

## Diphenylphosphinoxazoline Ligands with a Chiral Binaphthyl Backbone for Pd-Catalyzed Allylic Alkylation

Yoshitane Imai, Wanbin Zhang, Toshiyuki Kida, Yohji Nakatsuji, and Isao Ikeda\*

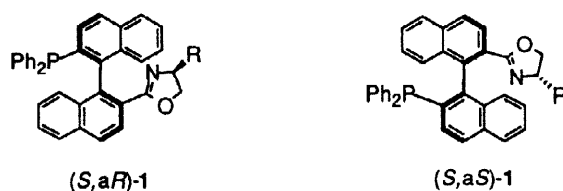
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

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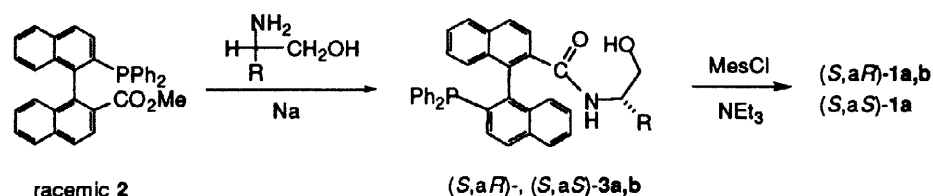
**Abstract:** Novel diphenylphosphinoxazoline ligands with a chiral binaphthyl backbone were prepared. It was interestingly found that the two diastereomeric ligands afforded two enantiomeric products, respectively, with excellent catalytic activities and enantioselectivities for the palladium-catalyzed allylic alkylation, regardless of the identical (*S*)-oxazoline ring existing in both ligands. This is the first example using an (*S*)-oxazoline ligand to afford an (*R*)-product for this reaction. © 1998 Elsevier Science Ltd. All rights reserved.

**Keywords:** asymmetric reaction; catalysis; oxazolines; biaryls.

Chiral oxazoline ligands derived from readily available aminoacids have found widespread use in metal-catalyzed asymmetric reactions and extensive efforts have been devoted to the preparation of their efficient structural derivatives.<sup>1</sup> It is well known that most of the earlier oxazoline ligands possess only one kind of chirality on oxazoline rings which render the ligands effective for a number of reactions.<sup>1</sup> Recently, some novel oxazoline ligands with multi-chiralities have been developed by several groups including ours independently.<sup>2–4</sup> Besides the chirality of the oxazoline ring, these ligands also possess the chirality of a backbone such as 1,3-dioxolane,<sup>2</sup> ferrocene<sup>3</sup> or biaryl.<sup>4</sup> Owing to the introduction of the chiral backbone, the asymmetric induction of these ligands can be effectively controlled by the combination of the chiralities of the oxazoline ring and the backbone in the ligands. Here we wish to report a new kind of diastereomeric oxazoline ligands **1** with a chiral binaphthyl backbone, which is, to the best of our knowledge, the first example of chiral P,N-chelating binaphthyl ligands. It is expected that by the introduction of a chiral binaphthyl backbone in these diphenylphosphinoxazoline ligands some interesting and effective asymmetric inductions may be found.



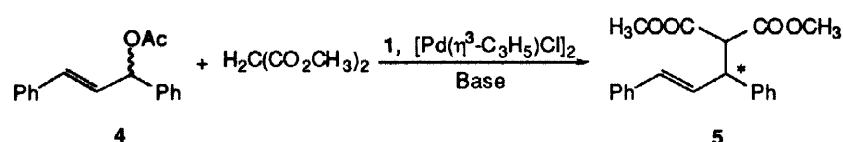
Ligands **1** can be synthesized from racemic diphenylphosphinocarboxylic esters **2** which were prepared from racemic binaphthol according to a reported method.<sup>5</sup> After the reaction of racemic **2** with (*S*)-aminoalcohol, the resulting two diastereomeric amides (*S*,*aR*)-**3** and (*S*,*aS*)-**3** were separated with silica gel column chromatography in 34–39% yields. Then, the amides (*S*,*aR*)-**3** and (*S*,*aS*)-**3** were treated with methanesulfonylchloride in the presence of triethylamine to afford ligands (*S*,*aR*)-**1** and (*S*,*aS*)-**1**, respectively, in 68–72% yields.<sup>6</sup> The absolute configurations of the two diastereomers of **1** were determined in comparison with those prepared from chiral 1,1'-bi-2-naphthol.



a: R=*i*-Pr, b: R=*t*-Bu

### Scheme 1

Palladium-catalyzed asymmetric allylic substitution, especially the alkylation of 1,3-diphenyl-2-propenyl acetate (**4**) with malonate (Scheme 2), is a significant carbon-carbon bond forming reaction in organic synthesis.<sup>7</sup> During the last few years, many kinds of chiral bidentate ligands have been developed for this model reaction. Among them, the oxazoline-containing ligands, particularly the oxazoline-containing P,N-chelating ligands, have been found to be efficient inducers of enantioselectivity.<sup>1,7</sup> With these two diastereomeric P,N-chelating ligands in hand, we first carried out this model reaction as a preliminary experiment (Scheme 2, Table 1).



