On the Mechanism of the Hydroxycarbonylation of Styrene with Palladium Systems

Inmaculada del Río,[a] Carmen Claver,*[a] and Piet W. N. M. van Leeuwen[b]

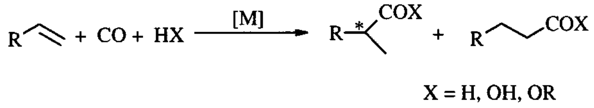
Keywords: Carbonylation / Palladium / Reaction mechanisms / Regioselective catalysis / P ligands

We present a review concerning the mechanism involved in the hydroxycarbonylation of styrene. We discuss the intermediates proposed in the literature, the effect of the acidic medium, the reactivity and kinetics, as well as the results of theoretical calculations on hydroxycarbonylation and related reactions. We have performed an in situ high-pressure NMR study to obtain more insight into the mechanisms that control the regioselectivity and have assessed how this is affected by the phosphorus ligand and the catalyst precursor. We observed palladium hydride and palladium acyl species and we suggest a catalytic cycle involving palladium hydride, palladium alkyl, and palladium acyl intermediates.

Introduction

Transition-metal-catalysed transformations of alkenes play a major role in synthesizing products of industrial importance. The catalytic routes are a safer and more selective alternative to conventional methods involving stoichiometric organic syntheses that lead to considerable amounts of by-products.[1]

Particularly useful are reaction sequences in which an alkene is inserted into a metal hydride and then CO is inserted to form new C−C bonds. Some of the most successful reactions, such as hydroformylation, alkoxycarbonylation, and hydroxycarbonylation, belong to this class of reaction (Scheme 1). In general, carbonylations are important processes since they lead to the production of oxygenated products from petrochemical hydrocarbons.



Scheme 1. General scheme for catalysed carbonylation reactions

Among the carbonylation reactions, hydroformylation using Co^{I} or Rh^{I} is now the largest industrial application of homogeneous catalysis by transition metal complexes for producing aldehydes and alcohols.[2,3] In hydroformylation chemistry, much progress has been made in recent years in

---

[a] Departament de Química Física i Inorgànica, Universitat Rovira i Virgili,
Pl. Imperial Tarraco 1, 43005 Tarragona, Spain
Fax: (internat.) +34-977/559-563
E-mail: claver@quimica.urv.es
[b] Institute of Molecular Chemistry,
Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands
Fax: (internat.) +31-20/525-6456
E-mail: pwnm@anorg.chem.uva.nl

Inmaculada del Río (left) received her Ph.D. in 2000 from the University Rovira i Virgili working on mechanistic aspects of hydroformylation and hydroxycarbonylation reactions.

Carmen Claver (right) is Professor of Inorganic Chemistry at the University Rovira i Virgili in Tarragona (Spain), a position she has held since 1991. She received her Ph.D. in 1978 from the University of Zaragoza (Spain) working in the field of organometallic chemistry with Prof. Luis A. Oro. Her present research is focused on fundamental aspects of homogeneous catalysis with transition metals, especially in asymmetric catalysis.

Piet W. N. M. van Leeuwen is Professor of Homogeneous Catalysis at the University of Amsterdam, a position he has held since 1989. He has spent much of his career at Shell Research in Amsterdam working in the area of homogeneous catalysis and organometallic chemistry. His present research is aimed at the development of novel transition metal homogeneous catalysts, using the full range of available tools and techniques.

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.

1434−1948/01/1111−2719 $ 17.50+.50/0

controlling the regioselectivity and understanding the mechanism of the process.[4]

Palladium systems have been used as catalysts in many carbonylation reactions, and their use in hydroxycarbonylation and alkoxycarbonylation reactions has been widely studied.[5] They have also been used as catalysts in many other carbonyl-based processes of industrial interest. The hydroxycarbonylation of butadiene, the dicarboxylation of alkenes, the carbonylation of alkenes, the carbonylation of benzyl and aryl halides, and oxidative carbonylations have recently been reviewed.[6]

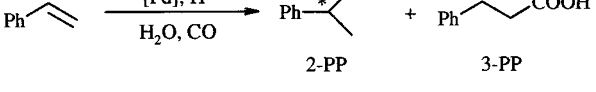
In the palladium-catalysed reactions, products such as alcohols, aldehydes, ketones, and oligoketones can be prepared by modifying the palladium complexes with different phosphorus ligands. The selective formation of ketones by the carbonylation of higher alkenes using Pd^{II} complexes has been reported.[7,8]

A major breakthrough regarding the activity of this type of catalyst was the discovery that palladium complexes modified with *cis*-diphosphanes can be used in the alternating copolymerization of ethene or propene with carbon monoxide. This is another Pd^{II}-catalysed process that has attracted the interest of industry in the last two decades.[9]

In hydroxycarbonylation, alkoxycarbonylation, and the amidocarbonylation of alkenes, the use of a palladium carbonylation catalyst to synthesize propionic and other acids has been widely studied. The catalysts were mainly designed for the carbonylation of alkenes in the presence of alcohols in order to prepare carboxylic esters, but were also found to work well in the synthesis of carboxylic acids and anhydrides.[10]

It seems appropriate to distinguish between aliphatic alkenes and functionalized vinylic substrates, including vinyl aromatics. The carbonylation of vinyl aromatics is important for the synthesis of 2-phenylpropionic acids/esters, a class of non-steroidal anti-inflammatory drugs.[11] Also, the linear products, i.e. 3-phenylpropionic acid and its esters, have found application as speciality chemicals. In view of the synthetic importance of the preparation of phenylpropionic acids, styrene was selected as a model substrate for use in carbonylation studies.

The palladium-catalysed hydroxycarbonylation of alkenes has attracted considerable interest in recent years as a means of obtaining carboxylic acids. In general, in acidic media, palladium salts in the presence of mono- or bidentate phosphanes afford mixtures of linear and branched acids (Scheme 2).[6]

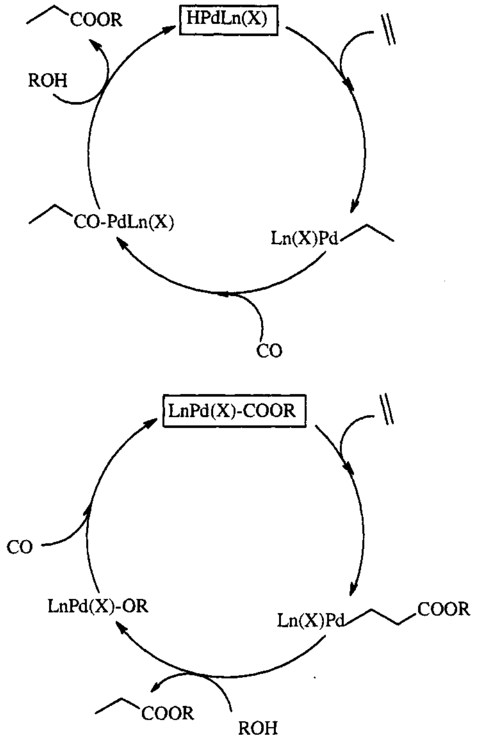


Scheme 2. Hydroxycarbonylation of styrene with palladium salts in acidic medium

This reaction has a number of associated problems, the most important of which is that metallic Pd^0 forms if the palladium species is not sufficiently well stabilized. Secondly, it is difficult to perform the reaction in an enantioselective fashion since the use of *cis*-chelate ligands provides linear acids. Also, because of the absence of a suitable nuclear spin on palladium, the characterization of its phosphane complexes in situ is more difficult than that of the corresponding rhodium or platinum complexes.

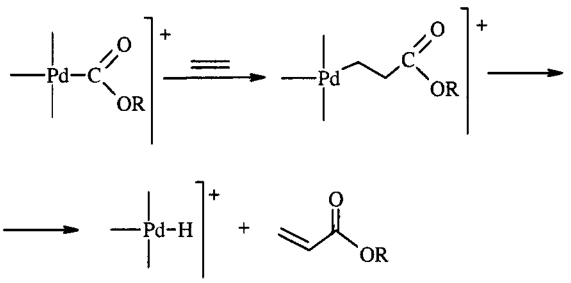
Although reports on the hydroxycarbonylation reaction with palladium systems have been published and several aspects of the mechanism have been discussed in the last few years, a review summarising the results and findings concerning the mechanism of this reaction is still lacking.

The related alkoxycarbonylation reaction has been studied in much greater detail[12−16] and two mechanisms have been suggested (Scheme 3).[17−21] One starts the cycle with a hydrido-metal complex.[19] In this cycle, an alkene inserts into a Pd−H bond, and then migratory insertion of CO into an alkyl−metal bond produces an acyl−metal complex. Alcoholysis of the acyl−metal species regenerates the palladium hydride and yields the ester. In the second mechanism, the crucial intermediate is an alkoxycarbonyl−metal complex.[20] Here, the insertion of the alkene into a Pd−carbon bond of the alkoxycarbonylmetal species is followed by alcoholysis to produce the ester and the alkoxymetal complex. The insertion of CO into the alkoxymetal species regenerates the alkoxycarbonylmetal complex.



Scheme 3. Mechanisms proposed for the alkoxycarbonylation of alkenes

Most researchers currently agree that the hydrido mechanism is more common than the alkoxycarbonyl path in the alkoxycarbonylation of alkenes with palladium systems. However, alkoxycarbonyl complexes may be plausible intermediates in carbonylation reactions of alcohols or in the formation of succinates and polyketone diesters with metals such as Co, Rh, or Pd.[7] The unifying mechanistic theme of these diverse reactions may be the generation of an alkoxycarbonylmetal intermediate, M−COOR.[20] Moreover, palladium alkoxycarbonyl complexes can produce the palladium hydride species in situ after insertion of the alkene and β-elimination of the unsaturated ester (Scheme 4), as was shown by Otsuka.[22]



Scheme 4. Formation of Pd-hydride species from Pd-methoxycarbonyl species

The regioselectivity in the hydroxycarbonylation of styrene with palladium precursor systems under appropriate reaction conditions was controlled by modifying the auxiliary phosphorus ligand.[23] When monophosphanes are used as ligands, the major product is 2-phenylpropanoic acid with practically total regioselectivity. In contrast, the use of diphosphanes as auxiliary ligands switches the regioselectivity in favour of the linear product. Moreover, the activity and regioselectivity in the hydroxycarbonylation of styrene are both sensitive to the nature of the counteranion of the acid. The regioselectivities obtained for mono- and diphosphanes are generally strongly dependent on the nature of the anion.[24] In spite of several studies of the regioselectivity of the reaction, a satisfactory explanation for the regioselectivity is not yet available.

The aim of this Microreview is to provide a systematic overview of the mechanistic aspects and kinetic studies that have been published, as well as to provide some insight into the regioselectivity by means of a mechanistic study. We have performed in situ high-pressure NMR studies to obtain information about the resting state of the catalyst depending on the reaction conditions, the catalyst precursor, and the phosphorus ligands. Finally, we have compared the results of these studies with those of the catalytic experiments in order to arrive at a proposal for a catalytic cycle.

Reactivity and Characterization of the Palladium Species Involved in the Hydroxycarbonylation Reaction

The reactivity of Pd−H species towards the coordination and insertion of the substrate, as well as the subsequent coordination and insertion of carbon monoxide to form the palladium acyl species, have been studied for stoichiometric as well as catalytic alkoxycarbonylation reactions. Not all of these experiments, however, have been performed under the same conditions as the hydroxycarbonylation reaction; they are nevertheless useful for discussing the hydroxycarbonylation mechanism. Similarly, studies of the reactivity of Pd^0 species towards CO or phosphanes or acids are of interest to us. We will start the discussion with Pd^0 complexes.

Pd^0 carbonyl phosphane complexes are believed to be intermediates in the palladium-catalysed hydroxycarbonylation of alkenes, although they do not necessarily participate in the catalytic cycle (vide infra). $[Pd(CO)(PPh_3)_3]$ was isolated from the reaction mixture that arose from the hydroxycarbonylation of cyclohexene with $[PdCl_2(PPh_3)_2]$ as the precursor. This complex was also prepared by the direct reaction of $[Pd(PPh_3)_4]$ with CO in benzene. For the $[Pd(CO)(PPh_3)_3]$ complex, ^{31}P and ^{13}C NMR spectra suggest a rapid dissociation of PPh_3 at room temperature and a tetrahedral structure in solution at −70 °C.[25] $[Pd(CO)(PPh_3)_3]$ proved to be inactive in the hydroxycarbonylation of alkenes, like $[Pd(PPh_3)_4]$. However, the addition of traces of hydrochloric acid promoted the formation, under carbon monoxide pressure, of a catalytically active system.[26]

The Pd^0 complexes can be produced from mixtures of Pd^{II} complexes with phosphanes. Thus, stable Pd^0 complexes were generated in situ from the cationic Pd^{II} complex $[Pd(PPh_3)_2](BF_4)_2$ when water and triphenylphosphane were present in solution. Triphenylphosphane was able to reduce the Pd^{II} metal centre to Pd^0, and was itself oxidized to triphenylphosphane oxide. This reduction was performed on a Pd^{II} complex in which the palladium ion was most likely ligated by a hydroxy group.[27]

The reduction of Pd^{II} to Pd^0 has also been investigated in the presence of both monodentate PPh_3 and bidentate dppp [1,3-bis(diphenylphosphanyl)propane]. ^{31}P NMR measurements showed that triphenylphosphane can reduce $Pd(OAc)_2$ to Pd^0 in toluene. Bidentate dppp is mainly responsible for the reduction in DMF, which results in dppp hemioxide and dppp dioxide. Both mono- and bidentate coordination of dppp in intermediate species were proposed on the basis of in situ NMR studies.[28]

The key intermediates, namely palladium hydride, palladium alkyl, and palladium acyl, were detected and characterized by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy for the homogeneous water-gas shift reaction and for the carbonylation of ethene to diethyl ketone catalysed by the $Pd(OAc)_2/PPh_3/CF_3COOH/H_2O$ system. The key palladium intermediate in both catalytic reactions was the hydride complex $[Pd(H)(PPh_3)_3]^+$. This cationic palladium hydride complex $[Pd(H)(PPh_3)_3]^+$ was formed by the oxidative addition of H^+ when the Pd^0 phosphane complex $[Pd(PPh_3)_4]$ was dissolved in an aqueous CF_3COOH solution. When the experiments were carried out starting with a Pd^{II} complex, it was shown that this complex was first reduced by CO (Scheme 5), giving CO_2 in the rate-determining step of the water-gas shift reaction.[8] Treating a solution of the hydride complex with CO at 25 °C resulted in a rapid rearrangement of a PdH^+ (a Pd^{II} species) and a Pd^0 species into the cationic dinuclear complex $[Pd_2(PPh_3)_4(\mu\text{-}H)(\mu\text{-}CO)]^+$.

