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Application of Immobilized Rhodium Catalyst Precursors in Enantio- and Chemoselective Hydrogenation Reactions

Jim A. M. Brandts* and Peter H. Berben

Engelhard de Meern B.V., Strijkviertel 67, P.O. Box 19, 3454 ZG De Meern, The Netherlands

Abstract:

Two different homogeneous catalyst precursor complexes, i.e. $[Rh(COD)_2]BF_4$ and $[Rh(COD)Cl]_2$, were immobilized on phosphotungstic acid-modified alumina to form γ-Al_2O_3/PTA/$Rh(COD)_2BF_4$ (1b) and γ-Al_2O_3/PTA/$[Rh(COD)Cl]_2$ (2b), respectively. These immobilized complexes have been modified with (*R*,*R*)-MeDuPHOS to form the immobilized chiral catalysts γ-Al_2O_3/PTA/Rh((*R*,*R*)-MeDuPHOS)(COD)BF_4 (1c) and γ-Al_2O_3/PTA/Rh((*R*,*R*)-MeDuPHOS)(COD)Cl (2c). It is shown that immobilization and subsequent modification by ligand exchange reactions of general precursor complexes is a powerful method to prepare chiral and achiral anchored rhodium catalysts. Enantioselective hydrogenation reactions show that the activity and selectivity differences between the homogeneous catalysts [((*R*,*R*)-MeDuPHOS)Rh(COD)]BF_4 (1a) and the in situ prepared [((*R*,*R*)-MeDuPHOS)Rh(COD)]Cl (2a) are larger than the differences between the immobilized analogues (1c, 2c). At elevated temperature and H_2 pressure the activity and selectivity of 1c are comparable to those of its homogeneous analogue. Complex 1b was also used to prepare γ-Al_2O_3/PTA/Rh(DiPFc)-(COD)BF_4 (1d) via a ligand exchange reaction with 1,1′-bis-(diisopropylphosphino)ferrocene (DiPFc). This complex was used as a selective and heterogeneous hydrogenation catalyst with special chemoselective hydrogenation properties. The described immobilized rhodium catalysts prepared from the general precursor complexes 1b and 2b display hydrogenation activity and selectivity comparable to those of their homogeneous analogues. Moreover, it is demonstrated that these catalysts can be reused multiple times with neither activity nor selectivity loss and that leaching can be minimized by using optimized reaction parameters.

Introduction

Reduction of unwanted side-product formation in C═C, C═O, and C═N double bond reductions is attractive both from an economic and environmental point of view. These reduction reactions can effectively be performed with stoichiometric amounts of hydride complexes, but equimolar amounts of salts have to be discarded as waste. Catalytic reduction with hydrogen is a more attractive alternative in terms of waste, selectivity, and ease.[1]

Both homogeneous and heterogeneous precious metal catalysts can perform these catalytic reduction reactions very effectively with the use of hydrogen as the only reagent.[2] Although heterogeneous precious metal catalysts can be very effective in hydrogenations, the chemo-, regio-, and especially enantioselectivity are more difficult to control. On the contrary, the properties of homogeneous catalysts can be tuned by changing both the electronic and steric influences on the catalytic center by modification of the ligands attached.[3,5] Optimization of homogeneous catalysts allows the generation of more active and selective catalysts. Despite the higher activity and selectivity, homogeneous catalysts have not widely replaced heterogeneous catalysts on industrial scale, partly due to the difficult product-from-catalyst separation.

One possible option to circumvent the problems of catalyst separation in homogeneously catalyzed reactions is immobilization of the catalyst to a support.[4] The obvious advantages would be the easy separation of the catalyst from the product (downstream product purification is simplified), the possibility for performing the reactions in a continuous mode, and higher turn-over numbers (TON) by reusing the catalyst.

