Effect of 2-Propanol on the Transfer Hydrogenation of Aldehydes by Aqueous Sodium Formate using a Rhodium(i)-sulfonated Triphenylphosphine Catalyst

Ágnes Kathó*ab, Imre Szatmáriab, Gábor Pappab, and Ferenc Joóab

Abstract: In water/2-propanol mixtures [RhCl(mtppps),] (mtppps = monosulfonated triphenylphosphine) was an efficient catalyst for the selective C=C reduction of trans-3-phenyl-2-propenal (trans-cinnamaldehyde) by hydrogen transfer from formate at temperatures as low as 30 °C. An outstandingly high catalyst turnover frequency of 1214 h−1 was determined at 70 °C. A possible mechanism of the reaction is suggested on the basis of kinetic studies and 1H- and 31P-NMR spectroscopic identification of the major Rh i species in the reaction mixtures as cis-mer-[H,PhX(mtpmpp)] (X = HCOO− or H2O). It was established that a large part but not all of the rate increase observed in water/2-propanol mixtures in comparison with systems with neat water as solvent was the consequence of complete dissolution of trans-cinnamaldehyde on the effect of the co-solvent. Nevertheless, the rate showed a significant further increase with increasing 2-propanol concentration even in homogeneous solution and this was ascribed to changes in the solvent structure. The high catalyst activity in this solvent mixture allowed the transfer hydrogenation of citral. Although good to excellent conversions were observed at 30–70 °C, a useful degree of selectivity in hydrogenation of C=C vs. C=O bonds could not be achieved.

Keywords: Aldehydes, Rhodium-phosphine catalyst, Sodium formate, Transfer hydrogenation, Water

1. Introduction

Homogeneous catalysis allows precise control of the composition and structure of molecularly dispersed catalysts resulting in their efficient use and in their ability to effectively govern selectivities of the catalysed reactions. Of the many examples, one may refer to the asymmetric hydrogenation of various prochiral substrates[1] or to the stereocontrolled olefin metathesis reactions.[2] Platinum group metal complexes feature frequently as catalysts for such reactions, often containing expensive ligands, so that recovery of such catalysts is a prerequisite for their practical application. This can be achieved relatively simply by using liquid biphasic reaction systems. In such reactions, the catalyst is dissolved in one of the liquid phases which is immiscible (slightly miscible) with the other liquid phase containing the substrate and the product.[1,2] In the most favourable cases, product isolation and catalyst recovery requires simple phase separation. Water is a most suitable solvent for such biphasic reactions,[3] since it does not mix well with many of the commonly used organic solvents. In addition, water is a natural solvent choice for reactions of substrates which dissolve preferably (or exclusively) in water or for reactions in which water is one of the reactants (such as hydration[5] of alkanes, nitriles, etc.). Consequently, it is a common situation in aqueous organometallic catalysis that the catalysts operate in an aqueous solution (phase) in contact with organic solvents.