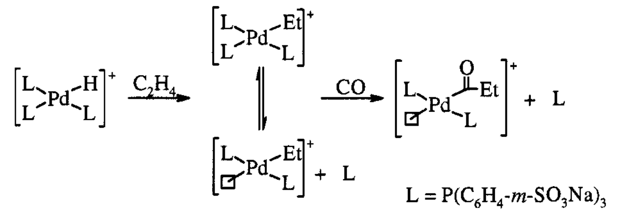
When a solution of the hydride complex was treated with ethene at −25 °C, a palladium alkyl complex formulated as $[Pd(Et)(PPh_3)_2]^+$ was formed. Similarly, exposure of a solution of the hydride complex to a CO/C_2H_4 (3:1) gas mixture at 25 °C led to a rapid, quantitative formation of the palladium propionyl complex *trans*-$[Pd\{C(O)Et\}(PPh_3)_2]^+$.[8] The cationic hydride, ethyl, and propionyl palladium complexes are relatively stable as a result of the polar solvent and the non-coordinating anion.

$$PdL_2X_2 + CO + H_2O \xrightarrow[\text{slow}]{-CO_2,\ -HX} PdL_n(H)X$$

$$PdL_n(H)X \underset{\text{fast}}{\rightleftharpoons} L_4Pd^0 + HX$$

Scheme 5. Formation of palladium hydride species in the presence of CO and water

A similar involvement of palladium hydride, palladium alkyl, and palladium acyl complexes as intermediates in the catalytic cycle of the palladium-catalysed hydroxycarbonylation of alkenes was demonstrated for the analogous reaction in the aqueous phase. When a solution of $Pd(OAc)_2$ and tppts (tppts = trisulfonated triphenylphosphane) in aqueous trifluoroacetic acid was placed under a CO atmosphere, the cationic hydride $[Pd(H)(tppts)_3]^+$ was formed by reduction of the Pd^{II} complex with CO and H_2O to $[Pd(tppts)_3]$ and subsequent protonation in the acidic medium. The reaction of the hydride complex with ethene produced an equilibrium mixture of two new compounds, $[Pd(Et)(tppts)_3]^+$ and $[Pd(Et)(tppts)_2]^+$. The fourth coordination site in the latter is presumably occupied by a solvent molecule. The mixture of the palladium alkyl complexes reacted readily with CO to afford *trans*-$[Pd\{C(O)Et\}(tppts)_2]^+$ (Scheme 6).[29] Once again, the stability of the cationic intermediates may be attributed to the ionic medium and the non-coordinating nature of the anion, which is even enhanced by the aqueous solvent. The authors showed that in the stoichiometric reaction the hydrolysis of the acyl species giving propionic acid is the slowest step in the sequence.



Scheme 6. The stepwise aqueous-phase hydroxycarbonylation of ethene

The intermediates involved in the palladium-catalysed methoxycarbonylation of ethene have also been characterized. The complex [Pd(L−L)(dba)] [L−L = 1,2-$(CH_2PtBu_2)_2C_6H_4$] reacts with HBF_4 or CF_3SO_3H in MeOH to produce a new compound that can be formulated as either the neutral complex [Pd(L−L)HX] or the solvated cation [Pd(L−L)H(MeOH)]X. This hydride complex reacts immediately with ethene at room temperature to form the cationic species [Pd(L−L)Et(MeOH)]X. On adding one equivalent of CO to the alkyl complex, the species [Pd(L−L){C(O)Et}(MeOH)]X is formed. Subsequent addition of a trace of MeOH to the solution leads to an immediate reaction regenerating the palladium hydride complex and forming EtCOOMe. It should be noted that the palladium hydride complex is stable even in the presence of oxidants (benzoquinone or oxygen) under these conditions. There was no evidence for the formation of any methoxycarbonyl complex.[30] For other systems, the formation of methoxycarbonyl palladium species is a well-documented process.[31,32] It should be noted, however, that the formation of methoxycarbonyl complexes under these conditions requires anhydrous conditions; in the presence of traces of water a hydroxycarbonyl-palladium species form, which rapidly loses carbon dioxide to give palladium hydride.[33] Thus, in the presence of water, hydride species will invariably be formed, which will initiate the catalytic cycle. This side reaction was efficiently suppressed by the addition of trimethyl orthoformate, which, under acidic conditions, transforms water into methanol.[34]

In the case of styrene, the mechanism of the methoxycarbonylation using $[Pd(OTs)_2(PPh_3)_2]$ formed in situ from $Pd(OAc)_2$, PPh_3, and TsOH in methanol has been investigated by isolating and characterising the intermediates. From the reaction mixtures, palladium hydridocarbonyl and palladium acyl complexes were isolated, and, accordingly, a palladium hydride mechanism has been proposed. Following exposure of the catalyst precursor system $Pd(OAc)_2$/$4PPh_3$/10HOTs to CO at 75 °C for 30 min., the complex $[Pd(H)CO(PPh_3)_2](OTs)$ was characterized. When the methoxycarbonylation was performed with $PdCl_2$ as the catalyst precursor, the acyl complex *trans*-$[PdCl(COCH_2CH_2Ph)(PPh_3)_2]$ was isolated.[35] The observation and isolation of the hydride, alkyl, and acetyl palladium species is, of course, strongly suggestive that they form part of the productive catalytic cycle; nonetheless, kinetic measurements are desirable to obtain further proof.

Palladium Hydride Complexes

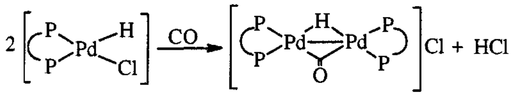
Palladium hydrides are of special interest due to their exceptional relevance to catalysis. Indeed, several hydrido complexes of palladium have been proposed as key intermediates in a number of palladium-catalysed reactions.[36−38] Also, the study of palladium hydride species has been the subject of some interesting reports and reviews.[39,40] However, the reactivity of palladium hydrido complexes has still not been adequately explored. Despite the exceptionally high affinity of palladium metal for hydrogen,[41] soluble molecular hydrides of palladium are rather unstable and in many cases they cannot be isolated but only generated and characterized in solution at low temperature. The stability of analogous hydrides increases dramatically on going from palladium to platinum; for instance, $[Pt(H)Cl(PPh_3)_2]$ is stable to air and moisture and has been fully characterized.[42]

Over the last few years, the chemistry of palladium hydrides has developed significantly and a number of neutral and cationic hydrido complexes of palladium have been prepared and characterized by a variety of techniques. In fact, all known general methods for synthesising transition metal hydrides can be used to prepare palladium hydride complexes.[40]

Neutral palladium hydride complexes of the type $[PdHCl(PPh_3)_2]$ can be synthesized by oxidative addition of strong acids, as in the oxidative addition of HCl to Pd^0 complexes such as $[Pd(CO)(PPh_3)_3]$ or $[Pd(PPh_3)_4]$.[43] Related hydride complexes have been synthesized using other monophosphanes such as PEt_3,[44,45] PCy_3,[43] and PBu_3.[46] The nature of the phosphane is important, since the more basic phosphanes stabilize the product of the oxidative addition, i.e. the hydride complex.

The cationic hydrido complexes of palladium can be prepared by several methods, for example by replacing an anionic ligand in neutral palladium hydrides with a neutral ligand,[47] or by the protonation of zero-valent palladium complexes.[45,48] There have been reports of the formation of palladium cationic hydrides with H_2O, CH_3CN, or other coordinated solvents.[49−51]

With diphosphane ligands, the hydride complexes of palladium *cis*-[PdHCl(P−P)] are apparently highly unstable and numerous attempts to synthesize such species have failed; instead, cationic dinuclear complexes of palladium $[(P-P)_2Pd_2(\mu\text{-}H)(\mu\text{-}CO)]^+$ are readily formed during carbonylation reactions (vide supra and Scheme 7). These dinuclear complexes have been isolated and characterized, and their reactivity towards alkenes under CO atmosphere has been studied. Apparently, it is important to stabilize the systems with CO and to create a bridging instead of a terminal hydride *trans* to the phosphane.[52−54]



Scheme 7. Formation of the dinuclear $[(P-P)_2Pd_2(\mu\text{-}H)(\mu\text{-}CO)]^+$ in the reaction of [(P−P)PdHCl] under a CO atmosphere

The fact that palladium hydride species are stabilized under CO pressure can favour the catalysis through the intermediacy of a palladium hydride species. Moreover, it is interesting that in the alkoxycarbonylation of alkenes catalysed by a $[PdCl_2(PPh_3)_2]/PPh_3$ system, the catalytic activity is higher in the presence of molecular hydrogen. This is most likely attributable to the formation of a Pd−H intermediate through the heterolytic splitting of H_2. This represents an alternative pathway for the formation of the initial hydride species. This route does not require the reduction of Pd^{II} prior to oxidative addition of H^+. The occurrence of heterolytic splitting of hydrogen rather than oxidative addition is further substantiated by the fact that no aldehyde has been detected in the reaction products.[8,55−57] The latter reaction would require oxidative addition of dihydrogen to a palladium(II) acyl species.

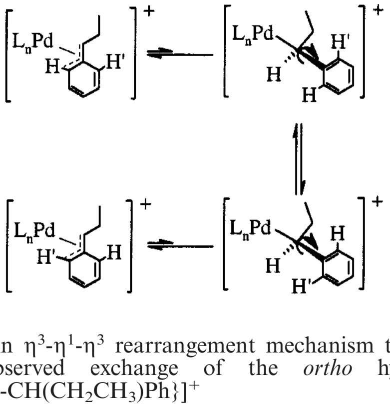
Palladium Alkyl Complexes

Palladium alkyl derivatives have also been synthesized and characterized, especially the benzyl derivatives, which are stabilized as η^3-benzylic species. Since one of the most interesting palladium−styrene intermediates is the palladium η^3-benzylic species, it is useful to discuss species of this type.

The benzyl palladium complexes *trans*-$[Pd(CH_2Ph)Cl(PPh_3)_2]$ have been synthesized by the oxidative addition of benzyl chloride to Pd^0 complexes such as $[Pd(PPh_3)_4]$.[58] However, these complexes proved to be unstable and the dinuclear complex $[Pd_2(CH_2Ph)_2(PPh_3)_2(\mu\text{-}Cl)_2]$ was formed.[59] Other palladium alkyl derivatives have been obtained by adding halogenated hydrocarbons to a suspension of $[Pd(PPh_3)_4]$.[60,61]

The structures of the arylpalladium complexes of the type *trans*-$[Pd(Ph)X(PPh_3)_2]$ (X = F, Cl, Br, I) were studied by single-crystal X-ray diffraction analysis and the relative affinities of the halide anions for the metal centre were studied using ^{31}P NMR spectroscopy.[62]

Palladium η^3-benzyl complexes have also been prepared by the insertion of styrene into the Pd−Me bond of the solvated cation [PdMe(L−L)S]. This η^3-coordination of the benzyl ligand has been elucidated by X-ray structure determination and NMR spectroscopy. NMR studies showed that the palladium η^3-benzyl complexes undergo two dynamic processes in solution, namely η^3-η^1 coordination of the benzyl group, and ligand exchange of coordination sites.[63] Kinetic and isotopic labelling experiments have been employed to determine the mechanism of this benzyl exchange reaction (Scheme 8).[64] These complexes are highly prone to β-hydride elimination.[33]



Scheme 8. An η^3-η^1-η^3 rearrangement mechanism that accounts for the observed exchange of the *ortho* hydrogens in $[(phen)Pd\{\eta^3\text{-}CH(CH_2CH_3)Ph\}]^+$

Palladium Acyl Complexes

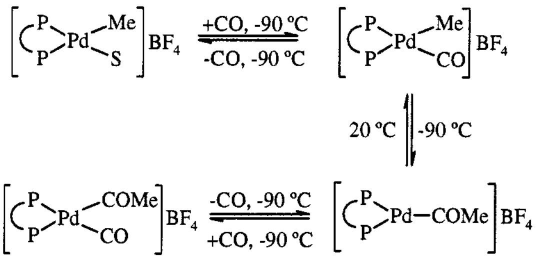
Since the 1970s, a key question has been the involvement of either acylpalladium or alkoxycarbonylpalladium species in the reaction cycle. In the 1970s, supporting evidence for both mechanisms was put forward.[18,20] A comparative study of the reactivity and catalytic activity in the alkoxycarbonylation of alkenes using the isolated palladium acyl complex $[PdCl(COR)(PPh_3)_2]$ (R = Et, *n*-Hex) (a key intermediate in the palladium hydride mechanism) and the palladium methoxycarbonyl complex [PdCl(COOMe)(PPh$_3$)$_2$] (an active species in the alkoxycarbonyl mechanism) was carried out by Cavinato and Toniolo.[19] With regard to the reactivity, the palladium acyl complex was found to react with an alkanol R′OH in the presence of added PPh$_3$ to yield the ester RCOOR′ and a mixture of [PdCl$_2$(PPh$_3$)$_2$] and [Pd(PPh$_3$)$_{3,4}$]. This was considered to be the slowest step of the hydride mechanism. When the isolated methoxycarbonyl complex [PdCl(COOMe)(PPh$_3$)$_2$] was treated with 1-hexene in methanol, under nitrogen and in the absence of carbon monoxide, the ester was not formed and the starting complex was recovered almost quantitatively, thus confirming that the step presumed to be the slowest in this cycle was indeed very slow. As regards the catalytic activity of these complexes, use of the acyl palladium complex as the catalyst precursor in the alkoxycarbonylation of ethene yielded almost stoichiometric amounts of the ester. When [PdCl(COOMe)(PPh$_3$)$_2$] was used as the catalyst precursor in the alkoxycarbonylation of 1-hexene in methanol, in the absence of added PPh$_3$ and in the presence of NEt$_3$ or carboxylate anions (to favour the formation of the methoxycarbonyl complex), no catalytic activity was seen and the precursor was recovered in the form of Pd^0-carbonylphosphane complexes. Only after prolonged reaction times was some of the methoxycarbonyl complex observed.[19]

Other acyl species of palladium have been synthesized and characterized. White crystals of *trans*-[Pd(CO*n*Pr)Cl(PPh$_3$)$_2$] were isolated in 70% yield after allowing the solution obtained following the alkoxycarbonylation of propene to stand for several hours at room temperature. This complex was found to be active in the alkoxycarbonylation of propene.[65] In situ IR spectroscopic studies were performed during the hydroxycarbonylation of ethene with [PdCl$_2$(PPh$_3$)$_2$], by which the intermediate species [Pd(COEt)Cl(PPh$_3$)$_2$] was observed. A mechanism involving Pd−H active species has been proposed.[66]

In favour of the participation of alkoxycarbonylpalladium species, the following two observations may be mentioned. The cationic complexes [(P−P)PdC(O)OCH$_3$(PPh$_3$)]$^+$ (P−P = dppe, dppp, dppb) undergo slow insertion of reactive alkenes such as norbornadiene.[33] The formation of diester[67][68] and diester end-group polyketones indicates that, under anhydrous conditions, cationic species may allow the insertion of alkenes into alkoxycarbonylpalladium species.[69]

As regards diphosphanes, the insertion of CO was studied for both neutral palladium chlorides and ionic triflate complexes containing the bidentate phosphanes dppe, dppp, dppb, and dppf.[70] Half-life times for the neutral complexes were between 18 and 36 min at 235 K and 25 bar of CO and the rates decreased in the order dppb > dppp > dppf >> dppe (170 min at 305 K). The ionic complexes were found to react with rates one or two orders of magnitude higher, even though acetonitrile was used as the solvent. Thus, carbon monoxide insertion should indeed be a fast step in the hydroxycarbonylation cycle.