### Scheme 2

**Table 1.** Palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate<sup>a</sup>

Entry	Ligand	Base	T (°C)	Time (h)	Yield (%)	ee (%) <sup>d</sup>	Enantiomer <sup>e</sup>
1	(S,aR)-1a	BSA-KOAc <sup>c</sup>	25	5	91	90	(R)-(+)
2	(S,aR)-1a	NaH	25	5	90	79	(R)-(+)
3 <sup>b</sup>	(S,aR)-1a	BSA-KOAc <sup>c</sup>	25	5	89	88	(R)-(+)
4	(S,aS)-1a	BSA-KOAc <sup>c</sup>	25	4	93	85	(S)-(-)
5	(S,aS)-1a	NaH	25	5	60	50	(S)-(-)
6	(S,aR)-1b	BSA-KOAc <sup>c</sup>	25	7	91	93	(R)-(+)
7	(S,aR)-1b	BSA-KOAc <sup>c</sup>	0	20	90	96	(R)-(+)

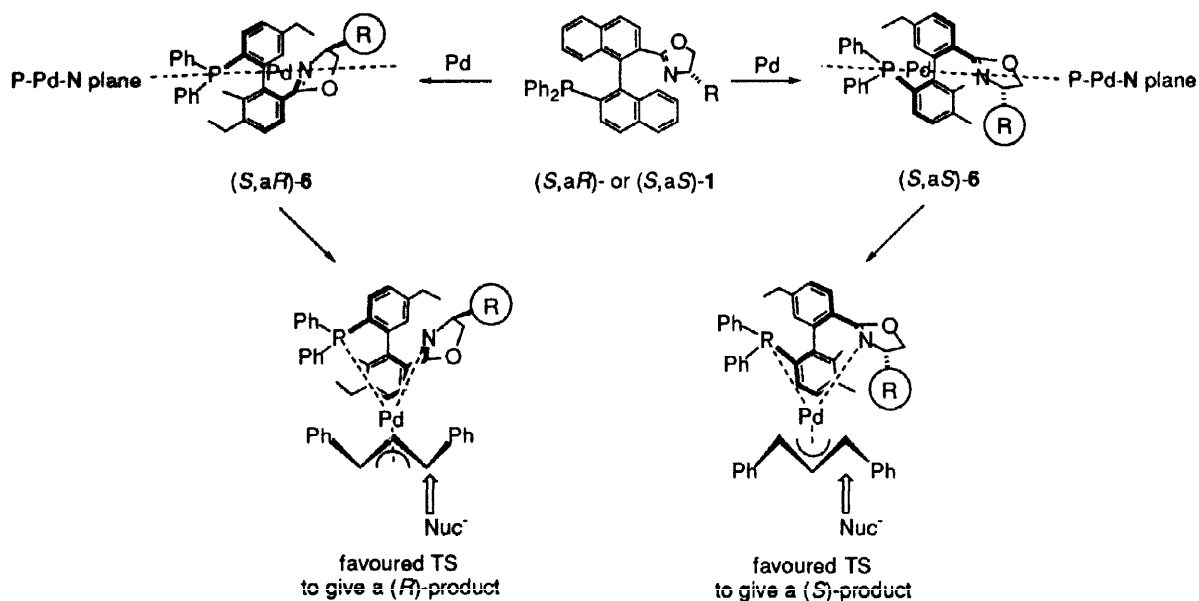
a) Reactions were conducted with **4** (1 mmol), nucleophile (3 mmol), and base (3 mmol) in 3 mL of THF under argon in the presence of the catalyst which was prepared by treating **1** (30 μmol) with [Pd(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)Cl]<sub>2</sub> (12.5 μmol) in 1 mL of THF for 1 h before use. b) CH<sub>2</sub>Cl<sub>2</sub> was used as the solvent. c) Where KOAc (20 μmol) was added. d) The enantiomeric excess was determined by <sup>1</sup>H NMR in the presence of shift reagent Eu(tfc)<sub>3</sub>. e) The absolute stereochemistry of the product was determined by comparison of the optical rotation with literature values.

