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Hydrocarboxylation of olefins using an amphiphilic palladium catalyst, activity and recycling properties NMR identification of some reaction intermediates

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Abstract

The high solubility in acidic solutions of *N*-bis(*N*′,*N*′-diethyl-2-aminoethyl)-4-aminomethylphenyl-diphenylphosphine (N3P) make it a suitable candidate for study and comparison to the more commonly studied trisulfonated triphenylphosphine (TPPTS) ligand in the palladium catalysed aqueous hydrocarboxylation reaction. The catalyst employing N3P shows an inverted regioselectivity compared to the TPPTS system. Non-coordinating anions give the best results in terms of activity and stability of the catalyst. Due to N3P amphiphilic character and contrary to sulfonated phosphines reaction, it is possible to recycle the catalyst, both by extracting the substrate and by extracting the catalyst into an organic solvent. The hydrocarboxylation of styrene, 1-octene and 4-penteneoic acid demonstrates that the reaction rate is strongly dependent on the solubility of the substrates. Using the water-soluble 3-buten-1-ol as substrate, two palladium zerovalent complexes, two palladium hydrides, one acyl and one alkyl complexes were identified by means of NMR and IR.

Keywords: Amphiphilic phosphine; Aqueous phase; Hydrocarboxylation; Palladium; Recycling

1. Introduction

The synthesis of carboxylic acids from olefins, carbon monoxide and water using a palladium catalyst, i.e., the hydrocarboxylation reaction (Fig. 1), has gained considerable attention during the last years, and the field has been reviewed several times during the last years [1]. The recent interest is due partly to the finding that the reaction can be conducted in neat water or in aqueous biphasic systems, employing sulfonated phosphines as ligands [2–4] and the use of a water-soluble catalyst is advantageous since water is one of the reactants. Water-soluble catalysts also facilitate separation of the product from the reaction mixture, as well as catalyst recovery.

The hydrocarboxylation reaction is used industrially in the production of the analgesic and anti-inflammatory drug ibuprofen, (2-(4-isobutylphenyl) propionic acid), where the reaction is one of the steps in the synthesis [5].

We have previously published a report on the synthesis and use of the amphiphilic phosphine N3P, *N*-bis(*N*′,*N*′-diethyl-2-aminoethyl)-4-aminomethylphenyl-diphenylphosphine (Fig. 2) [6]. The acidic conditions required in the hydrocarboxylation reaction and the high solubility of N3P and its complexes in acidic aqueous solutions make N3P a suitable candidate for study and comparison to the more commonly studied trisulfonated triphenylphosphine (TPPTS) ligand in the palladium catalysed aqueous hydrocarboxylation reaction. Due to its amphiphilic character, and contrary to sulfonated phosphines, it is possible to extract excess N3P and its complexes into an organic phase. This enables biphasic separation since the acid product is highly water-soluble. Compared to the most commonly used ligand for this reaction, trisulfonated triphenylphosphine (TPPTS), N3P is sterically less demanding and more electron rich, factors which might influence both the activity and the regioselectivity of the catalyst.

In this paper, results from palladium catalysed hydrocarboxylation of styrene, 1-octene and 4-penteneoic acid, employing N3P as the ligand are presented. In addition, the recycling properties of the catalyst system and NMR identification of some

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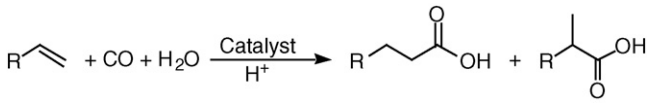

Fig. 1. The hydrocarboxylation reaction.

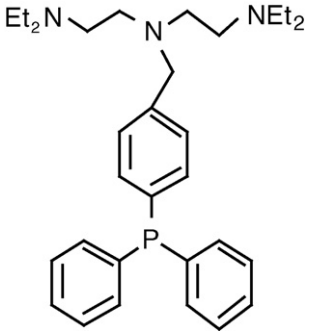

Fig. 2. N3P.

key intermediates in the catalytic cycle, using the water-soluble 3-buten-1-ol as substrate, are also described.

2. Experimental

2.1. General procedures

All chemicals of the highest grade purity were purchased from commercial sources and used as received, except N3P [6] and $PdCl_2(PhCN)_2$ [7], which were synthesised according to literature procedures. All solvents used in the manipulation of N3P and the catalysts were repeatedly degassed prior to use. Standard Schlenk technique was used in the manipulation of the catalysts and isolated compounds.