High-pressure NMR spectroscopy was also used to follow the synthesis of the chiral ionic square-planar [Pd(Me)CO(BDPP)]BF$_4$ compound [BDPP = (2*S*,4*S*)-2,4-bis(diphenylphosphanyl)pentane], an intermediate in CO insertion into the Pd−Me bond. This compound was formed in situ by the reaction of the solvated [Pd(Me)S(BDPP)]BF$_4$ with ^{13}CO and in a high-pressure NMR tube. Concomitant with the decomposition of [Pd(Me)CO(BDPP)]BF$_4$, the complex [Pd(COMe)CO(BDPP)]BF$_4$ was formed and CO insertion was followed by the coordination of another CO ligand. This reaction was found to be completely reversible at room temperature. Several experiments were carried out to investigate whether the methyl(carbonyl) complex was also an intermediate in the formation of the methoxycarbonyl compound [Pd(Me)(COOMe)(BDPP)], but this compound could not be obtained in this way (Scheme 9).[71] [Pd(Me)(COOMe)(BDPP)] has been reported previously as the product of insertion of CO into [Pd(Me)(OMe)(BDPP)] at low temperatures.[72] Low temperatures are imperative as otherwise β-hydride elimination would take place. Interestingly, insertion takes place in the Pd−O bond rather than the Pd−C bond, as has been reported previously for platinum.[73] There are no indications that this reaction is relevant to alkoxycarbonylation since in cationic alkyl palladium species the insertion of CO into the palladium alkyl bond is very fast.[70]



Scheme 9. Formation of palladium acyl complexes with diphosphane ligands under CO

Phosphorus-nitrogen ligands have been used for the study of the insertion of carbon monoxide into both ionic and neutral complexes.[74] In such complexes, the preferred structures have the methyl and acetyl groups *cis* to the phosphane ligand, as one would expect according to the *trans* influence. As a result, the insertion reaction for such P−N ligands is slower than those for either P−P or N−N ligands, because, in the first instance, migration leads to a less-stable isomer with the acetyl group *trans* to phosphorus. The details of such migration reactions in dissymmetric P−P* ligand complexes have been reported previously.[75][76]

A similar study has been performed concerning the reactivity of a cationic complex [(P,N)Pd(Me)(CO)]$^+$ towards CO and norbornene. Luinstra showed that in the presence of both an alkene and CO, the *trans* effect could be advantageously used to give faster reactions in some instances.[77] The same effect was reported by Mul et al.[78] This effect of ligand equilibria seems most relevant to polyketone synthesis, but similar effects can be envisaged for hydroxycarbonylation, casting some doubts on the rate measurements of stepwise stoichiometric reactions.

Benzylpalladium and (phenylacetyl)palladium complexes with two PMe_3 or PPh_3 ligands or a dppe ligand have been prepared as models for studying the mechanisms of carbonylation reactions by which benzyl halides are converted into singly and doubly carbonylated products.[58] The monodentate ligands give rise to *trans*-benzylPdX(L)$_2$ structures containing η^1-benzyl fragments. When non-coordinating anions are used, η^3-benzyl species are formed. Insertion of CO is a fast and reversible process. Examination of the reactions of the (phenylacetyl)palladium complexes with secondary amines and alcohols provided evidence for the operation of different types of mechanisms leading to amides and esters. Amide formation proceeds more rapidly when more basic amines are used. The amines coordinate first to the palladium, and then attack the acyl moiety, which is assisted by another molecule of base. Ester formation proceeds more rapidly when more acidic alcohols are used. It was suggested that after coordination to palladium the alcohols are deprotonated by the base, and then the oxygen attacks the acyl carbon atom. In cationic diphosphane acylpalladium complexes, in the absence of base, the order of reactivity is $H_2O > MeOH > EtOH >$ 2-PrOH, showing that the more acidic species react more rapidly.[79]

Effect of the Acidic Medium on Hydroxycarbonylation

The effect of the counteranion involved in the catalytic system has been studied, although its role is not yet fully understood. In the carbonylation of aliphatic and functionalized alkenes by cationic palladium complexes in the presence of hydrogen to give alcohols, aldehydes, ketones, or oligoketones, a selectivity control by the neutral ligand and anion was found. Non-coordinating anions primarily produce oligoketones, and increasing anion coordination strength shifts the selectivity towards aldehydes and alcohols.[7] For the latter, the heterolytic cleavage of hydrogen assisted by the more basic anions was proposed.

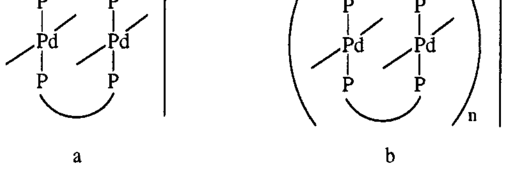
The regioselectivity of the alkoxycarbonylation of 1-arylethanols catalysed by Pd/acid systems is highly sensitive to the nature of the counteranion of the acid. Chloride anions favour branched products while weakly coordinating tetrafluoroborate and sulfonate anions favour linear products; the latter also enhance product yields.[80]

In the regioselective synthesis of ibuprofen by the $PdCl_2$/PPh_3/HCl-catalysed hydroxycarbonylation of 1-(4-isobutylphenyl)ethanol, the rate and selectivity of the reaction proved to be dependent on the concentration and nature of the halide ion used. It has been reported that hydrochloric acid plays a dual role in this reaction, firstly providing a proton, which promotes the dehydration of the alcohol, and secondly providing a chloride ion, which promotes the carbonylation step.[81]

In the asymmetric alkoxycarbonylation of alkenes catalysed by chiral palladium bis(dibenzophosphole) complexes, halide salts, such as LiCl or bis(triphenylphosphane)iminium chloride, and hydrogen at low pressure, were found to dramatically increase the extent of conversion without significantly decreasing the optical yield. Palladium species coordinated by halide are thought to prevent the aggregation of reduced palladium species.[82] In the asymmetric alkoxycarbonylation of styrene with palladium catalysts, both the degree of conversion and the asymmetric induction were found to be very low when acids such as MeCOOH, HCOOH, HCl, HBr, etc. were used instead of CF_3COOH.[83]

Finally, studies on the effect of the counteranion on the hydroxycarbonylation reaction have been performed. The effect of mineral acids as additives in the hydroxycarbonylation of 4-methylstyrene with $PdCl_2$/$CuCl_2$/PPh_3 has been studied. Efficient hydroxycarbonylation was only achieved after a halogen compound had been added; the addition of HCl improved the reaction rate significantly. This improvement was due to the effect of chloride ions rather than protons, as was proved by adding either other acids or other chloride salts.[84] Some reports have shown that the hydroxycarbonylation reaction also takes place if water is used instead of acid.[85,86]

In the course of a study on the use of palladium systems in the hydroxycarbonylation of styrene, we also explored how the counteranion of the acid affects this reaction when the Pd bears monophosphane and diphosphane ligands. To prevent the palladium precursor from introducing counteranions, we chose to perform a series of experiments using the catalyst precursor [$Pd_2(dba)_3$] in the presence of acids. We showed that activity and regioselectivity in the hydroxycarbonylation of styrene are sensitive to the nature of the counteranion of the acid. The regioselectivities obtained for monophosphanes and diphosphanes (branched and linear, respectively) can be changed by judicious choice of the counteranion. When a monophosphane such as PPh_3 was used as the ligand, coordinating anions such as halides were found to favour the formation of branched acids. However, weakly coordinating anions such as sulfonic acids were found to favour the formation of linear acids. On the other hand, the regioselectivity for the systems formed with the diphosphane dppb in the presence of Br^- and I^- was found not to favour the linear acid as other diphosphanes do.[23] It has been suggested that the diphosphane could be monocoordinated depending on the nature of the counteranion, but it might also suggest that dinuclear species with the diphosphane bridging between two different palladium centres are formed (Scheme 10).[70,74] A similar behaviour



Scheme 10. Dimeric and oligomeric palladium complexes with diphosphane ligands

has recently been reported in Pd-diphosphane systems used in carbonylation processes, where differences in catalytic activity and selectivity can be rationalized in terms of monodentate coordination of the diphosphane.[87,88]

Regioselectivity in the Palladium-Catalysed Carbonylation Reactions

In spite of the reported studies, which have compared systems showing opposite regioselectivities in the palladium-catalysed alkoxycarbonylation and hydroxycarbonylation reactions, the issue of regioselectivity is still far from understood.

Since the 1970s, regioselectivity in the alkoxycarbonylation of alkenes has been shown to depend on the nature of the phosphorus ligand. Pd/monophosphane catalytic systems produce mainly the branched ester, whereas Pd/diphosphane systems produce mainly the linear one.[89,90]

In 1976, Sugi and Bando reported an interesting study of the ethoxycarbonylation of styrene with carbon monoxide and ethanol in the presence of diphosphane palladium complexes $[PdCl_2\{Ph_2P(CH_2)_nPPh_2\}]$ ($n = 1-6, 10$).[91] When diphosphanes with $n = 3, 4, 5$ were used, ethyl 3-phenylpropionate was obtained in significant amounts. With dppe, $n = 2$, however, no conversion was found. Phosphanes with $n = 1, 6, 10$ gave ethyl 2-phenylpropionate as the predominant isomer, in the same way as monodentate phosphanes do. The conversion increased with n, but proved to be highest for monodentate phosphanes. These results were rationalized in terms of the stability of the chelate ring under the reaction conditions, assuming the formation of monophosphane complexes for ligands with high n, similar to those with the monophosphane ligands. The current explanation is based on *cis* complexes for bidentate ligands of lower n, and *trans* complexes for ligands having higher n and monodentate ligands, at least for the resting states of the catalysts. The highest selectivity in favour of the branched ester (99.5%) was obtained using PBu_3.[91]

In several studies, monophosphanes and diphosphanes have been used together. In the asymmetric alkoxycarbonylation of α-methylstyrene using the Pd/DIOP system, the addition of PPh_3 was found to increase the amount of the branched ester.[92] In the hydroxycarbonylation of alkenes, PPh_3 was added to the $Pd(OAc)_2$/dppb system; this improved the yield without significantly affecting the product distribution.[93]

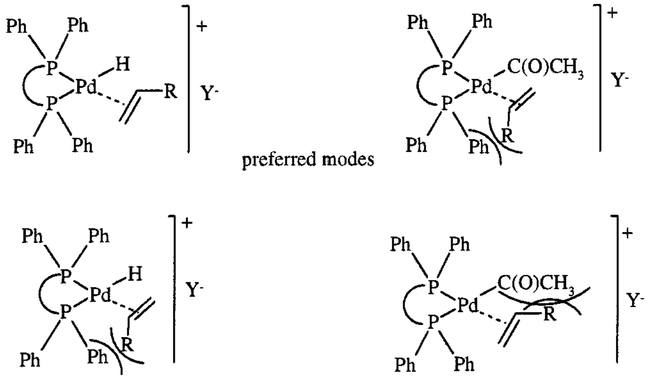
In some cases, a co-catalyst was added to the Pd/phosphane system, as in the hydroxycarbonylation of 1-heptene with $[HPdCl(PPh_3)_2]/SnCl_2$[94] and $[PdCl_2(PPh_3)_2]/Co_2(CO)_8$,[95] the hydroxycarbonylation of styrene with the $[PdCl_2(PPh_3)_2]/Co_2(CO)_8$ system,[96] and alkoxycarbonylation with the $[PdCl_2L_2]/SnCl_2$ or $GeCl_2$ systems (L = monophosphane).[48,55] In general, the co-catalyst increased the regioselectivity in favour of the linear product and decreased the rate of the reaction. In the asymmetric alkoxycarbonylation of styrene with the precursor $PdCl_2$ and chiral diphosphanes, the addition of $CuCl_2$ as a co-catalyst favoured the formation of the branched ester in good yield and with high enantiomeric excess.[97] In this case, however, the rigid structure of the iditol-derived ligand might have led to a non-chelating coordination, this being responsible for the high chiral induction. Monodentate coordination would be consistent with the high regioselectivity obtained in favour of the branched product.[98] A role of the MCl_2 salts that is frequently overlooked is that they may act as "chloride acceptors", thus assisting in the formation of weakly coordinating anions.

Interestingly, regioselectivity is seen to depend on the nature of the substrate. With aliphatic alkenes, the differences in isomeric composition are not as great as they are with vinyl arenes.[88] This can be explained in terms of π-benzylic stabilization of styrene in the styrylpalladium fragment obtained after insertion.[52,53] The steric bulk of the substrate is also important, as illustrated by the hydroxycarbonylation of simple and functionalized alkenes with $Pd(OAc)_2$/dppb/HCOOH. Control of the regioselectivity of the reaction depends in part on the effective bulk of the substituent group on the alkene; more hindered alkenes produce higher yields of the linear acid.[99] No pronounced influence of the electronic effects of the substrate on regioselectivity has been found in the alkoxycarbonylation and hydroxycarbonylation of 3,3,3-trifluoropropene and pentafluorostyrene catalysed by phosphane-palladium systems. When monophosphanes were used as ligands, the major product was the branched one, whereas when diphosphanes were used it was the linear one.[100] Thus, the fluoroalkenes follow the normal trend, although a higher preference for branched ones might have been expected.

Regioselectivity is often explained in terms of the following two mechanisms: (1) when styrene inserts into a metal−acyl bond, branched products are formed, and (2) when it inserts into a metal hydride, linear products are formed.[93][101] The regioselectivity of styrene insertion has been studied for the palladium-catalysed oligomerization of styrene and carbon monoxide. With diphosphanes, the insertion of the first styrene into the palladium hydride complex leads to the formation of a linear palladium alkyl species. This can be attributed to steric hindrance between the phenyl group of the styrene and the phosphane coordinated to the palladium centre. Insertion of styrene into the acyl palladium intermediate gives a branched insertion product.[100]

According to this interpretation, the different regioselectivities have a steric origin. In the first step, the hydride attacks the α-carbon of styrene, but the acyl species formed after insertion of CO attacks the styrene molecule at the β-carbon atom, as in our reaction (Scheme 11).[33] While this has proved to be correct for cationic complexes that act as polymerization or oligomerization catalysts, for hydroxycarbonylation this has yet to be confirmed (vide infra).

