Communication

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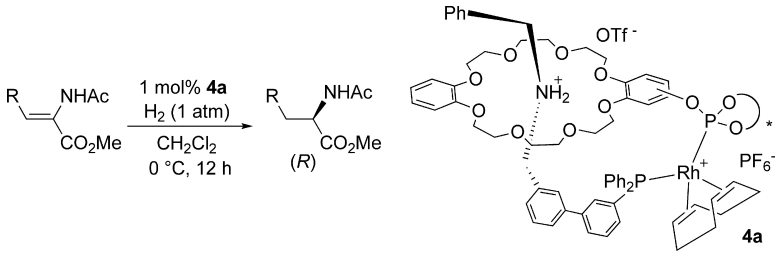

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Design and Preparation of a Chiral Ligand Based on a Pseudorotaxane Skeleton: Application to Rhodium-Catalyzed Enantioselective Hydrogenation of Enamides

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Supramolecular chemistry is one of the most rapidly growing areas of chemistry and greatly contributes to the development of numerous new innovative concepts in nanotechnology and molecular machines.[1] In this area, interlocked molecules such as catenanes, rotaxanes, and pseudorotaxanes have currently attracted a great deal of interest because of not only their peculiar structures but also their unique properties that can be applied to molecular shuttles, molecular wires, and drug delivery systems.[2] Especially, the combination of secondary ammonium salts and crown ethers has been extensively studied in rotaxane and pseudorotaxane synthesis because of their structural diversity and the high stability of crown ether/ammonium salt complexes.[3−5] The rotaxane and pseudorotaxane molecules can provide unique chemical fields based on noncovalent bonding between crown ethers and ammonium salts, but much less attention has so far been paid to the use of such chemical fields for synthetic reactions.[6]

On the other hand, supramolecular approach to prepare chelating bidentate ligands for homogeneous catalytic reactions such as hydrogenation and hydroformylation has recently appeared where attractive ligand−ligand interactions through noncovalent bonding play a critical role to generate libraries of defined chelate-ligand catalysts by simply mixing two different monodentate ligands.[7−12] These interesting reports, together with the potential chemical utility of interlocked supramolecular compounds mentioned above, prompted us to envisage the use of pseudorotaxane molecule for constructing a chiral environment where a key interaction in the molecules is a noncovalent hydrogen bonding (Figure 1). In this communication, we describe a preliminary result of design and preparation of a novel chelating bidentate chiral ligand based on a pseudorotaxane skeleton and its application to rhodium-catalyzed enantioselective hydrogenation of enamides.

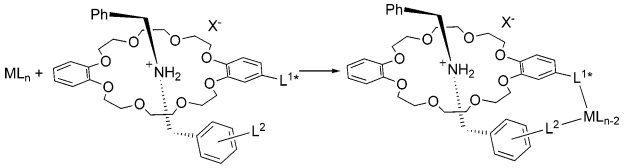
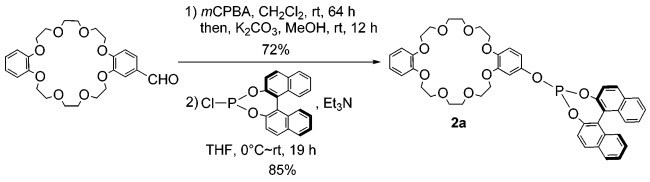


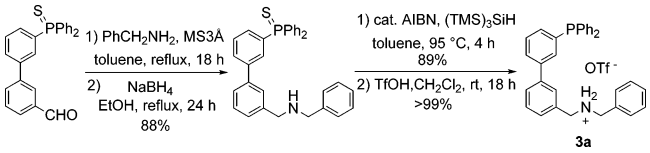
Figure 1. Design of a chiral ligand based on a pseudorotaxane skeleton.