N3P·$(HCl)_x$ was prepared by dissolving N3P in diethyl ether, and bubbling HCl (g) through the solution until precipitation of the salt occurred. Filtration afforded a white solid, which on analysis showed to contain varying amounts of HCl.

The NMR spectra were recorded at 21 °C, on a Varian Unity 300 MHz spectrometer with an observation frequency of 121 MHz for ^{31}P, using 85% H_3PO_4 as external standard, and of 300 MHz for ^1H. The high pressure NMR experiments were performed using a sapphire tube assembly [8].

The IR spectra were recorded on a Nicolette FT-IR spectrometer as Nujol mulls.

The hydrocarboxylation reactions were performed in a 50 ml Autoclave Engineers Hastaloy™ autoclave equipped with a sampling valve and a temperature and stirring speed control device.

2.2. Hydrocarboxylation reactions

In a typical experiment involving styrene or 1-octene, N3P (70 mg, 0.14 mmol) and two equivalents of acid were dissolved in 15 ml degassed water. Additional acid was added to set the pH to 1.8, after which the palladium complex $PdCl_2(PhCN)_2$ (6 mg, 0.016 mmol) was added and the mixture was stirred until complete dissolution. The solution was then transferred to the autoclave and the substrate added. In the experiments using styrene as the reacting olefin, *p-tert*-butyl catechol (6 mg, 0.036 mmol) was added as polymerisation inhibitor. The autoclave was closed and pressurised (25 bar) and vented three times before the heating and stirring was started. After having reached the set temperature the pressure was adjusted to the set value. The autoclave was cooled to room temperature and vented after reaction completion. The reaction mixture was then transferred to a Schlenk tube and extracted with 4 × 3 ml diethyl ether. The autoclave was rinsed with 2 × 3 ml diethyl ether. The composition of the combined organic phase was analysed by GLC. In the recycling experiments the aqueous phase from the initial run containing the catalyst was transferred to the autoclave and the pH was adjusted to the selected value, followed by addition of fresh substrate and polymerisation inhibitor before starting the reaction according to the above procedure.

The hydrocarboxylation reaction with 4-penteneoic acid followed the above protocol but the work-up was different. After completed reaction, the reaction mixture was transferred to a Schlenk tube and cooled in an ice bath, after which the pH was set to ≈12 by slow addition of aqueous NaOH. The resulting turbid solution was extracted with 3 × 3 ml toluene, leaving a colourless aqueous phase containing the sodium salt of the carboxylic acid products and unreacted 4-penteneoic acid. The water was removed under vacuum and the residue was examined by ^1H NMR to determine yield and regioselectivity. The combined toluene phases, containing catalyst and excess ligand, were extracted with 3 × 5 ml water containing methanesulfonic acid. The pH in the final combined aqueous phase was adjusted to 1.8 using additional amounts of methanesulfonic acid, and then transferred to the autoclave and the reaction started again following the above procedure.

2.3. Attempts to identify and isolate reaction intermediates using 3-buten-1-ol as the reacting alkene

2.3.1. Reaction sequence 1

$PdCl_2(PhCN)_2$ and N3P·$(HCl)_x$ (P/Pd = 10) were charged into an autoclave and dissolved in D_2O (C_{Pd} = 10 mM) and the resulting solution was then subjected to CO (g) at 50 bar and 50 °C for 15 min. After depressurisation, two equivalents of 3-butene-1-ol were added under CO. The immediate addition of THF provided a yellow precipitate which was analysed by NMR and IR. The stability of the precipitated complex was monitored by observing the peaks in ^{31}P NMR at 80 °C for 1 h after which the organic products were identified by IR.

2.3.2. Reaction sequence 2

$PdCl_2(PhCN)_2$ and N3P·$(HCl)_x$ (P/Pd = 5) were charge into a Schlenk tube and dissolved in D_2O (C_{Pd} = 5 mM). CO (g) was bubbled through the resulting solution at room temperature for 15 min and then two equivalents of 3-butene-1-ol were added while keeping the reaction mixture under a CO atmosphere. An aliquot of the solution was transferred to a HP NMR-tube and monitored by observing the ^{31}P spectrum first at 1 bar then at 50 bar CO. A 4 h after start of the experiments THF was added to

the remaining solution in the Schlenk tube, furnishing a yellow precipitate. The precipitate was separated and analysed by NMR and IR. The stability of the precipitated solid was monitored by ^{31}P NMR at 80 °C over a period of 1 h after which the organic products were identified by GC.