We have previously reported a systematic study into how palladium precursor systems and the phosphorus ligand affect the hydroxycarbonylation of styrene. Monophosphanes and diphosphanes behave differently when used as ligands in this reaction. Using monophosphanes, only Pd^{II} pre-



Scheme 11. Effect of steric hindrance on the stereochemistry of insertion of an alkene into a Pd−H bond and a Pd−C(O)CH_3 bond

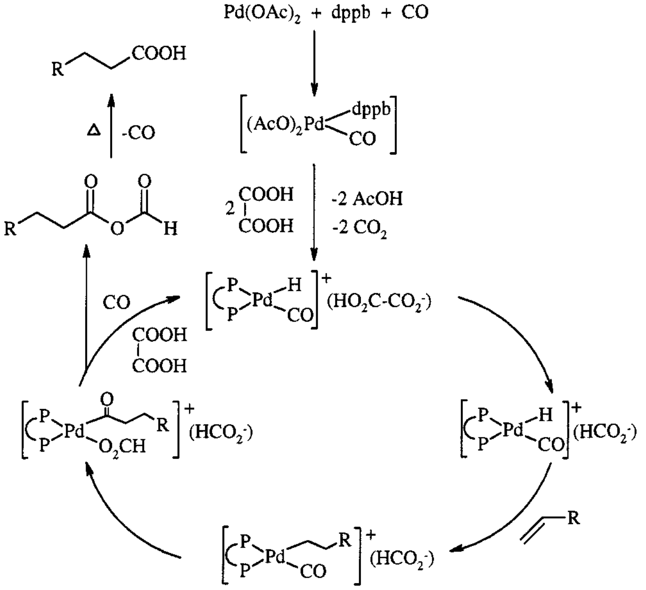
cursors containing chloride give reasonable activity. When diphosphanes are used as auxiliary ligands, the results obtained with Pd^0 and Pd^{II} precursors are similar. As far as regioselectivity is concerned, the branched acid is the major product with monophosphanes, while the linear acid is the major product with diphosphanes. Also, monophosphanes afford much faster catalysts. It has been suggested that different intermediates are involved in the catalytic cycle for monophosphanes and diphosphanes; the association/dissociation of counteranions and phosphanes may account for the differences between the two systems.[23]

Studies of the Mechanism of Palladium-Catalysed Carbonylations

The understanding of a catalytic process requires a combination of several techniques, such as kinetic studies, deuteration experiments, determination of the intermediates, and theoretical studies. Here, we review significant studies of hydroxycarbonylation or related reactions that have contributed to the understanding of the palladium hydroxycarbonylation mechanism.

In several instances in the literature, no experimental support is presented for proposed catalytic cycles, and it should be borne in mind that these proposals are often speculative and include at best circumstantial evidence. In general, in catalytic alkene carbonylation reactions involving palladium species, a palladium hydride is proposed as the species that starts the cycle. Subsequently, coordination and insertion of the substrate occurs, which is followed by the coordination and insertion of carbon monoxide, which leads to the proposed palladium intermediates (Scheme 3).[102]

A mechanism has also been proposed for the Pd^{II} acetate/oxalic acid systems used in the presence of a chelating phosphorus ligand in the hydroxycarbonylation of alkenes. The system consisting of oxalic acid in 1,2-dimethoxyethane (DME) allows relatively mild conditions and gives high regioselectivity in favour of the linear acid when 1,4-bis(diphenylphosphanyl)butane, dppb, is used.[97] A catalytic cycle was proposed for the hydroxycarbonylation reaction starting with a $[Pd(OAc)_2(dppb)(CO)]$ complex that reacts with two equivalents of oxalic acid to afford an ionic complex $[Pd(H)CO(dppb)]^+$. For subsequent steps, palladium alkyl and palladium acyl intermediates are proposed. Finally, the linear acid is formed by decarbonylation (Scheme 12).[103]

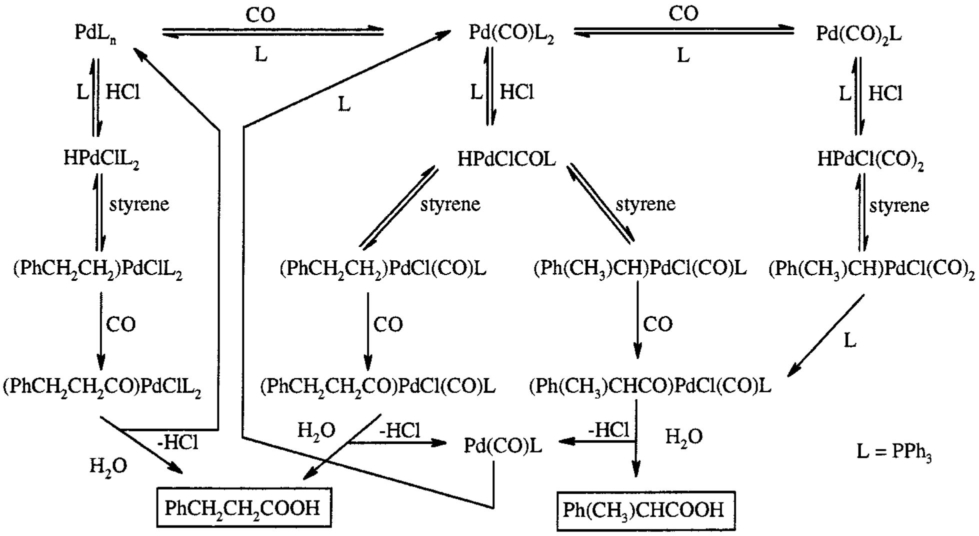


Scheme 12. Catalytic cycle proposed for the hydroxycarbonylation of alkenes with the $Pd(OAc)_2$/dppb/$H_2C_2O_4$ system

Kinetic Studies

A number of studies on the kinetics of the hydroxycarbonylation reaction with palladium systems have been reported.[104−106] These generally focus on how the carbon monoxide pressure, the concentration of styrene, the palladium precursor, the phosphane ligands, and water affect the activity and regioselectivity of the reaction.

The kinetics and mechanism of styrene hydroxycarbonylation catalysed by the complex $[PdCl_2(PPh_3)_2]$ have been reported. When water was added to the catalytic system up to $[H_2O] = 2$ M, the rate of formation of the linear acid increased. Higher CO pressures were found to favour the formation of the branched acid. This can be attributed to the formation of species containing coordinated CO as a result of displacement of the bulkier PPh_3 ligand.[103] The rates of linear and branched acid formation both show a linear dependence on the concentration of the catalyst. Triphenylphosphane decreases the rate of formation of the branched acid more than that of the linear one; the inhibiting effect of PPh_3 is enhanced by increasing $[H_2O]$. As the styrene content increases, the rate of formation of the linear acid remains virtually constant, while the rate of formation of the branched acid increases markedly.[105] These relationships are consistent with the hydride mechanism, which involves four routes for the formation of phenylpropionic acids and three types of catalyst precursors $[Pd(H)Cl(CO)_n(PPh_3)_{2-n}]$ ($n = 0-2$) in equilibrium, depending on the CO pressure and the concentration of the



Scheme 13. Proposed mechanism for the hydroxycarbonylation of styrene with the [PdCl$_2$(PPh$_3$)$_2$]/PPh$_3$ system, involving [Pd(H)Cl(CO)$_n$(PPh$_3$)$_{2-n}$] (n = 0−2) species

ligand. The regioselectivity of the intermediates with respect to 3-phenylpropionic acid drops from 100 to 0% as n increases from 0 to 2 (Scheme 13).[105]

More recently, a kinetic study of how the addition of SnCl$_2$ to the [PdCl$_2$(PPh$_3$)$_2$]/PPh$_3$ system affects the hydroxycarbonylation of styrene has been reported.[106] Adding an equimolar amount of SnCl$_2$ to [PdCl$_2$(PPh$_3$)$_2$] increases the selectivity in favour of the linear acid from 30 to 70%, which stems from an increase in the rate of formation of this product. Kinetic and spectroscopic data were used to explain the effect of SnCl$_2$. It was proposed that it involves the displacement of CO ligands from Pd^{II}-containing intermediates by the π-acceptor SnCl$_3^-$, and leads to a higher concentration of phosphane hydride complexes that selectively afford the linear acid (Scheme 13).[107]

A kinetic study of the hydroxycarbonylation of 1-heptene catalysed by [PdCl$_2$(PPh$_3$)$_2$]/PPh$_3$ complexes has also been reported. The rates of formation of the acids increased as the carbon monoxide pressure was increased and as the water concentration was increased up to [H$_2$O] = 2 M. The same mechanism as that for styrene was suggested (Scheme 13).[107]

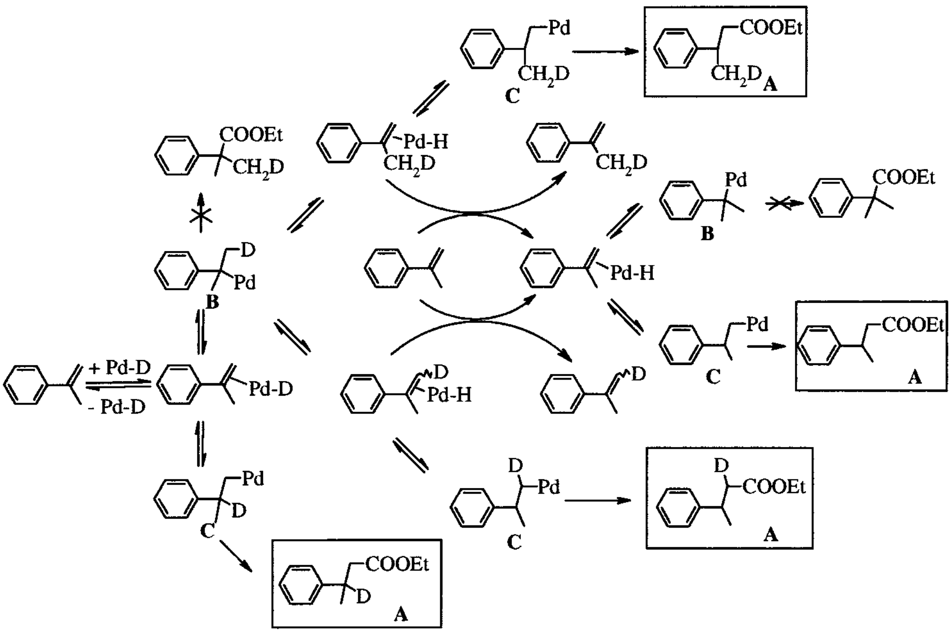
The kinetics of the alkoxycarbonylation of styrene have been studied using the Pd(OAc)$_2$/PPh$_3$/TsOH catalyst system. The reaction was found to be first order with respect to the catalyst concentration and zero order with respect to styrene up to 3.8 mol·dm^{-3}. At high concentrations of styrene (3.8−6.7 mol·dm^{-3}), the rate increased significantly. Water was found to promote the alkoxycarbonylation of styrene, although beyond 9.2·10^{-2} mol·dm^{-3} this effect was negligible. The rate increased when P_{CO} was below 3.4 MPa, but was not affected by higher partial pressures. A rate equation was proposed and the kinetic parameters were evaluated. A reaction mechanism involving palladium hydride, palladium alkyl, and palladium acyl species as intermediates has been proposed.[108]

In the Pd(OAc)$_2$/tppts-catalysed aqueous-phase hydroxycarbonylation of ethene, kinetic studies have shown that the conversion of a palladium acyl to a palladium hydride complex is a rate-determining, pseudo first-order reaction.[29]

Deuterium Labelling Experiments

Deuterium labelling has provided important information about the pathways that are operative in several catalytic reactions. A detailed investigation of the alkoxycarbonylation of styrene has been performed at various temperatures and conversions with the [PdCl$_2$(PPh$_3$)$_2$]/SnCl$_2$ system using labelled species, the content and distribution of deuterium in which was determined by mass spectral analysis and NMR (^{1}H, ^{2}H, ^{13}C) techniques. The large number of labelled species observed supports the assumption that the hydrido (Pd−H) route is the mechanism followed by this system. Significant deuteration of the unconverted styrene and the ester isomers formed was found in the alkoxycarbonylation of styrene with EtOD at low temperature (60 °C). Under more severe conditions, oligodeuterated species were formed in a less selective manner. The presence of deuterium in the unconverted alkene confirms the reversibility of the reaction (alkyl−metal intermediates readily undergo β-hydride elimination) and suggests that dissociation of the palladium alkyl intermediate occurred. Reversible alkene insertion/β-hydride elimination prior to carbonylation was deemed responsible for the incorporation of multiple deuterium atoms.[109]

A comparative study of the regioselectivity in styrene and α-methylstyrene alkoxycarbonylation in the presence of [PdCl$_2$(PPh$_3$)$_2$] and [PdCl$_2$(PPh$_3$)$_2$]/SnCl$_2$ catalyst precursors has been reported. When styrene was transformed with [PdCl$_2$(PPh$_3$)$_2$]/SnCl$_2$ as the precursor, the linear ethyl 3-phenylpropanoate was the major product. The formation of both the linear and branched palladium alkyls was reversible, so that deuterium labelling occurred at all carbon



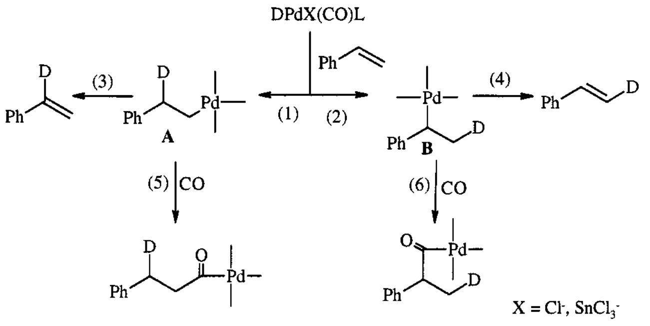
Scheme 14. Pathways for deuteration of α-methylstyrene and the derived deuterated isomeric esters

atoms of the side chains of the substrate and esters. In the absence of $SnCl_2$, the branched ethyl 2-phenylpropanoate was formed regioselectively and no deuterium was found adjacent to the phenyl rings. These results show that the routes leading to the linear metal-alkyls must be blocked.

