Pergamon

Tetrahedron Letters, Vol. 38, No. 15, pp. 2681-2684, 1997

0040-4039/97 $17.00 + 0.00

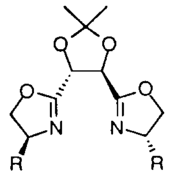
PII: S0040-4039(97)00428-0

Novel Axial Chiral Catalyst Derived from Biphenyl Ligand Bearing only Two *ortho*-Substituents[1]

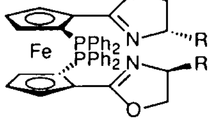
Yoshitane Imai, Wanbin Zhang, Toshiyuki Kida, Yohji Nakatsuji, Isao Ikeda*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

Abstract: The two diastereomers of novel C_2-symmetric bisoxazoline ligand bearing only two *ortho*-substituents **4** exist in equilibrium in solution. However, when the ligand was coordinated with Cu(I), only one of the two possible diastereomeric complexes, **5**-(*S*,*S*,*S*), was formed. With this complex as a chiral catalyst, up to 92% ee was attained for the asymmetric cyclopropanation of styrene with diazoacetate.

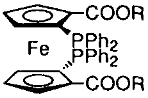
The chiral oxazolines derived from readily available aminoacids have found widespread use as chiral ligands in metal-catalyzed asymmetric reactions.[2] Our recent attention has been focused on the synthesis and application of novel bisoxazoline ligands with multi-chiralities such as **1**[3] and **2**[4], the former possesses the chirality of the 1,3-dioxolane group derived from tartaric acid and the latter possesses the planar chirality of ferrocene besides the chirality of oxazoline groups. Ligand **2** can be further modified to new ligand **3** which is the first C_2-symmetric ligand possessing only the planar chirality of ferrocene.[5] All of these ligands show excellent enantioselectivities in metal-catalyzed asymmetric reactions.[3-5] We here wish to report another novel C_2-symmetric chiral bisoxazoline ligand **4** derived from chiral 2-aminoalcohol and achiral 2,2'-biphenyldicarboxylic acid. When the ligand was coordinated with a metal such as copper(I), a stable axial chirality of biaryl was induced and only one of the two possible diastereomeric complexes was formed. With this complex as a chiral catalyst, excellent enantioselectivity was attained for the asymmetric cyclopropanation of styrene with diazoacetate.[6]