In homogeneous catalysis $[Rh(COD)Cl]_2$ and $[Rh(COD)_2]$-BF_4 (COD = 1,5-cyclooctadiene) are important general precursor complexes to prepare a number of symmetric and asymmetric Rh-based hydrogenation catalysts.[5] A simple ligand exchange reaction, in which one COD ligand is replaced by, for example, a chiral diphosphine ligand, gives the wanted, ligand-modified homogeneous catalyst. Immobilization of the Rh−precursor complexes would create the possibility to prepare a large number of different immobilized Rh catalysts by similar ligand exchange reactions. One of the most promising techniques for immobilization of these type of catalysts was reported by Augustine.[6] Both the precursor complexes as well as the ligand-modified homogeneous Rh-based catalysts can be anchored on a heteropoly acid-modified support (Scheme 1). Phosphotungstic acid (PTA) is especially suitable for this purpose. Interestingly, the immobilized catalysts prepared according

* Author for correspondence. E-mail: jim.brandts@engelhard.com.

(1) (a) Hudlicky, M. *Reductions in Organic Chemistry*; Halsted Press: New York, 1984. (b) Blaser, H.-U.; Studer, M. *Appl. Catal., A* **1999**, *189*, 191.

(2) (a) Augustine, R. L. *Heterogeneous Catalysis for the Synthetic Chemist*; Marcel Dekker: New York, 1996. (b) Nishimura, S. *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*; John Wiley & Sons: New York, 2001.

(3) (a) Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2024. (b) Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008. (c) Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998.

(4) (a) Pugin, B. *J. Mol. Catal.* **1996**, *107*, 273. (b) *Chiral Catalyst Immobilization and Recycling*; Vos, D. E., Vankelecom, I. F. J., Jacobs, P. A., Eds.; Wiley-VCH: New York, 2000.

(5) Ojima, I. *Catalytic Asymmetric Synthesis*, 2nd ed.; Wiley-VCH: New York, 2000.

(6) (a) Tanielyan, S. K.; Augustine, R. L. (Seton Hall University). U.S. Patent 6,025,295, 2000. (b) Augustine, R. L.; Tanielyan, S. K.; Anderson, S.; Yang, H. *Chem. Commun.* **1999**, 1257.

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Scheme 1

PTA = phosphotungstic acid
L =1,5-cyclooctadiene
1b: X = BF_4, **2b**: X = Cl

1c: P-P = (*R,R*)-MeDuPHOS, X = BF_4
2c: P-P = (*R,R*)-MeDuPHOS, X = Cl
1d: P-P = DiPFc, X = BF_4

to Augustine's method maintain a high degree of activity and selectivity and show minimum leaching.

It is known that the characteristics of the anion of the homogeneous catalysts (Cl, BF_4, PF_6, etc.) greatly influence the catalytic properties. Large differences between the different anions have been observed.[7] Interestingly, the anion effect in the immobilized analogues has not yet been addressed. One of the objectives of this study was to determine if such anion effects also exist for the immobilized catalysts prepared from different cationic rhodium complexes and PTA-modified alumina.

In this contribution, we present the immobilization and application of two different homogeneous catalyst precursor complexes, i.e., $[Rh(COD)_2]BF_4$ and $[Rh(COD)Cl]_2$ to form γ-Al_2O_3/PTA/$Rh(COD)_2BF_4$ (**1b**) and γ-Al_2O_3/PTA/$[Rh(COD)Cl]_2$ (**2b**), respectively. These complexes have been modified with (*R,R*)-MeDuPHOS to form the immobilized chiral catalysts γ-Al_2O_3/PTA/Rh((*R,R*)-MeDuPHOS)(COD)BF_4 (**1c**) and γ-Al_2O_3/PTA/Rh((*R,R*)-MeDuPHOS)(COD)Cl (**2c**). Complexes **1c** and **2c** and their homogeneous analogues were tested in chiral hydrogenation reactions, and the results were compared in terms of activity and selectivity. Moreover, the influence of experimental conditions on the stability towards leaching of the immobilized catalysts is demonstrated.

