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Asymmetric hydrogenation of (*E*)-α,β-bis(*N*-acylamino)acrylates catalyzed by a rhodium complex with *trans*-chelating chiral diphosphine ligand

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Abstract

The asymmetric hydrogenation of (*E*)-α,β-bis(*N*-acylamino)acrylates was promoted by a rhodium complex bearing a *trans*-chelating chiral diphosphine ligand (*R*,*R*)-(*S*,*S*)-PrTRAP, providing the corresponding optically active (2*S*,3*R*)-2,3-bis(*N*-acylamino)carboxylates with 79–82% ee. The 2,3-bis(*N*-acylamino)carboxylates isolated were readily hydrolyzed under acid to afford (2*S*,3*R*)-2,3-diaminocarboxylic acids in 95% yield without epimerization.

Optically active α,β-diamino acids are important constituents of antibiotics, such as antrimycin[1] and lavendomycin[2] et al. Although some syntheses of optically active α,β-diamino acids have been reported,[3–5] they have not been accessible by catalytic asymmetric hydrogenation of the corresponding olefinic precursor.

In a preceding paper, we reported that *trans*-chelating chiral diphosphines bearing linear alkyl substituents on the phosphorus atoms, (*S*,*S*)-2,2′-bis[(*R*)-1-(dialkylphosphino)ethyl]-1,1′-biferrocenes, [abbreviated to (*R*,*R*)-(*S*,*S*)-alkylTRAPs][6] are effective for asymmetric hydrogenation of β,β-disubstituted α-acetamidoacrylates catalyzed by rhodium complexes.[7] The optically active alkylTRAP–rhodium complex was also successfully applied for asymmetric hydrogenation of both (*Z*)- and (*E*)-β-oxy-α-acetamidoacrylates, giving optically active β-hydroxy-α-amino acids.[8] Herein, we wish to describe the asymmetric hydrogenation of (*E*)-α,β-bis(*N*-acylamino)acrylates by TRAP–rhodium complex catalysts (Scheme 1), which provides an efficient synthesis of optically active (2*S*,3*R*)-α,β-diamino acids after acid hydrolysis.

Several chiral diphosphine ligands were tested for the rhodium catalyzed asymmetric hydrogenation of methyl (*E*)-2-(*N*-acetylamino)-3-(*N*-benzyloxycarbonylamino)-2-alkenoate **1**, which was stereo-

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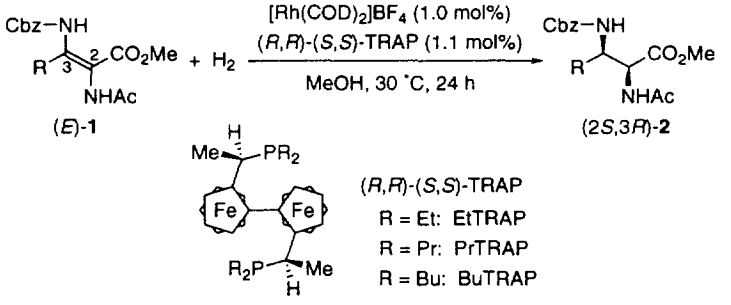


Scheme 1.

Table 1
Asymmetric hydrogenation of **1** catalyzed by TRAP–rhodium complex[a]

entry	R (**1**)	Ligand[b]	product	yield, %[c]	ee, %[d]	confign.
1	Me (**1a**)	EtTRAP	**2a**	94	76	(2*S*,3*R*)
2	Me (**1a**)	PrTRAP	**2a**	93	82	(2*S*,3*R*)
3	Me (**1a**)	BuTRAP	**2a**	99	75	(2*S*,3*R*)
4	Et (**1b**)	PrTRAP	**2b**	100	81	(2*S*,3*R*)[e]
5	Pr (**1c**)	PrTRAP	**2c**	90	80	(2*S*,3*R*)[e]
6	*i*-Bu (**1d**)	PrTRAP	**2d**	99	79	(2*S*,3*R*)[e]

