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Review

Advances in transition-metal catalyzed hydroxycarbonylation reactions in aqueous-organic two-phase system

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Abstract

A survey of the literature related to the aqueous organometallic chemistry and catalysis shows that the interest in the carbonylation reactions in two-phase systems has remarkably grown during the five last years and that most of carbonylation reactions conducted in homogeneous medium, i.e., the carbonylation of benzyl chloride, bromobenzene, allylic halides, phenethylbromide and olefins have been successfully applied under biphasic conditions. With allylic halides and benzyl alcohol, the catalytic activities appear even much higher than those obtained in homogeneous systems. Nevertheless the lack of stability of palladium–water soluble phosphine based catalyst often observed limits its reuse and constitutes at the present the major drawback of these processes. © 1999 Elsevier Science B.V. All rights reserved.

1. Introduction

Nowadays, environmental factors in addition to economic motives are more and more taken into consideration as driving force for technological innovations in the chemical industry. In this context, homogeneous catalysis can be regarded as particularly attractive. Indeed, the main advantage of homogeneous catalysis in comparison to its heterogeneous counterpart is that high activities and high selectivities can be achieved under mild conditions by tuning the coordination sphere of the metal. However, the major drawback of homogeneous catalytic systems is the difficulty to separate the catalyst (often based on expensive noble metal) from the reaction products and its recovery in an active form.

Among the different attempts to overcome this problem, the recourse of liquid–liquid two-phase system seems the more elegant and attractive one. Actually, in such a process, the catalyst is dissolved in a liquid phase that is immiscible with the phase that contains the substrate and reaction products. At the end of the reaction, a simple decantation allows to separate the phases and the catalytic system can be recycled [1]. Due to its immiscibility with most organic

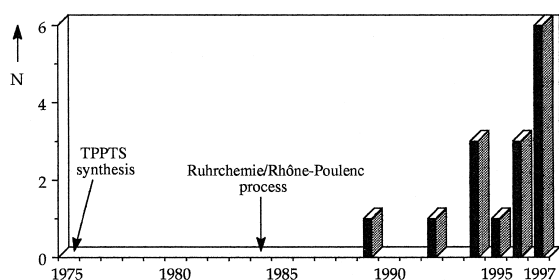* Corresponding author: Fax: +33-3-2179-1717; E-mail: monflier@univ-artois.fr

Fig. 1. Number (N) of publications annually on carbonylation reactions in two-phase system (excluding patent applications and hydroformylation).

compounds, water appears as a very appropriate solvent for the catalytic system [2]. Moreover, water minimizes the environmental impact of the process owing to its non-toxicity, non-flammability and the lack of odor. Transition metal complexes are generally dissolved in water by using ligands bearing polar substituents such as $-SO_3Na$, $-COONa$, $-NR_3^+X^-$ and $-(RO)_nR$ [3,4]. The industrial feasibility of this approach has been demonstrated in 1984 by Ruhrchemie with the hydroformylation of propylene by using the water-soluble ligand tris(sodium-*m*-sulfonatophenyl) phosphine (TP-PTS) discovered by Cornils et al. [5] and in 1975 by Kuntz [6–8].

Despite the numerous advantages of the biphasic catalysis and the importance of carbonylation processes in homogeneous medium [9,10], only little work has been devoted to the carbonylation reactions in an aqueous-organic two-phase system and most of it has been published these five last years as shown in Fig. 1.

Our aim is to review these carbonylation reactions and to discuss the efficiency of these biphasic processes. We will report in a first part *the carbonylation of organic halides*, in a second part *the carbonylation of alcohols* and, finally, *the hydroxycarbonylation of olefins*.

2. Hydroxycarbonylation of organic halides in aqueous-organic two-phase medium

In homogeneous medium, aryl, alkyl, vinyl or allyl halides can be easily carbonylated to

$$RX + CO + NuH \xrightarrow[\text{base}]{\text{"Cata"}} RCONu + (baseH)X$$

$$Nu = OH, R'O, H, NR_2 \ldots$$
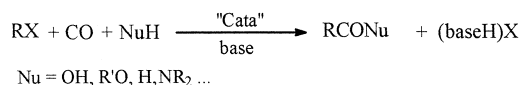
Scheme 1. Overview of transition-metal catalyzed carbonylations of organic halides.

lead to a wide variety of products such as aldehydes, esters, acids, amides, ketoesters, according to the nature of the nucleophilic group used as co-reagent [11] (Scheme 1).
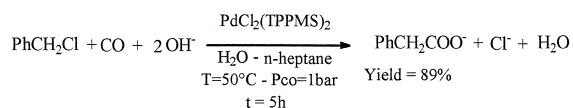
With water the reaction affords organic acids which are recovered in the presence of an excess of base as their carboxylate forms in aqueous phase. This behavior has given rise to aqueous-organic two-phase processes in which the catalyst is dissolved in organic medium and remains in this phase while the reaction products are recovered in aqueous phase [12]. Numerous works have been devoted to this process in which addition of a phase transfer agent is generally needed to improve the yield [13].

We will only focus our attention here on biphasic carbonylation reactions where water soluble ligands maintain the catalyst in the aqueous phase during the whole reaction course.