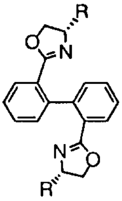
1



2

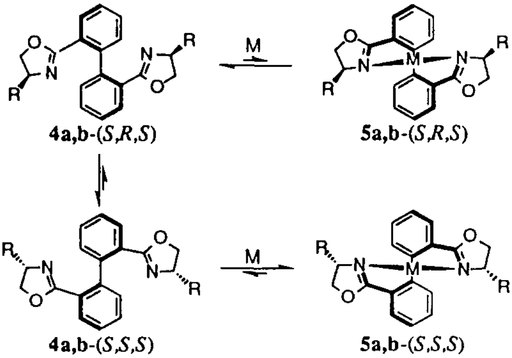


3



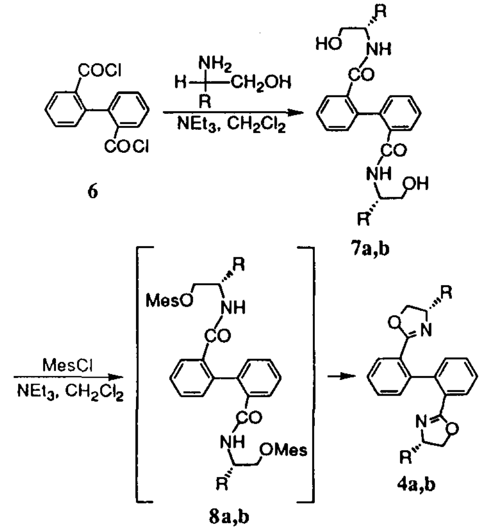
4

It has been pointed out that enantiomerically stable biphenyls require at least three *ortho*-substituents to avoid the racemization due to the rotation around the internal bond of the biaryls.[7] Since compound **4** has only two *ortho*-substituents, the two diastereomers, **4**-(*S*,*S*,*S*) and **4**-(*S*,*R*,*S*), should be present in equilibrium in solution due to the rotation, and one of the diastereomers, **4**-(*S*,*S*,*S*), should dominate over the other, **4**-(*S*,*R*,*S*), owing to the difference in the steric repulsion between the substituents on the oxazoline rings of the two diastereomers (Scheme 1, proposed according to an examination of CPK models). Upon coordinating with a metal, the spacial distance between the two coordination sites decreases, causing amplified difference in the steric repulsion between the substituents on the oxazoline rings of the two diastereomeric complexes, **5**-(*S*,*S*,*S*) and **5**-(*S*,*R*,*S*), and an additional difference in the steric repulsion between the substituent on the oxazoline ring and other coordinated moieties on the metal of the two diastereomeric complexes. Therefore, one of the diastereomeric complexes, **5**-(*S*,*S*,*S*) proposed, should form in preference to the other, **5**-(*S*,*R*,*S*), and the ratio of the two diastereomers of **5** should be larger than that of **4**. If the ratio is large enough, it may be possible to utilize the complex as an axial catalyst in asymmetric reaction.[8]



(a: R=*i*-Pr, b: R=*t*-Bu; M=Cu(I))

Scheme 1



Scheme 2 (a: R=*i*-Pr, b: R=*t*-Bu)

Compounds **4a,b** were readily synthesized from 2,2'-biphenyldicarboxylic acid and chiral aminoalcohol *via* the corresponding β-hydroxylamides **7a,b** and mesylates **8a,b** successively as intermediates (Scheme 2). Thus, 2,2'-biphenyldicarboxylic acid dichloride **6** was stirred with (*S*)-valinol and triethylamine in dichloromethane at 25 °C for 3 h to give **7a** in 77% yield. Then, a mixture of amide **7a**, methanesulfonyl chloride and triethylamine in dichloromethane was stirred at 25 °C for 4 h to give bisoxazoline compound **4a** in 83% yield as a colorless viscous liquid, without the isolation of the dimesylate intermediate **8a**.[9] In the same way, the oxazoline **4b** was prepared in about 60% overall yield from 2,2'-biphenyldicarboxylic acid and (*S*)-*tert*-leucinol.[10]

As expected, the two diastereomers of ligand **4** were observed in solution by ^{1}H NMR, existing in equilibrium due to the rotation around the internal bond in the biphenyl unit. In chloroform-*d* at 26 °C, the ratio of the two diastereomers of **4a** was 2.5:1 (**4a**-(*S*,*S*,*S*):**4a**-(*S*,*R*,*S*)),[9b] while the ratio of the two diastereomers of **4b** was 2.1:1 (**4b**-(*S*,*S*,*S*):**4b**-(*S*,*R*,*S*)).[10b] Though **4b** has bulkier substituents than **4a**, the diastereomer ratio of **4b** was slightly lower than that of **4a**. This may be ascribed to the reverse effect arising from the large steric repulsion between the oxazolinyl *tert*-butyl group on one benzene ring and 5,6-position protons of the other benzene ring in **4b**. We then investigated the equilibrium between the two diastereomers of **4a** at different temperatures and in different solvents (Table 1). As can be expected, lower temperature gave a higher ratio, and at -90 °C up to 8.5:1 ratio was obtained in methanol-d^4. At higher temperature, the ratio went down and at about 40 °C, the signals of the two diastereomers in ^{1}H NMR broadened to coalesce in both methanol-d^4 and chloroform-*d*. It was also shown that a polar solvent gave a larger ratio than a nonpolar solvent (Table 1, entry 4, 8, 10).

