VIP

Noncovalent Anchoring of Asymmetric Hydrogenation Catalysts on a New Mesoporous Aluminosilicate: Application and Solvent Effects

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Abstract: A new Brønsted acidic aluminosilicate, AlTUD-1, with ideal characteristics for catalyst immobilisation (mesoporous structure, high surface area, and high $Al_{tetrahedral}$/Si ratio), was used successfully for the noncovalent anchoring of two well-established asymmetric hydrogenation catalysts: $[Rh^{I}(cod)\{(R,R)\text{-MeDuPHOS}\}]BF_4$ (**1**) and $[Rh^{I}(cod)\{(S,S)\text{-DiPAMP}\}]BF_4$ (**2**). The new heterogeneous catalysts, **1**-AlTUD-1 and **2**-AlTUD-1, prepared by a straightforward ion-exchange procedure, were highly active and selective in the asymmetric reduction of dimethyl itaconate (**3**) and methyl 2-acetamidoacrylate (**4**), giving enantiomeric excesses of up to >98%. The catalysts showed similar behaviour to their homogeneous counterparts. Catalyst **2**-AlTUD-1 could be re-used multiple times without loss of enantioselectivity or activity. Leaching of Rh showed a significant dependence on the polarity of the solvent in which the catalysis was performed. By applying *tert*-butylmethyl ether (MTBE) as solvent, the loss of Rh could be reduced to <0.1%. The solvent also had a noteworthy effect on the enantioselectivity in the hydrogenation of **4** (an effect not seen with **3** as substrate), that is, in MeOH the *ee* was 92%, in MTBE it dropped to 26% when using **2**-AlTUD-1 as catalyst.

Keywords: asymmetric catalysis · hydrogenation · mesoporous materials · solvent effects · supported catalysts

Introduction

Transition-metal-catalysed asymmetric hydrogenation is becoming increasingly important for the production of enantiopure pharmaceuticals and agrochemicals. The Monsanto L-DOPA process[1] represents one of the most prominent examples of the successful implementation of this technology. In recent years highly enantioselective catalysts for a broad range of substrates such as olefins, ketones and imines[2] have been developed. However, large-scale applications of this mature methodology are often hampered by the difficult removal of the homogeneous catalysts. Heterogenisation of the metal complexes provides a way to greatly ease this separation and to improve the recycling of the expensive catalyst. A commonly applied technique is the covalent binding of the complex to a solid support.[3] Serious drawbacks of this approach are the time-consuming and difficult ligand modification as well as the not always predictable effects on activity and selectivity. Augustine et al. reported a very elegant method for the heterogenisation of ionic transition-metal complexes, which did not require any modification of the complexes and additionally, in some cases, improved their catalytic activity and selectivity.[4] This method utilised the cationic character of the complex to bind it noncovalently to an inorganic support, employing heteropoly acids as the anchors. Variations of this approach using different surface modification strategies to anchor by electrostatic binding have been reported by Hölderich et al.,[5] Hems and Hutchings,[6] and Broene et al.[7]

Inspired by these new anchoring techniques, we set out to utilise the new mesoporous aluminosilicate, AlTUD-1, as a support for chiral rhodium complexes. Here, we describe the preparation of this new aluminosilicate and its use in the im-

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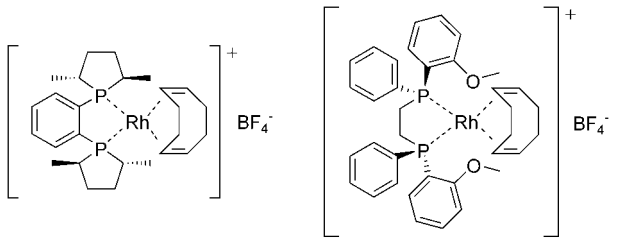
mobilisation of two established, asymmetric hydrogenation catalysts, [Rh^{I}(cod)((*R*,*R*)-MeDuPHOS)]BF_4 (**1**)[8] and [Rh^{I}(cod)((*S*,*S*)-DiPAMP)]BF_4 (**2**),[9] wherein cod is 1,5-cyclooctadiene. The application of these new heterogeneous catalysts in asymmetric hydrogenation and the striking influence of the solvent, a factor often ignored, were investigated.



1 **2**

Results and Discussion

The starting point for the development of the mesoporous aluminosilicate (AlTUD-1, pore diameter 20–500 Å) was the recent discovery of a new templating method for mesoporous networks.[10] This novel approach uses inexpensive, nonsurfactant chemicals to produce mesoporous materials with high surface areas (up to ca. 1000 m^2g^{-1}) and three-dimensional (3D) connectivities. The 3D pores should allow better accessibility of the catalyst compared with one-dimensional pore systems as found in materials such as MCM-41.[11]

For the purpose of immobilising cationic complexes on the material, an unusually low Si/Al ratio of about 4 is desirable. Preferably, to ensure a high Brønsted acidity, the aluminium center should display tetrahedral coordination. The templates described have the ability to stabilise metal alkoxides by complexation,[12] and thus seemed ideally suited for production of the desired aluminosilicate.

Initial experiments with the most frequently reported template triethanolamine, did not give satisfactory results. However, with tetraethyleneglycol (TEG)[13] as a template, a white solid, denoted as AlTUD-1, was obtained. The complete removal of the template was confirmed by IR spectroscopy, and the structural properties of AlTUD-1 were investigated with X-ray powder diffraction and N_2 physisorption.