2.1. Two-phase carbonylation of benzyl, aryl and allyl halides catalysed by water-soluble phosphine complexes of palladium

2.1.1. Carbonylation of benzyl chloride and related compounds

The first example of carbonylation using a catalyst in solution in the aqueous phase has been reported by Okano et al. [14,15]. It relates to the carbonylation of benzyl chloride into phenyl acetic acid using sodium diphenylphosphino-benzene-*m*-sulfonate (TPPMS) as water soluble ligand and $PdCl_2(TPPMS)_2 3H_2O$, **1** [16] as catalyst (Scheme 2). The catalytic system and

$$PhCH_2Cl + CO + 2\,OH^- \xrightarrow[\substack{H_2O - n\text{-heptane} \\ T=50°C - P_{co}=1bar \\ t = 5h}]{PdCl_2(TPPMS)_2} PhCH_2COO^- + Cl^- + H_2O$$

Yield = 89%

Scheme 2. Palladium catalyzed carbonylation of benzyl chloride.

Table 1
Carbonylation of benzyl chloride and various derivatives using biphasic systems

Substrate	Catalytic system	Ligand added	Solvent	Selectivity (%)	Yield (%)	Ref.
BC	PdCl$_2$(TPPMS)$_2$	no	Heptane	90	89	[14,15]
BC	PdCl$_2$(PPh$_3$)$_2$	no	Heptane	13	2.3	[14,15]
BC	PdCl$_2$(TPPMS)$_2$	no	C$_6$H$_6$	96	93	[14,15]
BC	PdCl$_2$(TPPMS)$_2$	no	Anisole	98	92	[14,15]
BC	PdCl$_2$(PPh$_3$)$_2$	no	Anisole	94	61	[14,15]
BC	Pd(OAc)$_2$	TPPTS	o-Xylene	92	88	[17]
4-FBC	Pd(OAc)$_2$	TPPTS	o-Xylene	82	82	[17]
2-FBC	PdCl$_2$	TPPTS	o-Xylene	96	94	[17]
2-MBC	Pd(OAc)$_2$	TPPTS	o-Xylene	84	84	[17]
2-CBC	PdCl$_2$	TPPTS	o-Xylene	82	80	[17]
4-CBC	PdCl$_2$	TPPTS	o-Xylene	86	83	[17]
BC	Pd(OAc)$_2$	BINAS	Toluene	98	97	[17]
BC	Pd(OAc)$_2$	BINAS	Toluene	74	63	[17]

BC = benzyl chloride, 2-FBC = 2-fluorobenzyl chloride, 4-FBC = 4-fluorobenzyl chloride, 2-MBC = 2-methylbenzyl chloride, 2-CBC = 2-chlorobenzyl chloride, 4-CBC = 4-chlorobenzyl chloride.
Other conditions: see Refs. [14,15,17].

the substrate are dissolved in an aqueous solution of sodium hydroxide (2.5 eq. of NaOH vs. substrate) and in an organic phase, respectively. The reaction is carried out under very mild conditions (1 bar CO, 50°C) to afford phenyl acetic acid (after acidification of the aqueous phase and extraction) with a high yield varying between 89 and 93% according to the solvent (see Table 1). In each case an induction period is observed. Its length increases with the free phosphine concentration initially introduced.

Performed in homogeneous organic medium with PdCl$_2$(PPh$_3$)$_2$ as catalytic precursor, the yields are worse and increase with the polarity of the solvent.

More recently, similar results (91% yield of phenyl acetic) were obtained by using Na$_2$[Ph$_2$-P(4-C$_6$H$_4$PO$_3$)] · 1.5 H$_2$O, **2** as water soluble ligand and PdCl$_2$ as catalytic precursor [18]. However, in this report as in the former, no attention was paid on the reuse of the catalytic system. Nevertheless important leaching of catalyst in organic phase can be feared according to the amphiphilic character of TPPMS and of the hybrid phosphine–phosphonate ligand **2**.

From these reasons, the reaction was reinvestigated using as ligands the water-soluble phosphines TPPTS and BINAS (Scheme 3) which

are much less miscible in common organic solvent than TPPMS or **2** [17,19].

With these phosphines, the carbonylation of benzyl chloride and of various fluoro or chloro substituted homologues is still achieved in high yield (see Table 1), but a high phosphine to Pd ratio (5:1) is needed to avoid rapid deactivation of the catalyst. These results show that the high efficiency observed previously with TPPMS or **2** is not connected with their amphiphilic character.

Interestingly the Pd(II)-TPPTS or Pd(II)-BINAS systems are still active at a pH of about two in contrast with the conventional biphasic process (catalyst dissolved in the organic phase). So, if the amount of base initially introduced is
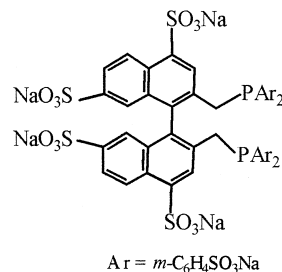
Scheme 3. Bis(disulfonatophenylphosphinomethyl)tetrasulfonatobinaphthene (BINAS).

adjusted to obtain a pH close to this value at the end of the reaction, more than 99% of the phenyl acetic acid sodium salt formed is protonated and dissolved in the organic phase. Therefore, a simple phases separation allows the isolation of the reaction products after solvent evaporation and the recovery of the catalytic system (Scheme 4).