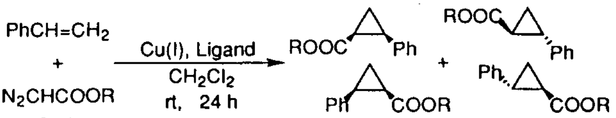
Table 1. Diastereomer ratio of 4a.

entry	solvent	temp (°C)	4a-(*S*,*S*,*S*) : 4a-(*S*,*R*,*S*)[a]
1	CD_3OD	-90	8.5 : 1
2		-60	7.9 : 1
3		-30	4.3 : 1
4		26	3.9 : 1
5		40	broad one peak
6	$CDCl_3$	-60	5.5 : 1
7		-30	4.1 : 1
8		26	2.5 : 1
9		40	broad one peak
10	C_6D_6	26	1.9 : 1

[a] Determined by ^{1}H NMR.

Next, we examined the complexation behavior of these ligands with a copper(I) triflate benzene complex [Cu(I)OTf(C_6H_6)$_{0.5}$] in solution. To a solution of ligand **4a** in dichloromethane-*d*^{2} was added 1 equiv. of the copper(I) triflate benzene complex and then the suspension was stirred at room temperature for 2 h under argon atmosphere. Interestingly, the ^{1}H NMR of the resultant clear solution showed the formation of only one of the two possible diastereomeric complexes with C_2-symmetry. The structure of this complex was tentatively assigned to **5a**-(*S*,*S*,*S*)[11] in which the steric repulsion between the two substituents on the oxazoline rings and between the substituent and the OTf group coordinated to Cu(I) is smaller than that in the complex **5a**-(*S*,*R*,*S*) by an examination of CPK models. The same behavior was also observed in the solution of chloroform-*d*. In the same way, ligand **4b** gave the same result as **4a** and afforded only one diastereomeric complex, **5b**-(*S*,*S*,*S*).[12] To the best of our knowledge, this is the first example of biphenyl derivatives bearing only two *ortho*-substituents with stable diastereomerically pure axial chirality.

In recent years, copper(I)-catalyzed cyclopropanation of olefin, especially styrene (Scheme 3), as an important asymmetric catalytic reaction has been investigated using various oxazoline compounds as chiral ligands, and high enantiomeric excess was reported.[1,13] In order to examine the ability of the present new kind of bisoxazoline compounds as chiral ligands, we also carried out the copper(I)-catalyzed cyclopropanation of styrene with diazoacetate using **4a,b** and a copper(I) triflate benzene complex as a preliminary experiment and up to 92% ee was attained for the *cis*-isomers of product **10b** when *l*-menthyl diazoacetate was used (Table 2).[14]



9a,b **10a,b**

Scheme 3 (**a**: R=Et, **b**: R=*l*-menthyl)

Table 2. Asymmetric cyclopropanation of styrene with diazoacetates catalyzed by copper(I)-bis(oxazolinyl)biphenyls.[a]

ligand	diazoacetate 9 (R)	yield[b] (%) of **10**	ratio[c] of *trans*/*cis*	% ee[d] (config)[e] *trans*	% ee[d] (config)[e] *cis*
4a	**9a** (Et)	72	74/26	49 (1R, 2R)	59 (1R, 2S)
4a	**9b** (*l*-menthyl)	60	79/21	70 (1R, 2R)	87 (1R, 2S)
4b	**9a** (Et)	69	68/32	74 (1R, 2R)	84 (1R, 2S)
4b	**9b** (*l*-menthyl)	60	81/19	84 (1R, 2R)	92 (1R, 2S)

a The reaction was carried out in dichloromethane in the presence of 1 mol% of the copper(I) catalyst at rt for 24 h under argon: dichloromethane (2.0 ml), styrene (1.0 mmol), diazoacetate (1.3 mmol), [Cu(I)OTf(C_6H_6)$_{0.5}$] (10 μ mol), ligand (11 μ mol). *b* Isolated yield of a mixture of *trans*-**10a,b** and *cis*-**10a,b**. *c* The ratio of *trans*-**10a,b**/*cis*-**10a,b** was determined by GC analysis.
d Determined by GC analysis with Chiraldex G-TA for **10a**, and with DB-1 for **10b**. *e* Absolute configuration of *trans*-**10a** and *cis*-**10a** was determined by measurement of their specific rotation values,[15] and that of *trans*-**10b** and *cis*-**10b** was determined by chemical correlation with **10a**.[f]
f Transformation of **10b** to **10a** was carried out in refluxing ethanol in the presence of a small amount of H_2SO_4.