The XRD pattern in Figure 1a shows one dominant signal, an intense peak around 0.65° θ, indicating that AlTUD-1 is a mesostructured material. The N_2 sorption isotherms (Figure 1b) show the mesoporous texture in what is a typical Type IV isotherm with a type H1 hysteresis loop, characteristic for mesoporous materials. Additional data, derived from the isotherm, illustrate that AlTUD-1 has a large surface area of about 600 m^2g^{-1} and a total pore volume of 1.1 cm^3g^{-1}. The pore size distribution is fairly broad and shows a maximum at 150 Å (inset). In the synthesis of the purely siliceous mesoporous silica (TUD-1) by this templating method, the pore-size distribution could be tuned by variation of the hydrothermal treatment time: a longer duration

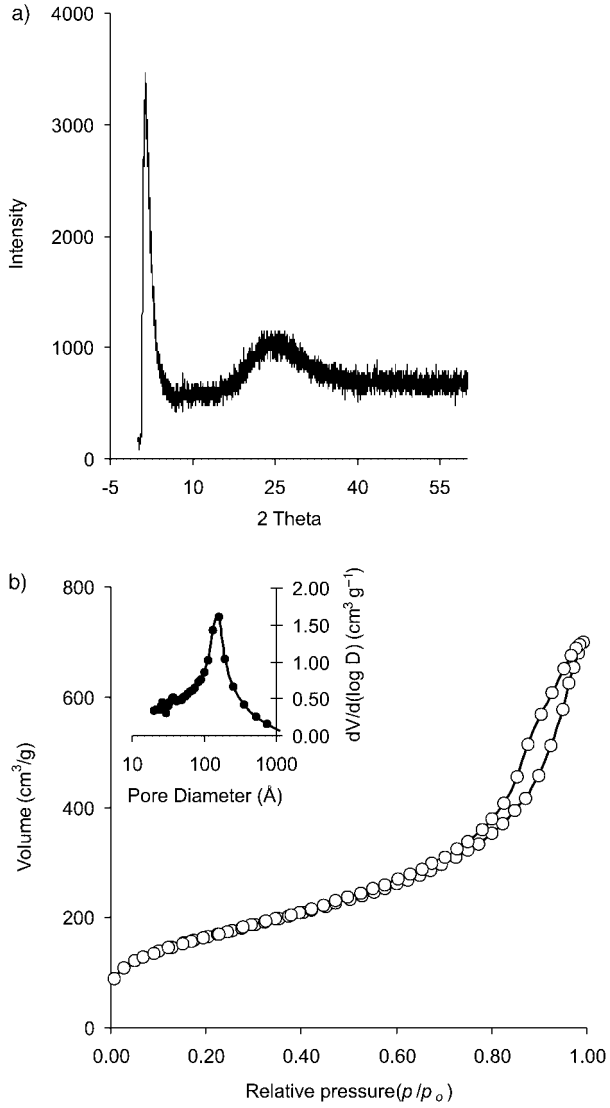


Figure 1. a) Powder XRD ($Cu_{K\alpha}$) pattern of AlTUD-1; b) nitrogen sorption isotherms of AlTUD-1. Inset: corresponding pore-size distribution.

increased the pore diameter. For AlTUD-1, variation in the hydrothermal treatment time had little to no effect on the pore-size distribution. This is, to a large degree, due to the faster formation of Al-O-Si bonds compared with Si-O-Si bonds, which renders the overall system less dynamic and, therefore, less sensitive towards changes in pore size with temperature. Increasing the time over a range of 3 to 24 h gave a pore diameter of 150–250 Å, all with the same broad distribution (see Figure 1b inset). Similarly, the surface area increased only marginally when prolonging the hydrothermal treatment from 3 to 24 h (~500–625 m^2g^{-1}). It can reasonably be assumed that AlTUD-1 exhibits a three-dimensional structure owing to the synthesis method used. Furthermore, all analyses of AlTUD-1 indicate that it is consistent with a TUD-1-like structure.

The nature of Al in AlTUD-1 was investigated by using ^{27}Al NMR spectroscopy (Figure 2). The spectrum exhibits a strong resonance at $\delta = 55$ ppm, which can be assigned to the desired Brønsted acidic, tetrahedrally coordinated Al

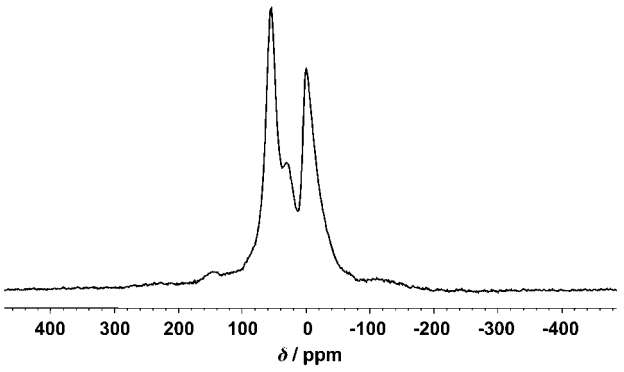
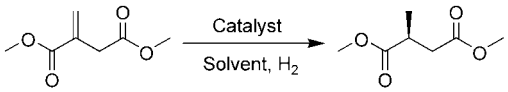


Figure 2. ^{27}Al NMR spectrum of AlTUD-1.