Owing to the easy separation of the reaction products and the catalytic phase, in an industrial outlook, the reuse of the catalytic system was thoroughly investigated with the system Pd-BINAS [17,20,21]. It appears that addition of the quantity of base needed to adjust the pH of aqueous catalytic solution to seven is sufficient to make a second run. However, conversion and selectivity are slightly lower than in the first run. The efficiency of the reaction still decreases more markedly after the third recovery since practically no conversion occurs. Addition of a fresh catalyst and ligand charge to aqueous phase has the effect to restore high conversion and selectivity proving that the deactivation is not due to the change of the reaction medium. It was also observed that the deactivation takes place more rapidly when the substrate to palladium ratio increases. Indeed, the maximum achievable turnover number of the catalyst varies between about 300 and 1200 when the initial substrate concentration in the organic phase decreases from 4 mol l^{-1} to 0.8 mol l^{-1}.

From a mechanistic point of view, it is generally accepted that palladium catalyzed carbonylation of benzyl halides starts with the oxidative addition of the substrate to a coordinatively unsatured Pd(0) species. The induction period

observed with TPPMS, TPPTS or BINAS could be assigned to the reduction of the Pd(II) precursor into the active Pd(0) species. For instance when $PhCH_2PdCl(TPPMS)_2$, supposed to be the key intermediate in the catalytic cycle, is synthesized separately [22] and used as catalyst under the same conditions as the Pd-TPPMS system no induction period is observed [14,15]. It is, however, noteworthy that recently, Papadogianakis et al. have reported the rapid reduction of $[PdCl(TPPTS)_3]^+$ to $Pd(TPPTS)_3$ under CO pressure (2 bar) [23]. Next steps could involve CO coordination and insertion to give an acyl palladium species. Subsequent nucleophilic attack of a hydroxide ion on the acyl group or chloride–hydroxide exchange followed by reductive elimination affords phenyl acetic acid. The catalyst decay is presumed to occur via the formation of inactive palladium agglomerates. Initially, while their size is sufficiently small, these Pd aggregates are stabilized by TPPTS and some catalytic activity might be preserved. During the reaction course, aggregation of palladium continues with a rate that increases with temperature. When the size of the Pd particle is to high, it cannot be maintained in solution by the ligand and precipitation into inactive palladium black starts, all the more easily as the ligand to Pd ratio is low.
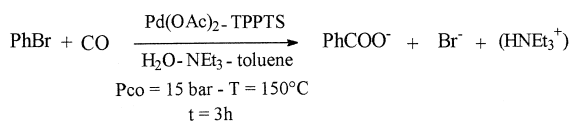
2.1.2. Hydroxycarbonylation of bromobenzene

As carbonylation of aryl chlorides under homogeneous conditions remains difficult and requires basic [24] or specially designed phosphines [25] or activation of the C–Cl bond [26], transposition of the reaction under biphasic conditions was checked with bromobenzene as model representative of this class of compound. Monteil et al. used this substrate with $Pd(OAc)_2$ as catalytic precursor and TPPTS as water soluble ligand [27,28]. The reaction is performed under 15 bar of CO pressure with triethylamine as base (2.2 eq. vs. substrate, Scheme 5).

The catalytic system is only active at a temperature higher than 120°C. Above 170°C the selectivity markedly decreases by formation of
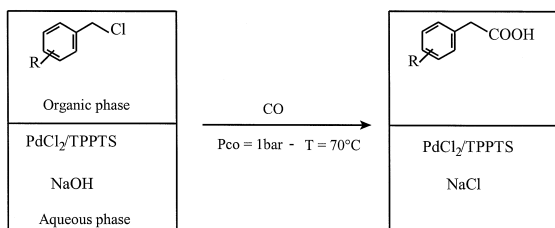
Scheme 4. Carbonylation of benzyl chloride with the Pd/TPPTS catalytic system.

$$PhBr + CO \xrightarrow[\substack{H_2O-NEt_3-toluene \\ Pco = 15\ bar - T = 150°C \\ t = 3h}]{Pd(OAc)_2-TPPTS} PhCOO^- + Br^- + (HNEt_3^+)$$

Scheme 5. Palladium catalyzed hydroxycarbonylation of bromobenzene.

by-products especially $PhCONEt_2$. A temperature of 150°C seems the best compromise. However, at this temperature, the stability of the catalytic system and consequently its efficiency requires the presence of a large excess of free phosphine. Indeed using a P/Pd ratio of five leads to the formation of Pd black and the conversion remains very low ($< 20\%$). For a P/Pd ratio = 12.5 or more, a total conversion is obtained. Moreover, the aqueous phase at the end of the reaction remains yellow and the Pd complex is recovered intact as proved by ^{31}P NMR analysis.