Complex **1b** was also used to prepare γ-Al_2O_3/PTA/Rh(DiPFc)(COD)BF_4 (**1d**) via a ligand exchange reaction with 1,1′-bis(diisopropylphosphino)ferrocene (DiPFc). This complex can be used as a very selective and heterogeneous hydrogenation catalyst with special chemoselective hydrogenation properties and exemplifies the advantages of this immobilization technique.

Experimental Section

Materials. All reactions were carried out using standard Schlenk techniques under inert nitrogen atmosphere unless stated otherwise. The phosphotungstic acid (Acros), dimethyl itaconate (Acros), 1,5-cyclooctadiene (Acros), γ-Al_2O_3 (Aldrich, activated, neutral, 150 mesh, SA 155 m^2/g), $[Rh(COD)Cl]_2$ (Engelhard), (*R,R*)-MeDuPHOS (Strem), [((*R,R*)-MeDuPHOS)Rh(COD)]BF_4 (Strem), 1,1′-bis(diisopropylphosphino)ferrocene (ChiroTech) were used without purifications. MeOH, EtOH, isopropyl alcohol, cyclohexane, CH_2Cl_2 (LabScan) were flushed with N_2 for several hours before use. $[Rh(COD)_2]BF_4$ was prepared from $[Rh(COD)Cl]_2$ and equimolar amounts of $AgBF_4$ and excess 1,5-cyclooctadiene. Chiral GC was measured with the use of a Chiraldex, β-cyclodextrin trifluoroacetyl, 30 m × 0.25 mm column; GC analysis was done with the use of a HP-1 methyl siloxane capillary 30 m × 320 μm × 0.25 μm column; ICP (inductively coupled plasma) analyses were determined on a ThermoJarrell Ash, Atom Scan 16; and XRF analyses were determined on a Philips Uniquant Analyzer.

Procedures. γ-Al_2O_3/PTA. The preparation method was used as described in the literature[6] using 100 g of γ-Al_2O_3 and 20 g of phosphotungstic acid. The final product (yield 120 g) contains 11.4 wt % W by ICP and was stored in air.

γ-Al_2O_3/PTA/$Rh(COD)_2BF_4$ (1b). Preparation method was used as described in the literature[6] using 100 g of γ-Al_2O_3/PTA and 0.82 g of $[Rh(COD)_2]BF_4$ (2.02 mmol). The final orange-colored product contains 0.20 wt % Rh and 10.2 wt % W by ICP.

γ-Al_2O_3/PTA/$[Rh(COD)Cl]_2$ (2b). A preparation method similar to that for **1b** was used with 100 g of γ-Al_2O_3/PTA and 0.50 g of $[Rh(COD)Cl]_2$ (1.01 mmol). The final yellow-to-orange-colored product contains 0.21 wt % Rh and 10.6 wt % W by ICP.

In Situ Prepared [((*R,R*)-MeDuPHOS)Rh(COD)]Cl (2a). To a 2-mL MeOH solution containing 0.0010 g of $[Rh(COD)Cl]_2$ (2.0 μmol) was added a 1-mL MeOH solution of (*R,R*)-MeDuPHOS (0.0013 g, 4.3 μmol). The yellow-colored solution was stirred for 2 h and was used as such.

γ-Al_2O_3/PTA/Rh((*R,R*)-MeDuPHOS)(COD)BF_4 (1c). In a 20-mL Schlenk vessel were placed 1.00 g of **1b** (20 μmol Rh) and 0.0076 g of (*R,R*)-MeDuPHOS (25 μmol). The air in the Schlenk was replaced by N_2 by three vacuum (10 min, oil pump)−N_2 cycles. To the solids 10 mL of MeOH was added, and the Schlenk vessel was shaken several times during 1 h. The color of the solid material changed from orange to yellow. After 1 h the upper layer was removed by decantation. The remaining solids were washed with MeOH (two times 10 mL). The solids were dried in vacuo and stored in inert atmosphere. The yellow solids (yield 0.99 g, quantitative) contained 0.20 wt % Rh, 10.3 wt % W by ICP analysis.