($Al_{tetrahedral}$) center. The signals at $\delta = 31$ and 0 ppm can be ascribed to pentacoordinate Al and hexacoordinate Al centers, respectively. It follows from the integration that approximately 43% of the Al is coordinated tetrahedrally. Although the addition of TEG did not completely suppress the formation of hexacoordinate Al centers, it did allow the formation of a mesoporous aluminosilicate with a high surface area and a $Si/Al_{tetrahedral}$ ratio of 9:1 (overall Si/Al = 4:1). This new material (AlTUD-1) with its large surface area, mesoporous structure, and high proportion of Brønsted acidic Al combines all the desired properties for an anionic carrier.

Table 1. Asymmetric hydrogenation of **3** in various solvents.[a]



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Entry	Catalyst	Solvent	Conv. [%]	**3**/Rh ratio	TOF [mol mol^{-1} h^{-1}]	*ee* [%]	Rh loss [mg L^{-1}] (%)[c]
1[b]	**1**	MeOH	100	1250	>1000	96	–
2[b]	**1**-AlTUD-1	MeOH	100	1250	>1000	98	2.00 (23)
3[b]	**1**-AlTUD-1	2-PrOH	100	200	>1000	96	0.35 (1.4)
4	**1**-AlTUD-1	MeOH	22	250	51	97	4.5 (15)
5	**1**-AlTUD-1	2-PrOH	32	325	105	96	0.78 (2.5)
6	**1**-AlTUD-1	CH_2Cl_2	26	250	62	98	0.29 (0.7)
7	**1**-AlTUD-1	EtOAc	11	175	19	98	0.29 (0.5)
8	**1**-AlTUD-1	MTBE	10	250	25	96	0.04 (0.1)
9	**1**-AlTUD-1	toluene	0	250	0	n.d.	n.d.

[a] Reaction was performed using the Avantium Quick Catalyst Screen platform; conditions: ~6 mg supported catalyst, $p_{initial}(H_2) = 5$ bar, volume 1.5 mL, [substrate] = 0.1 M, time = 60 min, *S* major enantiomer with (*R*,*R*)-MeDuPHOS as ligand. [b] Reaction was performed in a Parr hastelloy C autoclave; conditions: 100 mg supported catalyst, 50 mL solvent, $p(H_2) = 5$ bar, [substrate] = 0.1 M, time = 30 min, *S* major enantiomer with (*R*,*R*)-MeDuPHOS) as ligand. [c] Percentage of total amount Rh.

Complexes **1** and **2** were immobilised by straightforward ion exchange, using the three-dimensional mesoporous aluminosilicate (AlTUD-1). A high $Al_{tetrahedral}$/Rh ratio of approximately 10:1 was chosen, so that any cationic complex that is inadvertently mobilised during the hydrogenation reaction is surrounded by many vacant acidic sites, increasing the chances to be immobilised again. Both, pre-formed complexes and those prepared in situ, can be immobilised. The resulting immobilised catalysts are expected to have a virtually unmodified, and possibly even improved, catalytic behaviour. The immobilised catalysts, denoted as **1**-AlTUD-1 and **2**-AlTUD-1, respectively, were washed with ethanol or 2-propanol to remove any unanchored catalyst. Typically, a loading of 1 wt% Rh was obtained.

For a direct comparison of the immobilised and homogeneous catalysts, the catalytic behaviour of **1**-AlTUD-1 was studied in the asymmetric hydrogenation of dimethyl itaconate (**3**) (Table 1). No difference was found between chiral catalysts that were immobilised as synthesised and those that were prepared by addition of a solution of bis(1,5-cyclooctadiene)rhodium tetrafluoroborate and the chiral ligand to AlTUD-1. The comparison between the homogeneous catalyst (entry 1, Table 1) and **1**-AlTUD-1 (entry 2, Table 1) under identical conditions reveals that there is no decrease in either selectivity or activity upon anchoring **1** on AlTUD-1. However, significant leaching of Rh was observed, casting doubt on the heterogeneity of the reaction. We therefore screened other solvents using the Avantium Quick Catalyst Screen platform (entries 4–9, Table 1) to reduce this problem. When switching from the mechanically stirred autoclave to the magnetically stirred Quick Catalyst Screen platform, a significant drop in activity was observed (entry 3 versus entry 5, Table 1), whereas the enantioselectivity was hardly affected by the change of reaction vessel and stirring mode. The reduction in activity is principally due to a reduced mass-transfer of hydrogen from the gas to the liquid phase, caused by the different reaction vessel design. The reduction in hydrogen uptake slows down the reaction, since hydrogen is involved in the rate-determining step.[14a] Nevertheless, this system is suited to finding trends in the leaching of Rh. The lack of activity in toluene is not surprising, since aromatic compounds tend to form stable η^6-arene complexes with Rh^I.[15]

The screening revealed a similar loss of Rh with methanol as solvent, when compared with the original experiment. As expected, the Rh loss could largely be overcome by switching to less polar solvents. With the less polar, but still protic, 2-propanol as solvent, leaching of Rh could already be reduced by a factor of 6. When we used dichloromethane or ethyl acetate, both regarded as polar aprotic solvents, the Rh in solution could be reduced to 0.29 mg L^{-1}, corresponding to 0.5–0.7% of the total amount of Rh. Minimal leaching (0.04 mg L^{-1}, 0.1% of the original Rh) was obtained with the much less polar and aprotic *tert*-butylmethyl ether (MTBE). By simply switching the polarity of the solvent, the leaching of the catalyst could be reduced by a factor of 150.

