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Application of Tripodal Linker Units to Immobilized Rhodium Complex Catalysts for Asymmetric Hydrogenation

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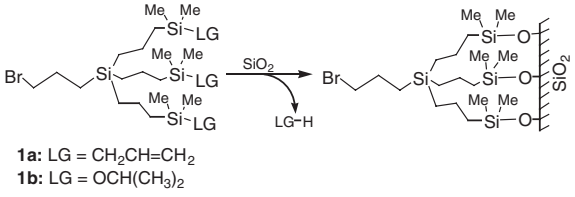
The tripodal linker unit with one bromopropyl group and three anchoring silicon atoms was used to immobilize a chiral phosphine–rhodium complex catalyst on an ordered mesoporous silica support. The rhodium and phosphorus leaching levels into the reaction solution after asymmetric hydrogenation were lower for this catalyst than for immobilized catalysts prepared using conventional triethoxysilane.

The immobilization of molecular catalysts via linkers, such as the trimethylene chain, on insoluble solid supports, such as silica, is a promising strategy for simplifying the separation of catalysts from reagents and products, as well as for facilitating catalyst recycling.[1] Immobilized molecular catalysts may be adapted to continuous flow processes. However, poor stability is a major drawback to immobilized metal complex catalysts.[2] The elimination of metal fragments from anchored ligands and the cleavage of the bond between a ligand and the support permit leaching of the metal and/or ligand into the reaction solution. Strong σ-donating[3] or chelating ligands[4] are occasionally effective for overcoming the former problem, whereas few attempts have been made to fortify ligand support bonds against leaching.[5]

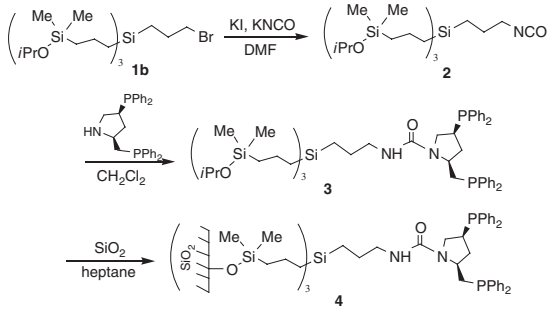
Recently, we developed a novel tripodal linker unit possessing three leaving allylsilyl or isopropoxysilyl groups (Scheme 1).[6] This linker unit binds tightly to the surface of a silica support via three independent siloxane bridges. The tripodal linker unit additionally contains a bromopropyl moiety to which various organic functional molecules, including auxiliary ligands for metal complexes, may be attached. This linker unit thus prevents grafted organic functional moieties from leaving the support. Here, we report application of the tripodal linker unit to the grafting of a chiral phosphine ligand onto mesoporous silica supports, and we describe the use of tethered rhodium complex catalysts for the asymmetric hydrogenation of cinnamic acid derivatives. The advantages of immobilized chiral catalysts have been well-documented in the literature.[7]



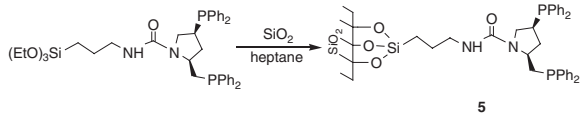
Scheme 1. Tripodal linker units and their grafting onto silica surfaces.

The tripodal linker unit containing three isopropoxysilyl moieties **1b** was prepared in a one-pot process via the iridium-catalyzed hydrosilylation of triallyl(3-bromopropyl)silane with dimethylchlorosilane, followed by treatment of the resulting tris(dimethylchlorosilyl) compound with triethylamine in isopropyl alcohol, as described previously.[6] The attachment of a chiral phosphine ligand to the linker unit was conducted as follows: **1b** was first converted to isocyanate **2** by reaction with potassium isocyanate in the presence of potassium iodide (Scheme 2). Then, the reaction of **2** with (2*S*,4*S*)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine yielded the tripodal chiral phosphine ligand **3**.[13] The grafting reaction of **3** onto the ordered mesoporous silica (TMPS-4)[8] was carried out in heptane under reflux for 24 h, giving the chiral pyrrolidinobisphosphine ligand-modified silica **4**.[9] To compare the effects of the linker structure on the catalytic performance, chiral ligand-modified silica **5** was prepared using conventional triethoxysilane according to reported procedures (Scheme 3).[9c] The organic contents in **4** and **5**, determined by elemental analysis of carbon, were 0.30 and 0.33 mmol g^{-1}, respectively, indicating that the tripodal linker secured surface loading levels that were comparable to those reached using a conventional trialkoxy linker.

The X-ray diffraction (XRD) pattern of the chiral ligand-modified silica **4** was similar to that of the parent mesoporous silica (Figure 1).[8] Three peaks were assigned to a 2D hexagonal structure, indicating that grafting of the pyrrolidinobisphosphine



Scheme 2. Synthesis and grafting of the tripodal chiral phosphine ligand onto the silica surface.



Scheme 3. Grafting of the chiral phosphine ligand containing triethoxysilyl groups onto the silica surface.