γ-Al_2O_3/PTA/Rh((*R,R*)-MeDuPHOS)(COD)Cl (2c). A method similar to that for the preparation of **1c** was used starting with 1.00 g of **2b**. The resulting yellow solid (yield 0.99 g, quantitative) contains 0.19 wt % Rh, 10.1 wt % W by ICP analysis.

γ-Al_2O_3/PTA/Rh(DiPFc)(COD)BF_4 (1d). A similar method was used as for the preparation of **1c** using 1.00 g of **1b** and 0.0096 g of 1,1′-bis(diisopropylphosphino)-

(7) (a) Blankenstein, J.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2001**, *23*, 4445. (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348. (c) For Alder ene reactions, see: Lei, A.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 8198

Table 1. **Hydrogenation of dimethyl itaconate using different catalysts[a]**

entry	catalyst	solvent	H_2 pressure (bar)	T (°C)	conversion (%) at 0.5 (min)	conversion (%) at 5 (min)	conversion (%) at 10 (min)	time[b] 98% (min)	TOF (h^{-1})[c]	ee (%)[d]
1	**1a**	MeOH	3.3	20	20.7	91.4	>99	<10	30000	96
2[e]	**1a**	MeOH	3.3	20	−	−	−	80	24000	95
3	**1a**	isopropyl alcohol[f]	3.3	20	26.7	94.6	>99	<10	32000	95
4	**2a**	MeOH	3.3	20	−	14.3	23.2	>60	1200	92
5	**1c**	isopropyl alcohol	3.3	20	−	19.4	34.5	120	2000	97
6	**1c**	isopropyl alcohol	6.6	20	7.1	43.1	68.4	40	5500	96
7	**1c**	isopropyl alcohol	6.6	50	16.9	82.2	96.5	12	17000	96
8[e]	**1c**	isopropyl alcohol	6.6	50	−	−	−	100	19000	96
9	**2c**	isopropyl alcohol	3.3	20	−	14.3	28.1	>60	1400	97
10	**2c**	isopropyl alcohol	6.6	50	15.2	74.8	93.7	15	13000	97

[a] Standard reaction conditions: 2−4 μmol Rh catalyst, 3.54 mmol dimethyl itaconate, 20 mL of solvent, 1000 rpm. [b] Time to reach 98% conversion. [c] Approximate turnover frequencies calculated at 20% conversion. [d] ee's determined at 98% conversion. [e] [dimethyl itaconate] = 1 M, 0.01 mol % catalyst. [f] Reaction mixture contains 10 vol % MeOH.

ferrocene (23 μmol). The resulting yellow solid (quantitative yield) contains 0.21 wt % Rh, 10.8 wt % W by ICP analysis.

Hydrogenation Tests. Standard hydrogenation reactions were carried out in a 50-mL stirred stainless steel Parr autoclave with a mechanic stirrer (1000 rpm). Reaction temperatures applied were between 20 and 60 °C. H_2 pressures between 0.7 and 6.6 bar were applied. Substrates were used as such without purifications. Solvents were flushed with N_2 for several hours before use. The reactor was loaded with the appropriate amount of catalyst (2−4 μmol Rh-based), purged with nitrogen, and a 20-mL solution (0.1−1.0 M in isopropyl alchol) containing the appropriate amount of substrate was added via a cannula. While stirring, the reaction was started by putting the reactor under H_2 pressure. The reaction progress was followed in time by taking samples at predetermined time intervals. Products were analyzed by (chiral) GC and ICP. After the reaction was completed, the stirring was stopped, the catalyst was allowed to settle, and the upper layer was removed. In reuse experiments a fresh batch of the dissolved substrate was added, and the procedure was repeated.