In comparison to the widely used organic solvents, water is not simply an alternative dissolving agent but has its own requirements and effects, too. First of all, in aqueous–organic biphase systems strongly hydrophilic catalysts are needed in order to maintain the catalyst exclusively in the aqueous phase. There are many hydrophilic ligands suitable for synthesis of water-soluble transition metal complex catalysts.[4] The most widely investigated ligands are the monosulfonated and trisulfonated triphenylphosphines (mtppps = sodium 3-diphenylphosphinobenzensulfonate,[6] and mtpptps = trisodium 3,3′,3″-phosphintriylbenzensulfonate,[7] respectively) as well as 1,3,5-triaza-7-phosphaadamantane (pta = 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane).[8] Recently, water-soluble N-heterocyclic carbene ligands and complexes have also received increasing attention.[9,10] The presence of water in the solvent may considerably influence the rates and selectivities of reactions performed in aqueous systems. For example, the [RhCl(mtppps),]-catalysed hydrogenation of fumaric acid proceeded much faster in water[10] than in water–diglyme mixtures or in pure diglyme. In contrast, the highest rate of hydrogenation of maleic acid was observed in diglyme as solvent and it decreased with increasing percentage of water in diglyme–water mixtures.[10b] Another interesting example is the hydrogenation of 2,6-hexadienoic (sorbid) acid. Hydrogenation of potassium sorbate in water with a [RhCl(mtppps),] catalyst was comparable to hydrogenation of sorbid acid in ethyl acetate with [RhCl(Ph3P),] concerning both the rates and the selectivities of the reactions. However, in a water–ethyl acetate biphase system and with [RhCl(mtppps),] as catalyst, hydrogenation of sorbic acid proceeded faster and more selectively than...
in any of the homogeneous solutions.\textsuperscript{[11]} There are examples of aqueous–organic biphasic reactions where the presence of water (often as a separate aqueous phase) has large effects even on reactions taking place in organic solution with an organo-soluble catalyst, such as the case of transfer hydrogenation of ketones from formate with half-sandwich Ru(II)-diamine cata-
lysts in which Xiao et al. have found large rate increases relative to the pure organic solvents.\textsuperscript{[12]} By a multilateral mechanistic study it was revealed that water directly participated in the hydrogen transfer pro-
cess.\textsuperscript{[12c]}

Selective hydrogenation of unsaturated aldehydes either to unsaturated alcohols or to saturated aldehydes is a synthetically most useful reaction. This transformation can be achieved by catalytic hydrogenation with H\textsubscript{2} or by catalytic hydrogen transfer from certain H-donors, of which 2-propanol and formic acid or formate salts are the most prominent. A specific way of transfer hydrogenation applies aqueous solutions of formate salts (most often HCOONa) and Rh(I)- or Ru(II)-tertiary phosphate complex catalysts. Although water-insoluble catalysts (such as [RuCl\(_2\)(PPh\(_3\))\(_2\)]) can also be used (and in that case they are dissolved in the alde-
hyde-containing organic phase in contact with an aqueous HCOONa solution),\textsuperscript{[13]} a more practical approach is to use wa-
ter-soluble catalysts dissolved in the aque-
ous formate phase.\textsuperscript{[14]} Several studies have revealed that in aqueous biphasic reactions of unsaturated aldehydes [Rh\(_2\)CIP\(_3\)],-type complexes selectively hydrogenated the carbon–carbon double bond,\textsuperscript{[15]} while the [RuCl\(_2\)(PR\(_3\))\(_2\)] catalysts showed pH-de-
pendent selectivity: in acidic solutions a slow hydrogenation of the C=C bond was observed, while in basic solutions the alde-
hyde function was rapidly hydrogen-
ated.\textsuperscript{[15c]} Accordingly, in biphasic transfer hydrogenations from aqueous HCOONa (slightly basic aqueous phase) selective reduction of unsaturated aldehydes to un-
saturated alcohols could be achieved.\textsuperscript{[17]}

Addition of alcohols to aqueous re-
action mixtures of hydrogenation, trans-
fer-hydrogenation, hydroformylation, etc. has often been found advantageous. For example, hydrogenation of trans-cinn-
amaldehyde (trans-3-phenyl-2-prope-
nal) was accelerated by ethylene glycol; in fact, the reaction showed the highest rate in pure ethylene glycol in which the Rh(I)-based catalysts, such as Rh\(_2\)(I)(-I)-
cysteine, were soluble.\textsuperscript{[18]} Ajou and Pinet studied transfer hydrogenation of various aldehydes and ketones in mixtures of wa-
ter and 2-propanol with a catalyst prepared in situ from [[RhCl(COD)]\(_2\)] + 15 mtpps (COD = 1,5-cyclooctadiene) in the presence of Na\(_2\)CO\(_3\) as base and found high conversions at 80 °C in 2 h.\textsuperscript{[19]} Under the reaction conditions the mixtures were homo-
geneous, and 2-propanol had a dual role as solvent and H-donor.