A good measure for solvent polarity is the normalised empirical parameter E_T^N,[16] which is based on the transition energy for the longest wavelength solvatochromic absorption band of a pyridinium *N*-phenolate betaine dye. This parameter also takes into account specific solute–solvent interactions, like hydrogen bonding and electron pair donation and electron pair acceptance interactions. The correlation between this parameter and loss of Rh is given in Figure 3.

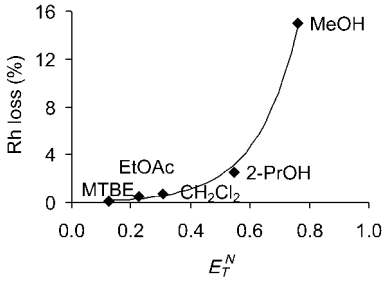


Figure 3. The correlation between the polarity of the solvent (E_T^N) and the loss of Rh (in percentage of total amount of Rh).

This exponential correlation can be rationalised by the increasing ability to stabilise charged species with increasing polarity. Whereas MTBE has almost no possibility to stabilise charges, ethyl acetate has the ability to stabilise positive charges by lone pair donation and its dipolar moment. However, ethyl acetate is far less efficient in the stabilisation of negative charges. Methanol on the other hand has the capability to stabilise both cations and anions, explaining the large amounts of Rh in solution.

The screening of various solvents also shows that the enantioselectivity in the hydrogenation of **3** with **1**-AlTUD-1 is independent of the solvent. The catalyst **1**-AlTUD-1 exhibits excellent enantioselectivities of up to 98% in all solvents. The enantioselectivity fluctuated only within 1 to 2% between different solvents.

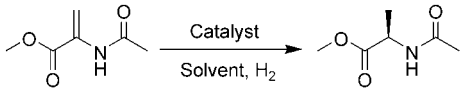
The encouraging results with **3** as substrate motivated us to investigate the asymmetric hydrogenation of the more highly functionalised substrate methyl 2-acetamidoacrylate (**4**) (Table 2, the reaction times are close to the shortest reaction times in which 100% conversion could be obtained for the best solvent/catalyst combination; all reactions gave quantitative yields when the reaction time was extended).

Again, **1**-AlTUD-1 in methanol gave results similar to the homogeneous catalyst, as was the case for **2**-AlTUD-1. Interestingly, the asymmetric hydrogenation of **4** with **2**-AlTUD-1 proceeded even in water. The homogeneous catalyst is poorly soluble in this solvent, but when using the immobilised catalyst, reasonable TOFs with moderate *ee* were obtained (entry 9, Table 2). Thus, immobilisation on AlTUD-1 also broadens the range of solvents for asymmetric hydrogenation.

Once more, significant leaching was observed with MeOH as the solvent. Analogous to the experiments with **3**, this leaching could be reduced by a change of solvent. The leaching could even be suppressed to <0.1%. Loss of Rh is slightly higher for **2**-AlTUD-1, especially when 2-propanol is used as solvent. Surprisingly, the amount of Rh leached in water is considerably lower than with methanol (entries 7 and 9, Table 2), although its E_T^N value is higher (1.00). This is due to the hydrophobic character of the cation.

The results with **2**-AlTUD-1 clearly show that the solvent also has an influence on the activity of the catalyst, where the TOF drops from >200 for methanol and ethanol (entries 7 and 8, Table 2) to 69 for 2-propanol (entry 10, Table 2). An obvious explanation could be the different solubility of H_2 in the various solvents. However, there is no correlation between the hydrogen solubility and the TOF (Table 3).

Table 2. Asymmetric hydrogenation of **4** in various solvents.[a]



4

Entry	Catalyst	$p(H_2)$[b] [bar]	Solvent	Conv. [%]	TOF [mol mol^{-1} h^{-1}]	*ee* [%]	Rh loss [mg L^{-1}] (%)[c]
1	**1**	1	MeOH	100	>350	>98	–
2	**1**-AlTUD-1	1	MeOH	100	>350	>98	4.9 (17)
3	**1**-AlTUD-1	1	MTBE	100	>350	90	0.01 (0.05)
4	**1**-AlTUD-1	1	EtOAc	100	>350	84	0.01 (0.05)
5	**1**-AlTUD-1	1	2-PrOH	100	>350	75	0.4 (1.6)
6	**2**	3	MeOH	100	>200	92	–
7	**2**-AlTUD-1	3	MeOH	100	>200	92	4.6 (20)
8	**2**-AlTUD-1	3	EtOH	100	>200	79	0.9 (4)
9	**2**-AlTUD-1	3	water	81	159	64	1.2 (5.6)
10	**2**-AlTUD-1	3	2-PrOH	26	69	44	1.3 (7.5)
11	**2**-AlTUD-1	3	MTBE	54	103	26	0.02 (0.09)
12	**2**-AlTUD-1	3	EtOAc	35	75	30	0.09 (0.45)

[a] Reaction was performed in a Parr hastelloy C autoclave, conditions: 50 mL solvent, [**4**] = 0.025 M, 0.1 g catalyst, **4**/Rh ratio = 100, *R* major enantiomer with (*R*,*R*)-MeDuPHOS) or (*S*,*S*)-DiPAMP) as ligand, reaction time: 20 min for **1** and 30 min for **2**. [b] Initial pressure. [c] Percentage of total amount Rh.

