed which display promising scope. This microreview will briefly mention the different mechanisms leading to C–H activation and describe the new systems leading to the catalytic formation of carbon–carbon bonds.

Introduction

Much research has been devoted during the past 20 years to the activation of the carbon−hydrogen bond,[1] whether it concerns intermolecular (Equations 1−3)[1a−1k] or intramolecular (cyclometallation, Equation 4) activation.[1l−1q] The first process is of special interest for the functionalisation of hydrocarbons, whereas the second one is of importance for the synthesis of fine chemicals where the production of by-products is minimized. A great deal of knowledge has been gained on the process of C−H bond activation and three main mechanisms identified, namely oxidative addition,[2] σ-bond metathesis,[3] and electrophilic

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Sylviane Sabo-Etienne (right) was born in 1956 in Tarbes (France). She studied at the Université Paul Sabatier, Toulouse, and obtained her "Thèse de Troisième Cycle" in 1980 working under the supervision of Prof. Danièle Gervais. She then entered the CNRS in 1980 and obtained her "Doctorat d'Etat" in 1984. In 1985 she went to the Université de Bretagne Occidentale in Brest, to work with Prof. Hervé des Abbayes. After a year working with Prof. Maurice Brookhart (Chapel Hill, USA) she returned to the Laboratoire de Chimie de Coordination where she is currently "Directrice de Recherche". Her research interests concern the chemistry and spectroscopic properties of polyhydride, dihydrogen, silane, and more generally σ-bond complexes, with particular focus on catalytic applications.

Bruno Chaudret (left bottom) was born in 1953 in Ferolles (France). He received his degree from the "Ecole Nationale Supérieure de Chimie de Paris" in 1975, his Ph.D. from Imperial College of Science and Technology, London, working under the direction of Prof. Sir Geoffrey Wilkinson in 1977 and his "Doctorat d'Etat" from the Université Paul Sabatier, Toulouse, working under the direction of Prof. René Poilblanc in 1979. He entered the CNRS in 1977 and was promoted to the position of "Directeur de Recherche" in 1988. His research interests concern the chemistry and spectroscopic properties of polyhydride, dihydrogen and more generally σ-bond complexes and their application in catalysis and for C−H activation as well as the synthesis, chemistry, and physical properties of nanoparticles of metals, alloys, and oxides.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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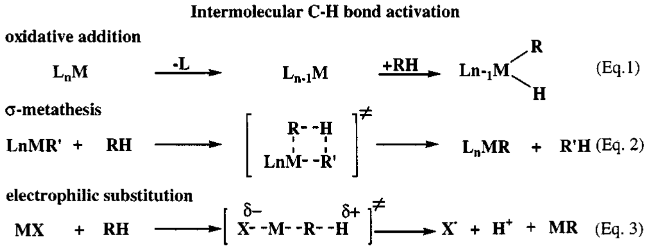
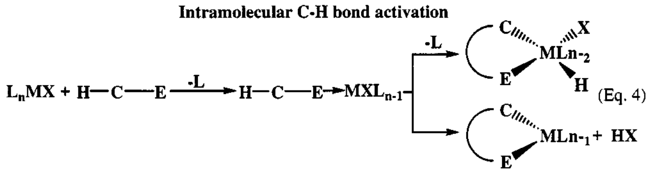
substitution,[4] all of which have been substantiated by stoichiometric studies.





However, despite this intense research activity, the number of catalytic processes including C−H bond activation as an elementary step have remained limited. This microreview will focus on the catalytic activation of cabon−hydrogen bonds leading to the formation of new carbon−carbon bonds. This will omit some very promising systems, such as that involving Pt(bipym) complexes recently described by Periana et al.[5] We will also omit the MERCAT process developed by Crabtree et al.[6] This is probably the most powerful system used to date to create new carbon−carbon and carbon−heteroatom bonds from alkanes, but it involves a mechanism based on electron transfer, and has recently been reviewed by Crabtree.

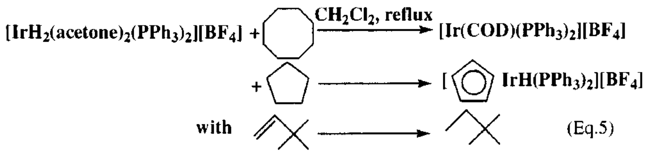
After the activation of a carbon−hydrogen bond, a new metal−carbon bond is generated. The new species has several possible pathways to react further: i) reductive elimination of an alkane in the case of an oxidative addition process; ii) β-elimination of the alkyl group to give an alkene; iii) insertion of small molecules into the metal−carbon bond leading to new functionalities. The first process is non-productive, we will consider only the latter two processes in the following review, and include the dehydrogenation processes as they formally generate a new carbon−carbon bond.

1. Alkane Dehydrogenation

With a Hydrogen Acceptor

Hydrocarbon dehydrogenation has been known in heterogeneous catalysis since 1937;[7] however, only recently have homogeneous systems been developed.

Alkane dehydrogenation could, in principle, be performed by good hydrogenation catalysts but this reaction is energetically unfavourable ($\Delta H \approx 30$ kcal·mol^{-1}). In order to circumvent this problem, Crabtree has employed a hydrogen acceptor, 3,3-dimethylbut-1-ene (*tert*-butylethylene), which is bulky enough to coordinate weakly to the transition metal centre, and which also shows a high enthalpy of hydrogenation. By using $[IrH_2(acetone)_2(PPh_3)_2][BF_4]$,[8] only stoichiometric reactions were observed (Equation 5).



