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Comparison of supports for the electrostatic immobilisation of asymmetric homogeneous catalysts

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Abstract

To determine the influence of the support on the asymmetric hydrogenation of dehydroamino acids using noncovalently immobilised catalysts, Rhodium-MonoPhos was successfully immobilised on four different anionic carrier materials: a mesoporous aluminosilicate (AlTUD-1), phosphotungstic acid on alumina (PWTUD), Nafion, and a Nafion silica composite (SAC-13). These supported catalysts were evaluated in the asymmetric reduction of methyl-2-acetamidoacrylate. Although most of the catalysts were highly selective, the activity and the loss of rhodium were strongly dependent on the type of support. PWTUD appeared to be the best support for this application, because it gave the catalyst with the highest activity and virtually no leaching in any solvent. Its superior anchoring ability derives from the additional bonding between the Rh and the phosphotungstic acid. Nafion, on the other hand, was by far the poorest support, giving very low activity. Immobilisation with this support relies on encapsulation rather than on ionic interactions. Its encapsulating properties not only prevent the complex from going into solution, but also prevent the substrate from reaching the catalytic site.

Keywords: Supported catalyst; Asymmetric catalysis; Hydrogenation; Immobilisation; Nafion; AlTUD-1

1. Introduction

The immobilisation of homogeneous catalysts on insoluble supports is a well-established methodology that combines the advantages of homogeneous and heterogeneous catalysts [1,2]. Heterogeneous catalysts have the benefit of easy separation and recyclability, whereas homogeneous catalysts generally have higher activities and superior selectivities. The merger of these two worlds is especially important in enantioselective catalysis, which is dominated by homogeneous catalysts that typically consist of noble (albeit toxic) metals and expensive chiral ligands. Therefore, catalyst recyclability is a major concern. One of the most attractive strategies for immobilisation relies on electrostatic interactions between the catalyst and the support rather than on covalent tethering, because it circumvents the need for time-consuming and often difficult ligand modification [3,4].

The important influence of these electrostatic interactions on activity and selectivity has long been recognized in homogeneous catalysis. One of the most striking examples is the effect of different halide ligands on the rhodium-catalysed asymmetric ring opening of oxabenzonorbornadiene [5], where the enantiomeric excess was increased from 45 to 98% simply by replacing Cl^- with I^-. Very recently, Pfaltz et al. demonstrated the importance of the anion in enantioselective hydrogenation [6]. His study revealed that in the asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene with Ir-PHOX, the reaction rate decreased significantly across the series $[Al\{OC(CF_3)_3\}_4]^- > [B(C_6F_5)_4]^- > PF_6 \gg BF_4^- > CFSO_3^-$. Surprisingly, in the electrostatic anchoring of asymmetric homogeneous catalysts, the study of the anion/anionic

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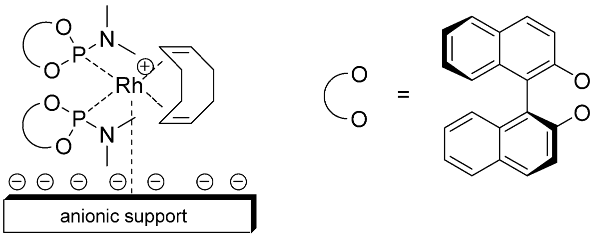

immobilised **1**

Fig. 1. Schematic representation of Rh-MonoPhos immobilised on an anionic support.

support has been neglected. Most authors compare an immobilised catalyst with its homogeneous counterpart; comparisons with other anionic support materials are lacking. The lack of a systematic study on the influence of the anionic support becomes even more surprising when considering that the anion also affects such characteristics as leaching, diffusion, and embedding of the catalyst. This absence of data leaves an important question—what is the best support for this application—unanswered.

To fill this void for the heterogenisation of asymmetric hydrogenation catalysts, Rh-MonoPhos (**1**) (depicted in Fig. 1) was immobilised on four different anionic carrier materials, and the behaviour of the four resulting heterogeneous catalysts for the hydrogenation of methyl 2-acetamidoacrylate (MAA) was systematically investigated. We selected the three-dimensional mesoporous aluminosilicate, AlTUD-1 [4,7] to represent the silicate-based materials used for immobilisation purposes. As a second support material, we selected the Augustine system, phosphotungstic acid (PW) on alumina, because this sets the standard for ionic anchoring. We selected Nafion as the ionic exchange resin, because it showed promising results in the field of asymmetric hydrogenation [8]. A drawback of this resin is its low surface area; for this reason, we selected SAC-13 as an additional support. SAC-13 is a commercially available Nafion silica composite that largely overcomes the aforementioned drawback of Nafion [9].

2. Experimental

2.1. General

Reactions and manipulations involving air-sensitive compounds were performed under a dry nitrogen atmosphere using standard Schlenk-type techniques. Dry solvents were purchased from Aldrich and deoxygenated by flushing with nitrogen for 1 h before use. Methyl 2-acetamidoacrylate [4], Bis(1,5-cyclooctadiene)rhodium tetrafluoroborate [10], (*R*)-MonoPhos [11], $[\mathrm{Rh}^{\mathrm{I}}(\mathrm{cod})((R)\text{-MonoPhos})_2]\mathrm{BF}_4$[2] [12], and AlTUD-1 ($S_{\mathrm{BET}}$, 600 m^2/g; total pore volume, 1.1 cm^3/g; pore diameter, 15 nm) [4] were prepared as described previously. Chloro(1,5-cyclooctadiene)rhodium dimer was purchased from Strem; all other reagents were purchased from Aldrich, Acros, or Fluka and used without further purification.