Table 3. The mole fraction solubilities ξ_{H_2} of hydrogen and the TOF in the asymmetric hydrogenation of **4** using **2**-AlTUD-1 as catalyst in various solvents.

Solvent	ξ_{H_2} (10^{-4})[a]	TOF [mol mol^{-1} h^{-1}]
methanol	15	>200
ethyl acetate	3.5	75
2-propanol	2.7	69
ethanol	2.1	>200
water	0.14[b]	159

[a] ξ_{H_2} at 10 bar H_2 and 25 °C.[17] [b] ξ_{H_2} at 1 bar H_2 and 25 °C.[17b]

Unexpectedly, the solvent also had a significant influence on the enantioselectivity of **1**-AlTUD-1 and **2**-AlTUD-1 in the hydrogenation of **4**. Whereas **3** was hydrogenated with

excellent enantioselectivity using **1**-AlTUD-1 in all solvents screened, the *ee* in the reduction of **4** varied between >98% for methanol and 75% for 2-propanol. Burk et al. reported essentially identical enantiomeric excesses in the solvents methanol, THF, dichloromethane, ethanol, 2-propanol, and ethyl acetate for the homogeneous hydrogenation of **4**.[8] The interaction between the support and the catalyst, which varies for different solvents, seems to influence the enantioselectivity in the hydrogenation of **4**. From these results, MTBE appears to be the ideal solvent when using **1**-AlTUD-1, since it combines high *ee* with virtually no loss of Rh for either substrate.

With regard to leaching, MTBE is also the first choice for **2**-AlTUD-1, but the enantioselectivity of **2-**AlTUD-1 drops dramatically (entry 11, Table 2). It appears that for this catalyst the solvent dependence of the enantioselectivity is even greater, ranging from 92 to 26 *ee*%. Once again the homogeneous complex shows different behaviour. Whereas Knowles reports a marginally better efficiency in higher alcohols,[1] here the enantiomeric excess decreases with higher alcohols. As for **1**-AlTUD-1, the interaction between support and catalyst seemingly plays a significant role. However, the relation between solvent and enantiomeric excess is not identical for both catalysts, which becomes particularly apparent for MTBE, ethyl acetate, and 2-propanol. For **1**-AlTUD-1, 2-propanol is the least suitable solvent, and MTBE is the second best. For **2-**AlTUD-1 MTBE is by far the poorest solvent, whereas it performs reasonably well in 2-propanol.

This dependence of the enantioselectivity on the solvent is unexpected. It is, however, not entirely surprising, since the energy difference responsible for an enantiomeric excess of 99.9% is only about 4 kcal mol^{-1}.[14] This energy difference is similar to that between solvated species, making the *ee* quite dependent on the solvent.

To confirm that the catalytic hydrogenation is indeed heterogeneous, the residual activity of the filtrate was measured in a filtration test.[18] A few minutes after the start of a normal hydrogenation procedure, **2**-AlTUD-1 was removed and the reaction was continued with the filtrate only. There is no additional conversion after the removal of the catalyst, (Figure 4), which clearly demonstrates that it is the heterogeneous catalyst that catalyses the reaction and that any Rh leached is inactive. This was also confirmed for **1**-AlTUD-1.

The recyclability of **1**-AlTUD-1 and **2**-AlTUD-1 was studied for all experiments described; results are depicted in Figures 5 and 6. In all solvents, with the exception of methanol, the activity of **1**-AlTUD-1 drops in the second run and in the third run. But with prolongation of the reaction time, 100% conversion could again be achieved in the fourth run, stressing the importance of short reaction times when comparing activities in consecutive runs. The enantioselectivity remains almost constant upon re-use and decreases only slightly in run 4, which can partially be explained by the altered reaction conditions. In MeOH the catalyst retains its activity in run 2, but is almost inactive in runs 3 and 4. The different behaviour in MeOH can be ascribed to the considerable leaching in this solvent. However, **2**-AlTUD-1 could be recycled without loss of activity or selectivity, even in MeOH.[1] In some cases the activity increased after run 1, which could be rationalised by the induction period needed to form the active species.[19]

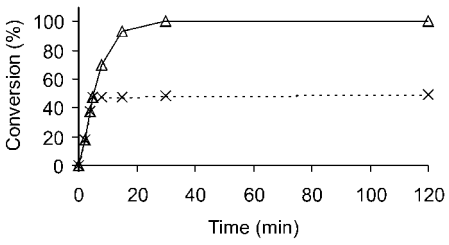


Figure 4. Determination of the heterogeneity of the AlTUD-1 supported catalysts by a filtration test. Lines: (△) conversion of **4** in MeOH, with **2**-AlTUD-1 as catalyst (entry 7, Table 2); (×) conversion of **4** in methanol, where the catalyst, **2**-AlTUD-1, was removed after 5 min.