When α-methylstyrene was used as the starting material, ethyl 3-phenylbutanoate (A) was predominantly obtained with both catalytic systems and there was no significant difference in the deuterium distributions obtained with the $[PdCl_2(PPh_3)_2]$ and $[PdCl_2(PPh_3)_2]/SnCl_2$ systems (Scheme 14). For the first time, this provides evidence for the formation of tertiary palladium alkyl species (B) with α-methylstyrene. These tertiary palladium alkyl species (B), although favoured over their primary counterparts (C), overwhelmingly underwent β-hydride elimination and, probably due to steric hindrance, the branched ester was not formed. Therefore, these intermediates undergo a slow migration of CO versus β-elimination. These results show that the different behaviour of primary, secondary, and tertiary palladium alkyl intermediates under alkoxycarbonylation conditions may account for the different regioselectivities.[110]

In the hydroxycarbonylation of styrene, the addition of $SnCl_2$ to the $[PdCl_2(PPh_3)_2]$ system also increases the selectivity in favour of the linear acid from 30 to 70%. Kinetic and spectroscopic data seem to indicate that this occurs through the displacement of a CO ligand from Pd^{II}-containing intermediates by the π-acceptor $SnCl_3^-$, as discussed above (Scheme 15).[104]

Scheme 15 shows that in systems containing chloride, when $X = Cl^-$, deuterium exchange occurs only at the β-position of the vinyl group; i.e. the rate of decomposition of species B (4) is higher than the rate of its carbonylation (6). The decomposition of species A (3) did not occur under the experimental conditions. Therefore, styrene insertion into a Pd−H bond was considered to be an equilibrium step in route (2) and an irreversible step in route (1). In the presence of $SnCl_2$, extensive deuterium exchange occurs at both the α and β positions; i.e. the rates of steps (3) and (4) become similar. This is consistent with the data on the ability of the $SnCl_3^-$ moiety to assist the β-elimination of hydrogen from hydrocarbon groups in transition metal complexes[111,112] and allowed the authors to suggest that the formation of an intermediate of type A according to route (1) with $X = SnCl_3^-$ is an equilibrium step (Scheme 15).[106]



Scheme 15. Study of the regioselectivity in the hydroxycarbonylation of styrene with deuterium labels

These studies prove that β-elimination takes place in the carbonylation reaction with the palladium catalyst. This was previously demonstrated for hydroformylation with a rhodium catalyst by means of deuterium labelling experiments.[113,114] However, the occurrence of β-elimination had already been deduced for other systems. In the hydroxycarbonylation of 1-octene with Pd/monophosphane systems at temperatures above 150 °C, dehydratocarbonylation was observed, this being the inverse reaction of hydroxycarbonylation. The acids formed reverted to the alkene, carbon monoxide, and water. Both the forward and reverse reactions proceeded with appreciable rates.[85]

Recently, deuterium labelling experiments have been used in the hydroxycarbonylation of acenaphthylene with the [$PdCl_2(MeCN)_2$] system in the presence of monophosphanes with different electronic properties. Deuteriocarboxylation of this substrate is, owing to the structure of the product, useful for determining the diastereoselectivity of the *cis*-addition of Pd−D to the alkene.[115]

Theoretical Studies

In an attempt to ascertain whether palladium hydride species or palladium alkoxycarbonyl species are the key intermediates in the Pd^{II}-catalysed alkoxycarbonylation of ethene, ab initio calculations were carried out to provide information on the transition state barriers of the elementary steps. The palladium hydride species was shown to be preferable to the palladium alkoxycarbonyl species as the key intermediate.[19] However, comparison of different routes remains a difficult task in view of the present state of the art. It can merely be concluded that the calculations are consistent with the experiments in that there is no prohibitive barrier for either route.[21]

In situ High-Pressure NMR Experiments

We have performed in situ high-pressure NMR studies of the hydroxycarbonylation of styrene using several palladium systems in order to obtain insight into the mechanisms that control the regioselectivity and the effects of the phosphorus ligand and the catalyst precursor. Similar in situ HPNMR studies have been performed for the rhodium hydroformylation[116,117] and palladium copolymerization reactions.[118] In particular, in the case of rhodium hydroformylation, this approach proved very useful for determining the intermediate species involved in the catalytic cycle.

In this study, the HPNMR spectroscopic investigations were carried out using $Pd(OAc)_2$ and [$PdCl_2(PhCN)_2$] as palladium precursors, which were modified with PPh_3 as a monophosphane or dppb as a diphosphane [dppb = 1,4-bis(diphenylphosphanyl)butane]. $H_2C_2O_4$ was used as the acid under CO atmosphere with [D_8]THF as the solvent. The system was stirred under pressure to favour the diffusion of the gas. The experimental conditions were chosen according to previous hydroxycarbonylation catalytic experiments.[23,24]

The System $Pd(OAc)_2$/PPh_3/$H_2C_2O_4$

HPNMR experiments were carried out at 30 bar CO and molar ratios of P/Pd = 4 and H^+/Pd = 25 with the $Pd(OAc)_2/PPh_3/H_2C_2O_4$ system. The system was heated to 100 °C to allow the catalytic species to form. The $^{31}P\{^1H\}$ NMR spectrum of the solution showed a sharp singlet at $\delta = 14.4$. The resonance of the oxidized phosphane was observed at $\delta = 32$. At room temperature, the same solution exhibited a broad signal at $\delta = 15.0$, together with the signal of the oxidized phosphane. When the temperature was lowered to −60 °C, the signal shifted downfield to $\delta = 23.6$; a second signal of low intensity simultaneously appeared at $\delta = -5.0$, which was assigned to the free PPh_3 ligand. Despite the acidic medium, no hydride signal was observed in the ^1H NMR spectra (Figure 1; Table 1).

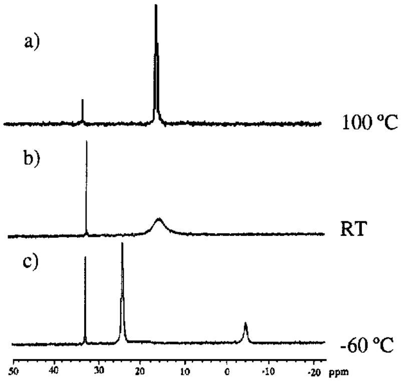


Figure 1. $^{31}P\{^1H\}$ NMR spectra for the reaction of $Pd(OAc)_2$ with PPh_3 under hydroxycarbonylation conditions at different temperatures: (a) 100 °C, (b) room temp., (c) −60 °C

In agreement with previously reported NMR spectroscopic data,[25] this behaviour may be rationalized in terms of ligand dissociation and a rapid ligand exchange according to an equilibrium between [$PdCO(PPh_3)_3$] and [$PdCO(PPh_3)_2$] + PPh_3. At low temperatures, [$PdCO(PPh_3)_3$] and free PPh_3 are observed.[27,28]

The HPNMR tube was then depressurized at room temperature and styrene (0.05 mL) was added under nitrogen (substrate/Pd = 4). The $^{31}P\{^1H\}$ NMR spectrum seen at 30 bar CO and room temperature remained unchanged. The temperature was then increased to 100 °C so as to reach carbonylation conditions. The formation of the acids was observed in the ^1H NMR spectrum, indicating the occurrence of hydroxycarbonylation. The major acid was the branched one, as reported previously for palladium systems with monophosphane ligands.[23] Simultaneously, the species observed in the $^{31}P\{^1H\}$ NMR spectra were those that had previously been observed when no substrate was added at these temperatures (Figure 1). When the system was cooled to −60 °C, decoalescence occurred in the same way as when there was no substrate. No hydride species were observed in the ^1H NMR spectra in the course of the experiment.

The System [$PdCl_2(PhCN)_2$]/PPh_3/$H_2C_2O_4$

Similar HPNMR experiments were performed for [$PdCl_2(PhCN)_2$]/PPh_3/$H_2C_2O_4$ at 30 and 10 bar CO, P/Pd = 4, and H^+/Pd = 25. The $^{31}P\{^1H\}$ NMR spectrum of the solution at 30 bar CO and 100 °C showed four broad signals: the signal of the oxidized monophosphane at $\delta = 33$, two minor signals at $\delta = 24.5$ and 22.9, and a major singlet at $\delta = 6.7$. A broad hydride signal was observed in the ^1H NMR spectrum at $\delta = -13$. At room temperature, the $^{31}P\{^1H\}$ NMR spectrum showed four sharp singlets at $\delta =$

Table 1. NMR spectroscopic data for the [Pd]/PPh_3/$H_2C_2O_4$ systems under hydroxycarbonylation conditions

Complex	$\delta^{31}P\{^1H\}$ (ppm)	δ^1H (ppm)	Ref.
PPh_3[a]	−5	–	–
oxidized PPh_3[a]	32	–	–
$[PdCO(PPh_3)_3]$	23.6 (−70 °C)	–	[25]
$[Pd(PPh_3)_3]$[a]	24.9	–	–
cis/*trans*-$[PdCl_2(PPh_3)_2]$[a]	23.0, 22.8	–	–
$[Pd(H)Cl(PPh_3)_2]$	23.0 (−70 °C)	−13 (H)	[43−46]
$[PdCl(PPh_3)_2(COCH_2CH_2Ph)]$	20.6	1.4; 2.2 (CH_2)	[35]
$[PdCl(PPh_3)_2\{COCH(CH_3)Ph\}]$	19.8	0.8 (CH_3); 2.8 (CH)	[35]

[a] NMR spectroscopic data from experimental results.

32.2, 24.9, 23.0, and 22.8 and a broad signal at δ = 6.8. When the system was cooled to −70 °C, the broad signal was shifted downfield to δ = 23 and a new signal appeared at δ = −6; this was assigned to free PPh_3. No hydride signal was observed in the ^1H NMR spectrum either at room temperature or at −70 °C (Figure 2; Table 1).

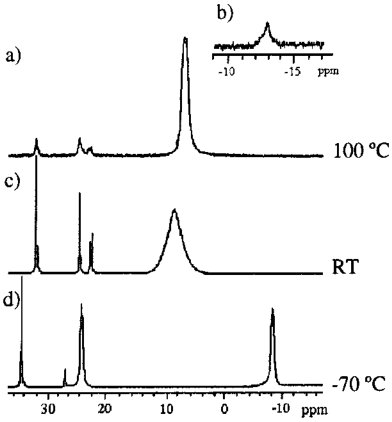


Figure 2. $^{31}P\{^1H\}$ and ^1H NMR spectra for the reaction of $[PdCl_2(PhCN)_2]$ with PPh_3 under hydroxycarbonylation conditions at different temperatures: (a) $^{31}P\{^1H\}$ NMR spectrum at 100 °C; (b) ^1H NMR spectrum at 100 °C; (c) $^{31}P\{^1H\}$ NMR spectrum at room temp.; (d) $^{31}P\{^1H\}$ NMR spectrum at −70 °C

As previously shown for the $Pd(OAc)_2/PPh_3$ system, a fast ligand exchange occurs at room temperature as well as at higher temperatures. However, the integrals of the phosphorus signals were different from those with the $Pd(OAc)_2/PPh_3$ system (Figure 1). These integrals may be indicative of the presence of a palladium complex with two monophosphanes coordinated as the $[Pd(H)Cl(PPh_3)_2]$ species.[43−46] These coordinated monophosphanes were responsible for the signal at δ = 23 in the $^{31}P\{^1H\}$ NMR spectrum and the corresponding hydride signal was observed at δ = −13 in the ^1H NMR spectrum. This hydride species is only observed at temperatures at or above 100 °C and under CO pressure.

The minor sharp singlets observed at room temperature at δ = 24.9 were attributed to the formation of $[Pd(PPh_3)_3]$ and those at δ = 23.0 and 22.8 to *cis*/*trans*-$[PdCl_2(PPh_3)_2]$. These complexes have previously been prepared in our laboratory for NMR assignment.

After cooling and depressurizing the HPNMR tube, styrene was added under nitrogen (substrate/Pd = 4). The solution was then pressurized with 30 bar CO and in the room temperature $^{31}P\{^1H\}$ NMR spectrum six sharp signals were observed at δ = 32.2 (oxidized monophosphane), 25.0, 23.1, 22.8, 20.6, and 19.8, together with a broad signal at δ = 0 (Figure 3, a). The singlets at δ = 25.0, 23.1, and 22.8 were assigned to the species previously observed in the absence of styrene, namely $[Pd(PPh_3)_3]$ and $[PdCl_2(PPh_3)_2]$. Two new singlets appeared at δ = 20.6 and 19.8 after the substrate was added, which were attributed to the palladium acyl complexes $[PdCl(PPh_3)_2(COCH_2CH_2Ph)]$ and $[PdCl(PPh_3)_2\{COCH(CH_3)Ph\}]$ (Table 1).[35] In the ^1H NMR spectrum, these palladium acyl complexes give rise to signals at δ = 1.4 and 2.2 due to the CH_2 of the linear isomer and at δ = 0.8 and 2.8 due to the CH_3 and CH of the branched acyl species, respectively. The major species was the linear palladium acyl species.

The broad signal observed at δ = 0 in the $^{31}P\{^1H\}$ NMR spectrum may be attributed to the species $[Pd(H)Cl(PPh_3)_2]$ that was previously observed in the absence of styrene at δ = 6.8 (Figure 2, c), despite there being no hydride signal in the ^1H NMR spectrum (Figure 3, a).

When the temperature was increased to 50 °C and 100 °C, hydroxycarbonylation was observed and in the $^{31}P\{^1H\}$ NMR spectrum the palladium acyl signals became broader (Figure 3, b,c). An exchange of PPh_3 between the palladium hydride and the palladium acyl species was observed.

The $^{31}P\{^1H\}$ NMR spectrum recorded after 24 hours was unchanged (Figure 3, d) and the ^1H NMR spectrum showed only 60% conversion to the acids with 64% regioselectivity in favour of the branched acid. When the temperature was increased to 120 °C (Figure 3, e), the rate of the reaction increased considerably and there was a faster phosphorus exchange between the palladium hydride and the palladium acyl species. After a few minutes, conversion reached 92% and the regioselectivity decreased to just 51% in favour of the branched acid. A dependence of the regioselectivity on the temperature was observed.

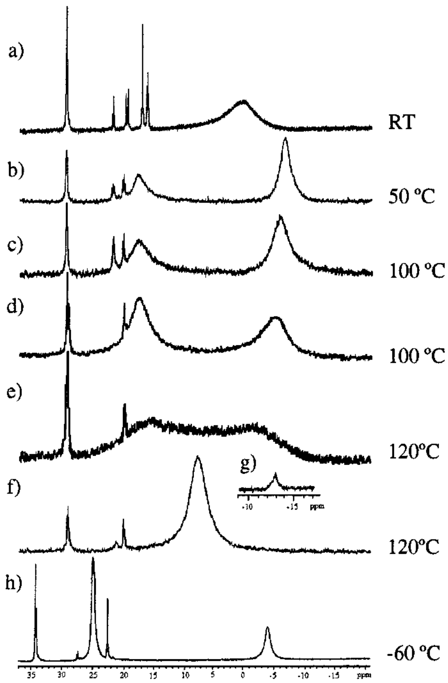


Figure 3. $^{31}P\{^{1}H\}$ and ^{1}H NMR spectra for the reaction of $[PdCl_2(PhCN)_2]$ with PPh_3 in the hydroxycarbonylation of styrene at different temperatures: (a) $^{31}P\{^{1}H\}$ NMR spectrum at room temp.; (b) $^{31}P\{^{1}H\}$ NMR spectrum at 50 °C; (c) $^{31}P\{^{1}H\}$ NMR spectrum at 100 °C; (d) $^{31}P\{^{1}H\}$ NMR spectrum after 1 day at 100 °C; (e) $^{31}P\{^{1}H\}$ NMR spectrum at 120 °C; (f) $^{31}P\{^{1}H\}$ NMR spectrum after 30 min at 120 °C; (g) ^{1}H NMR spectrum after 30 min at 120 °C; (h) $^{31}P\{^{1}H\}$ NMR spectrum at −60 °C

After 30 min, the hydroxycarbonylation was seen to be complete since the styrene and the palladium acyl complexes were no longer observed. A new hydride signal appeared at $\delta = -13$ (Figure 3, g). This signal was not observed in the course of the hydroxycarbonylation, possibly because it was below the detection level. The $^{31}P\{^{1}H\}$ NMR spectrum (Figure 3, f) was similar to that in the absence of styrene (Figure 2, a). Oxidized PPh_3, giving a signal at $\delta = 32$, and minor species such as $[Pd(PPh_3)_3]$ ($\delta = 25$) and $[PdCl_2(PPh_3)_2]$ ($\delta = 24$) were observed.