Hydrogenation was performed in a 100-mL Parr Hastelloy C autoclave (A1128HC). The rhodium and tungsten content of the immobilised catalysts was measured using instrumental neutron activation analysis (INAA) at the Interfaculty Reactor Institute (IRI), Delft. The Hoger Onderwijs nuclear reactor, with a neutronflux of 10^{17} neutrons/(s cm^2) was used as a source of neutrons, and the gammaspectrometer was equipped with a germanium semiconductor detector. Rhodium leaching was determined by analysing the reaction filtrates with graphite AAS on a Perkin–Elmer 4100ZL; tungsten leaching was determined by analysing the reaction filtrates with ICP on a Perkin–Elmer Optima 5300DV. The Nafion content of SAC-13 was determined by thermogravimetric analysis on a Cahn TG-131 (5 °C/min to 800 °C). N_2 desorption isotherms were measured on a Quantachrome Autosorb-6B at 77 K.

Conversions of the hydrogenation reactions were determined by ^{1}H-nuclear magnetic resonance (NMR) and gas chromatography (GC), using a Varian Star 3400 CX gas chromatograph with a CP wax 52 CB column (50 m × 0.70 mm; df = 2.0 μm), on column injection, a flame ionisation detector (FID) at 250 °C, and nitrogen as a carrier gas (10 psi). The oven program for MAA and its products was 60 °C for 2 min and 10 °C/min to 200 °C for 6 min. Enantiomeric excesses in the hydrogenation of MAA were determined by chiral GC using a Shimadzu GC-17A, equipped with a Chiralsil DEX CB column (25 m × 0.32 mm, df = 0.25 μm), He as carrier gas, a split injector (36/100) at 220 °C, and a FID at 220 °C. Retention times at 95 °C isotherm were 5.4 min for 2-acetamidoacrylate, 7.5 min for (*S*)-methyl 2-acetamidopropanoate, and 8.2 min for (*R*)-methyl 2-acetamidopropanoate.

2.2. Preparation TUD-$\mathrm{Al}_2\mathrm{O}_3$

TUD-$\mathrm{Al}_2\mathrm{O}_3$ was prepared according to the procedure of Shan et al. [13] At 45 °C, 15.32 g of aluminium isopropoxide (75 mmol) was added into a mixture of 13.8 g of absolute ethanol (300 mmol) and 13.5 g of anhydrous 2-propanol (225 mmol) under stirring. Then 14.6 g of tetraethylene glycol (75 mmol) was added. Finally, a solution of 13.8 g of absolute ethanol (300 mmol), 13.5 g of anhydrous 2-propanol (225 mmol), and 2.7 g of $\mathrm{H}_2\mathrm{O}$ (150 mmol) was added dropwise to this mixture. The resulting mixture was stirred for $\frac{1}{2}$ h at room temperature, followed by aging without stirring for 6 h, also at room temperature. The obtained wet gel was dried at 70 °C for 21 h and at 98 °C for 2 h, and then was hydrothermally treated at 160 °C for 3–21 h in an autoclave with a Teflon insert. Finally, the solids were calcined (at a rate of 1 °C/min to 550 °C, for 4 h at 550 °C and at a rate of 1 °C/min to 600 °C, for 10 h at 600 °C). TUD-$\mathrm{Al}_2\mathrm{O}_3$ was analysed by N_2 physisorption (Fig. 2), from which the following characteristics were derived: S_{BET}, 313 m^2/g; total pore volume, 0.61 cm^3/g; and pore diameter, 6 nm. PWTUD is made in situ from TUD-$\mathrm{Al}_2\mathrm{O}_3$ during the immobilisation, so no explicit structural data are available for this material. However, exploratory research showed that the presence of PW on the support reduced the sur-

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[2] Uncharacterised complex and it is probably a mixture of various species.

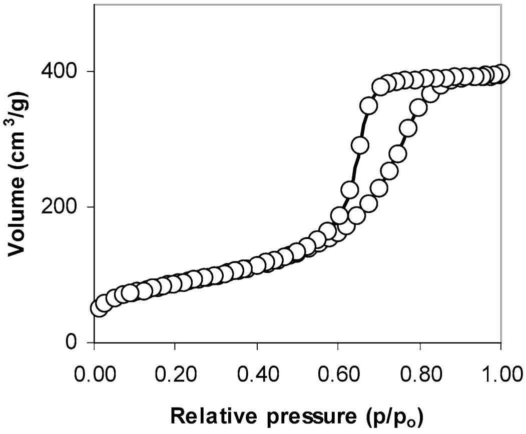


Fig. 2. Nitrogen sorption isotherms of TUD-Al_2O_3.

face area and pore volume only slightly, in accordance with the increase in sample weight.