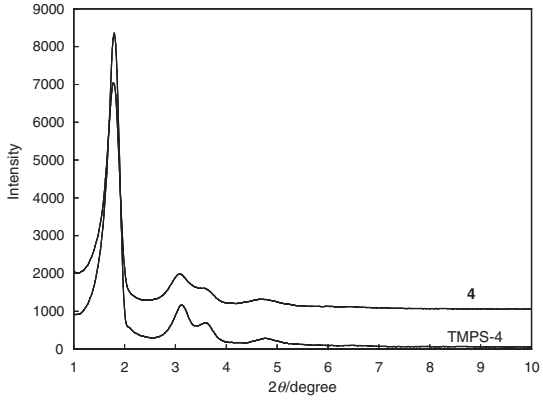


Figure 1. XRD patterns of **4** and the mesoporous silica support (TMPS-4).

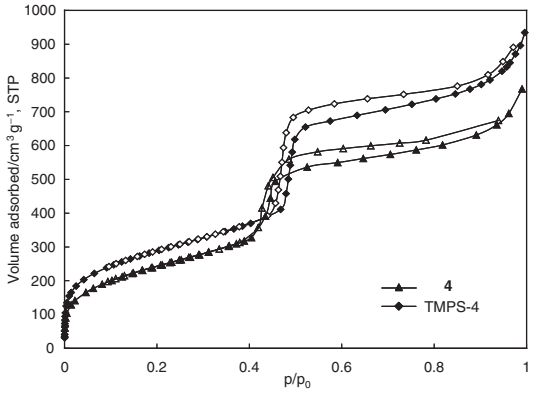


Figure 2. Nitrogen adsorption/desorption isotherms of **4** and the mesoporous silica support (TMPS-4).

unit via the tripodal linker unit preserved the mesoporous structure. The nitrogen adsorption/desorption isotherm of **4** showed a type IV sorption curve typical of mesoporous structures (Figure 2). Grafting of the tripodal chiral phosphine ligand reduced the pore volume from 1.46 to 1.18 $cm^3\,g^{-1}$ and narrowed the average pore size from 3.8 to 3.3 nm. However, **4** maintained a high surface area (868 $m^2\,g^{-1}$).

The chiral ligand-modified silicas **4** and **5** were further characterized by ^{29}Si, ^{13}C, and ^{31}P CP/MAS NMR spectroscopy. The ^{29}Si CP/MAS spectrum of **4** exhibited two peaks at 2 and 17 ppm, which corresponded to a single tetraalkyl-coordinated silicon center and three trialkylmonooxygen-coordinated silicon centers in **4**, in addition to the broad peaks around −100 ppm due to Q^3 and Q^4 silicon in silica (Figure 3A).[10] Both peaks at 2 and 17 ppm had shoulders around 6 and 15 ppm, which were probably due to species containing unreacted isopropoxysilyl groups. This was further confirmed by ^{13}C CP/MAS of **4** (vide infra).

Figure 3B shows the ^{29}Si CP/MAS spectrum of the modified silica **5**. Although condensation of conventional trialkoxysilanes with surface silanol groups in principle permits linkage through three siloxane bridges, the sole peak (−51 ppm) observed in the organosilane region was assigned to T^1 silicon.[11] This indicated that the chiral phosphine in **5** was predominantly bound to the silica surface via a single Si–O–Si bond.

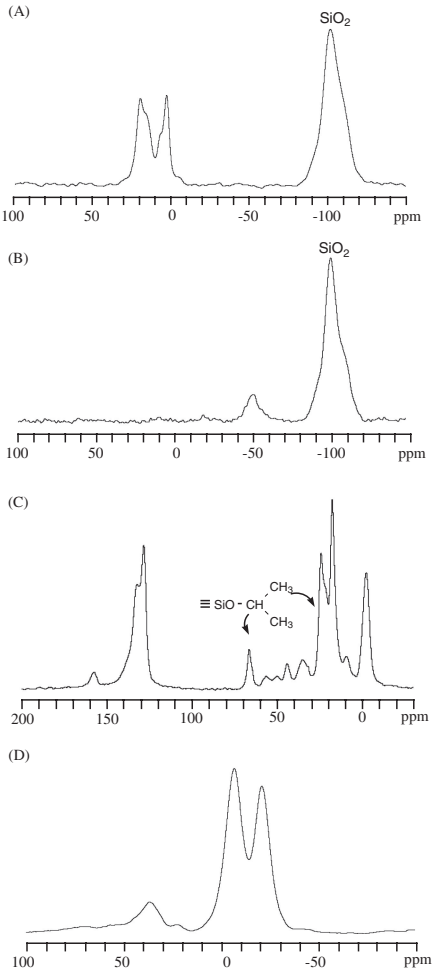
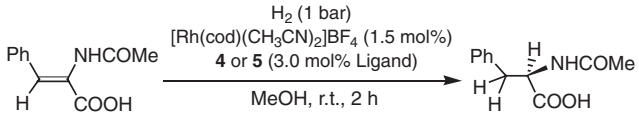


Figure 3. (A) ^{29}Si CP/MAS spectrum of **4**; (B) ^{29}Si CP/MAS spectrum of **5**; (C) ^{13}C CP/MAS spectrum of **4**; and (D) ^{31}P CP/MAS spectrum of **4**.