Organic co-solvents may have vari-
ous effects on the kinetics of a reaction catalysed by organometallic complexes in partially aqueous solutions. They may in-
crease the solubility of gaseous reactants (H\(_2\), CO, etc.) and that of slightly soluble substrates (alkenes, alkeny,
es, etc.). In bi-
phasic systems co-solvents may facilitate the phase transfer of the substrate to the catalyst-containing aqueous phase and the transfer of the product from the aqueous to the organic phase. Many of the organic substrates have such low solubility in wa-
ter that their reactions in aqueous–organic biphasic systems are impracticably slow. Addition of co-solvents often leads to for-
mation of homogeneous reaction mixtures characterized by higher reaction rates than their biphasic counterparts, however, iso-
lation of the product and recovery of the catalyst in these cases is no longer pos-
tible by simple phase separation. At the end of the reaction, phase separation can be induced by proper manipulation of the solvent composition (e.g. by increasing the amount of one of the solvents in the mixture, or by addition of a third solvent) and although at first this may not seem economical, smart engineering solutions can allow incorporation of induced phase separation even into industrial processes, such as the hydroformylation of long chain alkene.s.\textsuperscript{[46]}

A few common organic solvents (such as 2-propanol) may also act as H-donors in transfer hydrogenations; in addition, they may influence the formation of catalytical-
ly important metal complex intermediates (such as metal hydrides). Nevertheless, there are reactions where such effects can hardly be relevant for the observed dra-
matic rate increase. For example, we have found that transfer hydrogenation of alde-
hydes from aqueous HCOONa catalysed by [[RuCl\(_2\)(mntppms)]\(_2\)] (with added mtt-
ppms) was largely accelerated upon addi-
tion of 2-propanol as co-solvent; in case of trans-cinnamaldehyde 90% conversion was achieved in a water/2-propanol2/1 mi-
ture in contrast to 2.0% in water alone.\textsuperscript{[20]} In the homogeneous reaction mixtures of that study with no gaseous reactants, phase-transfer and solubility effects could not lead to the substantially increased rea-
tion rates. In order to get a deeper insight into the causes of this kinetic phenomenon, we decided to study a similar yet different reaction, i.e. the transfer hydrogenation of aldehydes from aqueous HCOONa cata-
lysed by [Rh\(_2\)(mntppms)]. Since in the case of unsaturated aldehydes this catalyst shows markedly different selectivity than [[RuCl\(_2\)(mntppms)]\(_2\)] + n mtpps, transfer hydrogenation of trans-cinnamaldehyde was investigated in detail; the results are reported below.

2. Results

Hydrogenation of trans-cinnamal-
dehyde (Scheme 1; A) may yield three products, namely 3-phenylpropanal (B), cinnamyl alcohol (3-phenyl-2-propanol, C), and 3-phenylpropanol (D). In general, unsaturated alcohols are regarded more valuable due to their role in synthesis es-
pecially in the fragrance industry.

![Scheme 1. Hydrogenation of trans-
cinnamaldehyde (trans-3-phenyl-2-propanal).](image)
two-sided (Fig. 4). At low aldehyde concentrations the conversion increased with increased substrate concentrations, while it showed decreasing values with [S]/[Rh] ratios higher than 50. However, the TOF vs [S]/[Rh] function is a conventional saturation curve with slight decrease of TOF values toward high substrate concentrations. Although substrate inhibition in transfer hydrogenation of aldehydes is a known phenomenon,[13,20] in this case it does not play an important role.

The hydrogenation activity of Wilkinson-type rhodium(i) complexes is often inhibited by additional phosphine ligands,
therefore this effect was also investigated. As shown on Fig. 5, the conversion of trans-cinnamaldehyde in transfer hydrogenation from aqueous formate increased up to a $[P]/[\text{Rh}]$ ratio of 5, then levelled off ($[P]$ includes the three mttpms ligands, too, bound in $[\text{RhCl(mttpms)}]$). This was the reason we used $[P]/[\text{Rh}] = 10$ in all other experiments.