We have designed to prepare a pseudorotaxane molecule (**1a**) by the interaction between a crown ether (**2a**) and a secondary ammonium salt (**3a**) as shown in Schemes 1 and 2 because the combination of crown ethers and secondary ammonium salts seems to be the most reliable for the formation of pseudorotaxane molecules.[2−5] As a wheel moiety, a crown ether bearing an optically active 1,1′-binaphthalen-2,2′-ylphosphite group (**2a**) was prepared from the corresponding crown ether[13] in a good yield.[14] On the other hand, as an axle moiety, an ammonium salt bearing a diphenylphosphino group of the benzene ring (**3a**) was prepared from the corresponding aldehyde[15] in a good yield.[14]

Scheme 1

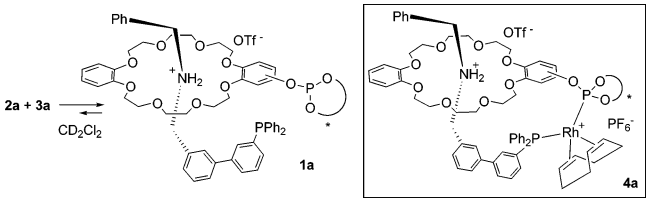


Scheme 2



The formation of **1a** was observed when an equal amount of wheel and axle moieties (**2a** and **3a**) was mixed in CD_2Cl_2 at 25 °C (Scheme 3). It was formed as a mixture of two diastereoisomers due to the planar chirality[16] of the pseudorotaxane skeleton. The structure of **1a** was determined by ^{1}H and ^{31}P NMR and FAB-MS (1236 [M−OTf]) spectra.[17] Detailed analysis of spectroscopic data indicates that **1a** exists in equilibrium with **2a** and **3a** under the present reaction conditions.[14] The addition of a cationic rhodium complex $[Rh(cod)_2]PF_6$ to the solution of this mixture in CD_2Cl_2 led to the quantitative formation of a new rhodium complex bearing a pseudorotaxane skeleton (**4a**) (Scheme 3). Here, the formation of only one diastereoisomer of **4a** was detected by ^{31}P NMR (δ 28.2 (dd, J_{Rh-P} = 143 Hz, J_{P-P} = 37 Hz, *P*Ph$_2$) and 121.7 (dd, J_{Rh-P} = 276 Hz, J_{P-P} = 37 Hz, *P*O$_3$)). Although the stereochemistry of the pseudorotaxane skeleton has not yet been determined, ^{1}H NMR and FAB-MS (1447 [M−OTf−PF_6]) spectra support the formation of the rhodium complex bearing the pseudorotaxane skeleton.[16] This result suggests that diastereoselective formation of the pseudorotaxane ligand is achieved through a reversible process in the formation of **4a** from **1a** and $[Rh(cod)_2]PF_6$. Thus, it is considered that the more stable rhodium complex was diastereoselectively formed from an equilibrium mixture as shown in Scheme 3.

Scheme 3



In order to obtain some information on the ability of the molecule **1a** as a chiral ligand, rhodium-catalyzed enantioselective hydrogenation[18] of methyl (*Z*)-α-acetamidocinnamate (**5a**) was investigated in CH_2Cl_2 at room temperature under 1 atm of H_2 by using

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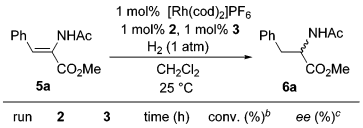
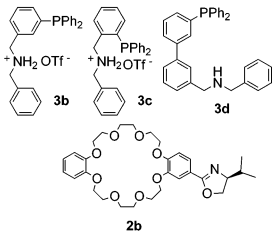
Table 1. Rhodium-Catalyzed Enantioselective Hydrogenation of Methyl (*Z*)-α-Acetamidocinnamate (**5a**) under 1 atm of H_2 by Using Pseudorotaxane Molecules (**1**), Prepared in situ from **2** and **3**, as Chiral Ligands[a]

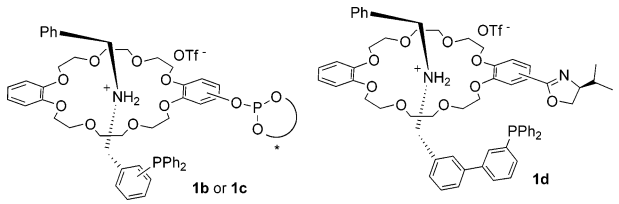




run	2	3	time (h)	conv. (%)[b]	*ee* (%)[c]
1	**2a**	**3a**	12	>99	77 (*R*)
2	**2a**	**3b**	16	>99	14 (*S*)
3	**2a**	**3c**	16	9	–
4	**2b**	**3a**	68	>99	15 (*R*)
5	**2a**	**3d**	48	6	–

[a] All reactions of **5a** (0.50 mmol) in CH_2Cl_2 (3 mL) under 1 atm of H_2 in the presence of a rhodium complex, generated in situ from $[Rh(cod)_2]PF_6$ (0.005 mmol), **2** (0.005 mmol), and **3** (0.005 mmol), at 25 °C. [b] Determined by ^1H NMR. [c] Determined by HPLC.