2.3. Immobilisation procedures

2.3.1. $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ on AlTUD-1

After 1.0 g of AlTUD-1 was dried at 200 °C under vacuum for 2 h, 45 mL of 2-propanol was added to the dried support. After 30 min of stirring, 0.15 g of $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ (0.15 mmol) in 40 mL of 2-propanol was added, and the resulting suspension was stirred for 3 h. The solid was collected by filtration and washed thoroughly with portions of 30 mL of 2-propanol until the washings were colourless (approximately 5 times). Finally, the catalyst was dried at 55 °C under vacuum for 2 h. The resulting catalyst loading was 11 $mg_{Rh}/g_{support}$, corresponding to an $Al_{tetrahedral}/Rh$ ratio of approximately 10.

2.3.2. $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ on PWTUD

TUD-Al_2O_3 was dried for 2 h under vacuum at 200 °C, and phosphotungstic acid (PW) was dried for 12 h under vacuum at 100 °C. To 1.9 g of TUD-Al_2O_3 was added 40 mL of 2-propanol, followed after 5 min of stirring by 0.358 g of PW in 20 mL of 2-propanol. The mixture was stirred for 30 min, after which 0.106 g of $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ was added. After 3 h of stirring, the solid was collected by filtration and washed thoroughly with portions of 30 mL 2-propanol until the washings were colourless (approximately 5 times). Finally, the catalyst was dried at 55 °C under vacuum for 2 h. The resulting catalyst loading was 1.4 mg_{Rh}/g and 93 mg_W/g.

2.3.3. $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ on Nafion

The sodium form of Nafion was prepared by washing the resin with 2 M NaCl until neutral, followed by thorough washing with water. Finally, the solid was dried at 150 °C under vacuum for 4 h. To 1.0 g of Nafion (Na^+) was added 35 mL of methanol, followed after 10 min of stirring by 0.15 g of $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ dissolved in 35 mL of methanol. The resulting suspension was stirred for 3 h. The solid was collected by filtration and washed thoroughly with portions of 30 mL methanol until the washings were colourless (approximately 5 times). Finally, the catalyst was dried at 55 °C under vacuum for 2 h. The resulting catalyst loading was 7.9 mg_{Rh}/g. Initially, immobilisation of $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ on Nafion was performed in 2-propanol, which resulted in low loading, as explained in Section 3. The catalysts resulting from immobilisation in methanol and 2-propanol are referred to as NafionC1 and NafionC3, respectively.

2.3.4. $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ on SAC-13

The sodium form of SAC-13 was prepared by washing the composite with 2 M NaCl until neutral, followed by thorough washing with water. Finally, the solid was dried at 150 °C under vacuum for 4 h. To 6.34 g of SAC-13 (Na^+) was added 30 mL of 2-propanol, followed after 10 min of stirring by 0.13 g of $[Rh^I(cod)((R)\text{-MonoPhos})_2]BF_4$ in 30 mL of 2-propanol. The resulting suspension was stirred for 3 h. The solid was collected by filtration and washed thoroughly with portions of 30 mL methanol until the washings were colourless (approximately 5 times). Finally, the catalyst was dried at 55 °C under vacuum for 2 h. The resulting catalyst loading was 1.4 mg_{Rh}/g.

2.4. Typical hydrogenation reaction

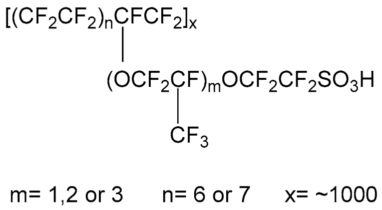
All hydrogenation experiments were performed at 20 °C using the amount of a supported catalyst corresponding to approximately 1 mg of rhodium, with the exception of NafionC3, for which, due to its low loading, only 0.06 mg of Rh was used. The catalyst was transferred to the autoclave under a nitrogen atmosphere, followed by 50 mL of substrate solution (0.05 M). The sealed autoclave was purged with hydrogen by pressurizing to 7 bar while stirring at 300 rpm, followed by releasing the pressure. This cycle was repeated five times, and finally the desired pressure (5 bar) was applied, and the stirring speed was increased to 1000 rpm. At the end of the reaction, the remaining hydrogen pressure was released, and the autoclave was purged three times with nitrogen, pressurizing to 5 bar while stirring at 300 rpm, followed by release. Under nitrogen atmosphere, the solution was separated from the catalyst by a syringe equipped with an Acrodisc GF syringe filter (1.0 µm pore size). After the solution was removed, fresh substrate solution was added to the used catalyst, and the hydrogenation procedure was repeated.

3. Results and discussion

3.1. Support structures

The four carriers selected have significantly different structures. The first carrier, AlTUD-1, is a purely inorganic material. This aluminosilicate, with a Si/Al ratio of 4, has a three-dimensional mesoporous structure and exhibits a maximum pore size distribution at 150 Å. The effective $Si/Al_{tetrahedral}$ ratio for the immobilisation of cations is 9. In addition, AlTUD-1 has a large surface area (ca. 600 m^2/g) and a total pore volume of 1.1 cm^3/g. Details of the analysis have been given elsewhere [4].