Figure 3C shows the ^{13}C CP/MAS spectrum of the modified silica **4**. The peaks at −3, 5–60, 125–140, and 157 ppm were assigned, respectively, to the methyl groups on silicon, the methylene and methyne carbons of the tripodal linker and the chiral pyrrolidinobisphosphine unit, the aromatic carbons on the phosphorus, and the ureidic carbonyl carbon, by comparison with the chemical shifts in the ^{13}C NMR spectrum of **3** in CD_2Cl_2. The ^{13}C CP/MAS spectrum revealed peaks that could be assigned to an isopropoxy group, the methyl peaks of which overlapped with the methylene peaks of the linker. This suggested that the isopropoxysilyl groups of **3** remained partially unreacted in **4**. However, the presence of the isopropoxide species on silica (*i*PrO–Si) formed by the reaction of the eliminated isopropyl alcohol and the surface silanol group could not be excluded. Thus, the chiral ligand-modified silica **4** may unfortunately contain bipodally and/or monopodally anchored species in addition to tripodal species. However, **4** showed apparent advantages in terms of reduced leaching during catalysis relative to **5** (vide infra). In the ^{31}P CP/MAS spectra of **4**, two peaks corresponding to the diphenylphosphino groups were observed at −21 and −7 ppm (Figure 3D). A minor peak observed at 36 ppm was probably due to the oxidized diphenylphosphino species.



Scheme 4. Asymmetric hydrogenation of ACA.

Table 1. Results of the asymmetric hydrogenation of ACA using the rhodium complex catalysts prepared from **4** and **5**[a]

Ligand	Yield/%[b,c]	ee/%[b]	Leaching of Rh/mg L^{-1}	Leaching of P/mg L^{-1}
4	98[d]	95	12	0.9
5	98	94	24	3.9

[a]ACA: 0.5 mmol, catalyst: 1.5 mol % on Rh, H_2: 1 bar, methanol: 7 mL, room temperature, 2 h. [b]Determined by HPLC using a Chiralpack AD-H column. [c]Sum of enantiomers. [d]Isolated yield was 96% after silica gel chromatography (ethyl acetate as eluent).

The catalytic performance of the chiral ligand-modified silica **4** was probed in the rhodium-catalyzed asymmetric hydrogenation of (*Z*)-α-(acetamido)cinnamic acid (ACA) in methanol under a hydrogen pressure of 1 bar at room temperature (Scheme 4). In the presence of a catalyst prepared by mixing $[Rh(cod)(CH_3CN)_2]BF_4$ with two equivalents of **4** (Rh: 1.5 mol %), the reaction was completed within 2 h to quantitatively yield *N*-acetylphenylalanine in 95% ee (Table 1). The enantioselectivity was comparable to that reported for the homogenously catalyzed reaction.[12] Although the catalytic activity and enantioselectivity of **4** were similar to those of the catalyst prepared from **5**, obvious differences in the leaching of metal and ligand were observed. After the reaction, the catalyst was separated by filtration, and the extent of rhodium and phosphorus leaching into the reaction solution was determined by ICP-AES. The leaching levels of the catalyst prepared from **4** (12 mg L^{-1} for Rh and 0.9 mg L^{-1} for P) were lower than those of the catalyst prepared from **5** (24 mg L^{-1} for Rh and 3.9 mg L^{-1} for P). The tripodal linker in **4** cannot inhibit the leaching of rhodium and phosphorus via de-coordination of rhodium and/or decomposition of the chiral phosphine part (e.g., cleavage of the NH–C(O)–N bond) during the asymmetric hydrogenation. However, firm immobilization utilizing the tripodal linker most likely effectively prevented the chiral phosphine–rhodium complex from leaving the silica support via cleavage of the Si–O–Si linkage.

The recyclability of the rhodium catalyst from **4** was assessed by hydrogenating ACA, removing the reaction supernatant via centrifugation and decantation, and recharging the reaction tube with ACA and a solvent. The recovered rhodium catalyst exhibited similar performances in the second and third runs as in the first run (Table 2).

In summary, we successfully used the tripodal linker unit to immobilize the chiral pyrrolidinobisphosphine ligand onto ordered mesoporous silica. The rhodium complex catalyst prepared from the silica-immobilized tripodal chiral phosphine ligand showed activity and enantioselectivity that were comparable to their homogeneous counterparts during asymmetric hydrogenation. Additionally, the catalyst containing the tripodal linker showed lower leaching levels of rhodium and phosphorus than the catalyst attached via a conventional trialkoxy linker.

Table 2. Catalyst recycling experiments for the asymmetric hydrogenation using the rhodium complex catalyst prepared from **4**[a]

Run	Yield/%[b,c]	ee/%[b]
1st	98	95
2nd	99	95
3rd	98	96

[a]ACA: 0.5 mmol, catalyst: 1.5 mol % on Rh, H_2: 1 bar, methanol: 7 mL, room temperature, 2 h. [b]Determined by HPLC using a Chiralpack AD-H column. [c]Sum of enantiomers.

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