



The biphasic transfer hydrogenation of aldehydes and ketones with isopropanol catalyzed by water-soluble rhodium complexes

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Abstract

Water-soluble rhodium complex generated in situ from $[\text{Rh}(\text{COD})\text{Cl}]_2$ and triphenylphosphine trisulfonate ($\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$, TPPTS) has been found to be a quite effective catalyst for transfer hydrogenation of aldehydes and ketones with isopropanol, under basic conditions. Thus, various aliphatic and aromatic aldehydes and ketones were selectively converted to the corresponding alcohols indicating the wide synthetic scope of the catalytic system. This latter can also be successfully recycled and re-used with only negligible loss of catalytic activity. © 2004 Elsevier B.V. All rights reserved.

Keywords: Transfer hydrogenation; Water-soluble catalyst; Ketones; Aldehydes; Isopropanol

1. Introduction

Reduction of ketones and aldehydes to the corresponding alcohols, which can be performed by a variety of methods, is one of the most important reactions in organic synthesis. Among the methods used, transfer hydrogenation [1] is an elegant strategy that can be accomplished with homogeneous [2–10], heterogeneous [11–18], perfluorinated [19], and water-soluble catalysts [20–23], using different hydrogen sources such as isopropanol and formic acid derivatives.

Although the considerable development of transfer hydrogenation of ketones catalyzed with transition metals, the mechanistic studies of this reaction are limited [2–4]. Hydridic metal intermediates are supposed to be involved during the catalytic cycles [1a,2–4], while direct transfer of hydrogen from alkoxy complex to the coordinated substrate was postulated for Meerwein–Ponndorf–Verley (MPV) reduction, promoted with aluminum alkoxide [1c]. Recently, Bäckvall and coworkers [24] and Noyori and coworkers [25] brought more evidence for hydridic route by isolating some ruthenium hydrides considered as intermediates.

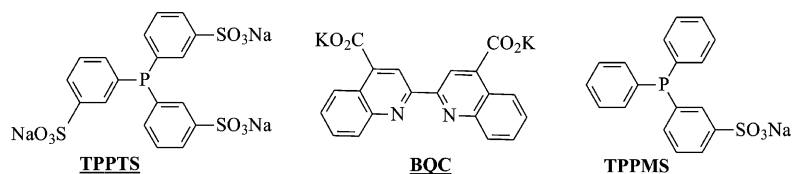
Despite the obvious economical and ecological importance of aqueous-phase catalysis [26], few catalytic systems

were reported for the hydrogen transfer reduction of aldehydes and ketones with sodium formate as reducing agent [20–22]. To the best of our knowledge, only water-soluble aminosulfonamide complexes were reported for the transfer hydrogenation of ketones with isopropanol [23]. However, the transformation was limited to acetophenones, 1-indanone, and 2'-acetonaphthone, and no attempts have been made to recycle the catalysts.

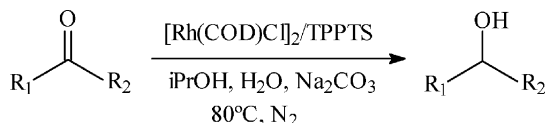
As part of our research program devoted to the synthesis of organic compounds in water, recently, we developed catalytic methods for, the hydration of nitriles to the corresponding amides [27], Oppenauer-type oxidation of secondary alcohols [28], and organic solvent-free oxidation of alcohols with *tert*-butyl hydroperoxide catalyzed by water-soluble copper complex [29]. We are interested in developing an effective recyclable water-soluble catalyst for Meerwein–Ponndorf–Verley-type reduction of ketones and aldehydes. In this paper we wish to report that $[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$ ($\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$, Scheme 1) system is very effective water-soluble catalyst for the hydrogen transfer reduction of a variety of aliphatic and aromatic ketones and aldehydes (equation). In addition to its wide synthetic utility, the catalytic system is easily recovered and recycled. $[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$ system has been reported to catalyze the hydrogenation of carbon dioxide to formic acid [30], and the transfer hydrogenation of α,β -unsaturated carboxylic acids with formates [31].