3. Results and discussion

3.1. NMR studies—identification of intermediates

The gross mechanistic features of the hydrocarboxylation reaction in the case of the TPPTS-based catalyst system have been verified by NMR identification of the key intermediates [9]. Initially, we were interested in whether the same catalytic cycle also applies for the N3P based catalyst, i.e., if similar intermediates could be identified. The precursor complex $PdCl_2(PhCN)_2$ dissolved smoothly in a D_2O solution of the hydrochloride salt of N3P·$(HCl)_x$ (P/Pd = 10, see Section 2.3.1) to furnish a solution with showed three resonances in its {H} ^{31}P NMR spectrum: one singlet resonance at −4.5 ppm, straightforwardly assignable to the free ligand, a triplet at 34.2 ppm, and a doublet at 30.2 ppm ($^2J_{P–P}$ 13.7 Hz). The shifts and coupling constant of the latter two resonances correspond well to those observed for cationic complexes of the general composition $[PdCl(L)_3]^+$ Cl^-, **1**, which has been shown to form under similar conditions using $PdCl_2$ and triphenylphosphine (TPP) [10] or TPPTS [11]. The room temperature spectrum run after subjecting the solution to CO (g) at 50 bar pressure and 50 °C for 15 min showed no peaks corresponding to complex **1** instead it exhibited two broad resonances centred at 22.7 ppm and 24.8 ppm. The up-field shift agrees with that of the TPPTS complex Pd(TPPTS)$_3$·9H_2O [12], hence complex **1** is reduced under CO to a mixture of zerovalent complexes viz. Pd(N3P)$_3$ **2** and Pd(N3P)$_4$ **3**, where complex **3** is predominant. The broad line-widths observed, compared to the narrow line-width (5.5 Hz) reported for Pd(TPPTS)$_3$·9H_2O and the observation of two separate peaks is probably a reflection of the smaller cone angle of N3P relative that of TPPTS, which enables the formation of the tetra-coordinated complex **3** and ligand interchange between the two complexes. The peaks get sharper and shift a little up-field (23.6 and 21.9 ppm) at 0 °C (Fig. 3a), but the line-width is still broad (179 Hz). The same spectrum taken under different conditions (P/Pd = 5, C_{Pd} = 5 mM, 1 bar CO, see Section 2.3.2) exhibits only one very broad resonance at 22.2 ppm (Fig. 3b) corresponding to the complexes **2** and **3** shifted closer together and in comparable amounts. This demonstrates that the CO pressure is not an important factor in the reduction step and that the ligand concentration controls the equilibrium (Eq. (1)) between the two zerovalent complexes **2** and **3**:

$$\text{Pd(N3P)}_3 + \text{N3P} \leftrightarrow \text{Pd(N3P)}_4 \quad (1)$$

We have not been able to verify the formation of a hydride by either ^{1}H or ^{31}P NMR at the pH at which dissolution of N3P·$(HCl)_x$ brings about. However, when the CO promoted reduction was carried out as described earlier [9], i.e., using a 60% (v/v) aqueous trifluoroacetic acid as the solvent, protonation of complexes **2** and **3** occurred virtually quantitatively, yielding two different hydrides which are stable enough to be observed by ^{1}H and ^{31}P NMR. Based on the observed NMR data, one of these hydride complexes is structurally identical to that earlier observed in the TPPTS based system, i.e., a planar or planaroid cationic palladium species with three phosphorus