Results and Discussion

Anchoring of homogeneous Rh catalysts on phosphotungstic acid (PTA)-modified supports using Augustine's immobilization technology can be achieved by following two different routes.[8] The first method is the reaction between a solution of a metal−ligand complex $[M(L)_n]^+[X]^-$ (where X = Cl, BF_4, OTf or another suitable counterion) and the PTA-modified alumina. In a second method the immobilized catalyst is formed by reaction of a cationic metal−precursor, e.g., $[Rh(COD)Cl]_2$ or $[Rh(COD)_2]BF_4$, on a support followed by modification with a ligand of choice. This latter method is preferable in case of having to screen many different ligands. This method also tends to give better reproducible results in terms of activity and leaching stability. A similar immobilization concept was reported by Hems et al.[9] Although $[Rh(COD)Cl]_2$ is a dimeric species, it is unclear at this moment if the immobilized form is monomeric or dimeric in character.

(8) Presented by R. L. Augustine at ChiraSource 2001, Philadelphia, PA, 2001.
(9) Hems, W. P.; Hutchings, G. J. Patent WO 02/36261, 2002

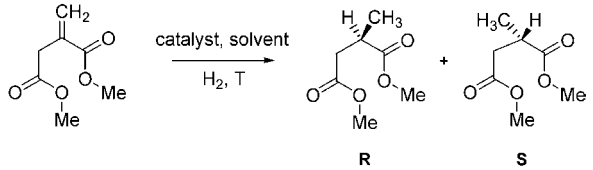


Figure 1. **Hydrogenation of dimethyl itaconate as model reaction to test the different catalysts.**

(*R,R*)-MeDuPHOS-Modified Precursor Complexes. Complex **1c** and **2c** were prepared by modification of **1b** and **2b** with (*R,R*)-MeDuPHOS, respectively. The immobilized catalysts **1c** and **2c** were tested in the hydrogenation of the prochiral substrate dimethyl itaconate (see Figure 1). For comparison reasons the homogeneous analogues [((*R,R*)-MeDuPHOS)Rh(COD)]BF_4 (**1a**) and the in situ prepared [((*R,R*)-MeDuPHOS)Rh(COD)]Cl (**2a**) were tested under similar reaction conditions. The data are collected in Table 1.

The rate of the catalyzed enantioselective hydrogenations showed a first-order dependency in substrate concentration (except **1b**). No evidence for catalyst activation times was found in the hydrogenation of dimethyl itaconate, similar to what was found by Cobley et al. for this substrate,[10] although it is known that the cyclooctadiene complexes of the rhodium catalysts can give rise to such phenomena at low s:c ratios.[11]

A significant difference in activity and selectivity was found between the homogeneous catalysts **1a** and **2a** under comparable reaction conditions (entries 1 and 4). Complex **2a** was approximately 20 times less active compared to **1a** and the enantioselectivety was lower as well (96% vs 92%). Moreover, slow deactivation of **2a** was observed during the reaction. It is known that these differences can be ascribed to the influence of the anion and that the (*R,R*)-MeDuPHOS-based rhodium catalysts work best with noncoordinating anions such as OTf^-, BF_4^-, or PF_6^-.

At room temperature and standard H_2 pressure the immobilized catalyst **1c** displayed a somewhat higher ee (97% vs 95%) but a lower activity compared to **1a** (entries

(10) Cobley, C. J.; Lennon, I. C.; McCague, R.; Ramsden, J. A.; Zanotti-Gerosa, A. *Tetrahedron Lett*. **2001**, *42*, 7481.
(11) (a) Drexler, H.-J.; Baumann, W.; Spannenberg, A.; Fischer, C.; Heller, D. *J. Organomet. Chem*. **2001**, *621*, 89. (b) Börner, A.; Heller, D. *Tetrahedron Lett*. **2001**, *42*, 223.

3 and 5). Catalyst **1c** is approximately 16 times less active, a phenomenon which can be explained in terms of transport limitation differences.[4b] The catalyst activity can be improved by increase of H_2 pressure (entry 6) or temperature (entry 7). The reaction parameter changes had no significant effect on the enantioselectivity.