The reaction rate showed a large temperature dependence (Fig. 6). Under the conditions of Table 1, a TOF of 41 h$^{-1}$ was determined at 30 °C, which increased to 276 h$^{-1}$ at 50 °C and to 1214 h$^{-1}$ at 70 °C. This latter value is unprecedentedly high for transfer hydrogenation of trans-cinnamaldehyde from aqueous formate with a water-soluble Rh(i)-tertiary phosphine catalyst. For comparison, in the biphasic hydrogenation of trans-cinnamaldehyde catalysed by $[\text{RhCl(mtppts)}]$ a TOF of 267 h$^{-1}$ was determined at 80 °C and 20 bar $H_2$.

A good linearity Arrhenius plot of $\ln$ TOF vs. $1/T$ ($R^2 = 0.9954$) yielded an apparent activation energy $E_a = 89$ kJ/mol.

The high catalytic activity in the transfer hydrogenation of trans-cinnamaldehyde encouraged us to attempt an industrially important reaction, namely the selective hydrogenation of citral (3,7-dimethyl-oct-6-en-1-al, a mixture of cis- and trans-isomers: geranial and neral). The results are shown in Table 2. The major products of the reaction were geraniol and nerol which are obtained by hydrogenation of the aldehyde function of geranial and neral, respectively. At 30 °C the reaction was fairly selective to geraniol (76% of all products); however, at higher temperatures its ratio among the products decreased to about 50%.

Selective hydrogenation of the conjugated C=C bond in citral yielding citronellal amounted to 15.1% at 70 °C (the isolated C=C bond was not hydrogenated at any of the studied temperatures). This C=C/C=O selectivity is different from that observed in hydrogenation of trans-cinnamaldehyde and may be the consequence of the higher degree of substitution of both olefinic bonds in citral.

### 3. Discussion

In this study we observed that reduction of trans-cinnamaldehyde by catalytic hydrogen transfer from HCOONa with the water-soluble $[\text{RhCl(mttpms)}]$ catalyst proceeded much faster in water/2-propanol mixtures than in water as the sole solvent and consequently the reaction could be run with high conversion already at 30 °C.

In search for the probable catalytically active Rh-species we studied the reaction of $[\text{RhCl(mttpms)}]$ with HCOONa in water/2-propanol = 4.0/3.5 v/v mixtures using $^1\text{H}$- and $^{31}\text{P}$-NMR spectroscopies. With standard decoupling techniques it was established that in the first few minutes following dissolution of $[\text{RhCl(mttpms)}]$, the solutions contained $\text{cis-mer-}[\text{H}_2\text{Rh(H-COO)(mttpms)}]$; however signals of $\text{cis-mer-}[\text{H}_2\text{Rh(H-O)(mttpms)}]$ appeared almost simultaneously (Fig. 7) and their intensity increased in time at the expense of those of the formato complex. In separate gas volumetric experiments it was determined that in such water/2-propanol mixtures $[\text{RhCl(mttpms)}]$ catalysed the decomposition of aqueous formate to $H_2$ and bicarbonate with a turnover frequency of 70 h$^{-1}$ at 30 °C. A plausible path of formation of the hydrido complexes is the initial replacement of Cl$^-$ by HCOO$^-$, followed by either nuclophilic attack of OH$^-$ on the formato carbon atom and subsequent rearrangement or by oxidative addition of $H_2$ produced by catalytic decomposition of HCOO$^-$.
[H,RhXP,] \( (X = Cl \) or \( H_2O \); \( P = mtppts \) or \( mppts \) or \( mttpms \)) was also revealed by \( ^1H- \) and \( ^3P \)-NMR spectroscopies.

Since HCOONa can also act as a mild base, and in the presence of bases 2-propanol is known to act as H-donor the question arises whether in our systems it behaves only as an inert solvent or whether it takes part in the hydrogen transfer reaction of aldehydes. To answer this question we attempted transfer hydrogenation of trans-cinnamaldehyde under our standard conditions, however, Na-formate was replaced by Na,CO or NaHCO (the latter compound accumulates in the reaction mixture during transfer hydrogenation or as a product of concomitant decomposition of formate). At 30 °C in 4 hours the conversion of trans-cinnamaldehyde was less than 1% with Na,CO, while no conversion at all was detected with NaHCO as a base. Accordingly, it can be concluded that in the above transfer hydrogenation experiments 2-propanol did not serve as an H-donor. On the basis of these findings and of the kinetic features of the reaction a possible catalytic cycle is shown on Scheme 2.