However, catalytic dehydrogenation of cyclooctane to cyclooctene was achieved at 150°C using $IrH_2(CF_3CO_2)$-$[P(p\text{-}F-C_6H_4)_3]_2$ with a total turnover number of 16.[9] A similar system was developed by Felkin, Ephritikhine, and Baudry with polyhydrides such as $ReH_7(PR_3)_2$, $IrH_5(PR_3)_2$, and $RuH_4(PR_3)_3$ as catalysts.[10] At 150°C turnover numbers reaching 70 were obtained for the best systems.

The reaction path is proposed to involve a mechanism which is the reverse to that of alkene hydrogenation,[11] and which also involves highly coordinatively unsaturated intermediates (see Figure 1).[10]

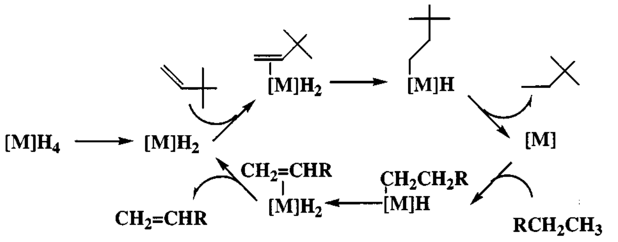


Figure 1. Proposed catalytic cycle for the dehydrogenation of saturated hydrocarbons

The first significant improvement was brought about by Goldman who performed the dehydrogenation reaction with $RhCl(CO)(PMe_3)_2$ as a catalyst and under a dihydrogen pressure of 69 bars. This system allows very high turnover numbers (1000) to be reached under mild conditions (60°C), but the problem is the necessary consumption of 6−8 mol of norbornene (used as hydrogen acceptor) per mol of dehydrogenated hydrocarbon. A number of linear and cyclic alkanes could be dehydrogenated in this way.[12]

More recently, Jensen et al. found that the complex $IrH_2[C_6H_3(CH_2P\mathit{t}Bu_2)_2\text{-}2,6]$ (very stable even at high temperatures) could dehydrogenate cyclooctane to cyclooctene at 200°C in the presence of *tert*-butylethylene with a turnover frequency of 12 min^{-1}.[13] The thermal stability of this compound results from the use of the "pincer" ligand $C_6H_3(CH_2P\mathit{t}Bu_2)_2\text{-}2,6$. Furthermore this system is able to dehydrogenate ethylbenzene or ethylcyclohexane to styrene, tetrahydrofuran to dihydrofuran,[14] cyclohexane to cyclohexene and benzene and decalin to octahydronaphthalene, tetrahydronaphthalene, and eventually naphthalene.[15] These reactions are slower than the dehydrogenation of cyclooctane. It is, however, remarkable that the formation of arenes does not poison the system.

Without a Hydrogen Acceptor

Whilst the interest of these systems is not in doubt, the presence of hydrogen acceptors make them unpractical. Therefore, several authors have looked for photocatalytic systems which avoid the use of hydrogen acceptors. Crabtree has shown that $IrH_2(CF_3CO_2)(PCy_3)_2$ is able to dehydrogenate cyclooctane to cyclooctene under UV irradiation with a turnover number of 7 at 25°C.[9] In this system, dehydrogenation of linear alkanes leads to a mixture of alkenes. Catalytic dehydrogenation of hexane, heptane, and octane has been carried out by Saito[16] using $RhCl(CO)(PR_3)_2$ (R = Me, Et, Ph), and Tanaka[17] using $RhCl(CO)(PMe_3)_2$. The reactions of Saito are carried out between 60 and 92°C and display a moderate variation in rate as a function of temperature, but no such variation as a function of the nature of the alkane substrate. The activity of the catalyst decreases in the order $PMe_3 > PEt_3 > PPh_3$. Tanaka's experiments were carried out under photolytic conditions and concern hexane as well as cycloalkanes such as cyclohexane and cyclooctane. In the case of hexane, 155 turnovers were obtained after 27 h, leading to (*E*)-/(*Z*)-2-hexene.

In all cases, the mechanism is proposed to involve β-elimination from an alkyl hydrido complex produced by oxidative addition of alkane to a coordinatively unsaturated species.

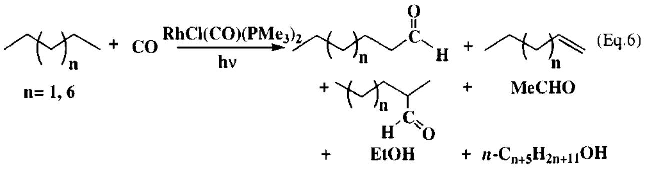
The best system was again found in 1997 by Goldman and Jensen, and involves the dehydrogenation of cyclodecane at 201°C under refluxing conditions leading to 360 turnovers after 24 h. The system is much less active for dehydrogenation of cyclooctane in a sealed tube at 200°C, thus suggesting the need for reflux.[18]

2. Formation of Carbon−Carbon Bonds

2.1 Insertion of Carbon Monoxide

The insertion of carbon monoxide into a carbon−hydrogen bond being thermodynamically unfavourable, all processes are photoassisted. Eisenberg was the first to show that square-planar iridium and rhodium complexes are able to catalytically insert carbon monoxide into a C−H bond of benzene when exposed to light ($\lambda > 366$ nm).[19] The complexes used were IrH(CO)(dppe), IrBr(CO)(dppe), $IrCl(CO)(PPh_3)_2$, and $RhCl(CO)(PPh_3)_2$ which gave rise to 2 catalytic cycles. A kinetic study carried out in the latter case shows that initial rates increase under reduced CO pressures, whereas larger turnover numbers were obtained under a high CO pressure.[19]