Catalyst **2c** is somewhat less active compared to the BF_4 equivalent **1c** (entries 5 and 9, entries 7 and 10), but the differences between the immobilized complexes and the homogeneous analogues are less distinct, both in terms of activity and selectivity. The difference in activity between the immobilized complexes **2c** and **1c** is less than a factor of 2, whereas this same difference between **1a** and **2a** is 25.

At low substrate-to-catalyst ratios (s:c = 100−300) catalyst **1c** could be reused more than 10 times with constant activity and enantioselectivity (ee = 96−97%). Neither Rh nor W leaching was observed. At higher substrate-to-catalyst ratios (s:c = 10000) the activity of the immobilized catalyst decreased upon reuse. Small amounts of Rh and W leaching could be detected, but no proof was found that this leached material contributed to the activity. Since the observed ee's remained unchanged, deactivation of the catalyst could be caused by substrate impurities. Although the phosphotungstic acid is able to catalyze the formation of *i*-propyl esters from methyl esters in the isopropyl alcholic solvent, only very small traces (<0.5%) of *i*-propyl esters were found in the products.

The results obtained by using the immobilized catalyst **1c** at high substrate-to-catalyst ratios are very comparable to those from the homogeneously catalyzed hydrogenation of dimethyl itaconate (entries 2 and 8) in terms of activity (reaction time to > 98% conversion: **1c** = 100 min, **1a** = 80 min) and selectivity (**1c** ee = 96%, **1a** ee = 95%) under the conditions that were used. Although the results of the two catalysts are comparable, different reaction conditions (increased temperature, increased H_2 pressure) had to be applied. Comparison between **1c** and its homogeneous derivative **1a** is delicate because the two catalysts are intrinsically different.

Complex 1b Modified with (DiPFc). Complex γ-Al_2O_3/PTA/Rh(DiPFc)(COD)BF_4 (**1d**) was prepared via a ligand exchange reaction with 1,1′-bis(diisopropylphosphino)ferrocene (DiPFc) and **1b** and was jointly developed by Chirotech Technology Limited and Engelhard Corporation. Complex **1d** is the immobilized equivalent of the homogeneous catalyst [Rh(DiPFc)(COD)]BF_4[12] and has similar activity and selectivity properties.[13] Catalyst **1d** is particularly useful for chemoselective hydrogenations of (sulfur-containing) alkenes, alkynes, and aldehydes.

However, **1d** can be separated from the product mixture by simple filtration techniques. Moreover, it can be reused several times, without loss of (chemo)selectivity or activity.

Of particular interest is the observation that the chemoselectivity of this catalyst allows reduction of alkenes, alkynes, and aldehydes in the presence of aromatic bromides, aromatic nitro groups, and sulfur. Conventional heterogeneous catalysts give more overhydrogenated side products or have only limited activity due to the poisoning effect of the sulfur. To demonstrate its practicability catalyst **1d** was used in the reduction 4-bromostyrene to bromo-4-ethylbenzene. At relatively mild reaction conditions (50 °C, 6.6 bar H_2, isopropyl alcohol, 0.1 mol % catalyst, [4-bromo-styrene] = 0.19 mol/L) the catalyst could be reused three times after full conversion (total TON = 4000) (see Figure 2).

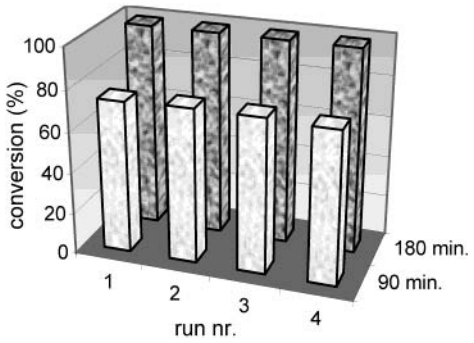
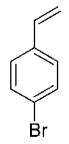
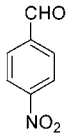
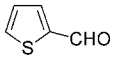


Figure 2. **Catalyst 1d is reused three times in hydrogenation of 4-bromostyrene.**

Table 2. **Selective hydrogenation using 1d and 10 % Pd/C[a]**

Substrate	Conversion (%)		Selectivity (%)	
	1d	10 % Pd/C	**1d**	10 % Pd/C
	>99	>99	>99	90[b]
	>99	42	>99	1[c]
	>99	8	>99	99

[a] Standard reaction conditions: 4 μmol Rh catalyst, 4 mmol substrate, 20 mL of isopropyl alcohol, 1000 rpm, 6.6 bar H_2 pressure, 50 °C. [b] Approximately 10% was ethylbenzene. [c] >96% = 4-carboxaldehyde aniline.

