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Simply Modified Chiral Diphosphine: Catalyst Recycling *via* Non-covalent Absorption on Carbon Nanotubes

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Dedicated to Professor Andreas Pfaltz on the occasion of his 60th birthday.

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: A new type of recyclable chiral catalyst system was developed by absorption of pyrene-modified Pyrphos rhodium catalyst onto carbon nanotubes *via* π-π stacking interaction. This modified catalyst was successfully applied in the asymmetric hydrogenation of α-dehydroamino esters for nine cycles without obvious deterioration of activity and enantioselectivity.

Keywords: absorption; asymmetric catalysis; carbon nanotube; catalyst recycling; pyrene

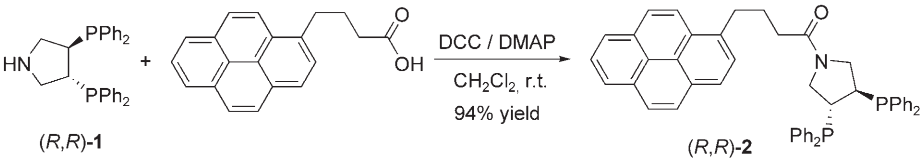
Asymmetric catalysis is a powerful, economically feasible tool for the synthesis of optically active molecules that serve as precursors for pharmaceuticals, agrochemicals, and flavorings, as well as functional materials. Many efficient, homogeneous chiral catalysts that exhibit high activities and enantioselectivities have been developed in the past few decades.[1] However, the considerable difficulty involved in separating these expensive chiral catalysts from products for reuse has restricted their applications in industrial processes.

The immobilization of chiral catalysts on various insoluble solid supports such as inorganic materials, organic polymers, or membranes can solve the problems arising from homogeneous catalysis.[2] However, these "heterogenized" catalysts usually suffer from decreased catalytic activities and enantioselectivities due to restriction by the solid matrix, which limits mobility and accessibility of the active sites. Thus, chiral catalysts that combine the advantages of homogeneous catalysts (high catalytic activity and enantioselectivity) and heterogeneous catalysts (easy separation and convenient recycling of the catalyst from the reaction mixture) have become a focus of intense research in recent years. For example, Chan and co-workers reported the synthesis of a soluble polyester-supported BINAP ligand based on the concept of "one-phase catalysis and two-phase separation". This supported chiral ligand showed a higher activity than the corresponding "free" ligand in the Ru(II)-catalyzed asymmetric hydrogenation of α-(6-methoxyl-2-naphthyl)-acrylic acid.[3]

Recent advances such as thermomorphic catalyst systems,[4] dendritic catalysts,[5] magnetically recoverable catalysts,[6] and self-assembled supported catalysts[7] have provided interesting alternatives for recovering and reusing chiral catalysts. However, the sophisticated designs generally result in increased cost of the chiral catalyst and/or catalyst system. In this communication, we describe a very simple and efficient approach to recycle and reuse a chiral Rh(I)/diphosphine catalyst for asymmetric hydrogenation *via* non-covalent absorption on carbon nanotubes (CNTs).

Since their discovery in 1991, CNTs have attracted considerable attention because of their unique mechanical, electronic, and chemical stability properties.[8] These properties have made CNTs very promising nanomaterials for many applications in chemistry.[9] However, only a few applications of CNTs in catalytic asymmetric reactions have been reported. García and co-workers[10] utilized single-well nanotubes (SWNTs) to support chiral vanadyl salen complexes *via* a covalent link for the heterogeneous asymmetric cyanosilylation of aldehydes, affording chiral α-hydroxy cyanides in 66% enantiomeric excess.

To develop a new method for recycling chiral catalysts, we designed a diphosphine ligand connected to a polyaromatic ring, which can be adsorbed onto



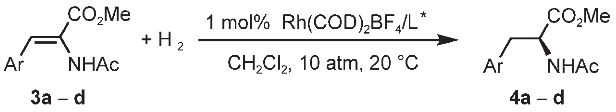
Scheme 1. Synthesis of pyrene-modified Pyrphos ligand **2**.

CNTs *via* π-π stacking.[11] Pyrene-modified Pyrphos ligand (*R*,*R*)-**2** was synthesized, and its complex with Rh(I) was found to be strongly adsorbed on CNTs in several solvents and weakly adsorbed in other solvents. This novel platform allows the "homogeneous" performance of the asymmetric reaction and the recycling of the chiral catalyst *via* general solid/liquid separation simply by changing the solvent.