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Scheme 1.



2. Experimental

2.1. Materials and instruments

All the substrates were purchased from Aldrich and used without further purification. $[\text{Rh}(\text{COD})\text{Cl}]_2$ and $[\text{Ir}(\text{COD})\text{Cl}]_2$ were acquired from Strem Chemical Co. TPPTS was prepared according to the literature method [32].

Routine NMR measurements were performed on a Bruker AC-200 spectrometer at 200 and 50 MHz, respectively, for ^1H and ^{13}C , using TMS as internal standard and CDCl_3 as solvent.

2.2. Typical procedure for the transfer hydrogenation with isopropanol

In a glass liner of a 45 ml autoclave and under an atmosphere of nitrogen, $[\text{Rh}(\text{COD})\text{Cl}]_2$ (0.01 mmol) and TPPTS (0.3 mmol) were dissolved in degassed water (10 ml) at room temperature. Then a solution of the substrate (5 mmol) in degassed isopropanol (3 ml) was added followed by sodium carbonate powder (1 mmol). The autoclave was flushed several times with 5 atm of N_2 and then placed in an oil bath at 80°C for the required reaction time (2 h for the aldehydes and 3 h for the ketones). The autoclave was cooled to room temperature then the mixture was extracted three times with deoxygenated diethylether (20 ml), under nitrogen atmosphere. The combined organic layers were dried (MgSO_4), evaporated to dryness, then analyzed by thin layer chromatography, ^1H NMR and ^{13}C NMR. Literature data and/or authentic samples were used for comparison. Yields were determined by ^1H NMR measurements.

For the recycling, the aqueous-phase obtained after removal of solvents was re-used with a fresh charge of a solution of the substrate (5 mmol) in degassed isopropanol (3 ml), and no additional TPPTS was added.

3. Results and discussion

In order to test the catalytic activity of various systems, the MPV-type reductions of benzaldehyde and acetophenone

were chosen as model reactions with different hydrogen sources. The main results obtained for these two compounds are, respectively, reported in Tables 1 and 2. The catalytic systems tested for these reductions are based on the water-soluble ligands $\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$ (TPPTS) and 2,2'-biquinoline-4,4'-dicarboxylic acid di-potassium salt (BQC, Scheme 1).

First the presence of the catalyst precursor and isopropanol together is required to achieve the reduction of benzaldehyde. Treatment of benzaldehyde (5 mmol) in the presence of catalytic amount of $[\text{Rh}(\text{COD})\text{Cl}]_2$ (0.01 mmol), TPPTS (0.3 mmol), and Na_2CO_3 (1 mmol) in a deoxygenated mixture of distilled water (10 ml) and isopropanol (3 ml) at 80°C selectively afforded benzyl alcohol in 98% yield (Table 1, entry 1). When molecular hydrogen or sodium formate were used, separately, instead of isopropanol, full conversion was obtained in the case of H_2 while HCO_2Na lead to 90% yield (Table 1, entries 4 and 5). Interestingly, the active catalyst generated from $[\text{Rh}(\text{COD})\text{Cl}]_2$ and TPPTS is much more active than $\text{RhCl}(\text{TPPMS})_3$ based on triphenylphosphine monosulfonate (TPPMS: $\text{Ph}_2\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})$, Scheme 1), since this latter catalyses the reduction of benzaldehyde with sodium formate in only 22% yield [20b]. The reaction was found to be considerably influenced by the ligand and catalyst precursor used. Indeed, dramatic decrease

Table 1
Transfer hydrogenation of benzaldehyde catalyzed by different water-soluble systems^a