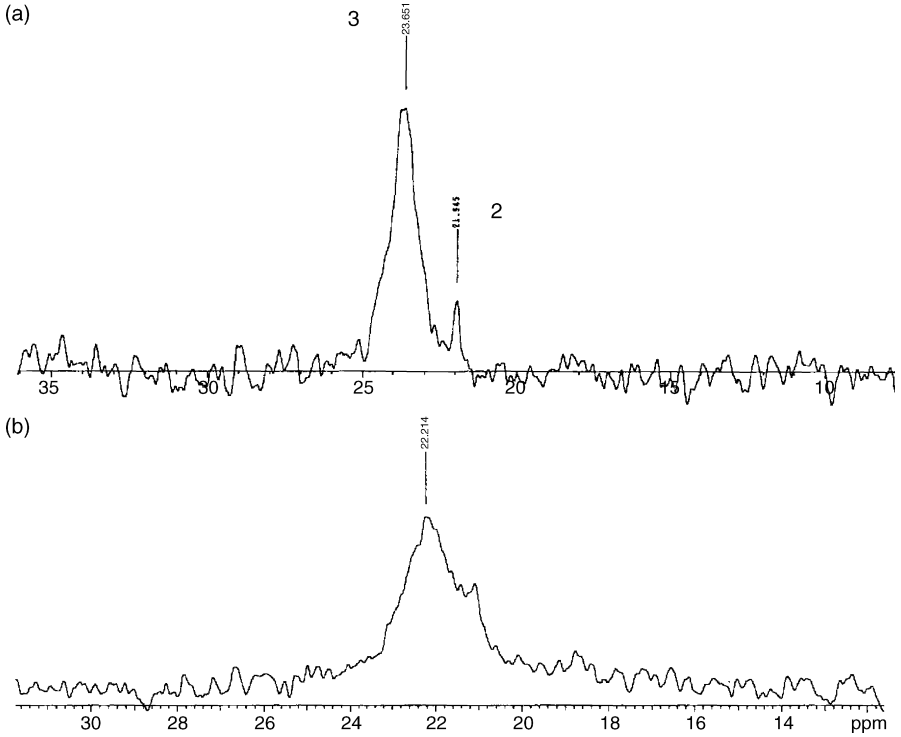

Fig. 3. ^{31}P {H} NMR spectra of the zerovalent complexes Pd(N3P)$_3$ **2** and Pd(N3P)$_4$ **3**: (a) P/Pd = 10; 0 °C; (b) P/Pd = 5; 25 °C.

atoms and one hydride, with a peak at −8.5 ppm consisting of a doublet of triplets ($^2J_{H–P(cis)}$ 13.5 Hz (trip), $^2J_{H–P(trans)}$ 175 Hz (d)). In the $\{^1H\}$ ^{31}P NMR spectrum, this resonance corresponds to a triplet at 19.7 ppm and a doublet at 26.3 ppm with $^2J_{P–P}$ of 37 Hz. Without decoupling these resonances were observed as one doublet of triplets with a $^2J_{H–P(trans)}$ coupling of 175 Hz and a broad resonance where the expected coupling of 13.5 Hz was lost in the line width.

The second hydride gave a pentet at −7.8 ppm with a $^2J_{H–P}$ of 39 Hz, consistent with a coupling between the hydride and four magnetically equivalent phosphorus atoms. In the $\{^1H\}$ ^{31}P NMR spectrum this hydride gave a singlet at 21.5 ppm, which in the decoupled mode transformed into a doublet with $^2J_{H–P}$ of 39 Hz. These NMR observations are consistent with a dimeric species with a hydride and a carbon monoxide molecule as bridging ligands and with a tetrahedral coordination around the two palladium atoms, $[Pd_2(\mu\text{-}H)(\mu\text{-}CO)(N3P)_4]^+$. A dimer of similar constitution is known from similar experiments employing triphenylphosphine as the ligand [13], but was reported not to appear using TPPTS [9].

The solution containing the mixture of the zerovalent complexes **2** and **3** reacted smoothly with 3-butene-1-ol to furnish a mixture of two new complexes viz. complex **4**, with a singlet resonance at 20.7 ppm and another complex, **5**, with a singlet resonance at 21.1 ppm in the ^{31}P NMR spectrum. The relative proportion of these two complexes varied over time—the peak corresponding to complex **4** dominated direct after addition of the alkene but, in time, the peak corresponding to complex **5** gradually increased in intensity at the expense of the peak corresponding to complex **4**. At a CO pressure of 50 bar the conversion is complete within 3 h and the inter-conversion cannot be reversed at even higher CO pressure. The constitution of these complexes cannot be deduced from the ^{31}P NMR spectrum but serendipitously, we found that the complexes can be precipitated from the aqueous solution by addition of THF or dioxane, although not in analytically pure form. The solid isolated direct after addition of 3-buten-1-ol proved to be complex **4** with a singlet peak in the ^{31}P spectrum at 20.7 ppm. The IR spectrum with a strong vibration at 1677 cm^{-1}, which is in the range of CO stretching frequencies of previously isolated palladium acyl complexes [14], indicates that it contains an acyl complex. The singlet in ^{31}P NMR leaves two alternative structures for this acyl complex **4**, as given in Fig. 4 (**4a**: *iso*-acyl; **4b**: *n*-acyl complexes). By thermal decomposition of the aqueous solution containing complex **4**, only the zerovalent complex **2** is visible in ^{31}P NMR, and the IR analysis showed the presence of α-methyl-γ-butyrolactone (1754 cm^{-1}) and butyraldehyde (1720 cm^{-1}).