We are currently studying other members of this kind of ligand (R= Me, Ph, CH_2Ph, etc.) to clarify the effect of the substituents on the oxazoline rings on coordination with Cu(I). The complexation behavior of this kind of ligand with other metals as well as other metal-catalyzed asymmetric catalyses is also under investigation in our laboratory.

References and Notes

1. Reported as a poster presentation at Osaka University, 43rd Symposium on Organometallic Chemistry, Japan, October 31 - November 1, 1996, Abstracts, 106-107.
2. For reviews: (a) Tongi, A.; Venanzi, L. M. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497-526. (b) Pfaltz, A. *ACC. Chem. Res.* **1993**, *26*, 339-345. (c) Doyole, M. P. *Catalytic Asymmetric Synthesis.* (Ed.: Ojima, I.), VCH publishers, New York, **1993**, p63. (d) Bolm, C. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 542-543.
3. (a) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron Asymmetry* **1996**, *7*, 2453-2462. This kind of ligands was also reported independently by the Andersson and the Knight groups, see: (b) Bedekar, A. V.; Andersson, P. G. *Tetrahedron Lett.* **1996**, *37*, 4073-4076. (c) Harm, A. M.; Knight, J. G.; Stemp, G. *Synlett* **1996**, 677-678.
4. (a) Zhang, W.; Adachi, Y.; Hirao, T.; Ikeda, I. *Tetrahedron Asymmetry* **1996**, *7*, 451-460. (b) Zhang, W.; Hirao, T.; Ikeda, I. *Tetrahedron Lett.* **1996**, *37*, 4545-4548.
5. Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron Lett.* **1996**, *37*, 7995-7998.
6. During our study on this work, two related ligands prepared from chiral biaryl and racemic biaryl were reported by the Corey and the Hayashi groups, but one of them needs the resolution of the biaryl material and the other needs the separation of the two diastereomers of the ligand; only one of the two diastereomers shows high enantioselectivity in both situations. See: (a) Gant, T. G.; Noe, M. C.; Corey, E. J. *Tetrahedron Lett.* **1995**, *36*, 8745-8748. (b) Uozumi, Y.; Kyota, H.; Kishi, E.; Kitayama, K.; Hayashi, T. *Tetrahedron Asymmetry* **1996**, *7*, 1603-1606.
7. (a) Meyers, A. I.; Meier, A.; Rawson, D. *Tetrahedron Lett.* **1992**, *33*, 853-856. (b) Rawson, D.; Meyers, A. I. *J. Chem. Soc., Chem. Commun.* **1992**, 494-496. (c) Mayers, A. I.; Himmelsbach, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 682-685.
8. (a) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis*, **1992**, 503-517. (b) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581-1590.