The synthesis of the pyrene-modified Pyrphos ligand (*R*,*R*)-**2** is very straightforward (Scheme 1). The reaction of (3*R*,4*R*)3,4-bis(diphenylphosphino)pyrrolidine (Pyrphos, *R*,*R*-**1**)[12] with commercially available 1-pyrenebutyric acid in the presence of 1,3-dicyclohexylcarbodiimine (DCC) and 4-(dimethylamino)pyridine (DMAP) afforded ligand (*R*,*R*)-**2** in high yield (94%).[13]

When evaluating the performance of ligand (*R*,*R*)-**2** in the Rh(I)-catalyzed asymmetric hydrogenation of α-dehydroamino esters **3**, we found that the introduction of a pyrenyl group into the Pyrphos ligand did not affect its enantioselectivity (Table 1). The uses of pyrene-modified Pyrphos (*R*,*R*)-**2** and *N*-acetyl-Pyrphos (Ac-Pyrphos) as ligands gave hydrogenation product **4a** in similar enantioselectivities (entries 1 and 2). The α-dehydroamino esters **3b–d** with electron-donating or -withdrawing substituents can also be hydrogenated efficiently with ligand (*R*,*R*)-**2**, providing the corresponding products **4b–d** with good enantioselectivities (92–96% *ee*) (entries 3–5).

Table 1. Asymmetric hydrogenation of α-dehydroamino esters **3**.[a]



Entry	Ligand	Ar	Product	*ee* [%][b]
1	Ac-Pyrphos	C_6H_5	**4a**	93
2	(*R*,*R*)-**2**	C_6H_5	**4a**	94
3	(*R*,*R*)-**2**	4-MeC_6H_4	**4b**	95
4	(*R*,*R*)-**2**	4-$MeOC_6H_4$	**4c**	96
5	(*R*,*R*)-**2**	4-ClC_6H_4	**4d**	92

[a] All reactions were carried out at a substrate concentration of 0.063 M; (substrate/catalyst/ligand = 100:1:1) under 10 atm of H_2 at 20 °C for 2 h. The conversion of substrate for all reaction was >99%.

[b] Determined by Chiral GC using a Supelco C.L.V. column.

The absorption of the chiral catalyst onto CNTs was studied. The Rh(I) catalyst **5** was generated *in situ* by the reaction of 1.0 mg (0.0025 mmol) Rh-$(COD)_2BF_4$ (COD = 1,5-cyclooctadiene) and 1.8 mg (0.0025 mmol) ligand (*R*,*R*)-**2**, followed by treatment with 15 mg CNTs in 4 mL solvent. After stirring for 15 min, the concentration of catalyst **5** in the upper solution was analyzed by UV/vis spectroscopy. Among the solvents tested, CH_2Cl_2 gave the lowest absorption of catalyst **5** on CNTs (50%), and the color of the upper solution was yellow (Figure 1 a). In contrast, catalyst **5** was mostly absorbed on CNTs in EtOAc (97%), and the upper solution was colorless (Figure 1 b). In THF and MeOH, 83% and 94%, respectively, of catalyst **5** was absorbed on CNTs.

On the basis of the absorption properties of catalyst **5** in different solvents, we chose CH_2Cl_2 as the solvent for the asymmetric hydrogenation of **3a**. When 15 mg CNTs were used in the hydrogenation of **3a** (0.25 mmol) with catalyst **5** (0.0025 mmol) in 4 mL CH_2Cl_2, the reaction was complete in 2 h at 10 atm of H_2 and 20 °C, providing the hydrogenation product in 93% *ee*. After the reaction, catalyst **5** was recovered by changing the solvent to EtOAc. The CH_2Cl_2 was evaporated, 4 mL EtOAc were added, and the mixture was stirred for 15 min. Catalyst **5** was separated by filtration. Increasing the amount of CNTs was favorable for recovering the catalyst but decreased the reaction rate and enantioselectivity (Table 2). Considering the recovery of catalyst, the reaction rate, and the enantioselectivity, we chose 15 mg CNTs and

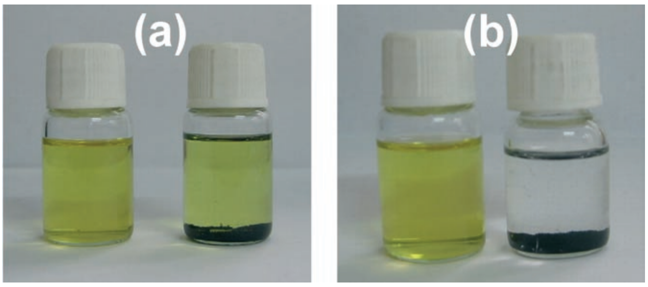


Figure 1. The absorption of chiral catalyst onto CNTs in different solvents. (**a**) CH_2Cl_2: no CNTs (*left*); added CNTs (*right*). (**b**) EtOAc: no CNTs (*left*); added CNTs (*right*).

Table 2. Optimizing the conditions for hydrogenation and recovery of catalyst.[a]

Entry	CNTs [mg]	Cat. **5** in solution [%][b]	Time [h]	Conv. [%]	*ee* [%]
1	0	100	2	100	94
2	10	65	2	100	94
3	15	50	2	100	93
4	20	36	3	100	91
5	25	33	4	100	90
6	30	27	6	99	86
7	100	<1.0	12	4	40

[a] *General conditions:* The catalyst **5** generated *in situ* from $Rh(COD)_2BF_4$ (1.0 mg, 0.0025 mmol) and (*R*,*R*)-**2** (1.8 mg, 0.0025 mmol) was treated with CNTs in 4 mL CH_2Cl_2 and stirred for 15 mins. The substrate **3a** (55 mg, 0.25 mmol) was hydrogenated under 10 atm of H_2 at 20 °C for a proper time.