The yellow solid isolated after letting complex **4** be converted to complex **5** showed neither no peak in the range of CO stretching vibrations nor did the GC analysis revealed any carbonylated product (acid or lactone) after thermal decomposition. The only organic product observed was butyraldehyde which is a result of isomerization of 3-buten-1-ol. All our experimental evidences point to that complex **4** is an acyl complex, possibly the *iso*-acyl **4a**, since the hydrocarboxylation product is α-methyl-γ-valerolactone. **4a** is the kinetically controlled complex which slowly converts to the thermodynamically controlled alkyl complex **5**. The rather high stability of complex **5** is a strong indication that it is a ring-closed complex with the oxygen atom of the alkene coordinating to the central palladium atom (Fig. 4).

3.2. Catalytic screening experiments

Initially we tried to establish suitable conditions (palladium precursor, Brönstedt acid, temperature and molar ratio Pd/P) for carrying out the hydrocarboxylation reaction using N3P as a ligand. $PdCl_2$ is commonly used as palladium source in in situ generation of the active catalyst, but $PdCl_2(PhCN)_2$, which is readily available and more reactive, offered certain advantages—the formation of the catalyst precursor $[PdCl(N3P)_2]^+Cl^-$ proceeded much faster, and $PdCl_2$ often left small amounts of insoluble material. Since no negative effect of the liberated benzonitrile was observed, all the experiments were carried out using the benzonitrile complex.

There have been differing opinions as to the influence of the anion of the Brönstedt acid on the hydrocarboxylation reaction and an example, demonstrating that coordinating anions e.g. Cl^-, Br^- or I^- lower the initial activity but raise the long-term activity, can be found [15]. Results from other investigations [3] show that coordinating anions decompose the hydride as a result of higher stability of cationic versus neutral hydrides [16]. We have studied four different acids in the hydrocarboxylation of styrene. From the results (Table 1) of the initial screening of the N3P based catalyst using these acids, it is clear that Brönstedt acids with non-coordinating anions give the best results in terms of conversion (%), and that methanesulfonic acid is the best. The trend in activity resembles the one found in the carbonylation of 1-(4-isobutylphenyl) ethanol [3], as in both cases organic sulfonic acids provide the best yield. With fluoroboric acid, the solubility of the N3P based catalyst posed a problem. Although the catalyst employing this acid appeared fully dissolved at temperatures above 70 °C, at room temperature the solubility is considerably lower, making the solution turbid. This restricted solubility makes catalyst recycling difficult and unreliable.

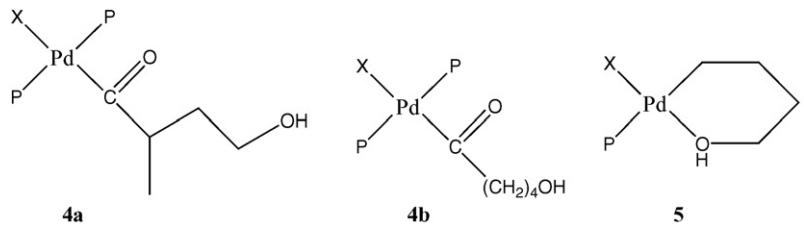

Fig. 4. Proposed structures for acyl complex **4** and alkyl complex **5** (X = Cl^-, D_2O, CO; P = phosphine).

Table 1
Influence of acid and olefin in the hydrocarboxylation reaction

Substrate	Acid	Conversion (%)	*n/i*
Styrene	TSA	76	3.4
	HBF_4	38	3.7
	HCl	26	3.0
	$MeSO_3H$	92	2.6
1-Octene	$MeSO_3H$	30	2.4

General reaction conditions: $P_{CO} = 50$ bar; $T = 100\,^{\circ}C$; precursor: $PdCl_2(PhCN)_2$ (0.016 mmol); ligand: N3P (0.14 mmol); styrene/Pd: 250; 1-octene/Pd: 100; polymerisation inhibitor for styrene: *p-tert*-butyl catechol (0.036 mmol); pH 1.8; solvent: H_2O; total volume: 15 ml; reaction time: 5 h.

