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Asymmetric Catalytic Hydrogenation Using Rhodium Diphosphinites Derived From D-glucose and D-mannitol

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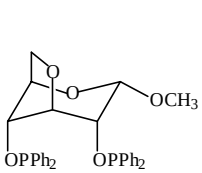
Abstract: Three diphosphinites were synthesized for preparing rhodium-diphosphinite complexes. The complexes were used for asymmetric catalytic hydrogenation of amino acid precursor α–acetamidocinnamic acid and its methyl ester. With all complexes, D-amino acid is the most abundant product.

Keywords: Asymmetric catalysis hydrogenation, rhodium diphosphinites, α–acetamidocinnic acid.

During past three decades, many reports have appeared describing the use of chiral ligands – transition metal complexes for asymmetric hydrogenation reaction[1]. Among the chiral ligands, chiral bis (phospines), 1,2-bis (aminophospines) and bis (phosphinites)[2] are well known for rhodium(I) complexes. Due to their easy accessibility from practical viewpoint, diphosphinite ligands have been reported till recently[3]. Chan *et al*[3a,c] and Zhang *et al*[3b] observe that increasing ligand rigidity is the key for the development of highly enantioselective reactions.

As chiral block, carbohydrate and derivatives have several advantages: configuration of every chiral carbon is determined; the materials are high optical purity and readily available; multi-chiral carbon and multifunctional group make it possible to derive various structures. D-glucose is a very cheap carbohydrate. When it was anhydrated from 3,6-sites, rigid cycle was constructed. Analogously, 1,3:4,6-dibenzylidene-D-mannitol has stabilized C_3, C_4 conformation.



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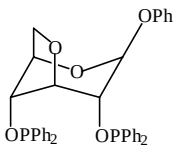

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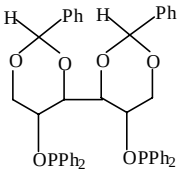

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In this paper, we report three new chiral diphosphinites derived from D-glucose (**ligand 1** and **2**) and D-mannitol (**ligand 3**) and their application in asymmetric hydrogenation. Diols were prepared by standard method [4] and then converted to the corresponding diphenylphosphinites by treatment with Ph_2PCl/pyriding at room temperature for 12hrs. As-synthesized diphenylphosphinites were purified with THF (**ligand 1** and **2**) or chloroform-petroleum ether (mp. 30-60°C) (**ligand 3**) under nitrogen

atmosphere and analyzed with elemental analysis and ^{31}P NMR spectrum[5]. Asymmetric hydrogenation of amino acid precursor α-acetamidocinnamic acid **(1a)** and its methyl ester **(2a)** was carried out with the cationic complex [(PO-OP)Rh(COD)]BF_4 prepared *in situ* by the diphosphinite, $[Rh(COD)Cl]_2$, KBF_4 in benzene for refluxing 12hrs, and with 1 atm of hydrogen at 25°C .

The results of the asymmetric hydrogenation of the substrates as summarized in **Table 1** show that D-amino acid derivatives are the most abundant products with all diphosphinites-rhodium complexes. Diphosphinite ligands **1** and **2** which have conformational rigidity result in high enantiomeric excess product. Diphosphinite ligand **3** leads to lower optical yield whether the substrate is α-acetamidocinnamic acid or its methyl ester. This may be ascribed to the flexibility of the chelate ring of the latter. Moreover, after longer reaction times, it is found that a cationic rhodium catalyst and neutral one coexisted in the reaction system where catalysts were synthesized *in situ* from ligands, $[Rh(COD)Cl]_2$ and KBF_4. These made the activity of the catalysts lower than equimolar cationic one[7].

Table 1 Asymmetric Hydrogenation of α-Acetamidocinnamic Acid or its Methyl Ester[a]

Substrate	Ligand	T (°C)	Yield (%)[b]	e.e (%)[c,d]	t(hr)
1a	1	25	89.5	40.8	6.0
2a	1	25	99.9	31.5	5.5
1a	2	25	93.4	57.1	7.5
2a	2	25	96.6	46.2	7.5
1a	3	25	85.6	25.6	5.0
2a	3	25	92.5	24.6	4.5

[a] In the presence of 1 mol% Rh chelate under 1 atm hydrogen at 25°C. [b] isolated yield. [c] Measured by standard method[2a]. [d] the R-configuration was obtained for all products comparing with the standard compounds[6].

On the other hand, anomeric effect of ligands exerts greatly influence on the stereo selectivity of the product. Rh-1 complex gives lower enantiomeric excess product than Rh-2 complex since the group OCH_3 lies in α-arrangement and OPh has the β-arrangement. In conclusion, rhodium-diphosphinite complexes having rigid eight number ring give better enanatiomeric excess of hydrogenation product than that of flexible nine number ring complex.

References and notes

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5. ^{31}PNMR of the ligands (ppm, $CDCl_3$, H_3PO_4 as external standard): 1: 118.2, 113.2. 2: 118.1, 115.0. 3: 108.9. Elemental Analysis Calcd for 1: C,68.38%; H,5.55% Found: C,68.14%; H,5.38%. Calcd for 2: C,77.37%; H,5.77% Found: C,77.48%; H,5.59%. Calcd for 3: C,72.71%; H,5.55% Found: C,72.53%; H,5.74%.
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