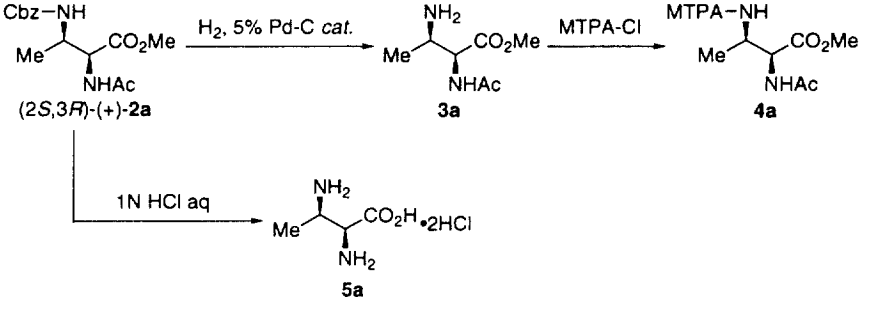
[a] All Reactions were carried out in MeOH (0.5 M) at 30 °C and 1 kg/cm^2 of hydrogen pressure for 24 h. **1**:[Rh(COD)$_2$]BF$_4$:Ligand = 100:1.0:1.1. [b] (*R*,*R*)-(*S*,*S*)-TRAP was used. [c] Isolated yield. [d] Determined by chiral HPLC analysis with SUMICHIRAL OA-4100. [e] Assigned by similarity to **2a** in the order of retention time in the HPLC analysis.

selectively prepared by dehydrative condensation of the corresponding methyl 2-(*N*-acetylamino)-3-ketoalkanoate and benzyl carbamate with sulfuric acid catalyst. The results are summarized in Table 1. Rhodium complexes coordinated with TRAP bearing linear alkyl *P*-substituents provided good catalytic activity and enantioselectivity for the asymmetric hydrogenation of (*E*)-**1a**. PrTRAP was superior to Et- and BuTRAP, giving 82% ee of (2*S*,3*R*)-(+)-**2a** without formation of its diastereomer (entries 1–3). The configuration of **2a** at the α-carbon was the same as those of products obtained from asymmetric hydrogenations of other β,β-disubstituted α-acetamidoacrylates catalyzed by an (*R*,*R*)-(*S*,*S*)-alkylTRAP–rhodium complex, reported previously.[7,8] It is notable that [Rh(COD){(*R*,*R*)-MeDuPHOS}]PF$_6$,[9] which is an effective catalyst for asymmetric hydrogenation of β,β-disubstituted α-acetamidoacrylates,[10,11] did not catalyze the hydrogenation of **1a**. A significant decrease of the enantiomeric excess of the product was observed by use of the substrate bearing the 3-*N*-phenoxycarbonyl group (63% ee, EtTRAP), suggesting that the 3-*N*-substituent of **1** may significantly influence the enantioselectivity of the asymmetric hydrogenation. α,β-Bis(*N*-acylamino)acrylates **1b–d** were also hydrogenated by a PrTRAP–rhodium catalyst, giving the corresponding optically active α,β-diamino acids derivatives **2b–d** with 79–81% ee (entries 4–6).

A typical procedure for the asymmetric hydrogenation of **1** is presented as follows. A mixture of (*R*,*R*)-(*S*,*S*)-PrTRAP (3.6 mg, 5.0 μmol) and [Rh(COD)$_2$]BF$_6$ (2.0 mg, 5.5 μmol) in MeOH (1.0 ml) was stirred for 10 min under an argon atmosphere, and then **1** (0.50 mmol) was added to the solution. Immediately, the reaction vessel was cooled to −78°C, and successively evacuated and filled with hydrogen gas. After stirring at 30°C for 24 h, the solution was condensed under reduced pressure. The residue was passed through a short silica gel column to give **2**.

As shown in Scheme 2, selective deprotection of the benzyloxycarbonyl group of **2a** was accomplished

by hydrogenolysis (100 kg/cm^2) with 5% palladium on an activated carbon catalyst in MeOH to give **3a**. The absolute configuration of (+)-**2a** was assigned as (2*S*,3*R*) by ^{1}H NMR analysis of the MTPA amide **4a**,[12] which was prepared by reaction of **3a** with MTPA chloride. In addition, optically active (2*S*,3*R*)-(+)-**2a** was readily converted into (2*S*,3*R*)-2,3-diaminobutanoic acid dihydrochloride **5a** without epimerization by hydrolysis with 10% hydrochloric acid at 100°C for 6 h in 95% yield {$[\alpha]_D^{25}$=+23.6 (*c* 1.00, H_2O)}.



Scheme 2.

In summary, we succeeded in the first catalytic enantioselective hydrogenation of (*E*)-α,β-bis(*N*-acylamino)acrylates **1** using cationic (*R*,*R*)-(*S*,*S*)-PrTRAP–rhodium complex, which gave 79–82% ee of *threo*-α,β-diamino acid derivatives (2*S*,3*R*)-**2** in high yield. The catalytic asymmetric hydrogenation will provide an efficient synthetic route of various optically active α,β-diamino acids.

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