A similar but more efficient system was developed by Tanaka al. Using $RhCl(CO)(PMe_3)_2$, it was possible to catalytically carbonylate benzene itself or benzene monosubstituted by methyl, methoxy, chloro, or cyano groups with efficiencies reaching that of 65 turnovers.[20] This system can be extended to the carbonylation of saturated hydrocarbons. In this case, products of both carbonylation and dehydrogenation are obtained, those involving the initial activation of the terminal methyl groups being the most abundant (Equation 6).[20b,21]



The mechanism of this reaction was studied at wavelengths shorter than 320 nm by Goldman et al.[22] Under these conditions, the authors propose that the first step is the oxidative addition of a benzene C−H bond to a photoexcited catalyst, and not photoextrusion of a ligand (CO or PR_3). Field et al. have prepared $RhHCl(Ph)(CO)(PMe_3)_2$ (2 isomers: *cis*-HCl and *trans*-HCl) by irradiation of $RhCl(CO)(PMe_3)_2$ in a benzene/tetrahydrofuran mixture at low temperatures in the absence of added CO.[23] Kinetic activation parameters ($\Delta H^{\neq}$ and $\Delta S^{\neq}$) for the interconversion of both isomers are in agreement with those obtained by Goldman, and strongly suggest the intermediacy of a photoactive intermediate such as $RhHCl(Ph)(CO)(PMe_3)_2$ in benzene photocarbonylation. Finally, Eisenberg has also shown that d^8-ruthenium complexes accomodating carbonyl and phosphane ligands are also active for the photocarbonylation of benzene.[24]

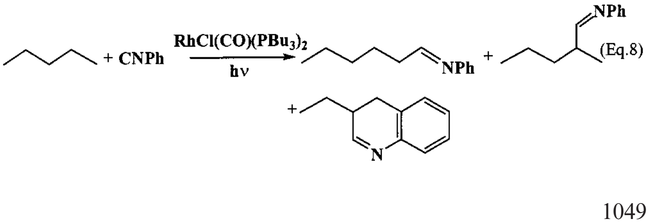
Sen and co-workers have studied electrophilic systems for the functionalization of alkanes.[1r] Whereas most systems concern the oxidation of alkanes, the reaction of $RhCl_3 \cdot 3\,H_2O$ with methane, dioxygen, and carbon monoxide in a mixture of C_3F_7COOH, $(CF_3)_2CHOH$, and D_2O produces methanol and acetic acid at 80°C with high efficiency. The proposed mechanism involves insertion of CO into a rhodium−methyl bond.[4k,4l] This direct formation of acetic acid is a promising method of activating methane.

2.2 Isocyanide Insertion

Insertion reactions of isocyanide groups (RNC, R = Ph, Me, *t*Bu, *p*-tolyl), a ligand formally similar to the carbonyl ligand, into a C−H bond of benzene have been carried out by Tanaka et al. using $RhCl(CO)(PMe_3)_2$. The reaction needs to be photoassisted and leads mainly to aldimines (Equation 7).[25]

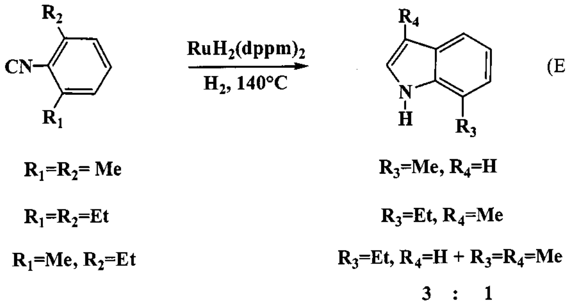
$$C_6H_6 + CNR \xrightarrow[h\nu]{RhCl(CO)(PMe_3)_2} PhCH{=}NR + PhCH_2NHR \quad \text{(Eq.7)}$$

In the case of linear alkanes, $RhCl(CO)(PBu_3)_2$ was used and the reaction was found to be only stoichiometric (Equation 8).



A similar reaction had been previously described by Jones et al. who showed that isocyanide insertion into the C−H bond of benzene could be catalysed at room temp. by $Fe(CNR)_3(PMe_3)_2$ (R = Me, *t*Bu, CH_2CMe, Ph, 2,6-xylyl) under UV light.[26] This reaction does not work for alkanes such as pentane or cyclohexane. The same reaction is possible using $RhCl(CNR')(PR_3)_2$ (R = Me, Et, *i*Pr and R′ = neopentyl, 2,6-xylyl, Me) as a catalyst, leading to 7.7 turnovers after 16 h in the best case (R = *i*Pr et R′ = neopentyl) but again no insertion of isocyanides into the C−H bond of alkanes was observed using this system.[27]

RuH(naphthyl)$(dmpe)_2$,[28] the first complex to be shown to activate C−H bonds of aryl and activated aliphatic C−H bonds, was reinvestigated by Jones for the synthesis of indoles from bulky isocyanides. 2,6-Xylyl isocyanide reacts at 60°C with RuH(naphthyl)$(dmpe)_2$ for 24 h in toluene to give *trans*-RuH[2-(7-methylindole)]$(dmpe)_2$ which isomerizes at 100°C to *cis*-RuH[2-(7-methylindole)]$(dmpe)_2$. The latter eliminates 7-methylindole at 140°C under 0.66 bar H_2 to yield $RuH_2(dmpe)_2$. The mechanism involves initial intramolecular C−H activation of a methyl substituent of the xylyl group attached to the isocyanide moiety. Using $RuH_2(dmpe)_2$, 3.6 turnovers could be obtained at 140°C (Equation 9).