Under these conditions an induction period of about 1 h is again observed and the reaction is complete after about 3 h (giving a TOF of 17 h^{-1}). Decantation of organic and aqueous phase is very easy but benzoic acid is obtained in its ammonium benzoate form dissolved in the aqueous phase, according to the excess of base used. Attempts to reuse this aqueous phase after addition of a new charge of bromobenzene and base was done. In a second run, carbonylation recurs but palladium is recovered as black precipitate despite the great excess of TPPTS used. ^{31}P NMR analysis of the aqueous phase shows mainly the presence of TPPTS oxide (OTPPTS) and $OPPh(m-C_6H_4SO_3Na)_2$ (OTPPDS). It should be noticed that these oxidations or transformation of TPPTS into OTPPTS or OTPPDS do not occur in the absence of palladium.

Moreover, inspired from the well admitted mechanism of methoxycarbonylation of aryl halides [29], the oxidative addition of bromobenzene on $Pd(TPPTS)_3$ [30] and the carbonylation of the resulting complex have been investigated [27,28]. At 35°C in methanol, bromobenzene slowly reacts (15 h) with $Pd(TPPTS)_3$ to give a white precipitate identified as PhPd-
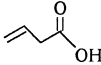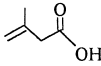
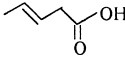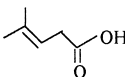$Br(TPPTS)_2$, **3**. In water, complex **3** rapidly evolves giving a deep-garnet solution. The ^{1}H NMR spectrum of a solution of **3** in D_2O is consistent with the presence of a [PhPd-$(TPPTS)_2$] fragmen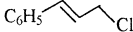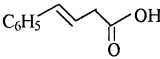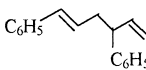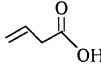t. By direct addition of PhBr to $Pd(TPPTS)_3$ in water, the same garnet complex is obtained as shown by its IR and NMR spectra. From these facts the formula Ph-$PdX(TPPTS)_2$, **4** (where X = OH or H_2O) was assigned to the garnet complex. This complex **4** can be easily carbonylated under ambient condition to lead to $Pd(COPh)X(TPPTS)_2$ (X = OH or H_2O). Its ^{31}P NMR spectrum is consistent with the one of $Pd(COPh)Br(TPPTS)_2$ prepared by ligand exchange in water–chloroform medium from the homologue $Pd(COPh)Br-(PPh_3)_2$. Thus, its appears that the carbonylation of a palladium phenyl bond is easier than the oxidative addition to palladium(0) species [31]. Moreover, as the same intermediates as in organic phase have been synthesized and characterized, one can assume that the catalytic cycle in aqueous phase is similar to the one previously published [29] except that in water the Br ligand of complex **3** is readily exchanged by an hydroxy or an aqua ligand.

2.1.3. Allylic halides

The catalytic system $PdCl_2(TPPMS)_2$ used by Okano et al. for the carbonylation of benzyl chloride [14,15] under biphasic conditions has also been tested by the same group for the carbonylation of various allylic halides in aqueous organic two-phase media (Table 2, Scheme 6) [32,33].

In the presence of a base, a rapid reaction takes place under very mild conditions ($P_{CO} = 1$ bar, $T = 30°C$) to give mainly β,γ unsaturated acids with yields varying between high to moderate. Interestingly, the yield is generally higher with allylic chlorides than with the bromides. This behaviour is attributed to the fact that allylic bromides are more prone to hydrolysis under these conditions. As the reaction is carried out in the absence of mass transfer agent, the influence of the nature of the organic sol-

Table 2
Carbonylation of allylic halides under biphasic conditions

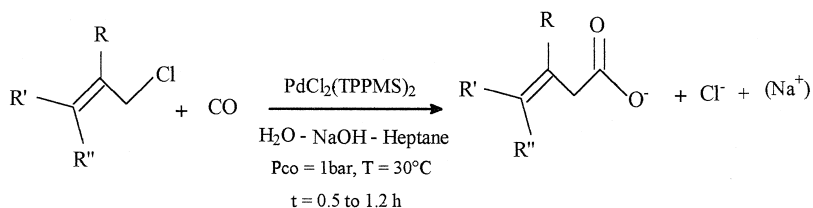| Allylic halide	Catalyst	t (h)	Products (Yields %)		Ref
Allyl bromide	PdCl$_2$(TPPMS)$_2$	1.2	(63)		[32]
(methallyl chloride)	"	0.5	(73)		[32]
(crotyl chloride)	"	0.5	(73)		[32]
(prenyl bromide)	"	0.2	(4)		[33]
C$_6$H$_5$ (cinnamyl chloride)	"	1.5	C$_6$H$_5$ (47)	C$_6$H$_5$ ... C$_6$H$_5$ (21)	[32,33]
Allyl chloride	PdCl$_2$(TPPTS)$_2$	1.3	(94)		[34]

Conditions: see Refs. [32–34].

vent on the efficiency of the reaction has been checked with cinnamyl chloride. Surprisingly, the polar solvents like THF or dioxane, which are expected to improve the mass transfer, lead to a lower yield than apolar solvent such as heptane.