The second system consists of a heteropoly acid—in this case phosphotungstic acid, $H_3PO_{40}W_{12}$ (PW)—supported on



$$[(CF_2CF_2)_nCFCF_2]_x$$
$$(OCF_2CF)_mOCF_2CF_2SO_3H$$
$$CF_3$$

m= 1,2 or 3 n= 6 or 7 x= ~1000

Scheme 1. Chemical structure of Nafion.

alumina [3]. Alumina was preferred over silica, because previous unpublished investigations showed an inadequate interaction between the heteropoly acid and silica, resulting in considerable leaching of PW from the surface. The alumina—PW interaction was much better, and no leaching of alumina occurred. Instead of the commercial alumina, a mesoporous alumina that structurally closely resembles AlTUD-1 was chosen, to allow a more accurate comparison between these two inorganic supports. This material, denoted as TUD-Al_2O_3, was prepared similarly to AlTUD-1 [13], resulting in a surface area of 313 m^2/g and a maximum pore size distribution at 60 Å. Because it is known that the presence of PW is crucial to the immobilisation of Rh complexes on alumina, TUD-Al_2O_3 was not selected as a separate support [14,15]. The ratio of PW to TUD-Al_2O_3 was fixed at 19 wt% PW. This system is referred to as PWTUD.

Nafion, as the solid equivalent of triflic acid, is the only fully organic support of the four supports studied. The triflate group ($CF_3SO_3^-$) is attached to the Teflon backbone (Scheme 1) of Nafion. The resin typically has a surface area of 0.02 m^2/g [9] and an equivalent weight of 1100 (molar mass divided by its valence). It consists of clusters (diameter, 40–50 Å) of the sulfonate-terminated groups separated by channels (diameter, 10 Å) within the hydrophobic matrix [16]. Although the surface area of Nafion is low, the triflate anion (a very popular and versatile anion in homogeneous catalysis) makes it a promising carrier.

SAC-13 overcomes Nafion's drawback of a low surface area by dispersing nanosized particles (200–600 Å) of Nafion in a porous silica matrix. The composite used had a surface area of 102 m^2/g with a very broad pore size distribution, 60–2000 Å, as determined by N_2 physisorption. The Nafion content of the material, which was analysed by thermogravimetric analysis (TGA), was 16 wt%, resulting in an equivalent weight of ∼6900.

Initial experiments with Nafion demonstrated that the strongly acidic sites had a negative influence on catalyst performance. Consequently, only the sodium forms of Nafion and SAC-13 were used.

3.2. *Immobilisation of Rh-MonoPhos*

Rh-MonoPhos was immobilised by straightforward ion exchange. In this procedure, an anionic site/Rh ratio in the range of 7–10 was selected, so as to ensure the reimmobilisation of any Rh species mobilised during catalysis and also to prevent catalyst clustering. The only exception to this is PWTUD; for this support, the procedure of Augustine et al. was adopted [17], which uses a PW/Rh ratio of 1, corresponding to three negative charges per Rh.

Table 1
The results of the immobilisation of Rh-MonoPhos on various supports[a]

Support	Rh loading (mg/g)	Rh uptake[b] (%)	Anionic site/Rh
AlTUD-1	12	66	15
PWTUD[c]	1.4	29	9
SAC-13	1.4	66	11
Nafion	0.5	4	175
Nafion[d]	7.9	52	15

[a] Immobilisations were performed in 2-propanol, see experimental section for details.

[b] The percentage of Rh immobilised relative to the Rh amount during the ion exchange.

[c] W loading = 90 mg/g.

[d] Immobilisation was performed in methanol.

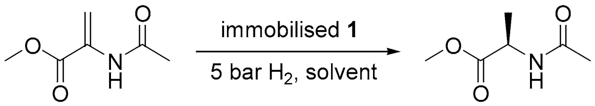
The results of the immobilisations are given in Table 1. The immobilisations were performed in accordance with procedures described previously (i.e., our previously published procedure [4] for AlTUD-1, SAC-13, and Nafion and the procedure from Augustine et al. [17] for PWTUD). This resulted in Rh loadings varying from 1 wt% for AlTUD-1 to 0.05 wt% for Nafion. AlTUD-1 is the best support with respect to Rh loading as well as Rh uptake. These high values are consistent with a material developed for the purpose of catalyst immobilisation. The extremely low loading of Nafion was surprising, however. This is emphasised by the anion to Rh ratio. Although all of the other supports achieved comparable anion-to-Rh ratios, ranging from 9 to 15, Nafion displayed a ratio at least 10 times higher. The large difference with SAC-13 is particularly noteworthy, because it contains the same type of anionic sites. This strongly indicates that the low loading of Nafion is due to the poor accessibility of the triflate groups. The dependence of Nafion's morphology on the solvent is well known [16].

In an effort to improve the accessibility of the negative charges and increase the Rh loading, the immobilisation on Nafion was repeated in methanol, a solvent that causes greater swelling of the resin [18]. Using this solvent, the Rh content was increased 16-fold, and an anion-to-Rh ratio equal to the other supports was obtained. As mentioned in Section 2, the catalysts resulting from immobilisation in methanol and 2-propanol are referred to as NafionC1 and NafionC3, respectively.

PWTUD is a three-component system; therefore, both the Rh loading and the PW loading are important. During ion exchange, 75% of the PW present in the mixture settles on the alumina, giving a PW loading of 117 mg/g. Although the Rh uptake is quite low (29%), it has the lowest anion-to-Rh ratio (i.e., 3). This is in line with the results described by Augustine [17].