The solubility of the catalyst is high in hydrochloric acid. The substrate conversion in hydrochloric acid, however, is low, as is the stability of the catalyst, and inevitably formation of various amounts of palladium black occurred. The low conversion can probably be attributed to decreased stability of the palladium hydride species due to the chloride ions present. The low stability of the complexes in hydrochloric acid, yielding palladium black are in contrast to previous observations regarding the TPPTS-based catalyst [15], for which it was claimed that chloride ions prevented the catalyst from decomposing.

The rate of product formation is strongly temperature dependent, and the higher the temperature the higher the reaction rate. However, the thermal stability of the catalyst system sets an upper limit, and 100 °C was found to be the highest temperature at which the catalyst, employing N3P as ligand, is stable, i. e. no metal particle formation was detectable at 50 bar CO. Thus, the conditions used for all the catalytic experiments were set to 100 °C and 50 bar CO.

The phosphine to palladium ratio influences the stability of the catalyst, and more than stoichiometric amounts of the ligand are needed to prevent catalyst decomposition, although in the ratio range of 5–12, it has only minor effects on the regioselectivity. A ratio of 9, which was used throughout this study, provided a stable catalyst.

3.3. Recycling experiments

In the hydrocarboxylation of styrene, the catalyst employing methanesulfonic acid could be recycled at least four times without loss of activity. In fact, a slight increase in activity occurred between the first and the second run (Fig. 5). This increase can be explained by either a longer activation time of the catalyst precursor **1** used in the first run, compared to the activation time of the resting state catalyst in consecutive runs, or that the chloride ions present in the precursor are lost in the recycling step, and this leads to a more active catalyst. Although the activity is retained during consecutive runs, we cannot exclude that catalyst decay is occurring to some extent. The retained activity then could be apparent due to the low substrate solubility (vide infra). However, in the recycling experiments, there was no formation of palladium black, nor did we observe any colouring of the ether extraction phases indicative of the loss of metal complex.

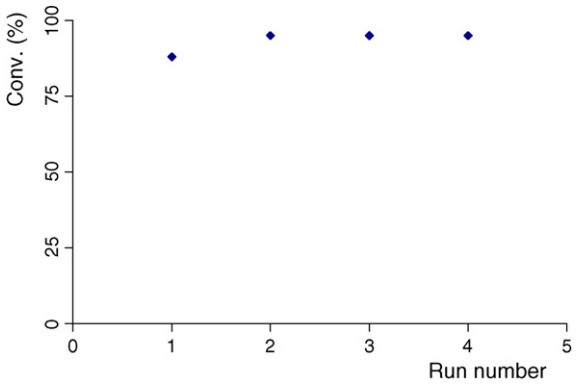

Fig. 5. Recycling of the catalyst in the hydrocarboxylation of styrene.

We have noted spectacular colour changes in the recycling procedure. During the extractions the colour of the aqueous solution changed from bright yellow to deep purple. This colour change was accompanied by a release of carbon monoxide from the over-saturated solution, but the solution regained its original yellow colour in the following catalytic run. Attempts to employ ^{31}P NMR to monitor which type of species gave rise to the purple colour were unsuccessful. However, palladium-carbonyl clusters involving phosphines are known to show strong colours [17].

Styrene is known to be susceptible to polymerisation under high temperature conditions, which is why a radical scavenger, *p-tert*-butylcatechol, was used. Without this additive polystyrene was always formed in visible amounts. Even in the experiments employing styrene, reported here, which all included *p-tert*-butylcatechol, we cannot exclude the formation of small amounts of visually undetectable polystyrene.

3.4. Regioselectivity

The linear to branched (*n/i*) ratio of the phenylpropionic acids formed was constant in the recycling experiments, but varied between 2.6 and 3.7 depending upon the acid used in the reaction (Table 1). This might be related to solubility differences. The highest *n/i* ratio was found for the least soluble catalysts, so it is possible that aggregation does occur to some extent, even at higher temperature, and that this affects the regioselectivity of the catalyst. More importantly, the observed regioselectivity is considerably different from that previously observed for TPPTS based catalyst, which gave a *n/i* ratio of 0.8 [2]. From the standpoint of product value, the observed high selectivity toward the linear isomer is a clear disadvantage—the branched isomer is the one related to the ibuprofen class of compounds, and thus the most valuable one. From the standpoint of a mechanistic understanding of the origin of regioselectivity our finding is, however, of interest. The electronic and steric properties of N3P are very similar to those of triphenylphosphine (TPP) [6]. It therefore differs from the bulkier and more electron deficient trisulfonated triphenylphosphine (TPPTS), and these differences are obviously enough to totally change the regiochemistry. Considering the regio-control, there are two different possibilities; the steric properties of the spectator ligands most likely affect