The solution was then cooled to −60 °C and, as previously observed in the absence of styrene (Figure 2, d), a broad signal appeared in the $^{31}P\{^{1}H\}$ NMR spectrum at $\delta = 24$ due to the complex $[Pd(H)Cl(PPh_3)_2]$, along with a signal due to the free phosphane at $\delta = -4$ (Figure 3, h).

To confirm the presence of the acyl species, we performed an experiment with the same $[PdCl_2(PPh_3)_2]/PPh_3/H_2C_2O_4$ system at 11 bar using a mixture of CO and ^{13}CO (10:1). Before the styrene was added, the species present were the same as those seen at 30 bar CO (Figure 2). After the addition of styrene at room temperature, the carbonyl signals of the palladium acyl complexes were observed in the ^{13}C NMR spectrum at $\delta = 234$ and 232. The temperature was then increased to 100 °C so as to reach hydroxycarbonylation conditions. This pressure favoured the formation of the linear acid and the ^{1}H NMR spectrum showed the presence of the hydride ($\delta = -13$) and the palladium acyl species.

During the hydroxycarbonylation, the temperature was lowered to −90 °C in an attempt to freeze out the intermediates of the reaction. The $^{31}P\{^{1}H\}$ spectrum was the same as that recorded without styrene (Figure 2, d; Figure 3, h), featuring signals due to the acyl complexes at $\delta = 19$ and 20. The temperature was then increased to 120 °C and at the end of the reaction the major product was the linear acid.

In conclusion, in the Pd/monophosphane systems, the palladium hydride species was only observed at high temperatures in the presence of carbon monoxide. Chloride ions favour the formation of this species. No hydrides were observed with the $Pd(OAc)_2/PPh_3$ system. With the $[PdCl_2(PhCN)_2]/PPh_3$ system at 30 bar CO, palladium acyl complexes were observed during the hydroxycarbonylation. At lower CO pressures, palladium hydride and palladium acyl species were observed. Similarly, the regioselectivity of the system was found to be dependent on the temperature and pressure; high temperatures and low pressures favoured the linear acid.

The System $Pd(OAc)_2/dppb/H_2C_2O_4$

Similar HPNMR experiments were performed with the $Pd(OAc)_2/dppb/H_2C_2O_4$ system at 60 and 20 bar CO, P/Pd = 4, and $H^{+}/Pd = 25$. At 60 bar CO, the system was heated to 120 °C to form the active species. The $^{31}P\{^{1}H\}$ NMR spectrum of the solution showed two broad signals at $\delta = 16$ and −6. Two resonances, corresponding to the oxidized diphosphane, were present at $\delta = 37$. A sharp hydride signal was seen in the ^{1}H NMR spectrum at $\delta = -5.6$. The $^{31}P\{^{1}H\}$ NMR spectrum of the same solution at room temperature showed a minor signal at $\delta = 27$ and a broad signal at $\delta = 14$, along with two signals due to the oxidized phosphane. On cooling to −70 °C, three broad signals were observed at $\delta = 27$, 16, and −14, the last of which was assigned to free dppb (Figure 4; Table 2).

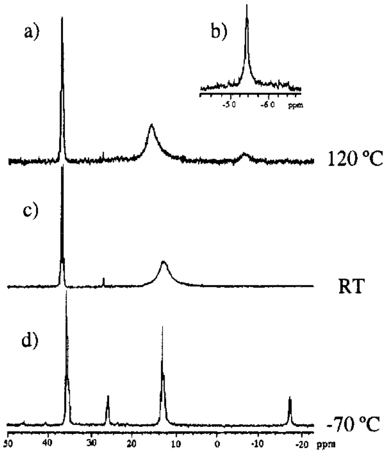


Figure 4. $^{31}P\{^{1}H\}$ and ^{1}H NMR spectra for the reaction of $Pd(OAc)_2$ with dppb under hydroxycarbonylation conditions at different temperatures: (a) $^{31}P\{^{1}H\}$ NMR spectrum at 120 °C; (b) ^{1}H NMR spectrum at 120 °C; (c) $^{31}P\{^{1}H\}$ NMR spectrum at room temp.; (d) $^{31}P\{^{1}H\}$ NMR spectrum at −70 °C

Table 2. NMR spectroscopic data for the [Pd]/dppb/$H_2C_2O_4$ systems under hydroxycarbonylation conditions

Complex	$\delta^{31}P\{^1H\}$ (ppm)	δ^1H (ppm)	Ref.
dppb[a]	−14	–	–
oxidized dppb[a]	37	–	–
$[Pd(dppb)_2]$	27 (−70 °C)	–	[119]
$[Pd(OAc)_2dppb]$	16 (−70 °C)	–	[28]
$[(dppb)_2Pd_2(\mu\text{-}H)(\mu\text{-}CO)]OAc$	23	−6.4 (μ-H)	[52,53]
$[PdCl_2dppb]$[a]	28	–	–

[a] NMR spectroscopic data from experimental results.

These spectra may be explained in terms of ligand dissociation and a rapid ligand exchange at high temperatures. The signal at δ = 27 may be attributed to the complex $[Pd(dppb)_2]$,[119] and that at δ = 16 to the species $[Pd(OAc)_2dppb]$.[28] These species can undergo exchange of free dppb at high temperatures, thereby accounting for the broad signal at δ = 16. There may also be a dinuclear species with two bridging chelate diphosphanes coordinated to two palladium centres, with a hydride and carbon monoxide or acetate in a *trans* arrangement (Scheme 10, a). One of the two signals at δ = 37 can be attributed to monooxidized monocoordinated diphosphane. The species [Pd(P−P)(P−P=O)] or $[Pd(OAc)_2(P-P=O)]$ may be formed, as has previously been suggested for the reduction of Pd^{II} species to Pd^0 as a means of initiating the catalytic cycle.[28] The sharp signal in the ^1H NMR spectrum at high temperatures did not show the expected large coupling constant for a hydride and a *trans* phosphorus atom (about 180 Hz). Therefore, the palladium hydride species did not have a hydride and the phosphane in a mutual *trans* arrangement. This species may correspond to the previously proposed dinuclear species.

The HPNMR tube was then depressurized at room temperature and styrene was added under nitrogen (substrate/Pd = 4). The $^{31}P\{^1H\}$ NMR spectrum at 60 bar CO and room temperature remained unchanged. The temperature was then increased to 120 °C so as to reach carbonylation conditions, and the formation of acids was observed in the ^1H NMR spectrum during the hydroxycarbonylation. As was previously reported for palladium systems with diphosphane ligands, the major product was the linear acid.[23] The species observed in the $^{31}P\{^1H\}$ NMR spectrum of the same solution were those that had previously been observed when no substrate was added at these temperatures (Figure 4). Furthermore, when the system was cooled to −70 °C, the behaviour was the same as that when no substrate was added. The hydride species was observed in the ^1H NMR spectrum only at high temperatures under carbon monoxide pressure. No palladium acyl species were observed.

An experiment was performed with the same system $Pd(OAc)_2$/dppb/$H_2C_2O_4$ at 20 bar CO with 1 bar of ^{13}CO. Prior to the addition of styrene, the species seen in the $^{31}P\{^1H\}$ NMR were the same as those seen at 60 bar CO (Figure 4) at the different temperatures, with only a minor singlet appearing at δ = 23. In the ^1H NMR spectrum, the sharp hydride signal was also present at δ = −5.6 and another minor broad signal was present at δ = −6.4. This palladium hydride signal and the $^{31}P\{^1H\}$ singlet at δ = 23 may be attributed to the dinuclear palladium species $[(dppb)_2Pd_2(\mu\text{-}H)(\mu\text{-}CO)]OAc$.[52,53]

When styrene was added and the system was heated to 120 °C, the $^{31}P\{^1H\}$ and ^1H NMR spectra were unchanged. In the ^{13}C NMR spectrum, however, a broad carbonyl signal due to a palladium acyl complex appeared at δ = 234. During the hydroxycarbonylation, formation of the linear acid was seen to be preferred. The system was cooled to −70 °C and the $^{31}P\{^1H\}$ NMR spectrum recorded at this temperature was the same as that when no styrene was added (Figure 4, d). The temperature was then increased to 120 °C once more and the reaction went to completion giving mainly the linear acid.

The System $[PdCl_2(PhCN)_2]$/dppb/$H_2C_2O_4$

Similar HPNMR experiments were performed with the $[PdCl_2(PhCN)_2]$/dppb/$H_2C_2O_4$ system at 60 bar CO, P/Pd = 4, and H^+/Pd = 25. The $^{31}P\{^1H\}$ NMR spectrum of the solution at 120 °C showed only free and oxidized dppb and a small signal due to the sparingly soluble $[PdCl_2dppb]$ complex at δ = 28. When styrene was added to the system, no activity was observed. After one week, a small broad signal had appeared at δ = 16 in the room temperature $^{31}P\{^1H\}$ NMR spectrum. This signal was similar to that for the $Pd(OAc)_2$ system (Figure 4, c), where a small amount of the linear acid was observed. This may explain the fact that the $[PdCl_2(PhCN)_2]$/dppb system requires high pressures and temperatures in the catalytic experiments.

In conclusion, for the $Pd(OAc)_2$/dppb system palladium hydride species have been observed at high temperatures in the presence of carbon monoxide. On the other hand, monophosphane systems need chloride ions to stabilize the hydride species. At 20 bar CO, an acyl complex and the hydride species were observed by ^{13}C NMR spectroscopy. In the presence of palladium species, the occurrence of monooxidized, monocoordinated diphosphanes cannot be discarded, but the regioselectivity has invariably been found to favour the linear acid. The fact that some enantiomeric excess was seen with chiral diphosphanes means that some diphosphane remained coordinated as a chelate.[23]

Discussion of the Catalytic Cycle

The key questions to be answered concerning the catalytic cycle, focussing on the hydroxycarbonylation of styrene, are:

− Is the starting point a palladium hydride or a palladium alkoxycarbonyl species?

− How does the regioselectivity relate to the ligand, anion, and solvents?

Of the two proposed mechanisms, most researchers agree that the hydride mechanism is more common than the alkoxycarbonyl path in the alkoxycarbonylation of alkenes with palladium systems. However, the involvement of alkoxycarbonyl species cannot be discarded as they are stable intermediates.[20] We must distinguish between hydroxycarbonylation and alkoxycarbonylation, as these reactions may have different characteristics. The prevailing mechanism for methoxycarbonylation is the hydride mechanism, but firm evidence has been presented for the occurrence of the methoxycarbonyl species as well. As examples, we mention double methoxycarbonylation leading to succinates,[67,68] the formation of methyl methacrylate from propyne,[120] and the formation of diesters during polyketone formation.[69] In two of these cases there is no choice, and the methoxycarbonyl species is the putative starting point. On the other hand, as pointed out by Sperrle and Consiglio,[121] it is difficult to present direct experimental evidence for either mechanism for the reactions producing monoesters or acids. For the very fast methoxycarbonylation of propene in methanol using alkyl diphosphanes, it was suggested[122,123] that palladium hydrido species were the starting points of the catalytic cycle as they were observed besides alkyl and alkanoyl species in separate NMR spectroscopy studies. Similar results have been reported[29] for the hydroxycarbonylation of propene in water using palladium complexes of tppts. However convincing it might seem though, it should be borne in mind that, strictly speaking, this remains circumstantial evidence. As we will discuss below, even kinetic measurements may not necessarily lead to clear-cut experimental evidence.

In the present study, like previous authors, we have observed palladium hydride intermediates and palladium acyl intermediates in the HPNMR experiments. The presence of hydroxycarbonyl species (or alkoxycarbonyl species[122,123]) below the detection limit responsible for the activity of the system is less likely because previous reactivity studies have shown that the alkoxycarbonyl species is less reactive than the hydride species.[16,87] This brings us to an important difference between alkoxycarbonylation and hydroxycarbonylation. The latter involves the PdCOOH fragment, which is highly unstable and rapidly degrades to palladium hydride and carbon dioxide. In the presence of oxidizing agents, divalent palladium dominates during the methoxycarbonylation, which leads to methoxycarbonyl species as the initiating group, provided that the system is anhydrous.[33,123] Tooze et al. reported an exception to this, a hydride being central to the catalytic cycle in the presence of an oxidizing agent, but it was not explicitly mentioned that this system was anhydrous. In the presence of water, the hydroxycarbonyl palladium species forms and hence palladium hydride will start the sequence.[16,122,123]

There are many other ways by which the palladium hydride species can be formed: (a) by β-elimination from the [PdCH(Ph)CH_2COOH] intermediate,[21] (b) by the formation of diacids, i.e. double carbonylation (the absence of minute amounts of these by-products in our experiments, as previously reported in catalytic experiments,[23] is incompatible with the presence of metal−carboxylic acid intermediates), (c) by reduction of phosphanes, (d) by addition of H_2, and (e) by β-elimination from [PdOCH_2R] species.[9,121] The deuterium exchange between the alkene and ROD found during the alkoxy- and hydroxycarbonylation[106,109,110] can only occur through reversible alkene insertion into a Pd−D bond, which strongly supports a reaction mechanism involving this step as well. The reversibility has implications for the regio- or enantioselectivity, as we will see below.

The regioselectivity and stereoselectivity have previously been discussed by Consiglio.[101,121] From the regioselectivity, it was concluded that the insertion of styrene into a metal−acyl bond leads to branched products, while its insertion into a metal hydride leads to linear products.[94,101,112] It is tempting to apply this finding to hydrocarboxylation as well. For the present systems, this is not the case as both the monodentate ligand systems, leading to mainly branched acid, and the bidentate ligand based systems, leading to mainly linear acid, imply insertions of styrene into a palladium hydride fragment. It has been argued[121] that insertion into a palladium hydride causes less steric constraints than insertion into a palladium alkoxycarbonyl species, and thus a lower stereospecificity can be obtained for the former. Indeed, high enantioselectivities were obtained in the formation of succinate.[67] This would make stereoselective hydroxycarbonylation difficult to accomplish. On the other hand, insertion of styrene into a palladium hydride bond may bring the aryl substituent in close proximity to a *cis* ligand, if this were a bulky and/or chiral ligand. We have previously reasoned that this steric interaction would stimulate the formation of linear products, which indeed seems to be the case for *cis* bidentate phosphane catalysts. A second problem arises from the reversibility of the insertion reactions. Alkene insertion is reversible, but so may be the insertion of carbon monoxide. If this were so, and the nucleophilic attack of water on the acyl group were to play a role in determining the overall rate, the selectivities under Curtin−Hammett conditions would be determined by all the rates and concentrations. In other words, the selectivities are determined by the differences in the overall final barriers. This may explain the low enantioselectivities obtained in many instances. It also complicates the discussion of the regioselectivity, as one pathway may involve complete equilibration while another may not.