More recently, the system PdCl$_2$(TPPTS)$_2$-NaOH was reported as particularly efficient toward the carbonylation of allyl chloride into β,γ butenoic acid under biphasic conditions. For instance an average turnover frequency of about 1900 h^{-1} was obtained instead of 360 h^{-1} with

PdCl$_2$(PPh$_3$)$_2$ (at 40°C and 1 bar CO pressure) [34].

To explain the unusual high activity observed with the biphasic system under atmospheric CO pressure in comparison with the classical homogeneous system, Okano et al. proposed that the reaction proceeds through a different mechanism. It is generally accepted that the first step of the catalytic cycle is the formation of a η^3-allyl palladium species. In the conventional process subsequent insertion of carbon monoxide into the allyl metal bond affords an allyl–

$$\text{R'} \overset{\text{R}}{\underset{\text{R''}}{\diagup}} \text{Cl} + \text{CO} \xrightarrow[\substack{\text{H}_2\text{O - NaOH - Heptane} \\ P_{CO} = 1\text{bar, T} = 30°C \\ t = 0.5 \text{ to } 1.2 \text{ h}}]{\text{PdCl}_2(\text{TPPMS})_2} \text{R'} \overset{\text{R O}}{\underset{\text{R''}}{\diagup}} \text{O}^- + \text{Cl}^- + (\text{Na}^+)$$

Scheme 6. Palladium catalyzed carbonylation of various allylic halides.
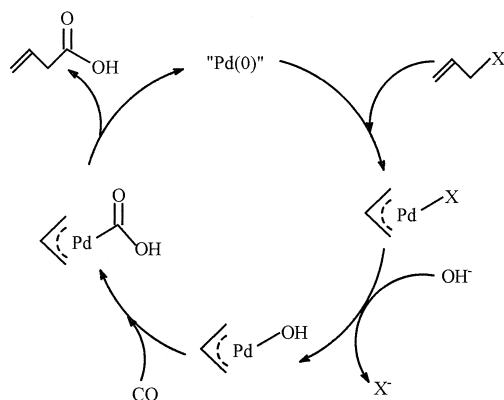
Scheme 7. Proposed catalytic cycle for the carbonylation of allylic halides.

CO–Pd complex which reacts with the nucleophile to give the reaction products [35]. However, it is known that this CO insertion into a $(\eta^3$-allyl)Pd bond is generally difficult [36]. In the case of the biphasic process, the easier formation in aqueous medium of a carboxyl-$(\eta^3$-allyl) palladium intermediate by CO insertion in a Pd–O bond is suggested. This step is followed by reductive elimination to give products and regenerate the active catalytic species (Scheme 7).

This example shows that in polar aqueous phase the catalytic intermediates could be different from those involved in organic phase. It may be deduced that using biphasic conditions could sometimes modify activity and/or selectivity for a given reaction.

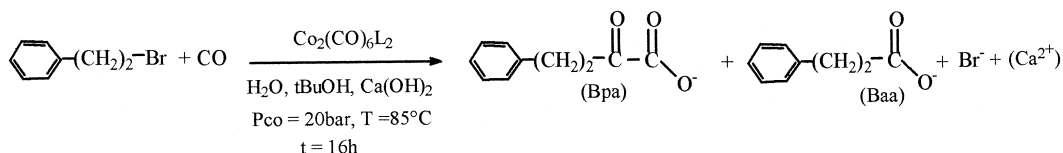## 2.2. Double vs. monocarbonylation of phenethyl bromide catalysed by water soluble cobalt complexes

In contrast with the above reactions, the carbonylation of phenethyl halides is better performed with cobalt complexes due to the very

easy β-H elimination with palladium complexes. Thus, the $Co_2(CO)_8$ catalyzed carbonylation gives benzylpyruvic acid (Bpa) or benzylacetic acid (Baa) according to the experimental conditions (Scheme 8) [37–39].

The water soluble complexes $Co_2(CO)_6(TP-PMS)_2$ and $Co_2(CO)_6(TPPTS)_2$ unlike $Co_2(CO)_6(PPh_3)_2$ are also active in carbonylation of phenethyl bromide but the benzylpyruvic acid and benzylacetic acid yields are lower than those obtained with $Co_2(CO)_8$ [40]. The use of these modified cobalt complexes induces also significant variations of the double vs. to mono carbonylation ratio. Indeed, this ratio was equal to 7, 2 and 1/3 for $Co_2(CO)_8$, $Co_2(CO)_6(TP-PTS)_2$ and $Co_2(CO)_6(TPPMS)_2$, respectively. Interestingly, the overall yield of carbonylation products and the Bpa/Baa ratio can be correlated with the $\nu(C=O)$ IR vibration of cobalt carbonyl complexes modified by water soluble ligands. As the $\nu(C=O)$ signal of the complex is considered as being representative of the basicity of the coordinated phosphine, it has been deduced that the basicity of the phosphine played a fundamental role toward the efficiency of the catalytic system and the double vs. monocarbonylation ratio [40].