(Eq. 9)

2.3 Alkene and Alkyne Insertion into Unsupported Carbon−Hydrogen Bonds

The insertion of alkynes into C−H bonds of benzene, *n*-hexane, cyclohexane, or diethyl ether can be achieved with $RhCl(CO)(PMe_3)_2$ in the presence of UV light. However, the reaction is less efficient than carbon monoxide or isocyanide insertion, and only 6 turnovers were obtained in the best case.[29] In addition to insertion products, the reaction in the case of benzene leads to dimers and trimers of acetylenes as well as biphenyl. The latter product, and other biaryls, can be obtained directly from the photolysis of arenes in the presence of $RhCl(CO)(PMe_3)_2$.[30] Cyclohexane, *n*-hexane, and diethyl ether react in the same way with phenylacetylene to give the corresponding α-substituted styrenes with a good regioselectivity but in low yield (from 19%/Rh for cyclohexane to 77%/Rh for *n*-hexane) and with the formation of several by-products.[29]

Some thermal systems involving insertion of unsaturated molecules into C−H bonds of benzene have been known for a long time. Thus, Hong et al. have shown that insertion of alkynes (RC≡CR′; R = Ph, Me, R′ = Ph; R = R′ = *p*-MeC_6H_4),[31] heterocumulenes,[32] aryl isocyanates (RN=C=O; R = Ph, *p*-MeC_6H_4, *p*-ClC_6H_4, α-$C_{10}H_7$),[32] ethylene,[33] monosubstituted ethylene (CH_2=CHCOR; R = OMe, OH, NMe_2, NMePh, Me),[34] disubstituted ethylene (RCH=CHR′; R = Me, Ph, CO_2Me, R′ = CO_2Me;[34] CH_2=CRR′; R = Me, R′ = CO_2Me)[34] and cyclic alkenes[34] into the C−H bonds of benzene, arenes (PhR; R = Me, OMe, F; Figure 2) or furans ($C_4H_3R''O$; R″ = H, Me, $MeCO_2$, MeCO, CHO; Figure 3) could be achieved at 220°C with $Rh_4(CO)_{12}$ as catalyst and under a pressure of CO. A maximum turnover number of 360 was obtained in the case of the addition of CH_2=$CHCO_2Me$ to benzene under 29 bars of CO. The reaction is favoured by the presence of electron-withdrawing substituents leading the authors to propose initial attack of a nucleophilic low-valent rhodium cluster onto the substrate C−H bond, followed by C−H bond cleavage and alkyne or isocyanate insertion. The CO pressure would be necessary to regenerate the active catalytic species. In some cases, secondary products can be formed, such as indenones in the case of the reaction between acetylenes and benzene, which result from CO insertion.

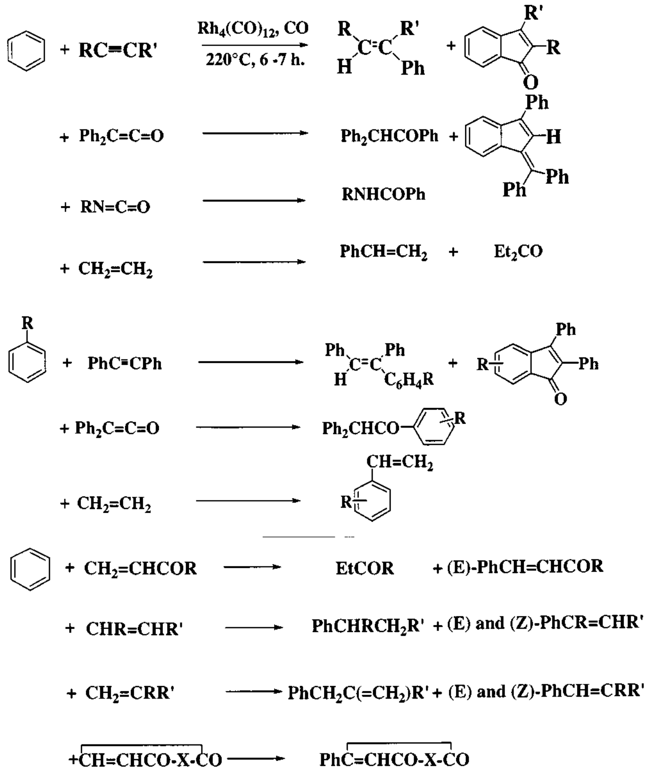


Figure 2. Carbon−carbon bond formation between arenes and unsaturated hydrocarbons catalysed by $Rh_4(CO)_{12}$

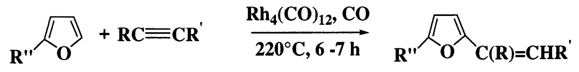
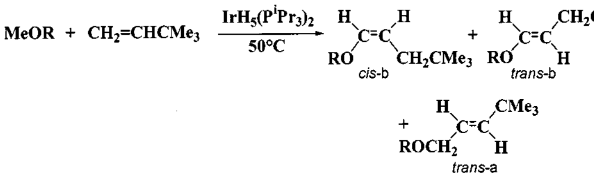


Figure 3. Carbon−carbon bond formation between furan and unsaturated hydrocarbons catalysed by $Rh_4(CO)_{12}$

An interesting coupling reaction between a C−H bond of methyl ethers (MeOR; R = CH_2CH_2OMe, C_6H_{11},

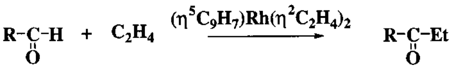
$C_6H_{10}Me$) and 3,3-dimethylbut-1-ene has been reported by Lin, Ma, and Lu with $IrH_5(PiPr_3)_2$ as the catalyst.[35] The reaction produces olefins and enol esters with a maximum turnover number of 12 after 24 h at 50°C (Equation 10).