3.3. *Hydrogenation with supported Rh-MonoPhos*

The four catalysts were tested in the hydrogenation of methyl 2-acetamidoacrylate (MAA, Scheme 2); the results are given in Tables 2–5. The reported turnover frequencies (TOFs)



Scheme 2. Test reaction for asymmetric hydrogenation catalysed by immobilised **1**.

Table 2
Results of the asymmetric hydrogenation of MAA catalysed by **1** immobilised on AlTUD-1[a]

Entry	Solvent	Time (min)	Conversion (%)	TOF[b] (mol/(mol h))	ee (%)	Rh loss (mg/L) [%][c]
Homogeneous	CH_2Cl_2	7	100	>1700	97	–
1	MTBE	7	20	350	94	0.32 [1.3]
2	MTBE	30	91	450	94	0.45 [1.8]
3	EtOAc	7	70	1300	92	1.27 [5.5]
4	EtOAc	10	99	1300	93	1.04 [4.5]
5	CH_2Cl_2	7	96	1600	83	0.76 [2.9]
6	2-PrOH	7	39	800	91	2.30 [9.4]
7	2-PrOH	25	100	>500	97	2.06 [8.4]
8	Water	35	75	290	95	0.21 [0.6]
9	Water	60	100	>220	95	0.11 [0.3]

[a] Initial pressure 5 bar H_2, 20 °C, 50 mL solvent, [MAA] = 0.05 M, 0.1 g catalyst with 1 wt% Rh.

[b] TOF ($mol_{substrate\ converted}/(mol_{cat}\ h)$), calculated at the indicated time.

[c] Percentage of total amount of Rh determined by AAS of the filtrate.

Table 3
Results of the asymmetric hydrogenation of MAA catalysed by **1** immobilised on PWTUD[a]

Entry	Solvent	Time (min)	Conversion (%)	TOF[b] (mol/(mol h))	ee (%)	Rh loss (mg/L) [%][c]	W loss (mg/L) [%][d]
1	MTBE	30	97	750	96	<0.05 [0.4]	<0.1 [<0.01]
2	EtOAc	7	83	2300	97	0.10 [0.7]	<0.1 [<0.01]
3	2-PrOH	25	96	800	93	0.18 [1.2]	2.6 [0.2]
4	Water	30	98	750	96	0.29 [2.0]	3.3 [0.26]

[a] Initial pressure 5 bar H_2, 20 °C, 50 mL solvent, [MAA] = 0.05 M, 0.7 g catalyst with 0.14 wt% Rh.

[b] TOF ($mol_{substrate\ converted}/(mol_{cat}\ h)$), calculated at the indicated time.

[c] Percentage of total amount of Rh determined by AAS of the filtrate.

[d] Percentage of total amount of W determined by ICP of the filtrate.

are all lower estimates, because they are derived from the conversion at the corresponding reaction time. Not all catalysts were tested in CH_2Cl_2, because this is an undesirable solvent for industrial application.

The first parameter of interest is the activity of the catalyst. For comparison of the carrier-dependent activities of MonoPhos, the TOFs were plotted versus carrier and solvent (Fig. 3). The findings reveal that in all solvents tested, PWTUD (Table 3) gives the most active catalyst, corresponding to the activation of the catalysts by the PW (as reported by Augustine et al. [3]). Also consistent with the results of Augustine et al., PWTUD produced a discoloration after hydrogenation of MAA that none of the other supports showed. Augustine et al. explained this discoloration by partial reduction of the tungsten in PW, which may be the cause of the activation [19]. These results support this hypothesis, because structurally AlTUD-1 and PWTUD are quite similar. Both have three-dimensional connectivity, but AlTUD-1 exhibits lower activity, although it should have better accessibility (higher S_{BET}, total pore volume, and pore diameter).

Table 4
Results of the asymmetric hydrogenation of MAA catalysed by **1** immobilised on SAC-13(Na^+)[a]

Entry	Solvent	Time (min)	Conversion (%)	TOF[b] (mol/(mol h))	ee (%)	Rh loss (mg/L) [%][c]
1	MTBE	30	55	275	92	0.21 [0.9]
2	EtOAc	30	97	460	98	2.5 [12]
3	CH_2Cl_2	7	55	1180	86	1.8 [8.8]
4	CH_2Cl_2	20	93	700	87	2.2 [11]
5	2-PrOH	30	70	332	96	3.5 [17]
6	Water	30	100	508	97	0.04 [0.12]

[a] Initial pressure 5 bar H_2, 20 °C, 50 mL solvent, [MAA] = 0.05 M, 0.7 g catalyst with 0.14 wt% Rh.

[b] TOF ($mol_{substrate\ converted}/(mol_{cat}\ h)$), calculated at the indicated time.

[c] Percentage of total amount of Rh determined by AAS of the filtrate.