Neither deactivation nor leaching of the catalyst (Rh, W leaching determined by ICP) was observed. The bromide-aromatic bond remained unaffected. A 10% Pd/C catalyst under similar reaction conditions gave 10% ethylbenzene as a result of dehalogenation (see Table 2).

Catalyst **1d** can also be used for the hydrogenation of other functionilized alkenes and alkynes in alcoholic solvents. Substrates such as 3-nitrostyrene, phenyl vinyl sulfone, 1-phenyl-1-hexyne, and 1-dodecyne could be converted to their corresponding hydrogenated products.[13] No overhydrogenation was observed when **1d** was used, but other products were found when 10% Pd/C was used as a catalyst. Conventional heterogeneous catalysts do not give these types of chemoselectivity as shown by the data in Table 2.

(12) Burk, M. J.; Harper, T. P. G.; Lee, J. R.; Kalberg, C. *Tetrahedron Lett.* **1994**, *35*, 4963.
(13) Burk, M. J.; Gerlach, A.; Semmeril, D. *J. Org. Chem.* **2000**, *65*, 8933.

Table 3. **Leaching data obtained from 1c-catalyzed reaction mixtures[a]**

entry	solvent	[substrate] (M)	reaction time (min)	T (°C)	Rh leach (% total Rh)	W leach (% total W)
1	MeOH	0.1	20	50	2.3	0.05
2	EtOH	0.1	20	50	1.5	0.05
3	isopropyl alcohol	0.1	20	50	<1[b]	<0.002[b]
4	cyclohexane	0.1	20	50	<1	<0.002
5	cyclohexane	1.0	20	50	<1	<0.002
6	isopropyl alcohol	1.0	20	50	1.2	0.008
7	isopropyl alcohol	1.0	20	20	<1	<0.002
8	isopropyl alcohol	0.1	1020	50	2.0	0.03
9[c]	isopropyl alcohol	0.1	20	50	7.3	0.06

[a] Standard reaction conditions: 0.1 mol % **1c**, substrate = dimethyl itaconate, 20 mL solvent, 1000 rpm, 6.6 bar H_2. [b] Below detection limits of ICP. [c] Addition of 0.1 mol % Et_3NHCl.

The activity of **1d** is very comparable to the homogeneous catalyst [Rh(DiPFc)(COD)]BF_4 in the case of alkene and alkyne hydrogenations. In aldehyde reductions the activity of [Rh(DiPFc)(COD)]BF_4 is usually significantly higher. Depending on the substrate, the reaction conditions (higher temperature, H_2 pressure) could be optimized to compensate for this difference.

Some acetal formation was observed in the aldehyde hydrogenations in alcoholic solvents, probably due to acid-catalyzed reaction between the alcohol and the aldehyde.

Catalyst Stability to Leaching. Although the reaction mechanism of the bonding between the homogeneous catalysts and the heteropoly acid-modified support remains unclear, some evidence suggests that the bond is mainly ionic in character. Addition of ionic components such as ammonium and potasium salts, causes leaching of at least a part of the immobilized complexes. However, the addition of, for example, $LiBF_4$ hardly causes leaching.[8] A weak covalent coordinating interaction between the Rh atom and the phosphotungstic acid oxygen atom(s) is also conceivable as was found for comparable Ir and Rh complexes by Finke et al.[14] No evidence was found that the counterion in the Rh complex is removed from the catalyst during the reaction between the PTA-modified alumina and the rhodium−precursor complexes. We were unable to detect Cl by ICP analysis in the removed liquids after the reaction between the modified alumina and [Rh(COD)Cl]$_2$. However, XRF analysis of **2b** could not confirm the presence of Cl. The relatively small amount of Cl in the final product **2b** (0.07 wt %) is very close to the detection limit of the XRF analysis technique. Experiments resulting in immobilized [Rh(COD)Cl]$_2$ products with higher Cl content should provide more clarity.