(Eq.10)

The mechanism of this reaction involves the formation of an unsaturated 14-electron intermediate, similar to that proposed by Felkin et al. for alkane dehydrogenation, which is able to insert into the activated C−H bond of the methyl ether. The absence of β-hydrogen allows the coupling reaction to occur. This reaction is followed by a rapid isomerisation of the olefin formed.

Finally, the coupling reaction between aldehydes and olefins involves the activation of a particular C−H bond. Milstein et al. have shown that $[(\eta^5C_9H_7)Rh(\eta^2C_2H_4)_2]$ catalyses the insertion of ethylene at 100°C under 69 bars into the C−H bond of aldehydes RC(O)H (R = Ph, p-$CF_3C_6H_4$, p-MeC_6H_4) with a turnover frequency of 4 h^{-1}(Equation 11).[36]



$$R{-}\underset{\underset{O}{\|}}{C}{-}H + C_2H_4 \xrightarrow{(\eta^5C_9H_7)Rh(\eta^2C_2H_4)_2} R{-}\underset{\underset{O}{\|}}{C}{-}Et \quad (Eq.\ 11)$$

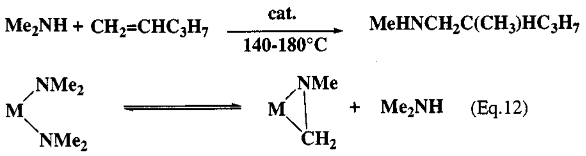
The reaction presumably proceeds by initial activation of the aldehyde C−H bond, as in the decarbonylation reactions of aldehydes catalysed by numerous transition metal complexes. It is, however, interesting to note that no decarbonylation product has been observed in this case.

2.4 Alkene and Alkyne Insertion into Potentially Chelating Systems

It has been shown in section 2.3 that most systems involving direct C−C coupling through C−H activation were relatively inefficient. It is, however, known from literature on organometallics that the activation of a C−H bond linked to a functional group (phosphane, amine, ketone, ...), thus maintaining it in close proximity to a metal centre, is much easier. This led several authors to investigate the functionalization of cyclometallated hydrocarbons. Lewis and Smith[37] have described the insertion of ethylene into the ruthenium−carbon bond of an *ortho*-metallated phosphite group. However, catalytic reactions were developed for systems containing a nitrogen or oxygen donor group as chelating assistant of the insertion reaction into the C−H bond.

Nitrogen Donor Chelating Assistants

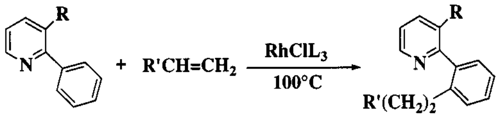
A catalytic amination reaction of olefines has been described by Nugent et al.[38] which does not involve, as expected, the formation of a C−N bond, but the formation of a C−C bond. The catalysts are amido transition metal complexes. The proposed mechanism involves the intermediacy of a metallacycle and the insertion of the olefin into the M−C bond (Equation 12).



$$Me_2NH + CH_2{=}CHC_3H_7 \xrightarrow[140\text{-}180°C]{cat.} MeHNCH_2C(CH_3)HC_3H_7$$

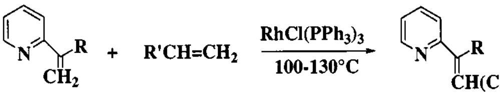
(Eq.12)

Recently, Lim, Kim, and Bang have described the catalytic alkylation of the phenyl ring of 2-phenylpyridine and 3-methyl-2-phenylpyridine in the *ortho* position relative to pyridine. Several olefins were used, namely $R'CH{=}CH_2$ [R' = $Me(CH_2)_2$, $Me(CH_2)_3$, $Me(CH_2)_5$, $Me_3C(CH_2)_2$, $Si(OEt)_3$, $Si(OMe)_3$], in the presence of the catalyst $RhCl(PPh_3)_3$ leading at 100°C to 10 turnovers in 22 h for the best system (Equation 13).[39]



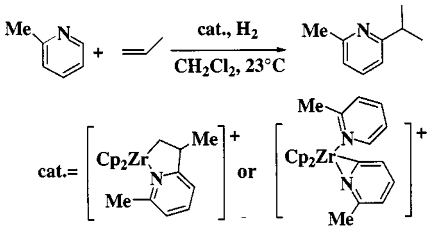
(Eq.13)

The intermediacy of an *ortho*-metallated hydridorhodium complex has been postulated. The reaction has been extended to carbon−carbon coupling reactions of substituted 2-vinylpyridines o-$RC({=}CH_2){-}C_6H_4N$ (R = Me, Ph) with the olefins $R'CH{=}CH_2$ previously mentioned.[40] This reaction leads to 10 turnovers at 100−130°C (in the best case) in the presence of the same rhodium catalyst (Equation 14).