Table 5
Results of the asymmetric hydrogenation of MAA catalysed by **1** immobilised on Nafion[a]

Entry	Catalyst	Time (min)	Solvent	Conversion (%)	TOF[b] (mol/(mol h))	ee (%)	Rh loss (mg/L) [%][c]
1	NafionC3	30	EtOAc	12	970	98	0.04 [3.0]
2	NafionC3	900	EtOAc	42	110	97	0.06
3	NafionC3	900	MeOH	2	5.9	–	0.9 [78]
4	NafionC3	30	Water	23	1850	96	0.01 [0.7]
5	NafionC3	900	Water	100	>270	92	0.01
6	NafionC1	900	MTBE	6	1.4	–	<0.005 [0.03]
7	NafionC1	30	EtOAc	16	80	98	0.02 [0.09]
8	NafionC1	1200	EtOAc	95	11	97	0.03
9	NafionC1	30	2-PrOH	5	27	–	0.15 [0.80]
10	NafionC1	1200	2-PrOH	30	4	91	0.17
11	NafionC1	30	MeOH	32	215	79	6.0 [40]
12	NafionC1	900	MeOH	100	>22	75	5.7
13	NafionC1	900	Water	100	>17	90	0.01 [0.05]

[a] Initial pressure 5 bar H_2, 20 °C, 50 mL solvent, [MAA] = 0.05 M, 0.1 g catalyst.

[b] TOF ($mol_{substrate\ converted}/(mol_{cat}\ h)$), calculated at the indicated time.

[c] Percentage of total amount of Rh determined by AAS of the filtrate.

The Nafion supports (Tables 4 and 5) also lack this additional interaction, because the sulfonate group is a textbook example of a noncoordinating ligand. Their activities do not even remotely match those obtained with PWTUD. In fact, both types of Nafion supports also perform worse than AlTUD-1, especially the pure Nafion resin.

The TOFs obtained with NafionC1 are only a fraction of those obtained with other supports. The low values of Nafion resin are most likely caused by poor swelling of the Nafion, which greatly hampers the accessibility of the catalyst inside the particles. To test this hypothesis, the hydrogenation with NafionC1 was also performed in MeOH (Table 5, entries 11 and 12), a solvent omitted for the other carriers due to the low selectivity of the Rh-MonoPHOS catalyst in this solvent. Indeed, in MeOH, TOFs approaching those of the other carriers are reached. When the TOFs of the various solvents are

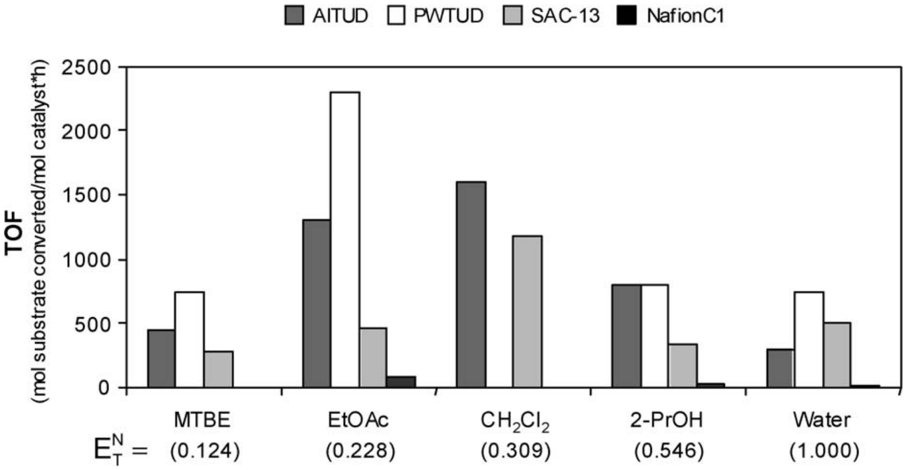


Fig. 3. TOFs of the various supported catalysts in several solvents. The normalised empirical parameter, E_T^N, [23] is a good measure for solvent polarity. (E_T^N is based on the transition energy for the longest-wavelength solvatochromic absorption band of a pyridinium *N*-phenolate betaine dye.)

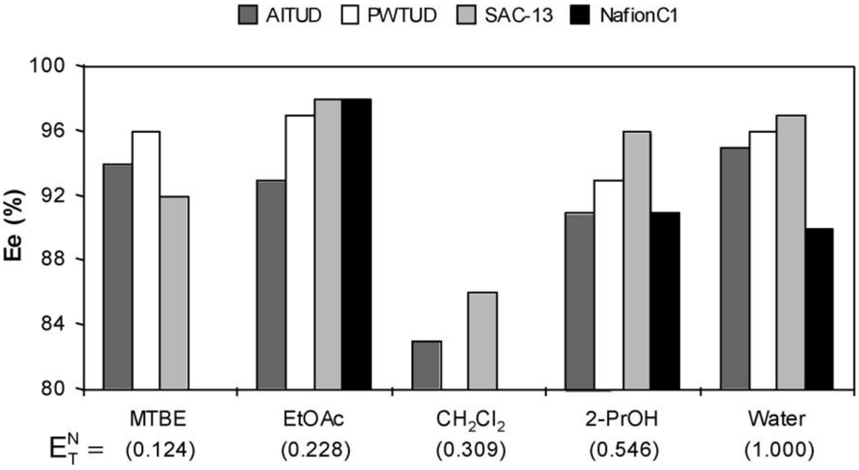


Fig. 4. ee of the various supported catalysts in several solvents. The normalised empirical parameter, E_T^N, [23] is a good measure for solvent polarity.

weighed against the corresponding solvent uptake of Nafion (Na^+-form), as determined by Yeo et al. [18] a dependence is observed: Nafion takes up 4 times as much methanol than water or 2-propanol, which corresponds fairly well to the difference in TOF.