Accordingly, 3-phenylpropanol was reduced to 3-phenylpropanol, albeit slowly, at 50 °C (11.9% conversion in 1 h). Other saturated aldehydes were also hydrogenated with this Rh-based catalyst by hydrogen transfer from formate. For example, under our standard conditions benzaldehyde was reduced with 60.3% conversion (reaction time: 1 h). We suggest that the reduction of the aldehyde function takes place with no prior coordination of the substrate to the metal and involves a hydride attack from cis-mer-[H,RhX(mppts)], as shown by the NMR investigations and accounts for the observed kinetic phenomena, such as the increase of reaction rate with increasing formate concentration (Fig. 3) and the lack of phosphine inhibition (Fig. 5).

Although the [RhCl(mppts)],-catalysed transfer hydrogenation of trans-cinnamaldehyde proved fairly selective towards formation of the saturated aldehyde 3-phenylpropanal, at longer reaction times or at higher temperatures substantial amounts of the saturated alcohol, 3-phenylpropanol were obtained.

In comparison to the effect of 2-propanol on the rate-increasing effect of 2-propanol the biggest part probably comes from the dissolution of aldehydes into the aqueous phase. Solubility of trans-cinnamaldehyde in water at 30 °C is 1.42 mg/ml and accordingly 0.0805 mmol of this compound is dissolved in 7.5 ml aqueous reaction medium. In the homogeneous solution of 1 mmol trans-cinnamaldehyde obtained with 4.0 ml water + 3.5 ml 2-propanol the aldehyde concentration is 12.4 times higher than in water alone. Nevertheless, this concentration gives an \([S]/[C]\) value of 100 which already implies the saturation value of TOF (see Fig. 4). It should also be mentioned that although the reaction mixtures were homogeneous already at 20% v/v 2-propanol concentration, the conversion of trans-cinnamaldehyde significantly increased further with increasing 2-propanol/water ratio (from 28% to 41%, see Fig. 2) and varied according to a maximum curve (with a plateau between 25 and 70 v/v propanol concentrations). It is of interest that changes in the solvent composition did not change the selectivity of the reaction; at 30 °C 3-phenylpropanol was obtained exclusively. Although we did not attempt repeated use of the same catalyst, we demonstrated that it could be recovered in the aqueous phase after the product and unreacted cinnamaldehyde were extracted from the water/2-propanol reaction mixtures with toluene.

In comparison to the effect of 2-propanol on the rate of transfer hydrogenation of trans-cinnamaldehyde from aqueous formate catalysed by Ru(ii)-mppts complexes (a 45-fold acceleration), the rate increase in the case of the [RhCl(mppts)],-catalysed reaction is smaller (6.5 x), and can be largely, although not completely, ascribed to the dissolution of the substrate.
into the aqueous reaction mixture. It is tempting to speculate that part of the effect originates from changes in the water/2-propanol solvent structure with changing composition. For example, the viscosity of water/2-propanol mixtures changes markedly with v/v 2-propanol concentration due to the regular H-bond network and propanol may co-exist with tetramethylsilane (TMS), sodium (DSS) or to external 85% H3PO4.

4.2 Catalytic Transfer Hydrogenation of Cinnamaldehyde

In a typical reaction 408 mg (6 mmol) sodium formate and 126 µl (1 mmol) cinnamaldehyde were added to a mixture of 4.0 ml water and 3.5 ml 2-propanol at T = 30 °C. 13 mg (0.01 mmol) [RhCl(mpptms)]2 and 28 mg (0.07 mmol) mpptms were dissolved in the deoxygenated solution and the mixture was stirred vigorously (or taken at a pre-set reaction time), diluted with 1 ml of water and extracted by toluene. The organic extract was filtered through a short silica plug and analysed by gas chromatography.

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