(Eq.14)

More unexpectedly, chelating assistance by the pyridine nitrogen atom is also involved in the functionalisation of *ortho* C−H bonds in pyridine. Jordan et al. have first described the alkylation of pyridines in *ortho* position relative to the nitrogen atom. The reaction occurs under H_2 at 23°C in the presence of cationic zirconium complexes, leading to up to 40 turnovers (Equation 15).[41]



(Eq.15)

The mechanism involves the initial formation of $[Cp_2Zr(\eta^2\text{-6-methylpyrid-2-yl})(THF)]^+$ from $[Cp_2ZrMe(THF)]^+$ through a σ-bond metathesis process. In this system intermediates were isolated and demonstrated to be active in the catalytic coupling of 2-methylpyridine with propene (see Figure 4).

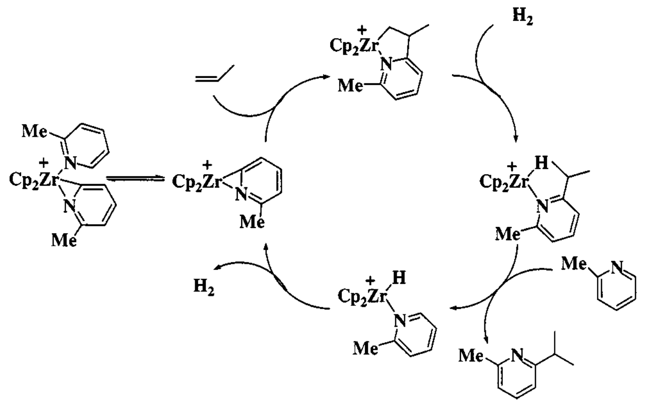
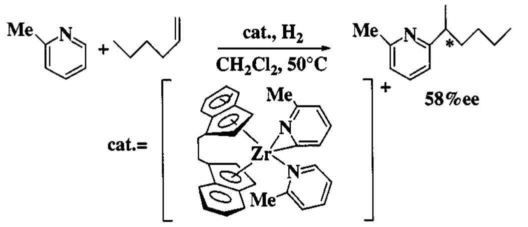


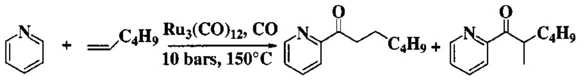
Figure 4. Reaction mechanism of coupling between 2-methylpyridine and propene catalysed by zirconium complexes

Recently, this reaction was extended to the regio- and stereoselective insertion of olefins into a methylpyridine C−H bond using chiral catalysts such as [$^{ch}Cp_2Zr(\eta^2$-pyrid-2-yl)]$^+$ [$^{ch}Cp_2$ = ethylenebis(indenyl) (EBI) or ethylenebis(tetrahydroindenyl) (EBTHI)].[42] The catalytic activity of the chiral complexes is 10 times lower, but at 50°C, in the presence of H_2, [(*S,S*)-(EBTHI)Zr(η^2-6-methylpyrid-2-yl)(2-methylpyridine)]$^+$, generated in situ from (*S,S*)(EBTHI)ZrMe$_2$, [HNBu$_3$][BPh$_4$], and 2-methylpyridine, catalyses the addition of 1-hexene to 2-methylpyridine to give (*R*)-2-methyl-6-(2-hexyl)pyridine with a 58% enantiomeric excess (Equation 16).



(Eq.16)

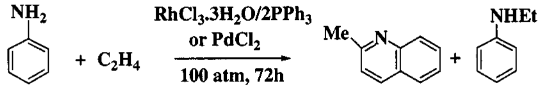
Moore et al. have shown that it is possible to insert two different molecules, namely carbon monoxide and olefins (R′CH=CH$_2$; R′ = H, C_4H_9, $C_{18}H_{37}$, Me$_3$C), into the C−H bond of pyridine in the *ortho* position relative to the nitrogen atom.[43] The reaction occurs at 150°C, under 10 bars of CO and leads to a turnover frequency of up to 300 h^{-1} when using 3,3-dimethyl-1-butene. The reaction can be extended to quinolines and to the use of cyclic alkenes but does not work for tri- and tetrasubstituted olefines. The authors present evidence for the implication of a trinuclear catalyst based on kinetic data and the absence of reactivity of photolytically generated mononuclear species (Equation 17).



(Eq.17)

A very similar system was used by Murai for the acylation of substituted imidazoles. The reaction is carried out under relatively harsh conditions (160°C, 20 bars of CO) and leads to a limited yield of coupling products; up to 23 turnovers in the best case.[44]

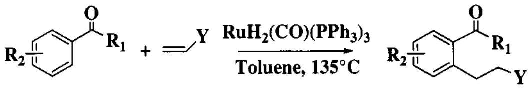
Finally, during attempts to catalyse olefin amination, Diamonds and co-workers observed a new cyclization reaction leading to the formation of 2-methylquinoline. The reaction conditions are severe (200°C, 101 bars, 72 h) and the yields modest (30 turnovers for the formation of *N*-ethylaniline and 10 turnovers for 2-methylquinoline), but this reaction represents the first catalytic synthesis of heterocycles and is thought to involve intermediate species containing *ortho*-metallated aniline (Equation 18).[45]



(Eq.18)

Oxygen Donor Chelating Assistants

Perhaps the most interesting and promising system for the functionalization of aromatic hydrocarbons in α-position relative to a functional group has been described by Murai and co-workers.[46−48] Initially, Murai (1993) described the alkylation of aromatic ketones using ruthenium catalysts, namely RuH$_2$(CO)(PPh$_3$)$_3$ (the most efficient example), Ru(H)$_2$(PPh$_3$)$_4$, Ru(CO)$_2$(PPh$_3$)$_3$, and Ru(CO)$_3$(PPh$_3$)$_2$.[46−48] The reaction was carried out in vigourously refluxing toluene, a temperature of 135°C being indicated by the authors, and led to ca. 50 turnovers of coupling product in the best case (Equation 19).