The relationship between poor activity and accessibility of Nafion is further stressed by the results obtained with NafionC3, the catalyst with low loading due to poor accessibility. Although the conversions with this catalyst are very low, the initial TOFs are very high. In water (Table 5, entry 4) it is even the most active catalyst per Rh. These results can be rationalised by the fact that on this support, all of the Rh complexes are immobilised on the outer anionic groups because the immobilisation for NafionC3 is performed in 2-PrOH; hence the Rh complex cannot enter the particles, resulting in the predominant loading at the external surface. Thus, for NafionC3, all active particles are highly accessible to the substrate, leading to the initial high activity.

By incorporating Nafion into a silica matrix, as in SAC-13, these accessibility problems are greatly reduced, as can be derived from the difference in TOFs. Nonetheless, SAC-13 is still outperformed by the PWTUD-supported catalyst by more than a factor of 2 in most solvents.

Fig. 3 also clearly shows that the activity is strongly dependent on the solvent. This dependence appears to be the same for all supports with the exception of Nafion, due to the reasons mentioned above. The highest activity is observed in CH_2Cl_2. When changing to a more polar or less polar solvent (i.e., a higher or lower E_T^N value), the TOF decreases. Thus, both MTBE and water give lower activities.

The influence of the anionic supports is less pronounced on the selectivity (Fig. 4) of the catalyst than on the TOF (Fig. 3). Again, PWTUD (Table 3) appears to be an excellent choice, although SAC-13 (Table 4) is marginally better in most solvents. AlTUD-1 (Table 2) gives somewhat lower but still very good enantioselectivities. With CH_2Cl_2 as a solvent, all catalysts display relatively low selectivities that do not exceed 87%. This minimum is unexpected, because CH_2Cl_2 together with EtOAc was the best solvent for hydrogenation with the homogeneous catalyst **1** [12]. Therefore, EtOAc remains the solvent of choice for hydrogenation with the supported catalysts.

To investigate how well the catalyst is immobilised, leaching studies were performed. Previously, we have shown that

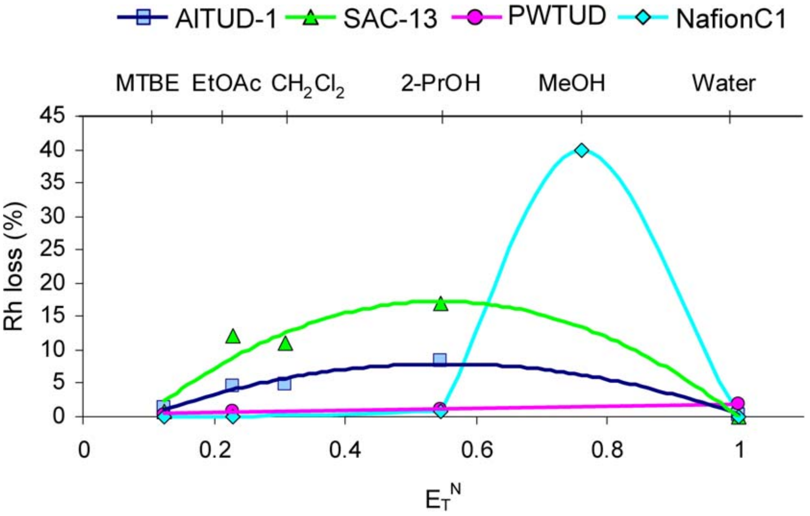


Fig. 5. The amount of Rh found in solution after hydrogenation and removal of the supported catalyst.

this is greatly dependent on the reaction solvent [4]. Here again, a distinct correlation between leaching and solvent is observed. (Fig. 5). In MTBE and water, all materials are equally suitable as supports, because virtually no leaching is observed in these solvents. In other solvents, significant differences between the materials are observed. As for the other parameters discussed previously, PWTUD (Table 2) exhibits the best properties. Virtually no loss of Rh in a wide range of solvents is observed, making it the support of choice. Surprisingly, NafionC1 (Table 5) performs almost as well. In methanol (Table 5, entry 11), however, Nafion lacks the ability to retain the Rh complex. This sharp contrast between methanol and the other solvents is rooted in the swelling properties of this support. As discussed above, Nafion has a more open structure in methanol compared with that observed in the other solvents, resulting in a high level of leaching. Thus, it can be concluded that the immobilisation of Nafion is based only partly on ionic interaction and to a significant extent on encapsulation.

This conclusion is supported by the leaching characteristics of SAC-13 (Table 4). Although Nafion and SAC-13 have the same anionic sites, the loss of rhodium demonstrates a different dependence on polarity, especially in the range of MTBE to 2-PrOH. Whereas Nafion exhibits an almost flat solvent/leaching dependence over this range, SAC-13 exhibits a logarithmic dependence, similar to AlTUD-1. The open structure of SAC-13 significantly decreases the possibility of encapsulation. Consequently, the influence of the solvent on the support structure is negligible, accounting for the observed differences in leaching behaviour between the various Nafion-based supports.