3. Palladium catalyzed carbonylation of 5-hydroxymethylfurfural (HMF), benzyl alcohol and 1-(4-isobutylphenyl)ethanol (IBPE) in water

In the scope of this review it seems us also relevant to include the carbonylation of different alcohols performed with a catalytic system in solution in water even if, according to the water solubility of these substrates, biphasic condi-

Scheme 8. Cobalt catalyzed double and mono carbonylation of phenethyl bromide.
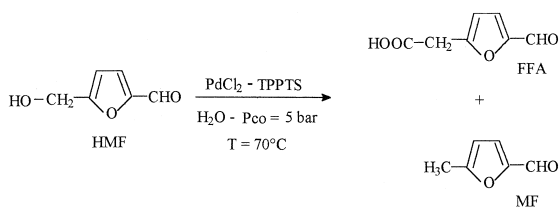
Scheme 9. Palladium catalyzed carbonylation of 5-hydroxymethylfurfural in water.

tions are not always used. Indeed the carbonylation of 5-hydroxymethylfurfural (HMF) [41,42], a compound representative of the carbohydrate class (see Scheme 9), of benzyl alcohol [43] (see Scheme 10) and 1-(4-isobutylphenyl)-ethanol (IBPE) [44,45], an ibuprofen precursor (see Scheme 11) have been successively reported by Sheldon et al.

In each case the reaction is catalyzed by the Pd/TPPTS combination dissolved in acidic aqueous medium. Interestingly with this system, the carbonylation of benzyl alcohol into phenyl acetic acid takes place under mild conditions whereas the classical hydrophobic Pd/PPh$_3$ system is practically inactive [46]. Alone, the carbonylation of activated benzyl alcohols such as 4-hydroxybenzyl alcohol is known with Pd/PPh$_3$.

The presence of both a Brønsted acid with a weakly or non coordinating anion and of TPPTS is essential to perform the reaction with a high yield. Indeed the conversion of 5-hydroxy-methylfurfural drops from 78% with p-CH$_3$C$_6$H$_4$SO$_3$H to 54% with HI. At the same time the selectivity in 5-formylfuran-2-acetic acid (FFA) decreases from 75 to 0% to the benefit of the reduction product: 5-methylfur-fural (MF) which is the only by product observed at moderate temperature and while the pH is not too low. A similar behavior is observed with IBPE: for instance in the presence of HI isobutyl styrene is obtained selectively whereas only traces are formed with p-CH$_3$C$_6$H$_4$SO$_3$H. The concentration of the acid has also a great influence on the efficiency of the reaction. In the case of IBPE the conversion

increases with increasing the amounts of p-CH$_3$C$_6$H$_4$SO$_3$H up to a maximum for a molar ratio H$^+$/IBPE = 2. At the same time the selectivity slightly decreases. However, even under the optimized conditions, the catalytic activity of Pd/TPPTS system remains low (turnover frequency = 2.3 h^{-1} instead of 950 h^{-1} with the conventional Pd/PPh$_3$ system). This low TOF has been attributed to the low solubility of IBPE in water and it has been proposed that the maximum activity observed with a relatively large amount of p-CH$_3$C$_6$H$_4$SO$_3$H could be due to the fact that this compound acts both as a protonic acid and as an amphiphilic reagent thus improving the distribution of IBPE between the organic and aqueous phase. In the same way when IBPE is dissolved in an organic phase (toluene) only traces of carbonylation products are obtained. Finally no activity is observed in the carbonylation of HMF and IBPE in the absence of TPPTS and this one increases to a maximum for a P/Pd ratio of about 6 for HMF and 10 for IBPE. Moreover other water soluble phosphines such as TPPMS, 2-pyridyl-diphenylphosphine and tris(2-pyridyl)phosphine lead to worse activities and selectivities.

The proposed catalytic cycle (see Scheme 12) to explain the carboxylic acid formation from alcohol involves as key intermediate the cationic alkyl-palladium species [R-PdL$_2$]$^+$, A which is obtained by oxidative addition of a carbenium ion (formed by reaction of the alcohol with the Brønsted acid) to Pd(TPPTS)$_3$ or by reaction of [HPdL$_3$]$^+$ with IBPE or with the olefin obtained by dehydration of IBPE. Migration of the alkyl group to the carbonyl group of the cationic alkyl-palladium intermediate [R-Pd(CO)L$_2$]$^+$, followed by a nucleophilic attack of water leads to the carboxylic acids.
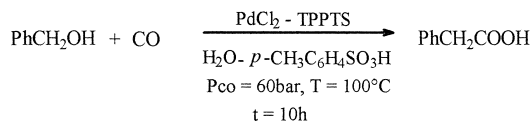
Scheme 10. Palladium catalyzed carbonylation of benzyl alcohol in water.
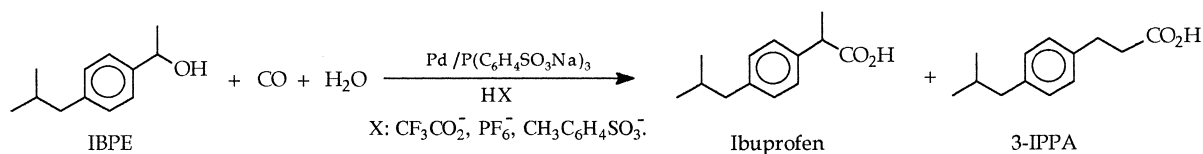
Scheme 11. Palladium catalyzed carbonylation of 1-(4-isobutylphenyl)ethanol into ibuprofen.