Scheme 4



some pseudorotaxanes prepared from a variety of wheel and axle moieties (**2** and **3**). Typical results are shown in Table 1. A high enantioselectivity was achieved only by the combination of **2a** and **3a**, and the use of other axles (**3b** and **3c**) in place of **3a** did not work successfully (Table 1, runs 1−3). On the other hand, when a crown ether bearing an optically active oxazoline moiety **2b** was employed in place of **2a**, hydrogenation proceeded, but with only a low enantioselectivity (Table 1, run 4). In these cases, pseudorotaxane molecules (**1b**−**d**) were formed from the corresponding **2** and **3** (Scheme 4), but no formation of new rhodium complexes was detected by the addition of cationic rhodium complex $[Rh(cod)_2]PF_6$ to the solution of **1b**−**d**. In the former cases, the distance between phosphine and phosphite moieties is too far to be coordinated to the rhodium atom. In the latter case, the coordination ability of the oxazoline moiety may be too weak to be coordinated to the rhodium atom. In addition, when secondary amine **3d** was used in place of its ammonium salt **3a**, the reaction hardly proceeded (Table 1, run 5).

Typical results of enantioselective hydrogenation of other (*Z*)-enamides (**5**) by using **1a** as a chiral ligand under the optimal reaction conditions are shown in Table 2.[19] In addition to the trisubstituted (*Z*)-α-acetamidocinnamates (**5**) (Table 2, runs 1−9), hydrogenation of methyl 2-acetamidoacrylate (**5j**) proceeded smoothly under the same reaction conditions with a high enantioselectivity (Table 2, run 10). Separately, when hydrogenation of **5a** was investigated by using only the crown ether **2a** as a chiral ligand, it proceeded sluggishly with a lower enantioselectivity (Table 2, run 1). In addition, the hydrogenation did not proceed smoothly even when 2 equiv of **2a** to the rhodium complex was used as a chiral ligand. These results indicate that only the rhodium complex **4a** coordinated to phosphine and phosphite moieties of the pseudorotaxane skeleton works as a good catalyst for enantioselective hydrogenation of enamides. To the best of our knowledge, this is the first successful example of the use of the pseudorotaxane molecule as a chiral ligand for homogeneous transition-metal-catalyzed asymmetric reactions.

Table 2. Rhodium-Catalyzed Enantioselective Hydrogenation of Methyl (*Z*)-α-Acetamidocinnamates (**5**) under 1 atm of H_2 by Using Pseudorotaxane Molecule (**1a**), Prepared in situ from **2a** and **3a**, as a Chiral Ligand[a]

run	R of **5**	conv. (%)[b]	*ee* (%)[c]	run	R of **5**	conv. (%)[b]	*ee* (%)[c]
1	Ph (**5a**)	>99 (34)[d]	90 (71)[d]	6	*m*-ClC_6H_4 (**5f**)	>99	94
2	*p*-MeC_6H_4 (**5b**)	>99	93	7	*o*-ClC_6H_4 (**5g**)	>99	91
3	*p*-$MeOC_6H_4$ (**5c**)	>99	94	8	1-naphthyl (**5h**)	>99	93
4	*p*-$NO_2C_6H_4$ (**5d**)	>99	93	9	2-naphthyl (**5i**)	>99	92
5	*p*-ClC_6H_4 (**5e**)	>99	90	10	H (**5j**)	>99	96

[a] All reactions of **5** (0.50 mmol) in CH_2Cl_2 (7 mL) under 1 atm of H_2 in the presence of a rhodium complex, generated in situ from $[Rh(cod)_2]PF_6$ (0.005 mmol), **2a** (0.005 mmol), and **3a** (0.005 mmol), at 0 °C for 12 h. [b] Determined by ^1H NMR. [c] Determined by HPLC. [d] In the absence of **3a**.

Supporting Information Available: Experimental procedures and spectroscopic data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) When $[Rh(cod)_2]BF_4$ was used as a catalyst in place of $[Rh(cod)_2]PF_6$, similar reactivity and enantioselectivity were observed under the reaction conditions.

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