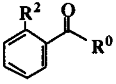
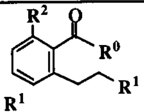
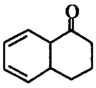
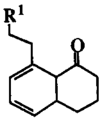
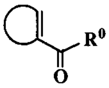
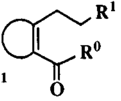
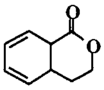
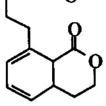
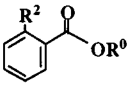
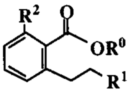
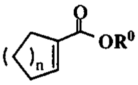
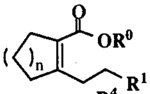
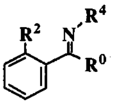
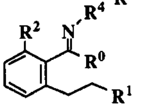


(Eq.19)

The scope of the reaction has proven to be fairly general. Thus, similar alkylation reactions were observed for acylbenzene derivatives,[46−48] α-tetralones,[49] α,β-enones,[50] lactones,[51] aromatic and heteroaromatic esters,[51] cyclic esters,[52] and aromatic imines[52] using substituted olefins[46−48,50−52] and alkynes.[49] Table 1 summarizes some of the reactions studied by Murai's group. This system has since then been extended by Weber et al. to the copolymerization of acetophenone with α,ω-dienes[53] as well as to the modification of unsaturated polymers,[54] whereas Woodgate used this system for alkylating hydroxyacetophenone and extended it to the functionalization of aromatic diterpenoids.[55]

The mechanism proposed by Murai involves the formation of a 16-electron ruthenium(0) intermediate produced by hydrogenation of the incoming olefin. The formation of triethoxyethylsilane (0.036 mmol) has been observed when RuH$_2$(CO)(PPh$_3$)$_3$ (0.04 mmol) was treated with 3 equiv. of triethoxyvinylsilane at 135°C for 1 min. The ruthenium complex was not identified. Addition of acetophenone (0.08 mmol), at 135°C and within 1 min, leads to the coupling product. An *ortho*-metallated intermediate, "RuH[*o*-C$_6$H$_4$−C(O)R]", is proposed (see Figure 5). Similar com-

Table 1. Some substrates used in Murai's reaction for coupling with an olefin $CH_2{=}CHR^1$

Substrate	Product	Reference
		46, 47, 48
		46, 48
		50
		51
		51
		57
		52

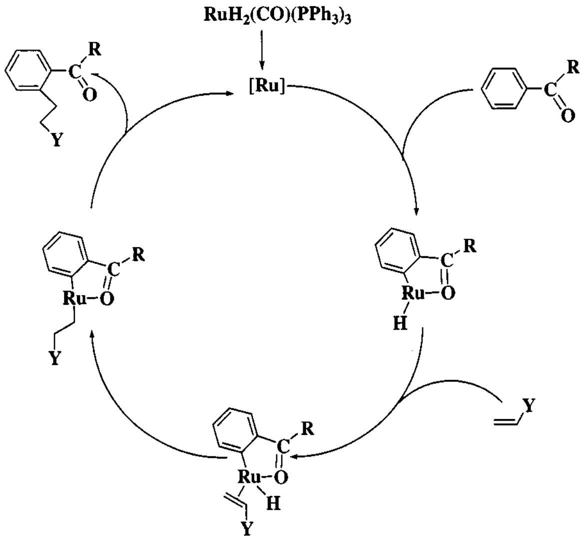


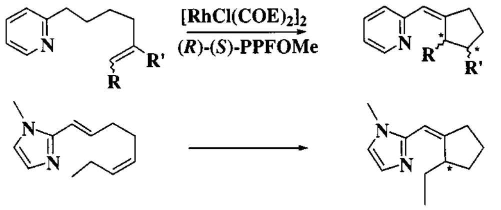
Figure 5. Mechanism proposed for Murai's reaction

plexes have been known since their first preparation by Cole-Hamilton and Wilkinson.[56] Hydrogen migration and carbon−carbon coupling would lead to the organic product and regenerate the active species [Ru].[46−52]

Trost et al. have studied the coupling of olefins with α-unsaturated esters catalysed by $RuH_2(CO)(PPh_3)_3$.[57] The catalytic activity is similar to that observed by Murai and the reaction is inhibited by the presence of a CO pressure or when carried out in a closed system, hence suggesting the need for CO to be eliminated for the reaction to proceed. The authors propose an active species "$RuS(PPh_3)_3$" stabilized by interaction with the solvent S.[57]

Weber et al. have recently mentioned the isolation of $[Ru\{MeC(O)C_6H_4CH{=}CH_2\}(CO)(PPh_3)_2]$ through the reaction of *o*-acetylstyrene with $[RuH_2(CO)(PPh_3)_3]$ in the presence of styrene at 120°C.[58] Such a complex could be a model for a late intermediate in the catalytic alkylation cycle and catalyses the copolymerisation of acetophenone and 1,3-divinyltetramethyldisiloxane.