As mentioned above, the curves in Fig. 5 for SAC-13 and AlTUD-1 are very similar, consistent with a similar type of immobilisation between support and catalyst, although there are significant differences in the strength of this interaction. AlTUD-1 is approximately twice as effective in retaining the catalyst complex. In these materials, the Rh loss initially increases as the solvent stabilizes charges more readily; however, when the solvent is too polar, it no longer can solubilise the catalyst due to the hydrophobic ligands, and thus leaching in water is very low.

As stated earlier, PWTUD demonstrates high stability against leaching in all solvents, presumably also in MeOH, as can be derived from the work of Brandts et al. [20]. In these authors' investigation on the immobilisation of Rh-MeDuPHOS on Al_2O_3/PW, the immobilised catalyst exhibited a Rh loss of 2.3% in MeOH in the hydrogenation of dimethyl itaconate as opposed to ca. 1% in 2-PrOH. PWTUD thus shows a distinctly different behaviour from the other supports, that is, an almost linear dependence of the loss of rhodium on the solvent. This difference may be caused by an additional interaction between PW and Rh, namely a Rh–O bond. Evidence for this additional interaction can be found in the UV data of $Rh(DiPAMP)^+$ with various counterions, as reported by Augustine et al. [19]. The complexes with noncoordinating counterions, including BF_4^-, SbF_6^-, and $CF_3SO_3^-$, had spectra distinguished by absorption doublets at 340 and 460 nm. The complexes with Cl^- and AcO^- had these counterions bound directly to the Rh and showed only a single adsorption bond at around 280 and 285 nm, respectively. When these complexes were treated with PW and washed thoroughly, they all showed only a single absorption, at 285 nm. This similarity with the AcO^- complex suggests the presence of a bond between Rh and the oxygen of PW. A bonding interaction of this type has also been observed directly in solution between heteropoly acids and $[Rh(cod)(CH_3CN)_2]BF_4$ [21]. Thus, the multiply charged PW anion has distinctly different properties than the singly charged sulfonate groups of Nafion and SAC-13 and the evenly dispersed charges of AlTUD-1. Tungsten leaching in 2-PrOH is slightly higher compared with values reported by Brandts [20], possibly due to differences between the surface of TUD-Al_2O_3 and γ-Al_2O_3.

The final factor of interest for immobilised catalysts is their recyclability. Representative results of the recycling experiments are given in Fig. 6. Every catalyst was recycled four times in all solvents reported. The catalysts exhibited almost complete retention of selectivity and activity on reuse in almost all of the

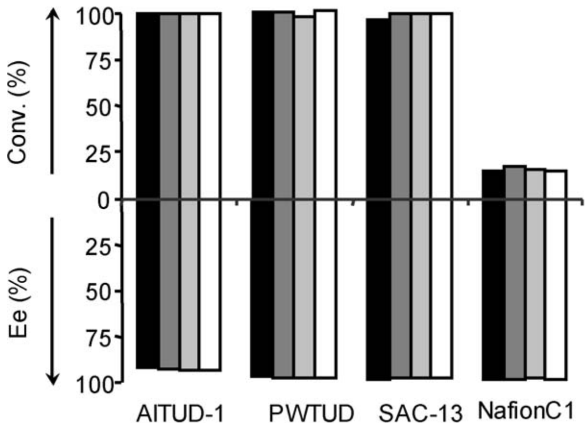


Fig. 6. Recycling of **1** immobilised on the various supports in the asymmetric hydrogenation of MAA in EtOAc. Reaction times are in line with those in the corresponding table. Different bars represent consecutive runs.

solvents, except for those that caused substantial leaching. Furthermore, the heterogeneity of the various catalyst systems was confirmed by a so-called "filtration test" in which the solid catalyst was removed under an inert atmosphere at the reaction temperature (20 °C) before completion of the reaction, followed by continuation of the hydrogenation to screen for any remaining activity in solution [22]. Although the nature of the anionic support had a significant effect on catalyst activity and selectivity, as well as leaching characteristics, it had no detectable effect on catalyst recyclability.

4. Conclusion

The objective of this study was to select the best support for the noncovalent anchoring of asymmetric hydrogenation catalysts. We can safely conclude that PWTUD outperformed the other supports in almost every aspect. Immobilisation of Rh-MonoPhos on this support resulted in the catalyst with the highest activity, but, especially with respect to leaching, this was by far the best anionic carrier. Virtually no leaching in any solvent was observed, and the enantioselectivity remained excellent. This catalyst's superior anchoring ability derives from the type of bonding between Rh and the phosphotungstic acid, which is thought to be partially covalent. AlTUD-1, a good second choice as support material, lacks this additional binding interaction and thus is much more sensitive to the polarity of the solvent with respect to leaching. SAC-13 behaves similarly with respect to leaching but is far inferior in terms of activity. The immobilisation of complexes on the Nafion resin, in contrast, relies on encapsulation rather than ionic interactions. Its encapsulating properties not only prevent the complex from going into solution in all solvents except methanol, but also prevent the substrate from reaching the catalytic site.

This systematic investigation of support effects clearly demonstrates the need to study all aspects of catalysis with immobilised catalysts. Research should not only focus on the catalytic complex when searching for the best catalyst. The type of support greatly influences all of the relevant parameters associated with asymmetric hydrogenation. The solvent of the reaction can make the difference between a moderate catalyst and an exceptional one. A better understanding of these and other interactions involved in catalysis will greatly facilitate the ongoing search for better catalysts.

Acknowledgments

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