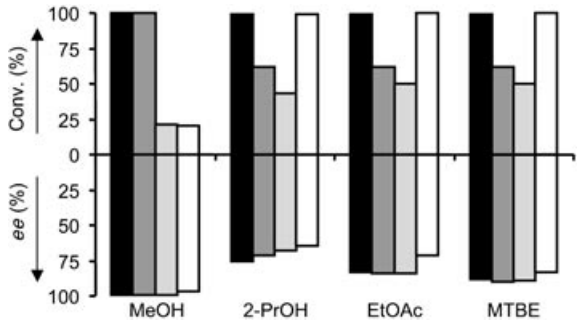


Figure 5. Recycling of **1**-AlTUD-1 in the asymmetric hydrogenation of **4** using conditions described in Table 2. Different bars represent consecutive runs. For run 4 modified conditions were used: $p_{initial}(H_2) = 5$ bar, time 120 min.

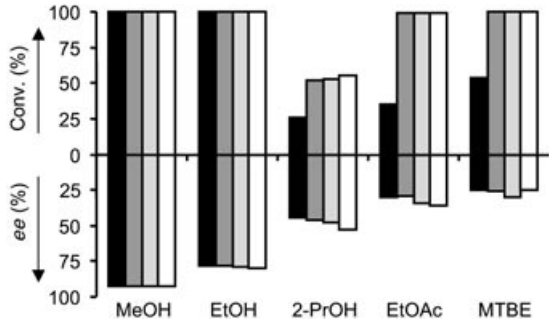


Figure 6. Recycling of **2**-AlTUD-1 in the asymmetric hydrogenation of **4** using conditions described in Table 2. Different bars represent consecutive runs.

The deactivation of **1**-AlTUD-1 cannot only be ascribed to the decreasing amount of Rh in successive runs, since this effect should be equal for **1**-AlTUD-1 and **2**-AlTUD-1. Another reason why this cannot be the only explanation is that the magnitude of deactivation is almost independent of the solvent. Even in MTBE, in which leaching is <0.1%, the same decrease of activity is observed. The dissimilarity in recyclability between the two catalysts should most likely be

[1] Mass transfer limitations were investigated, but did not seem to occur.

attributed to their different stabilities. The instability of Rh-DuPHOS complexes has been described earlier.[20] The catalyst probably decomposes at the end of the reaction or during the recycling procedure.

Conclusion

The ability to readily separate and recycle homogeneous catalysts was achieved by noncovalently anchoring this type of catalyst on a new aluminosilicate. These new catalysts showed a virtually identical behaviour to their homogeneous counterparts. Upon recycling, the immobilised catalyst **2**-AlTUD-1 displayed neither loss of activity nor of selectivity. **1**-AlTUD-1 was not fully recyclable, which is in line with the known instability of the homogeneous catalyst. The advantage of not having to modify the complex for the immobilisation and the absence of a negative influence of the immobilisation make this methodology fast and reliable for positively charged, proven homogeneous systems.

The choice of solvent is extremely important when applying this methodology. This factor not only influences the activity, but also the enantioselectivity of the catalyst and the leaching of Rh. The remobilisation of the Rh complex from the support shows an exponential increase with increasing polarity of the solvent. To minimise leaching, apolar solvents are recommended, but solvents like ethyl acetate and dichloromethane already give satisfactory results. Furthermore, this new immobilisation of the catalysts makes it possibile to combine catalysts and substrates that are normally incompatible owing to different solubilities. Thus, a new carrier material allows the straightforward immobilisation of transition-metal catalysts, while simultaneously broadening their applicability.