It was surprising that the two diastereomers (S,aR)-**1** and (aS,S)-**1** afforded two enantiomeric products (R)-**5** and (S)-**5**, respectively, with excellent catalytic activities and enantioselectivities, regardless of the identical (S)-oxazoline ring existing in both ligands. From literature it was known that all of the (S)-oxazoline ligands derived from (S)-aminoacids so far afforded an (S)-product<sup>1,7</sup> and, therefore, this is the first

example using an (*S*)-oxazoline ligand to obtain an (*R*)-product for this reaction. In addition, although several oxazoline ligands with multi-chiralities have been reported for other reactions, the same enantiomeric product was obtained with both diastereomeric ligands when they have the same chirality on the oxazoline ring in all of these cases.<sup>24,8</sup> Thus, the present result is the first example where the chiral backbone other than the chiral oxazoline group of the ligands played a dominant role in the determination of the chiral sense of the enantioselection.

From Table 1 it was also known that the substituent on the oxazoline ring affected the ee results and a bulkier group gave a better ee. Thus, as the substituent was changed from isopropyl to *tert*-butyl, the ee was changed from 90% to 93% at 25 °C. Like the cases of most other chiral ligands,<sup>7c</sup> the base used affected the ee largely and the best result was obtained with *N,O*-bis(trimethylsilyl)acetamide (BSA) as a base in the present case. Reaction temperatures had some effect on enantioselectivities also and up to 96% ee was attained with (*S,aR*)-**1b** as a ligand at 0 °C.

In order to explain the attainment of different enantiomers by the two diastereomeric ligands, respectively, we examined the CPK models of the palladium complexes of the ligands, (*S,aR*)-**6** and (*S,aS*)-**6**. It was found that in both cases the P-Pd-N coordination plane and the C=N-C plane of the oxazoline ring formed a large angle which placed the substituent on the oxazoline ring of (*S,aR*)-**6** above the coordination plane and the substituent of (*S,aS*)-**6** below the coordination plane (Figure 1). Therefore, the different chiral senses of the enantioselection observed by the two diastereomeric ligands can be explained in accordance with the model proposed by Helmchen et al. (Figure 1).<sup>9</sup>



**Figure 1.** Model explaining the observed selectivities

In conclusion, a new kind of chiral oxazoline ligands with a chiral binaphthyl backbone **1** has been developed and some interesting and effective asymmetric inductions have been found for the palladium-catalyzed asymmetric allylic substitution with this kind of diastereomeric ligands. Further studies on the application of this kind of ligands for other metal-catalyzed asymmetric reactions are underway.

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- 6 (*S*,*aR*)-**1a**:  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.13-6.95 (m, 22H), 3.71 (dd, 1H,  $J$ =8.0, 9.6 Hz), 3.58 (m, 1H), 3.33 (t, 1H,  $J$ =8.0 Hz), 0.58 (d, 3H,  $J$ =6.4 Hz), 0.52 (d, 3H,  $J$ =6.8 Hz).  $[\alpha]_{\text{D}}^{25} = +7.0$  ( $c$  = 0.50 in  $\text{CH}_2\text{Cl}_2$ ). FAB-MS :  $m/z$  : 550 ( $\text{M}^+$ ). IR (KBr) 1636, 1734, 2960  $\text{cm}^{-1}$ . (*S*,*aS*)-**1a**:  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.17-6.97 (m, 22H), 3.79 (dd, 1H,  $J$ =7.0, 9.4 Hz), 3.62 (m, 1H), 3.44 (t, 1H,  $J$ =7.0 Hz), 0.53 (d, 3H,  $J$ =7.2 Hz), 0.45 (d, 3H,  $J$ =6.8 Hz).  $[\alpha]_{\text{D}}^{25} = -2.0$  ( $c$  = 0.50 in  $\text{CH}_2\text{Cl}_2$ ). FAB-MS :  $m/z$  : 550 ( $\text{M}^+$ ). IR (KBr) 1375, 1720, 2960  $\text{cm}^{-1}$ . (*S*,*aR*)-**1b**:  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.12-6.92 (m, 22H), 3.67 (dd, 1H,  $J$ =8.0, 10.0 Hz), 3.57 (dd, 1H,  $J$ =8.0, 10.0 Hz), 3.43 (t, 1H,  $J$ =8.0 Hz), 0.53 (s, 9H).  $[\alpha]_{\text{D}}^{25} = +4.8$  ( $c$  = 0.50 in  $\text{CH}_2\text{Cl}_2$ ). FAB-MS :  $m/z$  : 564 ( $\text{M}^+$ ). IR (KBr) 1712, 2960  $\text{cm}^{-1}$ .
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- 8 The only exception is that reported by Hayashi's group in which two diastereomeric ligands with the same oxazoline ring afforded two enantiomeric products, respectively: one product with up to 87% ee, while the other with only 3% ee.<sup>4c</sup>
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