[b] Determined by UV/vis spectrum.

Table 3. Recycling catalyst experiments.[a]

Run	Time [h]	Conv. [%]	*ee* [%]
1	2	100	93
2	2	100	93
3	3	99	93
4	4	100	93
5	5	95	93
6	6	98	93
7	8	97	93
8	10	97	92
9	12	95	92
10	12	15	92

[a] *Reaction conditions:* $Rh(COD)_2BF_4$/(*R*,*R*)-**2**/**3a**/CNTs = 0.0025 mmol/0.0025 mmol/0.25 mmol/15 mg in 4 mL CH_2Cl_2 under 10 atm H_2 at 20 °C for the appropriate time.

0.0025 mmol catalyst **5** for the catalyst recycling experiment.

By absorption on CNTs, catalyst **5** was successfully recycled and reused in the asymmetric hydrogenation of **3a**. As shown in Table 3, catalyst **5** was reused for nine cycles without obvious deterioration in activity or enantioselectivity (entries 1–9). To our knowledge, this represents the best reported result for the recycling and reuse of the highly air-sensitive Pyrphos-derived catalyst. When recovered catalyst **5** was reused for 10th run, the activity of the catalyst droped dramatically, although the high enantioselectivity (92%) remained (entry 10).

In conclusion, a new type of recyclable chiral catalyst system was developed that utilizes absorption of a pyrene-modified Pyrphos rhodium catalyst onto CNTs by π-π stacking interactions. With this catalyst system, the asymmetric hydrogenation of α-dehydroamino esters was performed homogeneously, and the chiral catalyst was recovered *via* general solid/liquid separation simply by changing the solvent. This strategy for catalyst recycling has potential widespread applications in organic synthesis.

Experimental Section

General Procedure for Hydrogenation Reaction and CNTs-Assistant Catalyst Recycling

A mixture of $[Rh(COD)_2]BF_4$ (1.0 mg, 0.0025 mmol) and ligand (*R*,*R*)-**2** (1.8 mg, 0.0025 mmol) was stirred at room temperature for 15 min in CH_2Cl_2 (4 mL) under nitrogen. The resulting solution of catalyst **5** was directly transferred to a 20-mL glass vessel charged with substrate **3a** (55 mg, 0.25 mmol), CNTs (15 mg)[14] and a magnetic stirring bar. The vessel was put into a stainless steel autoclave, and the autoclave was closed and pressurized with H_2 to 10 atm. The reaction mixture was stirred (1100 rpm) under the H_2 pressure at 20 °C for a proper time. After the reaction, the hydrogen pressure was carefully released and 20 μL COD were added immediately. The CH_2Cl_2 was removed under reduced pressure, 4 mL EtOAc were added and the mixture was stirred for 15 min. The catalyst **5** absorbed onto the CNTs was recovered *via* filtration under nitrogen atmosphere and dried under reduced pressure, which was directly used for next cycle. The filtered EtOAc layer was used to determine the conversion of substrate and the enantiomeric excess of the hydrogenation product by GC on a Supelco C.L.V. column.

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[13] Mp 152–154 °C; $[\alpha]_D^{20}$: +117 (*c* 1.0, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.33$ (d, $J = 9.2$ Hz, 1H), 8.18–7.97 (m, 7H), 7.83 (d, $J = 7.6$, 1H), 7.40–7.28 (m, 8H), 7.23–7.10 (m, 12H), 4.04–3.94 (m, 1H), 3.86–3.70 (m, 2H), 3.37 (t, $J = 7.2$, 2H), 3.27–3.21 (m, 1H), 2.92–2.82 (m, 2H), 2.25–2.19 (m, 2H), 2.18–2.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.2$, 135.5, 135.3, 135.1, 134.9, 134.5, 134.4, 132.5, 130.4, 130.0, 128.8, 128.3, 128.1, 127.9, 127.6, 126.5, 126.3, 125.6, 124.7, 124.0, 123.7, 122.6, 47.6, 47.0, 38.0, 36.3, 32.8, 31.8, 25.5; ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = -11.57$, -11.63; HR-MS (ESI): $m/z = 710.2743$, calcd. for $C_{48}H_{42}NOP_2^+$ ($[M+H]^+$): 710.2736.

[14] Purchased from Shenzhen Nanotech Port Co. Ltd. Multiwall carbon nanotubes prepared by the chemical vapor deposition method, 3–5 walls, <10 nm diameter, >95% purity, <5% amorphous, <0.2% ash, 5–15 μm length.