Intramolecular association of sulfonated substituents of the neighbouring TPPTS ligand via hydrogen bonding in aqueous phase is proposed to justify the preference of the *cis*-coordination of TPPTS in the different Pd species. In the presence of a large excess of ligand or of a Brønsted acid with a strongly coordinating anion such as I^-, the free coordination site of the intermediate A is occupied so that coordination of CO is inhibited, which explains the drop of activity observed in these cases.

An alternative mechanism in which the formation of an hydroxocarbonyl-alkyl-palladium intermediate by nucleophilic attack of water on the coordinated carbonyl group of $[R\text{-}Pd(CO)\text{-}L_2]^+$ is followed by reductive elimination of the acid cannot be totally ruled out. However, as hydroxocarbonyl species are generally readily decomposed in acidic medium, this last proposal seems less likely.

4. Palladium catalyzed hydroxycarbonylation of olefins in a two-phase system

Hydroxycarbonylation of olefins into carboxylic acids in a two-phase system has been simultaneously and independently discovered by our research group [47], by Papadogianakis et al. [48] and by Xie et al. [49]. The catalytic system consists of a TPPTS palladium complex in acidic medium and allows to achieve in high yields and selectivities the hydroxycarbonylation of a wide range of substrates such as styrene derivatives [50] and linear α-olefins [50] (Table 3, Scheme 13).

However, whereas very high activities have been observed with propene at high substrate/Pd ratio [48], hydroxycarbonylation of
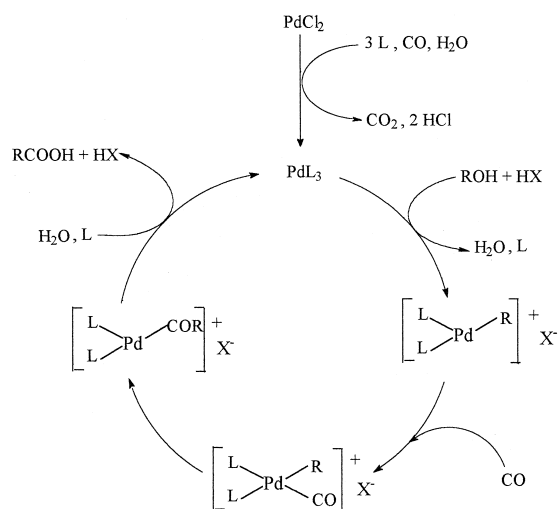
Scheme 12. Proposed catalytic cycle for carbonylation of alcohol.

Table 3
Biphasic hydroxycarbonylation of various olefins

Olefin	Acid	t (h)	T (°C)	Yield (%)	i/n Ratio	TOF (h^{-1})	Ref.
IBS	APTS	10	65	55	5.1	3	[48]
Styrene	HCl	6	100	98	1.1	25	[47]
4-Methyl-styrene	HCl	6	100	92	1.5	16	[47]
DMS	HCl	6	100	35	0.5	6	[47]
Propene	APTS	0.5	110	70	0.7	1390	[48]
1-Decene	HCl	6	100	2	1	1	[47]
1-Decene[a]	HCl	6	100	60	0.37	–	[50]

IBS = 4-isobutylstyrene, DMS = 2,4-dimethylstyrene, APTS = Acid *p*-toluenesulfonic.
[a]Addition of dimethyl-β-cyclodextrin: cyclodextrin/decene = 0.07.
Other experimental conditions see references indicated in the table.

$$R-CH=CH_2 \ + \ CO \ + \ H_2O \xrightarrow[\substack{HX}]{Pd/P(C_6H_4SO_3Na)_3} R-CH_2-CH_2-CO_2H \ + \ R-\underset{\underset{CH_3 \ (i)}{|}}{CH}-CO_2H$$

$$X: Cl^-, Br^-, I^-, CF_3CO_2^-, PF_6^- \ ...$$

R: Hydrogen, alkyl (C_1 to C_{14})

Or

R: — (aromatic ring) — R_1

R_1: CH_3, Cl, F, CF_3
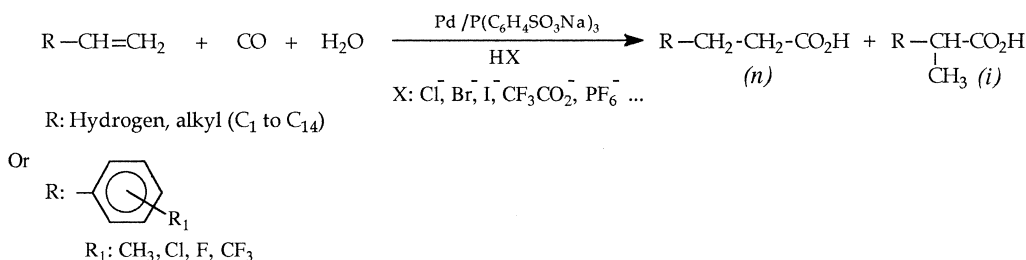
Scheme 13. Palladium catalyzed hydroxycarbonylation of olefins into carboxylic acids.2c