Entry	Catalytic system	Hydrogen donor	Yield (%)
1	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	<i>i</i> PrOH	98
2 ^b	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	<i>i</i> PrOH	97
3 ^c	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	<i>i</i> PrOH	98
4 ^d	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	H_2	100
5 ^e	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	HCOONa	90
6 ^f	$[\text{Rh}(\text{COD})\text{Cl}]_2/\text{BQC}$	<i>i</i> PrOH	7
7	$[\text{Ir}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	<i>i</i> PrOH	17
8 ^d	$[\text{Ir}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	H_2	9
9 ^e	$[\text{Ir}(\text{COD})\text{Cl}]_2/\text{TPPTS}$	HCOONa	4
10 ^f	$[\text{Ir}(\text{COD})\text{Cl}]_2/\text{BQC}$	<i>i</i> PrOH	19

^a Reaction conditions: benzaldehyde (5 mmol), TPPTS (0.3 mmol), $[\text{M}(\text{COD})\text{Cl}]_2$ (0.01 mmol), Na_2CO_3 (1 mmol), water (10 ml), *i*PrOH (3 ml), 80°C , N_2 , 2 h.

^b Second cycle of entry 1.

^c Third cycle of entry 1.

^d Fourteen atmosphere of hydrogen molecular pressure was used.

^e Twenty-six millimoles of sodium formate were used.

^f BQC was used in 0.15 mmol.

Table 2

Transfer hydrogenation of acetophenone catalyzed by different water-soluble systems^a

Entry	Catalytic system	Time (h)	Yield (%)
1	[Rh(COD)Cl] ₂ /TPPTS	2	72
2	[Rh(COD)Cl] ₂ /TPPTS	3	93
3 ^b	[Rh(COD)Cl] ₂ /TPPTS	3	90
4 ^c	[Rh(COD)Cl] ₂ /TPPTS	3	90
5 ^d	[Rh(COD)Cl] ₂ /TPPTS	3	88
6	[Rh(COD)Cl] ₂ /TPPTS	24	91
7 ^e	[Rh(COD)Cl] ₂ /TPPTS	24	49
8 ^f	[Rh(COD)Cl] ₂ /TPPTS	3	37
9 ^f	[Rh(COD)Cl] ₂ /TPPTS	24	74
10 ^f	[Rh(COD)Cl] ₂ /TPPTS	36	80
11 ^g	[Rh(COD)Cl] ₂ /BQC	3	4
12	[Ir(COD)Cl] ₂ /TPPTS	3	0
13 ^g	[Ir(COD)Cl] ₂ /BQC	3	13
14 ^h	[Rh(COD)Cl] ₂ /TPPTS	3	32
15 ⁱ	[Rh(COD)Cl] ₂ /TPPTS	3	9

^a Reaction conditions: acetophenone (5 mmol), TPPTS (0.3 mmol), [M(COD)Cl]₂ (0.01 mmol), Na₂CO₃ (1 mmol), water (10 ml), *i*PrOH (3 ml), 80 °C, N₂.

^b Second cycle of entry 2.

^c Third cycle of entry 2.

^d Fourth cycle of entry 2.

^e The reaction was performed without sodium carbonate.

^f The reaction was performed at 65 °C.

^g BQC was used in 0.15 mmol.

^h Hydrogen molecular (14 atm.) was used in stead of *i*PrOH.

ⁱ Sodium formate (26 mmol) was used in stead of *i*PrOH.

in the conversion of benzaldehyde was observed when BQC is used in place of TPPTS, or when [Rh(COD)Cl]₂ was substituted by its iridium analog (Table 1, entries 6–10).