Experimental Section

General: Reactions and manipulations involving air-sensitive compounds were performed under an atmosphere of dry nitrogen using standard Schlenk techniques. Dry solvents were purchased from Aldrich and flushed with nitrogen for an hour before use. Dimethyl itaconate (DMI) from Acros was purified by crystallisation from methanol by cooling to −78 °C. Bis(1,5-cyclooctadiene)rhodium tetrafluoroborate was prepared according to a literature procedure.[21] 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. Hydrogenations were performed in a 100-mL Parr hastelloy C autoclave (A1128HC) or using the Avantium Quick Catalyst Screen platform: 96 small scale pressure reactors with a volume of 8 mL in parallel. These reactors are equipped with a Teflon insert and utilise magnetic stirring. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer in KBr from 4000–450 cm^{-1}. ^1H and ^{13}C NMR spectra were obtained on a Varian Inova 300 MHz or a Varian VXR-400S spectrometer, relative to TMS. ^{31}P NMR spectra were recorded on a Varian Inova 300 MHz relative to 1% H_3PO_4 and were ^1H decoupled. ^{27}Al MAS experiments were performed at 9.4 T on a Varian VXR-400 S spectrometer operating at 104.2 MHz with pulse width of 1 ms. We used 4-mm zirconia rotors with a spinning speed set to 6 kHz. The chemical shifts are reported with respect to $Al(NO_3)_3$ as external standard at $\delta = 0$ ppm. The rhodium content of the immobilised catalysts was measured using instrumental neutron activation analysis (INAA), which was performed at the Interfaculty Reactor Institute (IRI), Delft. The "Hoger Onderwijs Reactor" nuclear reactor, with a neutronflux of 10^{17} neutrons $s^{-1}cm^{-2}$, was used as a source of neutrons, and the gammaspectrometer was equipped with a germanium semiconductor as detector. Rhodium leaching was determined by analysing the reaction filtrates with graphite AAS on a Perkin Elmer 4100ZL. N_2 desorption isotherms were measured on a Quantachrome Autosorb-6B at 77 K and X-ray powder diffraction patterns were recorded by using $Cu_{K\alpha}$ radiation on a Philips PW 1840 diffractometer equipped with a graphite monochromator. Conversions of the hydrogenation reactions were determined by ^1H NMR and GC analysis, using a Varian Star 3400 CX GC with a CP wax 52 CB column (50 m × 0.70 mm, df = 2.0 μm), on column injection, FID at 250 °C and nitrogen as carrier gas (10 psi). Oven program for **3** and its products: 60 °C (2 min), 5 °C min^{-1} to 185 °C (3 min). Oven program for **4** and its products: 60 °C (2 min), 10 °C min^{-1} to 200 °C (6 min). Enantiomeric excesses in the hydrogenation of **3** were determined by chiral HPLC using a Chiralcel OD column (250 × 4.6 mm) with 2-propanol/hexane (2:98) as eluent, a flow of 0.8 mL min^{-1}, and UV detection at 215 nm. Retention times (min): (*R*)-dimethyl 2-methylsuccinate (10), dimethyl itaconate (15), and (*S*)-dimethyl 2-methylsuccinate (19). Enantiomeric excesses in the hydrogenation of **4** 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, split injector (36/100) at 220 °C and FID at 220 °C. Retention times (min) at 95 °C isotherm: 2-acetamidoacrylate (5.4), (*S*)-methyl 2-acetamidopropanoate (7.5), and (*R*)-methyl 2-acetamidopropanoate.

Synthesis of [Rh^I(cod){(*R*,*R*)-MeDuPHOS}]BF_4 (1): [Rh(cod){(*R*,*R*)-MeDuPHOS}]BF_4 was prepared by a slightly modified literature procedure.[8] [Rh(cod)$_2$]BF_4 (0.12 g, 0.29 mmol) and (*R*,*R*)-MeDuPHOS (0.09 g, 0.29 mmol) were dissolved in CH_2Cl_2 (8 mL) and stirred for 30 min. Slowly diethyl ether (28 mL) was added, yielding an orange precipitate, which was collected by filtration. Yield 0.10 g (59%). ^1H NMR ($CDCl_3$): δ = 1.03 (dd, ^3J(H,H) = 6.6 Hz Hz, ^3J(P,H) = 15.0 Hz, 6H; CH_3), 1.46 (dd, ^3J(H,H) = 7.2 Hz Hz, ^3J(P,H) = 18.3, 6H; CH_3), 1.63 (m, 4H; CH_2), 1.93 (m, 2H; CH, CH_2), 2.30–2.80 (m, 12H; CH_2, CH), 2.61 (m, 2H; CH, CH_2), 2.71 (m; CH, CH_2), 5.07 (br, 2H; CH=C), 5.63 (br, 2H; CH=C), 7.70 ppm (m, 4H; Ph); ^{31}P NMR ($CDCl_3$): δ = 77.15 ppm (d, ^1J(Rh,P) = 148.1 Hz).

Synthesis of [Rh^I(cod){(*S*,*S*)-DiPAMP}]BF_4 (2): [Rh(cod){(*S*,*S*)-DiPAMP}]BF_4 was synthesised according to the procedure of Knowles et al.[9] [{Rh(cod)Cl}$_2$] (0.27 g, 0.55 mmol) was added to (*S*,*S*)-DiPAMP (0.50 g, 1.1 mmol) in 90% MeOH. The slurry became orange and after 1 h stirring gave a red-orange solution. The complex was precipitated by the slow addition of $NaBF_4$ (0.18 g) in water (1.37 mL). After 1 h of additional stirring a red-orange solid was obtained by filtration. The solid was washed with water and recrystallised from ethanol, yielding 0.69 g (84%). ^1H NMR ($CDCl_3$): δ = 2.32–2.39 (m, CH_2; 12H), 3.62 (s, 6H; OCH_3), 4.64 (br, 2H; CH=C), 5.30 (br, 2H; CH=C), 6.93–7.04 (m, 6H; Ar), 7.50 (m, 2H; Ar), 7.66 (m, 6H; Ar), 7.97 ppm (m, 4H; Ar); ^{31}P NMR ($CDCl_3$): δ = 48.5 ppm (dd, J(Rh,P) = 151 Hz, ^2J(P,P) = 38 Hz).