Insertion reactions of alkenes and carbon monoxide using cationic palladium catalysts in alcohols and water may give rates of tens of thousands of turnovers per hour at 100 °C or even below.[29,87] The oxalic acid based systems are several orders of magnitude slower, for which there may be a number of reasons. Firstly, sites may be blocked by coordinating anions or by excess phosphanes. Secondly, low concentrations of alkenes may be found, especially in biphasic reactions.[29] Thirdly, palladium may be present in a state other than the required PdH^+ species, for example as Pd^0 species or as inactive dimers. Populating resting states of the latter two types diminishes the reactivity of the system, as we reported above. Stable palladium hydrides are obtained when two phosphanes occupy *cis* positions with respect to the hydride. We found that monophosphanes do indeed provide the fastest catalysts and the diphosphanes provide much slower catalysts in the oxalic acid system.[23] In line with this, bidentate phosphanes having wide bite angles, which can also form *trans* complexes, give the most effective catalysts amongst the group of bidentate ligands.[23] Alkylphosphanes should give more stable hydride species as well, but in this system they show no activity and other side reactions must be followed, such as phosphonium salt formation perhaps.

Strong acids and polar media shift the equilibrium (Scheme 5) between Pd^0 and PdH^+ to the right. Indeed, high activities can be obtained[29,102] in water when soluble alkenes such as ethene and propene are used, but naturally this is not the case for styrene. Non-coordinating anions (i.e. the conjugate bases of strong acids) are also preferred in order to enhance coordination of alkenes and CO. Nevertheless, chloride has often been found to give the best results,[40] which may perhaps be ascribed to the higher stability of palladium hydrides when chloride anions are present. Acidic systems have an intrinsic drawback. If the nucleophilic attack on the acyl-palladium species is indeed rate determining, the strongest nucleophile present is water itself rather than the more nucleophilic hydroxide. This may be compared the very fast reaction of acyl palladium species and methoxy anions observed by Tóth.[16]

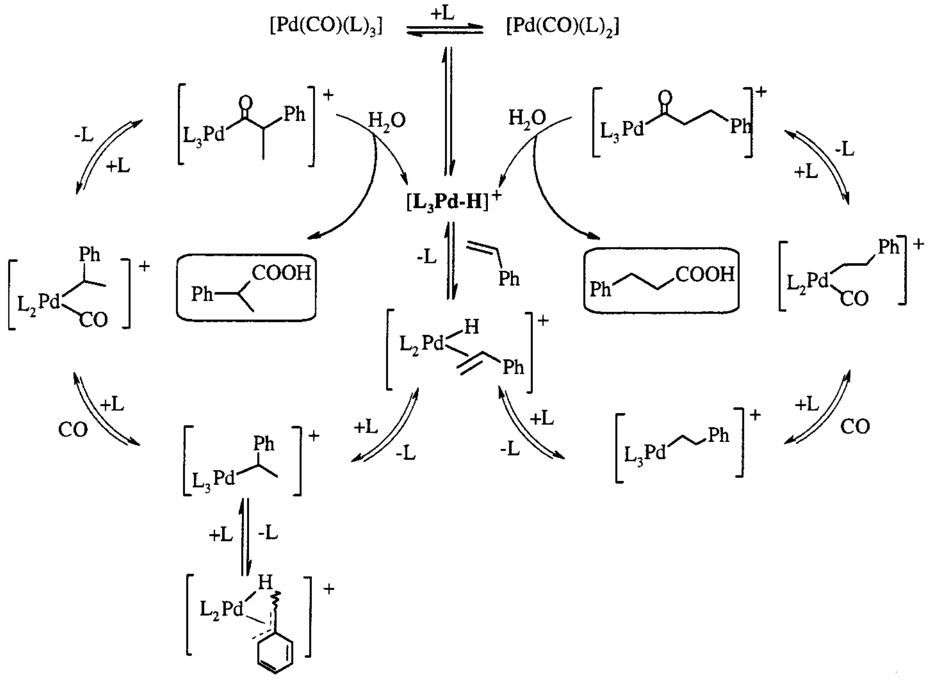
In an attempt to bring together the previously discussed reports and our in situ HPNMR study, we have summarized the catalytic cycle for the hydroxycarbonylation of styrene in Scheme 16.

A pre-equilibrium between different Pd^0 species bearing phosphane and carbon monoxide ligands is proposed; the stabilities of these species depend on the nature of the acidic medium and the phosphorus ligands, as demonstrated in the HPNMR spectra of the $Pd(OAc)_2/PPh_3/H_2C_2O_4$ system (Figure 1). This Pd^0 species can be formed by the methods discussed above, by oxidation of the phosphane,[27,28] or in the presence of CO and H_2O.[8,29] Because the acid used (AcOH) is not very strong, little hydride will be formed.

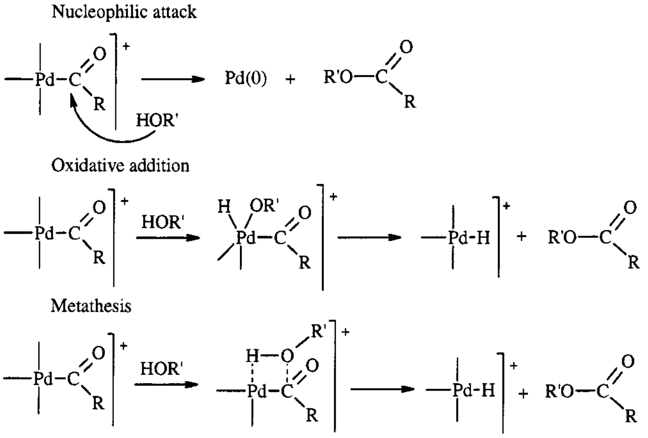
The insertion of styrene into the palladium hydride bond leads to two alkyl isomers, which can interconvert through β-elimination. Previous catalytic experiments,[85] kinetic studies,[106] and deuterium labelling methods[109,110] have demonstrated the occurrence of this β-elimination reaction.

For the branched palladium alkyl intermediate, stabilization through the formation of π-benzylic species[53,63] must also be taken into account. Thus, the regioselectivity may not yet be determined at this stage. The alkyl-alkanoyl equilibrium may reside on the side of the alkyl species, particularly for those π-benzylic species for which the insertion may be relatively slow, as has also been found for allyl palladium species.[124] The palladium acyl intermediates are formed by the insertion of carbon monoxide into the palladium−alkyl bond. The equilibrium between the palladium hydride species and palladium acyl species proposed in this catalytic cycle is in agreement with the reversibility of the CO insertion in the palladium alkyl bond, which was also verified by catalytic experiments.[71,77] Equilibration may even extend all the way between Pd^0 species and palladium acyl intermediates during hydroxycarbonylation (Scheme 17). Depending on the conditions, it seems likely that linear alkyl formation is irreversible whereas branched alkyl formation is reversible, even further down to alkanoyl formation. At least the trend will be in this direction.

Indeed, in the hydroxycarbonylation of styrene, kinetic and deuterium labelling studies have demonstrated that for the branched alkyl intermediate β-elimination is faster than



Scheme 16. Proposed catalytic cycle for the hydroxycarbonylation of styrene



Scheme 17. Different proposals for the final step in the palladium carbonylation reactions

CO insertion, but that for the linear alkyl intermediate carbonylation is faster than β-elimination.[106,109,110]

In the HPNMR experiments using ^{31}P as the probe, we could not establish whether or not equilibration was operative all the way from the hydride to the alkanoyl, because exchange of the phosphane ligand probe between the free and complexed species proved to be the fastest reaction, thus prohibiting the observation of exchange of CO or styrene. Phosphane exchange occurs on the NMR time scale and if reversible insertions were to have rates of only a few percent of that of this exchange, they would still be faster than the overall catalytic process.

We consider next the regioselectivity. The HPNMR experiments and the previously described kinetic studies[104,105,108] have shown that regioselectivity is dependent on the pressure and temperature. High temperatures and low CO pressures favour formation of the linear acid as these conditions favour β-elimination from the stabilized π-benzylic species to give the linear palladium alkyl species.

Previously, we have offered a tentative explanation for the different regioselectivities of monophosphanes and diphosphanes. The reason for the high degree of linearity achieved with diphosphane catalysts is not the higher temperatures used. Catalytic experiments performed under identical conditions (20 bar CO, 150 °C, and P/Pd ratio = 4) with PPh_3 as the monophosphane led to a branched/linear ratio of 73:27, while the ratio was 28:72 for the diphosphane dppb.[23] We surmise that *cis*-coordinated diphosphanes versus *trans*-coordinated monophosphanes could be the key to regioselectivity control. In a *cis*-diphosphane complex, a strong interaction between the moieties on the phosphane and the aryl group of styrene leads to the formation of linear alkyl-palladium species. Reversibility plays an important role and we still have insufficient knowledge about this. Branched alkanoyl species are probably slightly more stable than linear ones, but nucleophilic attack on the latter may be faster and thus the regioselectivity under Curtin−Hammett conditions is hard to predict.

Complexes containing fewer phosphanes coordinated to the palladium form more of the branched acid.[104,105] Similarly, more hindered alkenes afford the linear acid.[99] In conclusion, the regioselectivity remains an extremely delicate issue. It is still difficult to predict given the complex kinetics involved, with rates depending on the pressure, temperature, counteranion, and phosphorus ligand.

Finally, the mechanism of the last step is not so clear and is often neglected. For the palladium carbonylation reactions, nucleophilic attack of $R'O^-$ would generally lead to Pd^0 and H^+, with oxidative addition occurring as the next step. Alternatively, the oxidative addition of R′OH to Pd^{II}, in other words a sort of α-bond metathesis, may be considered (Scheme 17).

All evidence for the recently published, fast catalyst points to the fact that the hydrolysis step is rate determining. For the many systems mentioned above, the rates vary by many orders of magnitude. On the one hand, this may be due to the intrinsic effects of the ligands, anions, and solvents on the rate, but on the other hand it may also be due to the effects these factors have on the resting states, including those outside of the catalytic cycle. Monodentate ligands give the fastest reactions.

Polyketone catalysis employing a variety of *cis*-chelating bidentate ligands shows that insertion reactions are fast (several thousands of insertions per hour), while termination at 80−100 °C occurs only several times per hour. The latter depends on the time that the growing chain end exists as an alkyl or an acyl species, but at high CO pressures appreciable amounts of acyl palladium chain ends are present.[78] Thus, an acyl species *trans* to a phosphane ligand reacts relatively slowly[79] with water or an alcohol as the nucleophile, whereas insertion reactions are fast. In monophosphane systems, the group *trans* to acyl is a solvent molecule and in this case insertion reactions are slower and the acyl group is more susceptible to nucleophilic attack due to the smaller *trans* influence.

Conclusion

The reports that we have reviewed herein have shown that the hydroxycarbonylation reaction involves a palladium hydride mechanism and that palladium hydride, palladium alkyl, and palladium acyl are the intermediates of this reaction.

Previous kinetic and deuterium labelling studies proved the involvement of a β-elimination reaction. We have now performed in situ HPNMR experiments on different systems. Pd^0, palladium hydride, and palladium acyl species were observed during the hydroxycarbonylation reaction. We propose an equilibrium between the Pd^0 and the palladium acyl species in a catalytic cycle.

Control of the regioselectivity of the hydroxycarbonylation has proved to be dependent on the phosphorus ligand, the counteranion, the pressure, and the temperature. The regioselectivity remains a complicated issue and equilibration between several intermediates seems likely to play a major role, except in the case of diphosphane systems, where steric hindrance leads to predominantly irreversible, linear alkyl formation.

Acknowledgments

We thank the Spanish Ministerio de Educación y Ciencia for financial support (DGES PB-97-0407-C05-01) and the Generalitat de Catalunya (CIRIT) for awarding a research grant (to I. del Río). We thank Ramon Guerrero and J. Chris Slootweg for their helpful contributions.

