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Enantioselective Heck-type hydroarylation of norbornene with phenyl iodide catalyzed by palladium/quinolinyl-oxazolines

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Abstract

Enantioselective Heck-type hydroarylation of norbornene with phenyl iodide catalyzed by the palladium complex of quinolinyl-oxazolines is described. Using DMSO as the solvent and $HCOOH/Et_3N$ as the hydride source, *exo*-2-phenybicyclo[2.2.1]heptane is produced in reasonable yields and up to 74% ee. © 2000 Elsevier Science Ltd. All rights reserved.

Palladium-catalyzed arylation and alkenylation of olefins, known as the Heck reaction, is one of the most efficient catalytic methods for carbon–carbon bond formation in organic synthesis.[1] During the last decade, asymmetric Heck reactions have attracted great attention, and a number of highly enantioselective chiral ligands have been developed to enhance chiral discrimination in these reactions.[2] However, asymmetric Heck-type hydroarylations of olefins, addition of aryl halides or triflates to carbon–carbon double bonds, have not been well studied. In 1991, Brunner reported an asymmetric hydroarylation of norbornene and norbornadiene with aryl iodides using chiral bisphosphine ligands, and around 40% ee was achieved.[3] Later on, Achiwa reached around 70% ee in the asymmetric hydroarylation of norbornene with phenyl triflate by using chiral P–N ligands.[4,5] We recently designed and synthesized quinolinyl-oxazolines **1** as ligands in copper(I)-catalyzed cyclopropanation of styrene with diazoacetates.[6] Herein, we wish to describe our investigations on ligands **1** that provide the first examples of efficient bisnitrogen ligands in Heck-type hydroarylation. The enantioselectivities (up to 74% ee) produced by ligands **1** in the reaction of norbornene with phenyl iodide are comparable to those given with Achiwa's P–N ligands.[4]

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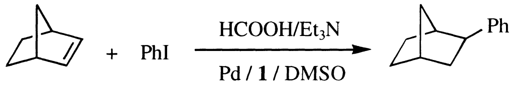

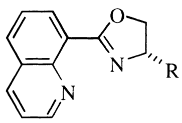

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Ligands **1** were found to be effective for chiral discrimination in the palladium-catalyzed hydroarylation of norbornene with phenyl iodide. The reactions were carried out in DMSO, catalysts were prepared in situ, and HCOOH/NR$_3$ was used as the hydride source. *exo*-2-Phenylbicyclo[2.2.1]heptane was produced exclusively in hydroarylation of norbornene with phenyl iodide using ligands **1**. The results are summarized in Table 1. In initial attempts, reactions were run at 65°C as others commonly were in the literature, and 47% ee was obtained when 5 mol% of palladium acetate was used. As the temperature dropped to 25°C, the enantiomeric excess increased to 67% although a longer time was needed to complete the reaction. This was different from the results in the hydroarylation reaction with bisphosphine ligands where the enantioselectivity was shown to be temperature independent.[3]

Table 1
Asymmetric hydroarylation of norbornene with PhI catalyzed by palladium complex of ligand **1b**[a]

Pd (mol %)	Base	Temp (°C)	Time (h)	Yield (%) [b]	ee (%) [c]
Pd(OAc)$_2$ (1)	Et$_3$N	65	4	58	20
Pd(OAc)$_2$ (5)	Et$_3$N	65	4	80	47
Pd(OAc)$_2$ (2)	Et$_3$N	40	16	41	45
Pd(OAc)$_2$ (5)	Et$_3$N	40	16	57	56
Pd(OAc)$_2$ (1)	Et$_3$N	25	84	43	44
Pd(OAc) (5)	Et$_3$N	25	66	52	67
Pd(dba)$_2$ (5)	Et$_3$N	25	58	60	73
Pd(dba)$_2$ (5)	*i*-Pr$_2$NEt	25	96	31	68
Pd(dba)$_2$ (5)	Proton Sponge	25	59	65	72

[a] Pd/Ligand/Norbornene/PhI/HCOOH/Base = 0.05/0.1/1/3/3/3.5. Solvent is DMSO.

[b] Isolated yield. [c] Determined by HPLC (Chiralcel OJ column, *n*-hexane/2-propanol = 9/1, 1 ml/min).

It was observed that using less catalyst reduced both the yield and % ee of the hydroarylation product. Pd(dba)$_2$[7] was also used as a precatalyst in hydroarylation of norbornene with phenyl iodide, and higher enantioselectivities were obtained than with Pd(OAc)$_2$. As a comparison, other bases have been tested. Proton sponge[8] was found to be the same effective base as triethylamine, whereas diisopropylethylamine gave slower reaction and low chemical yield.

Table 2 shows the effect of ligand in asymmetric hydroarylation of norbornene with PhI. Ligands **1b** and **1c**, with benzyl and isopropyl at C4 in the oxazolin ring, had the highest enantioselectivities. (4*S*)-2-(2-Pyridinyl)-4-benzyl-2,3-dihydrooxazole, the ligand developed by Brunner,[9] was also investigated but it provided only 29% ee and 44% yield of the product.

Table 2
Effect of the ligand in Pd-catalyzed asymmetric hydroarylation of norbornene with PhI[a]

Ligand	Time (h)	Yield (%) [b]	ee (%) [c]
1a (R=Me)	14	42	51
1b (R = Bn)	58	60	73
1c (R = *i*-Pr)	43	54	74 [d]
1d (R = Ph)	14	57	28
1e (R = *t*-Bu)	14	47	18

[a] Pd/Ligand/Norbornene/PhI/HCOOH/Et_3N = 0.05/0.1/1/3/3/3.5, DMSO, 25 °C.
[b] Isolated yield. [c] Determined by HPLC (Chiralcel OJ column, *n*-hexane/2-propanol: 9/1, 1 ml/min). [d] $[\alpha]_D^{20}$ -30.9 (c 1.0, chloroform).

In conclusion, we have demonstrated that chiral bisnitrogen ligands quinolinyl-oxazolines are the ligands of choice in asymmetric Heck-type hydroarylations. Further improvements of the ligands are under investigation.

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