the stability of the palladium alkyl complex formed by insertion of the olefin in the Pd–H bond, bulkier ligands promote formation of the linear alkyl complex. Based on steric arguments alone, the N3P ligand would give predominantly the branched isomer. On the other hand, if the insertion of the olefin in the Pd–H bonds yields two isomeric Pd-alkyls (linear and branched) which are in rapid equilibrium and which insert CO at different rates, there would be mainly electronic rather than steric control. Unfortunately, since the two spectator ligands N3P and TPPTS differ with respect to both steric bulk and donor strength, they do not provide a clear-cut answer as to the cause of the regio-control.

3.5. Mass-transfer

A slow rate of phase boundary mass transfer frequently causes problems with the reaction rate in biphasic reaction mixtures, and this is also the case when applying catalyst based on the N3P ligand in the hydrocarboxylation reaction. This is evident by comparing the conversions for 1-octene and styrene under the same reaction conditions. Styrene, having a reported solubility of 1.1 mmol/l in water [2], is much more water-soluble than 1-octene and has a conversion of 92% while 1-octene of only 30% (Table 1). Still, it is probably the solubility of styrene in water which determines its reaction rate. Additionally, we observed that 1-octene slowly isomerises under the reaction conditions, and the product mixture contained approximately 10% of 2-ethyl heptanoic acid. The influence of phase boundary mass transfer on the reaction rate also became evident by comparing reaction rates for both styrene and 1-octene in neat form or dissolved in toluene—a much higher reaction rate was found by adding the reactant olefins in undiluted form directly to the aqueous reaction mixture. Even so, the reaction rate is most likely limited by the low water solubility of these two substrates.

The importance of mass-transfer rates is also nicely demonstrated in the reaction of 4-penteneoic acid. Initially, this substrate was chosen to evaluate the possibility of using a "reverse" recycling procedure to recover and reuse a catalytic system based on an amphiphilic phosphine ligand. 4-Penteneoic acid represents a class of alkenes highly soluble in water, and its product in the hydrocarboxylation reaction, adipic acid, is even more water-soluble. This, of course, makes the separation of catalyst and product, and hence the catalyst recycling, cumbersome. Although in the case of penteneoic acid it is possible to separate the substrate and the product from the catalyst by repeated extractions, this method poses the risk of introducing air into the system, ultimately leading to oxidation of phosphine ligands. One can also easily find substrates/products with solubility so close to that of the amphiphilic catalysts that separation becomes virtually impossible. In such a case, the amphiphilic catalyst presents a clear advantage over the mere water-soluble ones (e.g. catalysts employing sulfonated phosphines), since an amphiphilic catalyst can be transferred into an organic phase while keeping the reactants/products in a basified aqueous phase. Compared to the normal recycling procedure for amphiphilic catalysts, extraction of the catalyst into toluene represents a reverse procedure, in that the aqueous phase contains the product, for which any appropriate method of work-up can be used to recover the product.

Table 2
Hydrocarboxylation of penteneoic acid

Substrate (pentenoic acid)	Conversion (%)	*n/i*
Run (1)	94	3.1
Run (2)	91	3.1

General reaction conditions: $P_{CO} = 50$ bar; $T = 100\,^{\circ}C$; precursor: $PdCl_2(PhCN)_2$ (0.016 mmol); ligand: N3P (0.14 mmol); substrate/Pd: 560; pH 1.8; acid: $MeSO_3H$; solvent: H_2O; total volume: 15 ml; reaction time: 1 h.

The results using 4-pentenoic acid, displayed in Table 2, demonstrate that the reverse recycling procedure can be applied with only a minor loss in activity. Pentenoic acid reaches 94% conversion in one hour while styrene needs five hours for 92% conversion. This, again, is a strong indication that the solubility of styrene limits its rate of reaction. The linear to branched ratio of 3.1 is slightly higher than the selectivity in the 1-octene reaction. Coordination of the carbonyl group on 4-pentenoic acid to the palladium atom in the alkyl intermediates would lead to seven or six-membered ring structures for the linear and branched alkyl complexes, respectively. Based on the higher stability of a six-membered ring, the branched isomer is expected, providing carbonyl interaction occurs. The preferential formation of the linear isomer observed, however, indicates that the carboxylic group on the substrate plays no role in determining the regioselectivity.