Synthesis of methyl 2-acetamidoacrylate (4): The procedure of Gladiali et al. was used to methylate 2-acetamidoacrylic acid.[22] The 2-acetamidoacrylic acid (6.45 g, 50 mmol) was added to acetone (300 mL), followed by K_2CO_3 (13.82 g, 100 mmol). The mixture was stirred mechanically and heated to 60–65 °C. Iodomethane (10.64 g, 75 mmol) was added slowly and the suspension was stirred overnight at the same temperature. The precipitate was removed by filtration and the acetone was removed by evaporation. The residue was dissolved in a small amount of ethyl acetate/petroleum ether (7:3) and filtered over silica. The volatiles were removed by evaporation and the residue was crystallised from n-hexane, yielding 5.86 g (82%) of a colourless solid. M.p. 50–51 °C; ^1H NMR ($CDCl_3$): δ = 2.14 (s, 3H; CH_3CO), 3.85 (s, 3H; OCH_3), 5.88 (d, ^2J(H,H) = 1.2 Hz, 1H; *H*CH), 6.60 ppm (d, ^2J(H,H) = 1.2 Hz, 1H; HC*H*); ^{13}C NMR ($CDCl_3$): δ = 24.7 (CH_3(CO)), 53.0 (CH_3O), 108.7 (CH_2), 130.9 (CCH_2), 164.6 ($COOCH_3$), 168.9 ppm ((CO)N).

Preparation of AlTUD-1: Aluminium isopropoxide (6.12 g, 0.03 mol) was added to a mixture of absolute ethanol (27.6 g, 0.60 mol), anhydrous 2-propanol (27.05 g, 0.45 mol) and tetraethyl orthosilicate (25.0 g, 0.12 mol) under stirring at 45 °C. This was followed by the addition of tetraethylene glycol (29.1 g, 0.15 mol). Finally a solution of absolute ethanol (27.6 g, 0.60 mol), anhydrous 2-propanol (27.05 g, 0.45 mol) and H_2O (5.41 g, 0.30 mol) was added dropwise to this mixture. The resulting mixture was stirred for 0.5 h at room temperature, followed by aging without stirring

for 6 h, also at room temperature. The resulting wet gel was dried at 70 °C for 21 h and at 98 °C for 2 h; it was then hydrothermally treated at 160 °C for 3–21 h in an autoclave with Teflon insert. Finally the solids were calcined (with 1 °C min^{-1} to 550 °C, 4 h at 550 °C, with 1 °C min^{-1} to 600, 10 h at 600 °C). Elemental analysis gave a Si/Al ratio of 3.8–4:1. An $Al_{tetrahedral}$/Si ratio of 0.11:1 was determined by ^{27}Al MAS (see Figure 2). For other analyses see Figure 1 in Results and Discussion.

Immobilisation procedure for 1: AlTUD-1 (1.1 g) was dried at 200 °C under vacuum for 2 h. Some 2-propanol (45 mL) was added to the dried support. After 30 min stirring, **1** (88.4 mg, 0.146 mmol) in 2-propanol (20 mL) was added and the resulting suspension was stirred for 3 h. The solid was collected by filtration and washed thoroughly with portions of 2-propanol (30 mL) until the washings were colourless (approx. 5 times). Finally the catalyst was dried at 55 °C under vacuum for 2 h. Rh loading was determined by INAA: 11.5 mg Rh g^{-1} support, which corresponds to an $Al_{tetrahedral}$/Rh ratio of approximately 10:1.

Immobilisation procedure for 2: AlTUD-1 (1.1 g) was dried at 200 °C under vacuum for 2 h. Absolute ethanol (45 mL) was added to the dried support. After 30 min stirring, **2** (166.0 mg, 0.219 mmol) in absolute ethanol (20 mL) was added and the resulting suspension was stirred for 3 h. The solid was collected by filtration and Soxhlet extracted with absolute ethanol overnight. Finally the catalyst was dried at 55 °C under vacuum for 2 h. Rh loading was determined by INAA: 12.2 mg Rh g^{-1} support, which corresponds to an $Al_{tetrahedral}$/Rh ratio of approximately 10:1.

Typical hydrogenation reaction: All hydrogenation experiments were performed with 0.1 g of immobilised catalyst (~1 wt % Rh). The catalyst was transferred to the autoclave under a nitrogen atmosphere, followed by 50 mL of substrate solution (concentrations and solvents given in Tables 1 and 2). The sealed autoclave was purged with hydrogen by pressurising to 7 bar while stirring at 300 rpm, followed by release of pressure. This cycle was repeated five times and finally the desired pressure 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 a 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 removal of the solution, fresh substrate solution was added to the used catalyst and the hydrogenation procedure was repeated. All catalysts were reused in this way several times.

Hydrogenation using the Avantium Quick Catalyst screen: The small-scale pressure reactors were charged with **1**-AlTUD-1 (6 mg), followed by 1.5 mL of a 0.1 M solution of **3**. The following solvents were screened in parallel: methanol, ethyl acetate, dichloromethane, 2-propanol, MTBE, and toluene. The reactors were simultaneously pressurised to 5 bar, followed by release of pressure to purge the system with hydrogen. This cycle was repeated five times, after which the reactors were again pressurized to 5 bars and stirred at 1500 rpm for 1 h.

Filtration test: To determine the heterogeneity of the reaction, the activity of the filtrate was measured using a filtration test. A hydrogenation reaction was carried out according to the typical hydrogenation procedure described above. After 5 min (17–25 % of normal reaction time) the hydrogenation reaction was stopped by releasing the hydrogen pressure and purging with nitrogen. The solution was withdrawn from the autoclave with a syringe equipped with an Acrodisc GF syringe filter (1.0 μm pore size) and the solution was stored under nitrogen. The catalyst was removed from the autoclave and the stored solution was transferred back into the autoclave under a nitrogen atmosphere. The hydrogenation reaction was then continued using the typical hydrogenation procedure. After filtration no additional conversion was observed.

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