higher α-olefins required meanwhile mass transfer promoters due to their low water solubilities. Among the various mass transfer promoters tested, the chemically modified cyclodextrins are the most efficient [50]. For instance, the selectivity obtained during 1-decene hydroxycarbonylation reached 90% with the per(2,6 di-*O*-methyl)-β-cyclodextrin, against 53% for 1-methyl-2-pyrrolidinone (one of the most suitable co-solvents) and 20% without mass transfer promoter. In the case of styrene derivatives, the effect of various aromatic ring substituents on the activity and the selectivity has been reported. The hydroxycarbonylation rates decrease with steric hindrance of the reacting double bond and with the presence of the electron-withdrawing groups on the aromatic ring; the normal to branched acids ratio is not sensitive to the electronic properties (electron-withdrawing or electron-donor group) of the aromatic ring substituents but rather to steric hindrance around the α-carbon atom of the double bond [51].

The catalytic activity of this water soluble palladium complex of trisulfonated triphenylphosphine was found to be greatly dependent on the pH values of the aqueous solution. For instance, the reaction rate is very low at pH = 7 and increases notably by adding a Brønsted acid. In both cases, i.e., acids of coordinating or non-coordinating anions, maximum activities are obtained for low pH values (pH = 1.8–2). By analogy with the behavior of the hydrophobic complex $Pd(PPh_3)_4$ in aqueous trifluoroacetic solution [52], it is assumed that the presence of this strong acidic medium is necessary to gener-

ate a palladium hydride complex from the zero valent palladium complex $Pd(TPPTS)_3$. The insertion of the olefin into the palladium-hydride bond, followed successively by carbon monoxide insertion and nucleophilic attack of water leads then to carboxylic acids as described in Scheme 14.

At the same time, the palladium hydride complexes can be regenerated. In this catalytic cycle, the key species $Pd(0)(TPPTS)_3$ is rapidly generated from palladium(II) chloride under carbon monoxide and in the presence of TPPTS [23].
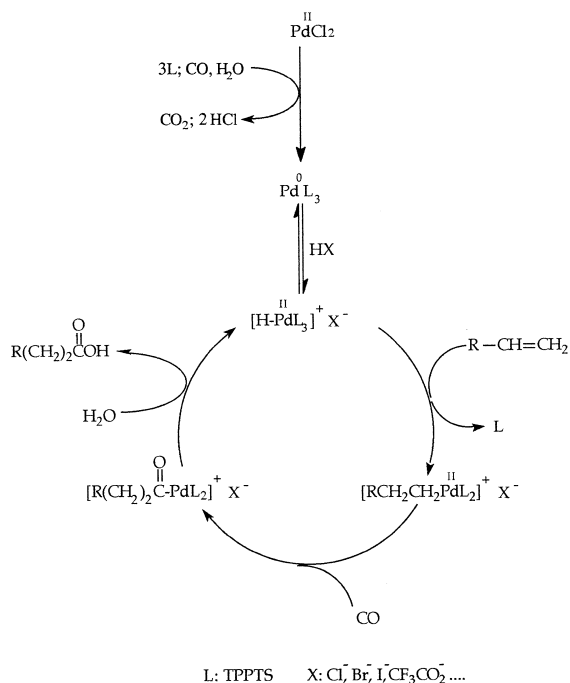
Scheme 14. Proposed catalytic cycle for the palladium catalyzed hydroxycarbonylation of olefins in two-phase system.

Recently, we have found that the nature of the anion of the acid greatly affects the stability of the above catalytic system. So, whatever the reaction temperature, a rapid decrease in the catalytic activity occurred in the case of reactions conducted with acids possessing non-coordinating anions (PF_6^- and BF_4^-). Furthermore, the formation of large aggregates at the boundary phase and the precipitation of black palladium were always observed at the end of these reactions. With acids possessing coordinating anions (Cl^-, Br^-, I^-), the decomposition of the catalytic system is much less important [53]. The role of these anions and more particularly of (I^-) remains nevertheless unclear as Papadogianakis et al. [48] have reported that under their conditions practically no reaction occurs with HI.

5. Conclusion

This review devoted to the hydroxycarbonylation reaction shows clearly that various carbonylation reactions known in homogeneous organic medium are transposable under biphasic conditions. Indeed the carbonylation of a large variety of substrates has been achieved in high yields and selectivities in aqueous-organic two-phase system. In some cases better results than those obtained in the organic homogeneous counterpart process are even observed. Catalytic intermediates different in aqueous phase than those involved in organic medium could explain this difference. However, the low carbonylation rates due to a mass transfer limitation and more markedly the catalyst deactivation prevent undoubtedly the development to an industrial scale of bromobenzene, 1-(4-isobutylphenyl)ethanol and olefins carbonylations. Obviously, the catalysts deactivation requires other studies to be understood further and to be controlled. In the future, some fruitful developments in asymmetric carbonylation and alternating copolymerization of olefins and carbon monoxide [54–57]

should again extend the scope of biphasic carbonylation.

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