Besides the main product, adipic acid, 8% 2-methyl-1,5-pentanedioic acid was also observed as a result of isomerization of 4-pentenoic acid.

4. Conclusions

The hydrocarboxylation of styrene, 1-octene and 4-penteneoic acid using a palladium catalyst employing the amphiphilic phosphine N3P demonstrates that the reaction rate is strongly dependent on the solubility of the substrates.

Using N3P in the hydrocarboxylation reaction it is possible to recycle the catalyst, both by extracting the substrate and by extracting the catalyst into an organic solvent. This is a clear advantage compared to the more commonly used ligand, trisulfonated triphenylphosphine (TPPTS). The catalyst employing N3P also shows an inverted regioselectivity compared to the TPPTS system.

A whole range of reaction intermediates, from zerovalent complexes to alkyl and acyl complexes were identified by means of NMR.

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References

[1] F. Bertoux, E. Monflier, Y. Castanet, A. Mortreux, J. Mol. Catal. 143 (1–3) (1999) 11;
W.A. Hermann, Synthetic Methods of Organometallic and Inorganic Chemistry: Catalysis, vol. 10, Thieme, Stuttgart, Germany, 2002, p. 42;
I. del Rio, C. Claver, P.W.N.M. van Leeuwen, Eur. J. Inorg. Chem. (2001) 2719.

[2] F. Bertoux, S. Tilloy, E. Monflier, Y. Castanet, A. Mortreux, J. Mol. Catal. 138 (1) (1999) 53.

[3] G. Verspui, G. Papadogianakis, R.A. Sheldon, Catal. Today 42 (1998) 449;
G. Verspui, J. Feiken, G. Papadogianakis, R.A. Sheldon, J. Mol. Catal. 146 (1–2) (1999) 299.

[4] M.S. Goedheijt, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, Chem. Commun. (1998) 2431.

[5] V. Elango, K.G. Davenport, M.A. Murphy, G.N. Mott, E.G. Zey, B.L. Smith, G.L. Moss, European Patent Appl. EP 0,400,892 (1990).

[6] M. Karlsson, M. Johansson, C. Andersson, J. Chem Soc. Dalton Trans. (1999) 4187.

[7] J.R. Doyle, P.E. Slade, H.B. Jonassen, Inorg. Synth. 6 (1960) 218.

[8] A. Cussanelli, U. Frey, D.T. Richens, A.E. Merbach, J. Am. Chem. Soc. 118 (1996) 5265.

[9] G. Verspui, I.I. Moiseev, R.A. Sheldon, J. Organomet. Chem. 586 (1999) 196.

[10] S. Yamazaki, Polyhedron 4 (1985) 1915.

[11] G. Papadogianakis, J.A. Peters, L. Maat, R.A. Sheldon, J. Chem. Soc. Chem. Commun. (1995) 1105.

[12] G. Papadogianakis, L. Maat, R.A. Sheldon, Inorg. Synth. 32 (1998) 25;
C. Binkowski, J. Cabou, H. Bricout, F. Hapiot, E. Monflier, J. Mol. Catal. 215 (2004) 23;
F. Monteil, P. Kalck, J. Organomet. Chem. 482 (1994) 45.

[13] V.N. Zudin, V.D. Chinakov, V.A. Nekipelov, V.A. Likholobov, Y.I. Yermakov, J. Organomet. Chem. 289 (1985) 425.

[14] K. Suzuki, M. Nishida, Bull. Chem. Soc. Jpn. 46 (1973) 2887;
P.E. Carrou, R.F. Heck, J. Am. Chem. Soc. 98 (14) (1976) 4115;
Cavinato, G:, L. Toniolo, A. Vavasori, J. Mol. Catal. 219 (2) (2004) 233.

[15] F. Bertoux, E. Monflier, Y. Castanet, A. Mortreux, J. Mol. Catal. 143 (1–3) (1999) 23.

[16] V.V. Grushin, Chem. Rev. 96 (1996) 2011.

[17] K. Kudo, M. Hidai, Y. Uchida, J. Organomet. Chem. 33 (1971) 393.