One possible explanation for the experimental results is to assume that the heteropoly acid not only binds the anion but also influences the anion−cation interaction of the rhodium complex. This will have an effect on the reactivity and selectivity of the bonded Rh complex. Immobilization of [Rh(COD)Cl]$_2$ on the heteropoly acid-modified support will thus influence the Rh−Cl bond. These interactions could effect the coordinating ability of the Cl anion to the rhodium cation. A shift towards more noncoordinating characteristics, similar to those of BF_4, could explain why the differences between the homogeneous (**1a**, **2a**) are larger than the differences between the immobilized complexes (**1c**, **2c**). However, more evidence is needed to verify this hypothesis.

The bond between the rhodium complex and heteropoly acid-modified support (ionic interaction) is fairly strong but is still susceptible towards leaching. This susceptibility, however, strongly depends on the nature (i.e., ligands) of the immobilized complex. An immobilized Rh catalyst prepared from **1b** and ligand X might leach in MeOH under standard reaction conditions, while another catalyst prepared from **1b** and ligand Y is stable. This leaching stability is influenced by the polarity of the reaction environment, and a correlation between leaching and solvent polarity was found. Using alcoholic solvents leaching of the Rh complexes decreased from MeOH > EtOH > isopropyl alcohol. In MeOH some leaching was detected in dimethyl itaconate hydrogenations using **1c** and **2c** as catalysts. In isopropyl alcohol the leaching was reduced below the detection limits of ICP. In cyclohexane no leaching was ever observed (see Table 3, entries 1−5). Parameters such as substrate concentration, addition of ammonium salts, temperature, and reaction time were investigated for their influence on the catalyst stability towards leaching (Table 3).

An increase in the dimethyl itaconate concentration (entries 3 and 6), prolonged reaction or stirring times (entries 3 and 8) and the addition of Et_3NHCl (entries 3 and 9) resulted in more leaching of rhodium. A decrease in reaction temperature (entries 6 and 7) decreased the amount of rhodium in the reaction mixture. These results show how parameters such as reaction media, reaction temperature, substrate concentration, and purity influence the catalyst leaching stability. The ratio between the amounts of Rh and W found in the reaction mixtures indicates that the interaction between the PTA and the support is fairly strong under the reaction conditions used. The interaction between the rhodium and PTA, or between the rhodium and other heteropoly acids,[15] is the more leaching-sensitive interaction. All this knowledge can be used to optimize the leaching stability of the immobilized hydrogenation catalysts.

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Conclusions

The immobilization and subsequent modification by ligand exchange reactions of the general precursor complexes $[Rh(COD)Cl]_2$ and $[Rh(COD)_2]BF_4$, is a powerful method to prepare a number of chiral and achiral anchored rhodium complexes. At elevated temperature and H_2 pressure the Rh catalysts immobilized on PTA-modified alumina have activity and selectivity properties comparable to those of the homogeneous analogues. Chiral hydrogenation reactions show that the activity and selectivity differences between the homogeneous catalysts bearing different anions (BF_4: **1a**, Cl: **2a**) are larger than the differences between the immobilized analogues (**1c**, **2c**). This immobilization technology is very suitable to prepare a library of ligand-modified immobilized Rh catalysts. Parameters such as solvent (polarity), substrate, substrate concentration, substrate purity, temperature, and reaction time can be tuned to optimize leaching stability. It has been demonstrated that leaching can be minimized, provided that the reaction parameters used are optimized. Due to its leaching stability under optimized conditions, the catalysts can be reused several times without losses in activity and selectivity.

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