More recently, Murai et al. have extended their study to the intramolecular asymetric coupling of substituted 1-(2-pyridyl)-1,5-dienes (Equations 20 and 21) or substituted 1-(1-methyl-2-imidazolyl)-1,5-dienes using a different catalytic system: $[RhCl(COE)_2]_2$ in the presence of alkyl (*R*)-1-[(*S*)-2-(diphenylphosphanyl)ferrocenyl] ether {alkyl = Me [(*R*)-(*S*)-PPFOMe], Et}.[59] The reaction proceeds at 25°C giving rise to 2 turnovers after 20 h and an enantiomeric excess of 78%. Up to 15 turnovers can be obtained at 120°C within 1 h but the enantiomeric excess decreases to 71%.



(Eq.20)

(Eq.21)

In our group, we have recently prepared a series of hydrido dihydrogen complexes containing *ortho*-metallated ligands (see Figure 6). For example, the reaction of 2-phenylpyridine leads to a new complex displaying interesting spectroscopic properties.[60a] These complexes are reminiscent of the intermediates proposed by Murai. This led us to attempt the same reaction with acetophenone and benzophenone. Hydrido dihydrogen complexes containing *ortho*-metallated aromatic ketones can thus be synthesized. These complexes further react with CO to give carbonyl hydrido complexes corresponding to precursors in Murai's cycle. The bis(dihydrogen) complex $[Ru(H)_2(H_2)_2(PCy_3)_2]$[60b] and the complexes containing *ortho*-metallated aromatic ketones were tested as catalysts for Murai's reaction in order to validate the catalytic cycle and define the role of CO. The reactions were carried out at room temp. in the presence of ethylene (20 bars). A catalytic reaction was observed when using $[RuH_2(H_2)_2(PCy_3)_2]$ or $[RuH(H_2)[OC(R)C_6H_4](PCy_3)_2]$ (R = Me, Ph) leading to the alkylation of the phenyl group in the *ortho* position of the ketone substituent. 10 turnovers are obtained under these conditions for the alkylation of acetophenone after 20 h, and 20 turnovers in the alkylation of benzophenone (see Figure 7). In the latter case, the reaction produces almost exclusively the dialkylated product. However, when using the carbonyl hydrido complexes $[RuH(CO)\{OC(R)C_6H_4\}(PCy_3)_2]$ (R = Me, Ph) no reaction was observed, even upon heating the solution. This suggests that the need for a high temperature in Murai's reaction is due to the necessity to eliminate CO from the coordination sphere of the ruthenium centre.

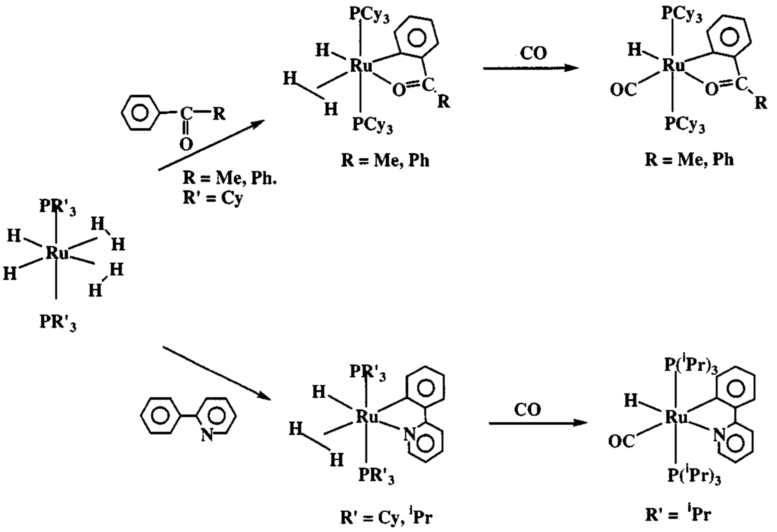


Figure 6. Synthesis of hydrido(dihydrogen)ruthenium complexes containing *ortho*-metallated ligands

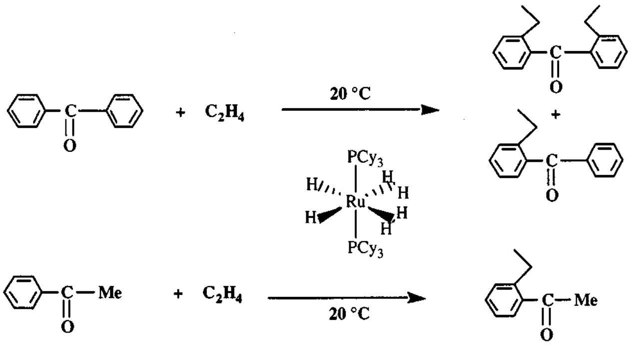


Figure 7. Alkylation reactions catalysed at room temp. by $RuH_2(H_2)_2(PCy_3)_2$

Conclusion

In conclusion, in this microreview we have briefly presented some of the latest results concerning the functionalization of C–H bonds through the formation of C–C bonds. If the alkane dehydrogenation is still difficult and requires harsh conditions, the catalytic insertion of alkenes into aromatic C–H bonds seems to be one of the most promising reactions regarding synthetic applications, especially if these reactions can be carried out under mild conditions (at room temperature for example). The development of such reactions would then avoid the by-products of conventional routes, salts in particular, and this research could therefore lead to new "environmentally friendly" processes.

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Received December 17, 1998
[I98434]