---

[1] R. A. Sheldon, *Organic Synthesis – Past, Present and Future*, *Chem. Ind.* **1992**, 903–906.
[2] P. W. N. M. van Leeuwen, G. van Koten, in *Catalysis: An Integrated Approach* (Eds.: R. A. van Santen, P. W. N. M. van Leeuwen, J. A. Moulijn, B. A. Averill), Elsevier, Amsterdam, **1999**, 2nd edition, chapter 6.2.
[3] M. Beller, B. Cornils, C. D. Frohning, C. W. Kohlpaintner, *J. Mol. Catal.* **1995**, *104*, 17–85.
[4] P. W. N. M. van Leeuwen, C. Claver, *Recent Advances in Rhodium-Catalyzed Hydroformylation*, Kluwer Academic Publishers, CMC series vol. 22, Dordrecht, **2000**.
[5] B. E. Ali, H. Alper, in: *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Willey-VCH, Weinheim, **1998**, chapter 2.2.
[6] A. Höhn, in: *Applied Homogeneous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Herrmann), VCH, Weinheim, **1996**.
[7] E. Drent, P. H. M. Budzelaar, *J. Organomet. Chem.* **2000**, *593–594*, 211–225.
[8] V. N. Zudin, V. D. Chinakov, V. M. Nekipelov, V. A. Rogov, V. A. Likholobov, Y. I. Yermakov, *J. Mol. Catal.* **1989**, *52*, 27–43.
[9] E. Drent, P. H. M. Budzelaar, *Chem. Rev.* **1996**, *96*, 663–681.
[10] [10a] E. Drent (Shell), EP 55 857, **1981**. – [10b] E. Drent, L. Petrus, S. A. J. van Langen (Shell), EP 282 142, **1988**.
[11] [11a] C. Botteghi, S. Paganelli, A. Schionato, M. Marchetti, *Chirality* **1991**, *3*, 355–369. – [11b] J.-P. Rieu, A. Boucherle, H. Cousse, G. Mouzin, *Tetrahedron* **1986**, *42*, 4095–4131.
[12] C. W. Lee, H. Alper, *J. Org. Chem.* **1995**, *60*, 250–252.
[13] K. Nozaki, M. L. Kantam, T. Horiuchi, H. Takaya, *J. Mol. Catal.* **1997**, *118*, 247–253.
[14] S. Oi, M. Nomura, T. Aiko, Y. Inoue, *J. Mol. Catal.* **1997**, *115*, 289–295.
[15] D. Zim, R. F. de Souza, J. Dupont, A. L. Monteiro, *Tetrahedron Lett.* **1998**, *39*, 7071–7074.
[16] W. Clegg, G. R. Eastham, M. R. J. Elsegood, R. P. Tooze, X. L. Wang, K. Whiston, *Chem. Commun.* **1999**, 1877–1878.
[17] R. F. Heck, *J. Am. Chem. Soc.* **1972**, *94*, 2712–2716.
[18] J. Knifton, *J. Org. Chem.* **1976**, *41*, 793–797.
[19] G. Cavinato, L. Toniolo, *J. Organomet. Chem.* **1990**, *398*, 187.
[20] D. Milstein, *Acc. Chem. Res.* **1988**, *21*, 428–434.
[21] M. Kawana, S. Nakamura, E. Watanabe, H. Urata, *J. Organomet. Chem.* **1997**, *542*, 185–189.
[22] S. Otsuka, A. Nakamura, T. Yoshida, M. Naruto, K. Ataka, *J. Am. Chem. Soc.* **1973**, *95*, 3180–3188.
[23] I. del Río, N. Ruiz, C. Claver, L. A. van der Veen, P. W. N. M. van Leeuwen, *J. Mol. Catal.* **2000**, *161*, 39–48.
[24] I. del Río, N. Ruiz, C. Claver, *Inorg. Chem. Commun.* **2000**, *3*, 166–168.
[25] F. Morandini, G. Consiglio, F. Wenzinger, *Helv. Chim. Acta* **1979**, *62*, 59–61.
[26] K. Bittler, N. V. Kutepow, D. Neubauer, H. Reis, *Angew. Chem.* **1968**, *80*, 329–335.
[27] [27a] C. Amatore, A. Jutand, M. J. Medeiros, *New J. Chem.* **1996**, *20*, 1143–1148. – [27b] C. Amatore, E. Carré, A. Jutand, M. A. M‘Barki, *Organometallics* **1995**, *14*, 1818–1826. – [27c] F. Ozawa, A. Kubo, T. Hayashi, *Chem. Lett.* **1992**, 2177–2180.
[28] Z. Csákai, R. Skoda-Földes, L. Kollár, *Inorg. Chim. Acta* **1999**, *286*, 93–97.
[29] G. Verspui, I. I. Moiseev, R. A. Sheldon, *J. Organomet. Chem.* **1999**, *586*, 196–199.
[30] G. R. Eastham, B. T. Heaton, J. A. Iggo, R. P. Tooze, R. Whyman, S. Zacchini, *Chem. Commun.* **2000**, 609–610.
[31] D. Milstein, *J. Chem. Soc., Chem. Commun.* **1986**, 817–818.
[32] K. Y. J. Kim, K. Osakada, K. Sugita, T. Yamamoto, A. Yamamoto, *Organometallics* **1988**, *7*, 2182–2188.
[33] G. P. C. M. Dekker, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, C. F. Roobeek, *J. Organomet. Chem.* **1992**, *430*, 357–372.
[34] P. W. N. M. van Leeuwen, W. L. Groeneveld, *Inorg. Nucl. Chem. Lett.* **1967**, *3*, 145–146.
[35] A. Seayad, S. Jayasree, K. Damodaran, L. Toniolo, R. V. Chaudhari, *J. Organomet. Chem.* **2000**, *601*, 100–107.
[36] P. M. Maitlis, *The Organic Chemistry of Palladium*, Academic Press, New York, **1971**, vols. 1 and 2.
[37] J. Tsuji, *Organic Synthesis with Palladium Compounds*, Springer-Verlag, New York, **1980**.
[38] R. F. Heck, *Palladium Reagents in Organic Synthesis*, Academic Press, New York, **1985**.
[39] B. M. Trost, *Chem. Eur. J.* **1998**, *4*, 2405–2412.
[40] V. V. Grushin, *Chem. Rev.* **1996**, *96*, 2011–2033.
[41] F. A. Lewis, *Platinum Met. Rev.* **1994**, *38*, 112.
[42] J. C. Bailar, H. Itatani, *Inorg. Chem.* **1965**, *4*, 1618–1620.
[43] K. Kudo, M. Hidal, T. Murayama, Y. Uchida, *Chem. Commun.* **1970**, 1701–1702.
[44] M. L. Scheneider, H. M. M. Shearer, *J. Chem. Soc., Dalton Trans.* **1973**, 354–356.
[45] R. F. Jones, J. R. Fisher, D. J. Cole-Hamilton, *J. Chem. Soc., Dalton Trans.* **1981**, 2550–2555.
[46] J. Grévin, P. Kalck, *J. Organomet. Chem.* **1994**, *476*, C23–C24.
[47] M. L. H. Green, H. Munakata, *J. Chem. Soc., Chem. Commun.* **1971**, 549.
[48] V. N. Zudin, V. D. Chinakov, V. M. Nekipelov, V. A. Likholobov, Y. I. Yermakov, *J. Organomet. Chem.* **1985**, *289*, 425–430.
[49] D. Braga, P. Sabatino, C. Bugno, P. Leoni, M. Pasquali, *J. Organomet. Chem.* **1987**, *334*, C46–C48.
[50] M. Sommovigo, M. Pasquali, P. Leoni, P. Sabatino, D. Braga, *J. Organomet. Chem.* **1991**, *418*, 119–126.
[51] P. Leoni, M. Sommovigo, M. Pasquali, S. Midollini, D. Braga, P. Sabatino, *Organometallics* **1991**, *10*, 1038–1044.
[52] I. Tóth, C. J. Elsevier, *Organometallics* **1994**, *13*, 2118–2122.
[53] M. Portnoy, D. Milstein, *Organometallics* **1994**, *13*, 600–609.
[54] P. J. Perez, J. C. Calabrese, E. Bunel, *Organometallics* **2001**, *20*, 337–345.
[55] J. Knifton, *J. Org. Chem.* **1976**, *41*, 2885–2890.
[56] G. Cavinato, L. Toniolo, C. Botteghi, S. Gladiali, *J. Organomet. Chem.* **1982**, *229*, 93–100.
[57] G. Cavinato, L. Toniolo, C. Botteghi, *J. Mol. Catal.* **1985**, *32*, 211.
[58] Y-S. Lin, A. Yamamoto, *Organometallics* **1998**, *17*, 3466–3478.
[59] P. Fitton, J. E. McKeon, B. C. Ream, *Chem. Commun.* **1969**, 370–371.
[60] P. Fitton, M. P. Johnson, J. E. McKeon, *Chem. Commun.* **1968**, 6–7.
[61] A. C. Albéniz, N. M. Catalina, P. Espinet, R. Redón, *Organometallics* **1999**, *18*, 5571–5576.
[62] J. P. Flemming, M. C. Pilon, O. Y. Borbulevitch, M. Y. Antipin, V. V. Grushin, *Inorg. Chim. Acta* **1998**, *280*, 87–98.
[63] G. Gatti, J. A. López, C. Mealli, A. Muso, *J. Organomet. Chem.* **1994**, *483*, 77–89.
[64] F. C. Rix, M. Brookhart, P. S. White, *J. Am. Chem. Soc.* **1996**, *118*, 2436–2448.
[65] B. Bardi, A. Del Pra, A. M. Piazzesi, L. Toniolo, *Inorg. Chim. Acta* **1979**, *35*, L345–L346.
[66] Y. G. Noskov, M. I. Terekhova, E. S. Petrov, *Kinet. Katal.* **1993**, *34*, 1001–1004.
[67] S. C. A. Nefkens, M. Sperrle, G. Consiglio, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1719–1720.
[68] C. Bianchini, G. Mantovani, A. Meli, W. Oberhauser, P. Brügeller, T. Stampfl, *J. Chem. Soc., Dalton Trans.* **2001**, 690–698.
[69] E. Drent, J. A. M. van Broekhoven, M. J. Doyle, *J. Organomet. Chem.* **1991**, *417*, 235–251.

[70] G. P. C. M. Dekker, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, *Organometallics* **1992**, *11*, 1598−1603.
[71] I. Tóth, C. J. Elsevier, *J. Am. Chem. Soc.* **1993**, *115*, 10388−10389.
[72] I. Tóth, C. J. Elsevier, *Chem. Commun.* **1993**, 529−531.
[73] H. E. Bryndza, J. C. Calabrese, M. Marsi, D. C. Roe, W. Tam, J. E. Bercaw, *J. Am. Chem. Soc.* **1986**, *108*, 4805−4813.
[74] G. P. C. M. Dekker, A. Buijs, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, W. J. J. Smeets, A. L. Spek, Y. F. Wang, C. H. Stam, *Organometallics* **1992**, *11*, 1937−1948.
[75] P. W. N. M. van Leeuwen, C. F. Roobeek, H. van der Heiden, *J. Am. Chem. Soc.* **1994**, *116*, 12117−12118.
[76] P. W. N. M. van Leeuwen, C. F. Roobeek, *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 73−75.
[77] G. A. Luinstra, P. H. P. Brinkmann, *Organometallics* **1998**, *17*, 5160−5165.
[78] W. P. Mul, H. Oosterbeek, G. A. Beitel, G.-J. Kramer, E. Drent, *Angew. Chem. Int. Ed.* **2000**, *39*, 1848−1851.
[79] M. A. Zuideveld, P. C. J. Kamer, P. W. N. M. van Leeuwen (to be published).
[80] M. C. Bonnet, A. L. Monteiro, I. Tkatchenko, *J. Mol. Catal.* **1999**, *143*, 131−136.
[81] E. J. Jang, K. H. Lee, J. S. Lee, Y. G. Kim, *J. Mol. Catal.* **1999**, *138*, 25−36.
[82] T. Hayashi, M. Tanaka, I. Ogata, *J. Mol. Catal.* **1984**, *26*, 17−30.
[83] G. Cometti, G. P. Chiusoli, *J. Organomet. Chem.* **1982**, *236*, C31−C32.
[84] J.-Y. Yoon, E. J. Jang, K. H. Lee, J. S. Lee, *J. Mol. Catal.* **1997**, *118*, 181−187.
[85] D. M. Fenton, *J. Org. Chem.* **1973**, *38*, 3192−3198.
[86] D. Kruis, N. Ruiz, M. D. Janssen, J. Boersma, C. Claver, G. van Koten, *Inorg. Chem. Commun.* **1998**, *1*, 295−298.
[87] W. Clegg, G. R. Eastham, M. R. Elsegood, R. P. Tooze, X. L. Wang, K. Whiston, *Chem. Commun.* **1999**, 1877−1878.
[88] J. G. Knight, S. Doherty, A. Harriman, E. G. Robins, M. Betham, G. R. Eastham, R. P. Tooze, M. R. J. Elsegood, P. Champkin, W. Clegg, *Organometallics* **2000**, *19*, 4957−4967.
[89] G. Consiglio, M. Marchetti, *Chimia* **1976**, *30*, 26−27.
[90] G. Consiglio, S. C. A. Nefkens, C. Pisano, F. Wenzinger, *Helv. Chim. Acta* **1991**, *74*, 323−325.
[91] Y. Sugi, K. Bando, *Chem. Lett.* **1976**, 727−730.
[92] G. Consiglio, *J. Organomet. Chem.* **1977**, *132*, C26−C28.
[93] B. E. Ali, H. Alper, *J. Mol. Catal.* **1993**, *80*, 377−381.
[94] M. I. Terekhova, E. S. Petrov, *J. Gen. Chem. USSR* **1985**, *55*, 842−843.
[95] M. I. Terekhova, T. E. Kron, Y. G. Noskov, E. S. Petrov, *Neftekhimiya* **1996**, *36*, 330−335.
[96] Y. V. Tel'Naya, Y. G. Noskov, E. S. Petrov, *Zh. Obshch. Khim.* **1995**, *65*, 1391−1392.
[97] H. Zhou, J. Hou, J. Cheng, S. Lu, H. Fu, H. Wang, *J. Organomet. Chem.* **1997**, *543*, 227−228.
[98] B.-H. Xie, C.-G. Xia, S.-J. Lu, K. J. Chen, Y. Kou, Y.-Q. Yin, *Tetrahedron Lett.* **1998**, 7365−7368.
[99] B. E. Ali, H. Alper, *J. Mol. Catal.* **1992**, *77*, 7−13.
[100] T. Fuchikami, K. Ohishi, I. Ojima, *J. Org. Chem.* **1983**, *48*, 3803−3807.
[101] C. Pisano, A. Mezzetti, G. Consiglio, *Organometallics* **1992**, *11*, 20−22.
[102] S. Tilloy, E. Monflier, F. Bertoux, Y. Castanet, A. Mortreux, *New J. Chem.* **1997**, *21*, 529−531.
[103] B. E. Ali, H. Alper, *J. Mol. Catal.* **1993**, *80*, 377−381.
[104] Y. G. Noskov, E. S. Petrov, *Kinet. Catal.* **1993**, *34*, 902−908.
[105] Y. G. Noskov, E. S. Petrov, *Kinet. Catal.* **1994**, *35*, 672−677.
[106] Y. G. Noskov, E. S. Petrov, *Kinet. Catal.* **1997**, *38*, 520−526.
[107] T. A. Kron, Y. G. Noskov, M. I. Terekhova, T. S. Petrov, *Zh. Fiz. Chim.* **1996**, *70*, 82−86.
[108] A. Seayad, A. A. Kelkar, R. V. Chaudhari, L. Toniolo, *Ind. Eng. Chem. Res.* **1998**, *37*, 2180−2187.
[109] C. Benedek, G. Szalontai, A. Gömöry, S. Tõrös, B. Heil, *J. Organomet. Chem.* **1999**, *579*, 147−155.
[110] C. Benedek, S. Tõrös, B. Heil, *J. Organomet. Chem.* **1999**, *586*, 85−93.
[111] I. Cipres, J. Jenck, P. Kalck, *J. Mol. Catal.* **1990**, *58*, 387−392.
[112] M. Gómez, G. Muller, D. Sainz, *Organometallics* **1991**, *10*, 4036−4045.
[113] R. Lazzaroni, R. Settambolo, A. Raffaelli, S. Pucci, G. Vitulli, *J. Organomet. Chem.* **1988**, *339*, 357−365.
[114] R. Lazzaroni, A. Raffaelli, R. Settambolo, S. Bertozzi, G. Vitulli, *J. Mol. Catal.* **1989**, *50*, 1−9.
[115] J. Real, E. Prat, S. González-Cabello, M. Pagès, A. Polo, *Organometallics* **2000**, *19*, 4715−4719.
[116] C. Bianchini, H. M. Lee, A. Meli, F. Vizza, *Organometallics* **2000**, *19*, 849−853.
[117] I. del Río, O. Pàmies, P. W. N. M. van Leeuwen, C. Claver, *J. Organomet. Chem.* **2000**, *608*, 115−121.
[118] K. Nozaki, T. Hiyama, S. Kacker, I. T. Horváth, *Organometallics* **2000**, *19*, 2031−2035.
[119] C. Amatore, G. Broeker, A. Jutand, F. Khalil, *J. Am. Chem. Soc.* **1997**, *119*, 5176−5185.
[120] J. Keijsper, P. Arnoldy, M. J. Doyle, *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 248−255.
[121] M. Sperrle, G. Consiglio, *Chem. Ber./Recueil* **1997**, *130*, 1557−1565.
[122] R. Eastham, B. T. Heaton, J. A. Iggo, R. P. Tooze, R. Whyman, S. Zacchini, *Chem. Commun.* **2000**, 609−610.
[123] R. P. Tooze, K. Whiston, A. P. Malyan, M. J. T. Taylor, N. W. Wilson, *J. Chem. Soc., Dalton Trans.* **2000**, 3441−3444.
[124] R. J. van Haaren, H. Oevering, G. P. F. van Strijdonck, P. C. J. Kamer, P. W. N. M. van Leeuwen (to be published).

Received March 20, 2001
[I01103]