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Preparation and application of a polymer-supported chiral π-allylpalladium catalyst for the allylation of imines

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Abstract

The polymer-supported chiral π-allylpalladium catalyst **8** was applied to the asymmetric allylation reaction of imines **9** with allyltributylstannane. The catalyst was very stable and could be reused several times with high catalytic activity, although the enantioselectivity was not necessarily high. © 1999 Elsevier Science Ltd. All rights reserved.

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In catalytic asymmetric synthesis, polymer-supported chiral catalysts offer the following advantages over the usual homogeneous catalysts; easy recovery and potential recycling of expensive chiral catalysts, simplified product purification and the possibility of carrying out the desired transformation in a continuous-flow system. Although many examples of asymmetric reactions with chiral transition-metal catalysts that employ polymer-supported *chiral ligands containing P, N and O atoms* have been given over recent years,[1,2] to the best of our knowledge, asymmetric reactions with polymer-supported *chiral π-allylpalladium* catalysts have not been reported so far. We recently reported the asymmetric allylation reaction of imines with allyltributylstannane catalyzed by the chiral π-allylpalladium catalyst **1** (Fig. 1, **1**). Mechanistic studies revealed that the unsymmetrical bis-π-allylpalladium complex **2** is a reactive intermediate for this allylation; the allyl group reacts as a nucleophile with an imine and the other sterically bulky chiral π-allyl group acts as a nontransferable π-allyl ligand (Fig. 1, **2**).[3] It occurred to us that if a nontransferable chiral π-allyl ligand is bound to a polymer and another π-allyl group is transferred as a nucleophile selectively to imines (Fig. 1, **3**), we may carry out the polymer-supported catalytic asymmetric allylation of imines. It was thought that the reaction of a chloromethylated polymer resin with a chiral source containing a hydroxyl group, which afterwards can be converted to a bis-π-allylpalladium species, would be suitable to make a polymer-bound chiral reagent (Fig. 1, **4**).

According to this design, we chose estrone as a chiral source, which was bound to the PS/DVB copolymer with a chloromethylated functionality (Scheme 1).[4] To a mixture of chloromethylated polystyrene

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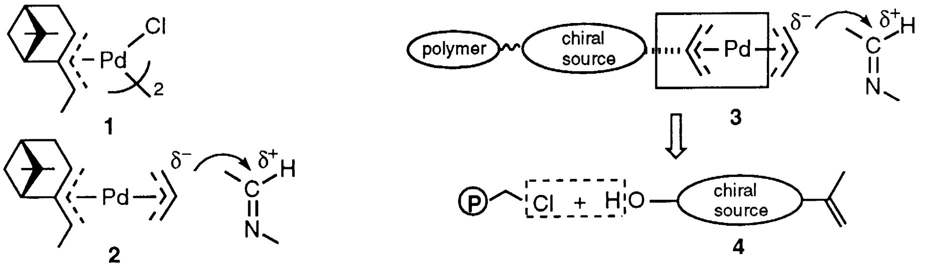
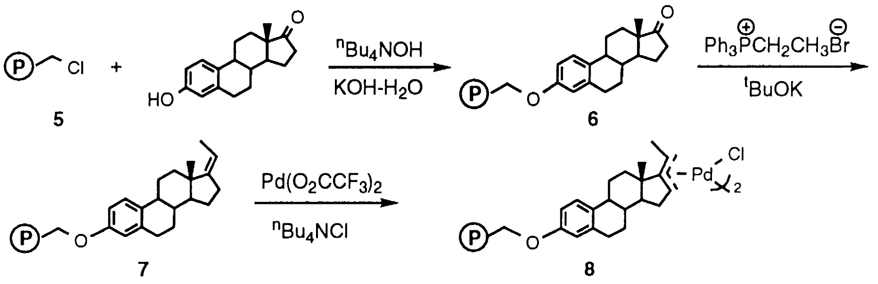


Fig. 1.

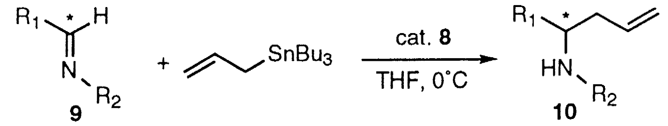
5 (2.685 g; Cl, 0.97 mmol/g) and estrone (7.042 g, 10 equiv.) in 30 mL of *o*-dichlorobenzene were added a 40% solution of tetrabutylammonium hydroxide (0.3 mL) and aqueous solution of NaOH (1.6 g, 5 mL H_2O). The mixture was placed in an oil bath at 80°C and stirred magnetically for 3 days. After filtration the resulting polymer was washed repeatedly with methanol, water, THF:H_2O (3:1), THF, acetone, dichloromethane and methanol, and then dried overnight at 60°C under vacuum. Chlorine analysis showed no chlorine present in the product. The resulting polymer **6** indicated a new infra-red band at 1740 cm^{-1} (C=O); cf. 1720 cm^{-1} (C=O for estrone). The polymer-supported exoethylidene **7** was prepared by treating the polymer **6** with excess of triphenylphosphonium ethyl bromide (10 equiv.) and ^{t}BuOK (9.5 equiv.) in THF under reflux for 41 h. The product **7** was filtered off, washed, and dried as described above. The strong C=O band at 1740 cm^{-1} disappeared in the infra-red spectrum of **7**. The polymer-supported exoethylidene **7** (0.97 g, 0.5 mmol) and palladium trifluoroacetate (166 mg, 0.5 mmol) were stirred at ambient temperature in 5 mL THF for 6 h, and then tetra-*n*-butylammonium chloride (153 mg, 0.55 mmol) was added. The resulting mixture was left under stirring for 1 h. It was then filtered, washed as described above, and dried overnight under vacuum at room temperature.[5] Thus, the yellow polymer-supported chiral π-allylpalladium catalyst **8** was prepared. ICP analysis indicated that the ratio of Pd was 4.6 wt%; if the exoethylidene group attached to the polymer resin was completely converted to the π-allylpalladium functionality the ratio should be 7.5 wt% indicating that there would be free ethylidene groups in the resulting polymer.