Based on these results and as we are interested in the reduction of ketones, we re-examined the activity of the catalytic systems in the reduction of acetophenone (Table 2). When acetophenone was reduced with isopropanol under the same conditions as for benzaldehyde, 1-phenylethanol was obtained with 72% yield (Table 2, entry 1). An increase in the reaction time to 3 h led to 93% yield (Table 2, entry 2). No further increase in yield was observed when the reaction was repeated for 24 h (Table 2, entry 6). The role of the base as promoter was demonstrated in the entry 7, since only 49% yield was achieved without the presence of sodium carbonate. At 65 °C, the catalytic system is still active performing the reduction of acetophenone with *i*PrOH in 80% yield after 36 h (Table 2, entries 8–10). As in the case of benzaldehyde, both the choice of the metallic precursor and the ligand affected the reaction in the expected manner. Indeed, the use of BQC instead of TPPTS, or iridium complex instead of rhodium one lead to poor yields (Table 2, entries 11–13). When molecular hydrogen and sodium formate are used as hydrogen donors, [Rh(COD)Cl]₂/TPPTS system gave very low yields (Table 2, entries 14 and 15). Same behavior was previously observed in the case of water-soluble catalyst RuCl₂(TPPMS)₂ which is very active for the reduction of aldehydes with HCO₂Na,

and failed to catalyze the reduction of acetophenone [20a].

Of particular significance in aqueous-phase catalysis is the ability to isolate the products by simple decantation, and to recover and recycle the catalyst. The stability of [Rh(COD)Cl]₂/TPPTS during the reduction of both benzaldehyde and acetophenone is evidently very good as the catalyst aqueous solutions, carefully separated from the organic phases under nitrogen atmosphere, could be reused with only a negligible loss of activity (Table 1, entries 1–3; and Table 2, entries 2–5). It is important to point out that no metallic precipitates were observed, and the aqueous phases containing the catalyst remained clear-yellow solutions. The reactions performed under an air atmosphere, led to the decomposition of the catalyst and to the formation of metallic rhodium. Under these conditions, the problems of reproducibility were encountered and only very low conversions were obtained.

In the light of these results, [Rh(COD)Cl]₂/TPPTS/*i*PrOH prove to be efficient for the hydrogen transfer reduction of benzaldehyde and acetophenone. Thus, various aromatic and aliphatic aldehydes and ketones were subjected to reduction with same method (Table 3). As can be seen, both aldehydes and ketones underwent smooth, selective and quantitative transformation into the corresponding alcohols within 2–3 h. The catalytic system proved to tolerate the presence of heterocycles (Table 3, entries 5 and 6). In the case of substituted cycloalkanones [Rh(COD)Cl]₂/TPPTS gave poor stereoselectivity since the ratios *trans/cis* are close to one (Table 3, entries 16 and 17).

Table 3

Transfer hydrogenation of aldehydes and ketones catalyzed by [Rh(COD)Cl]₂/TPPTS^a

Entry	Substrate	Time (h)	Yield (%)
1	Benzaldehyde	2	98
2	<i>p</i> -Anisaldehyde	2	86
3	<i>p</i> -(Diethylamino)benzaldehyde	2	84
4	Dodecylaldehyde	2	83
5	2-Furaldehyde	2	100
6	2-Thiophenecarboxaldehyde	2	72
7	Acetophenone	3	93
8	4'-Methoxyacetophenone	3	86
9	Benzophenone	3	96
10	9-Fluorenone	3	100
11	Propiophenone	3	78
12	Cyclohexanone	3	98
13	Cyclopentanone	3	87
14	Cyclooctanone	3	74
15	5-Nonanone	3	97
16 ^b	2-Methylcyclopentanone	3	90
17 ^c	4- <i>t</i> -Butylcyclohexanone	3	87

^a Reaction conditions: substrate (5 mmol), TPPTS (0.3 mmol), [Rh(COD)Cl]₂ (0.01 mmol), Na₂CO₃ (1 mmol), water (10 ml), *i*PrOH (3 ml), 80 °C, N₂.

^b *Trans/cis* = 55 : 45.

^c *Trans/cis* = 40 : 60.

4. Conclusions

In conclusion, the system $[\text{Rh}(\text{COD})\text{Cl}]_2/\text{TPPTS}/i\text{PrOH}$ effects selectively the transfer hydrogenation of aliphatic and aromatic aldehydes and ketones with good to excellent yields, under basic conditions. The catalytic system can also be recycled and re-used with only negligible loss of catalytic activity.

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