9. (a) **4a**: $[\alpha]_D^{26} = -141.5$ (c, 0.50, $CHCl_3$). MS(m/z) 377 ($(M+1)^+$). IR (neat, cm^{-1}) 1657(C=N). (b) Based on an examination of CPK models, the major diastereomer was tentatively assigned to the sterically less crowded **4a**-(*S*,*S*,*S*) and the minor diastereomer to the more crowded **4a**-(*S*,*R*,*S*). **4a**-(*S*,*S*,*S*): ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, 2H, *J*=7.8 Hz, ArH), 7.47 (t, 2H, *J*=7.2 Hz, ArH), 7.37 (m, 2H, ArH), 7.32 (d, 2H, *J*=7.2 Hz, ArH), 4.13 (t, 2H, *J*=9.3 Hz, OCH), 3.85 (m, 2H, NCH), 3.74 (t, 2H, *J*=7.8 Hz, OCH), 1.69 (m, 2H, Me_2CH), 0.81 (m, 12H, CH_3). **4a**-(*S*,*R*,*S*): ^1H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, 2H *J*=7.2 Hz, ArH), 7.40 (t, 2H, *J*=7.2 Hz, ArH), 7.37 (m, 2H, ArH), 7.23 (d, 2H, *J*=7.2 Hz, ArH), 4.01 (t, 2H, *J*=7.2 Hz, OCH), 3.85 (m, 4H, NCH and OCH), 1.64 (m, 2H, Me_2CH), 0.87 (d, 6H, *J*=6.6 Hz, CH_3), 0.81 (m, 6H, CH_3).
10. (a) **4b**: $[\alpha]_D^{26} = -101.4$ (c, 0.50, $CHCl_3$). MS(m/z) 405 ($(M+1)^+$). IR (neat, cm^{-1}) 1655(C=N). (b) The assignment of the two diastereomers of **4b** is the same as that of **4a**. **4b**-(*S*,*S*,*S*): ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, 2H, *J*=7.8 Hz, ArH), 7.44 (m, 2H, ArH), 7.37 (m, 2H, ArH), 7.27 (m, 2H, ArH), 4.07 (t, 2H, *J*=8.6 Hz, OCH), 3.83 (m, 2H, NCH), 3.78 (t, 2H, *J*=8.6 Hz, OCH), 0.79 (s, 18H, CH_3). **4b**-(*S*,*R*,*S*): ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, 2H, *J*=7.8 Hz, ArH), 7.37 (m, 4H, ArH), 7.21 (d, 2H, *J*=7.2 Hz, ArH), 3.94 (m, 4H, OCH), 3.83 (m, 2H, NCH), 0.79 (s, 18H, CH_3).
11. **5a**-(*S*,*S*,*S*): ^1H NMR (400 MHz, CD_2Cl_2) δ 7.60 (m, 2H, ArH), 7.41 (m, 4H, ArH), 7.06 (m, 2H, ArH), 4.54 (t, 2H, *J*=9.4 Hz, OCH), 4.31 (m, 2H, OCH), 4.03 (m, 2H, NCH), 1.47 (m, 2H, Me_2CH), 0.47 (d, 6H, *J*=6.8 Hz, CH_3), 0.42 (d, 6H, *J*=6.8 Hz, CH_3). MS(m/z) 439 ($(M-OTf)^+$).
12. **5b**-(*S*,*S*,*S*): ^1H NMR (400 MHz, CD_2Cl_2) δ 7.67 (m, 2H, ArH), 7.41 (m, 4H, ArH), 7.05 (m, 2H, ArH), 4.53 (t, 2H, *J*=9.6 Hz, OCH), 4.43 (m, 2H, OCH), 4.04 (m, 2H, NCH), 0.53 (s, 18H, CH_3). MS(m/z) 467 ($(M-OTf)^+$).
13. Selected papers: (a) Tokunoh, R.; Tomiyama, H.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 2449-2452. (b) Pique, C.; Fähndrich, B.; Pfaltz, A. *Synlett* **1995**, 491-492. (c) Evans, D. A.; Woerpel, K. A.; Scott, M. J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 430-432. (d) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553-1565.
14. The Corey and the Hayashi groups also carried out the related asymmetric cyclopropanation and higher ee was attained with the (*S*,*S*,*S*) diastereomer and lower ee with the (*S*,*R*,*S*) diastereomer of their ligands in both cases.[6] These results also support the assignment of our complex to **5**-(*S*,*S*,*S*) with which higher ee was attained.
15. Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726-728.

(*Received in Japan* 6 *January* 1997; *revised* 25 *February* 1997; *accepted* 28 *February* 1997)