Scheme 1.

We tested this catalyst **8** in the asymmetric allylation of imines **9** with allyltributylstannane. The results are summarized in Table 1. Since the catalyst **8** swelled better in THF than in DMF, THF was chosen as a solvent.[6] DMF was an effective solvent for the imine allylation reaction with chiral π-allylpalladium catalyst **1**.[3] The allylation reaction of **9a** using 1.2 equiv. allyltributylstannane in THF at 0°C gave **10a** in 76% yield with 42% ee (entry 1). Although the allylation of **9b** gave a very good yield (91%), a lower ee was observed (13%; entry 2); the enantioselectivity was the same as that using the chiral π-allylpalladium catalyst **1**. The reactions of **9c** and **9d** were very sluggish, giving the corresponding homoallylamines **10c** and **10b** in low yields with 38 and 35% ee, respectively (entries 3 and 4). The allylation reaction of **9e**

Table 1
Asymmetric allylation of imines **9** catalyzed by polymer-supported chiral π-allylpalladium catalyst **8**



entry	imine **9**	R^1	R^2	reaction time (h)	yield of **10** (%)[a]	ee (%)[b,c]
1	**9a**	Ph	Bn	140	**10a** 76	42 (*S*)
2	**9b**	Ph	Ph	134	**10b** 91	13 (*S*)
3	**9c**	*p*-$MeOC_6H_4$	Bn	228	**10c** 45	38 (*S*)
4	**9d**	Ph	Pr	240	**10d** 24	35 (*S*)
5	**9e**	2-naphthyl	Bn	168	**10e** 77	26 (*S*)
6	**9f**	PhCH=CH	Bn	168	**10f** 89	38 (*S*)
7	**9g**	*c*-Hex	Bn	186	**10g** 98	36 (*S*)

[a] Isolated yield based on **9**. [b] The ees were determined by a chiral HPLC (CHIRALCEL OD). [c] The absolute configurations were assigned by comparing the optical rotations with reported data.[3]

gave **10e** in 77% yield with 26% ee. The imines prepared from aliphatic aldehydes (**9f** and **9g**) gave **10f** and **10g** in very good yields (89 and 98%) with 38 and 36% ee, respectively (entries 6 and 7). These results clearly indicate that the polymer-supported chiral π-allylpalladium catalyst **8** is effective for the catalytic allylation reaction of imines with allyltributylstannane, the catalytic activity of which is comparable to that using the homogeneous chiral π-allylpalladium catalyst **1**, although the enantioselectivity obtained with **8** is lower than that with the homogeneous system.

A representative procedure for the allylation reaction of imines is as follows. To a mixture of polymer-supported chiral π-allylpalladium catalyst **8** (94 mg, 0.04 mmol Pd) and the imine **9a** (78 mg, 0.4 mmol) in 2 mL THF at 0°C was added allyltributylstannane (159 mg, 0.48 mmol). The mixture was stirred for 140 h, and then filtered. The reaction progress was monitored by TLC, and the allyltributylstannane disappeared after 140 h. The catalyst was washed with THF, and the filtrates were combined. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (hexane:ethyl acetate=5:1), giving **10a** in 76% yield. The optical purity was determined by HPLC analysis using a chiral column.

We next investigated the stability of the catalyst in order to recycle it. The results of repeated use of the catalyst for the allylation of **9a** are summarized in Table 2. Using the fresh catalyst **8**, **10a** was obtained in 76% yield with 42% ee (run 1). The use of the recovered catalyst gave **10a** in 78% yield with 47% ee (run 2). Again, the catalyst was recovered and used repeatedly. Essentially, same yields and ees were

Table 2
Recycle use of the catalyst **8** for the allylation of **9a**[a]

run	**10a**, yield (%) / reaction time (h)	ee (%)	run	**10a**, yield (%) / reaction time (h)	ee (%)
1	76 / 140	42	3	75 / 145	45
2	78 / 135	47	4	71 / 147	45

[a] All the reactions were carried out in THF in the presence of the polymer-supported chiral π-allylpalladium catalyst **8** (94 mg) at 0°C; Imine 9a (78 mg, 0.4mmol) and allyltributylstannane (159 mg, 0.48mmol) were used for the reactions.

obtained by the use of the catalyst recovered either from the reaction of run 2 or from that of run 3. It is interesting that even a slightly higher ee was obtained by the use of the recovered catalyst. These results clearly indicate that the polymer-supported chiral π-allylpalladium catalyst is very stable and can be used repeatedly.

In summary, we have prepared the polymer-supported chiral π-allylpalladium catalyst **8** for the first time. The catalyst was very stable and can be reused with high catalytic activity for allylation reaction of imines, although the enantioselectivities were not necessarily high.

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