Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 6, pp. 1603-1606, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0957-4166/96 $15.00 + 0.00

PII: S0957-4166(96)00193-0

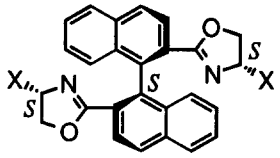
Homochiral 2,2'-Bis(oxazolyl)-1,1'-binaphthyls as Ligands for Copper(I)-Catalyzed Asymmetric Cyclopropanation

Yasuhiro Uozumi, Hirokazu Kyota, Eiji Kishi, Kenji Kitayama, and Tamio Hayashi*

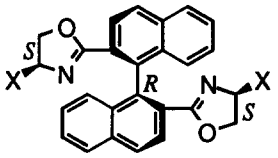
Department of Chemistry, Faculty of Science, Kyoto University, Sakyo, Kyoto 606-01, Japan

Abstract: Homochiral 2,2'-bis[4-(alkyl)oxazol-2-yl]-1,1'-binaphthyls, which possess both binaphthyl axial chirality and carbon centred chirality, were prepared from 1,1'-binaphthyl-2,2'-dicarboxylic acid and 2-alkyl-2-aminoethanols in high yields. Asymmetric cyclopropanation of styrene with diazoacetates in the presence of 2 mol % of copper(I) triflate and (*S*)-2,2'-bis[(*S*)-4-(*t*-butyl)oxazol-2-yl]-1,1'-binaphthyl gave optically active 2-(phenyl)cyclopropanecarboxylates of up to 97% ee. Copyright © 1996 Elsevier Science Ltd

Chiral oxazolines have been widely and successfully used as powerful moieties inducing high stereoselectivity in a variety of asymmetric reactions.[1,2] In particular, optically active bis(oxazolyl) compounds have attracted considerable attention as chiral ligands for transition metal-catalyzed asymmetric reactions.[2,3] On the other hand, axially chiral biaryls, endowed with a C_2-symmetry axis, display wide utility as chiral templates for stoichiometric and catalytic asymmetric reactions.[4] However, there have been very few reports on bis(oxazolyl) ligands whose basic skeleton is an axially chiral biaryl.[5] During our studies on the design of new chiral reagents, we have prepared optically active 2,2'-bis(oxazolyl)-1,1'-binaphthyls **1**[6] which are expected to be effective as chiral ligands for several types of transition metal-catalyzed asymmetric reactions. Here we report their preparation and use in copper(I)-catalyzed asymmetric cyclopropanations.



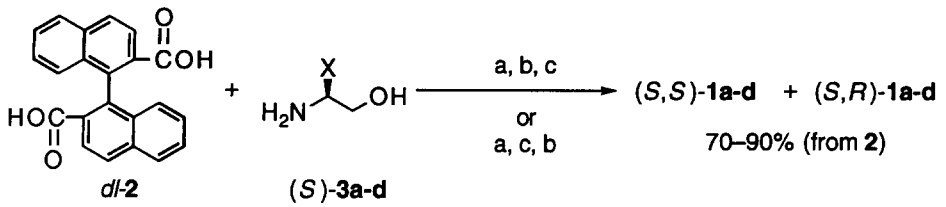
(*S*,*S*)-**1a-d**



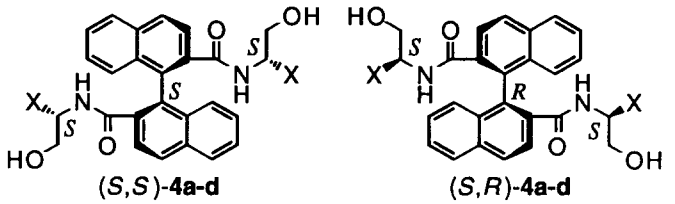
(*S*,*R*)-**1a-d**

a: X = *t*-Bu
b: X = *i*-Pr
c: X = Ph
d: X = CH_2Ph

Owing to the axial chirality in the binaphthyl and the carbon centred chirality in the oxazoline, a pair of diastereomeric isomers occur in 2,2'-bis[4-(alkyl)oxazol-2-yl]-1,1'-binaphthyl **1**. We have prepared both of the isomers, (*S*,*S*)-**1** and (*S*,*R*)-**1**, starting with racemic 1,1'-binaphthyl-2,2'-dicarboxylic acid (*dl*-**2**)[7] and optically active 2-alkyl-2-aminoethanols, (*S*)-**3** (Scheme 1).[1] Thus, *dl*-**2** was condensed with (*S*)-2-amino-3,3-dimethylbutanol ((*S*)-*t*-leucinol) (*S*)-**3a** by way of binaphthyldicarbonyl dichloride to give amides **4a** as a mixture of diastereomeric isomers (*S*,*S*)-**4a** and (*S*,*R*)-**4a** in a quantitative yield. The isomers were readily separated by column chromatography on silica gel (eluent: EtOAc/hexane = 4/1), and they were subjected to the oxazoline ring formation by treatment with triphenylphosphine-carbon tetrachloride in the presence of triethylamine[8] to give (*S*)-2,2'-bis[(*S*)-4-(*t*-butyl)oxazol-2-yl]-1,1'-binaphthyl (*S*,*S*)-**1a** in 93% yield and its



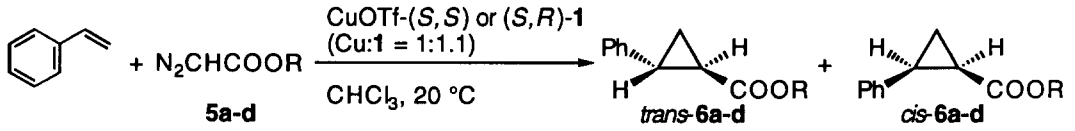
conditions:
a) $SOCl_2$, then **3**
b) Ph_3P, CCl_4, reflux
c) separation



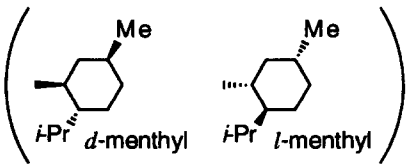
Scheme 1

isomer (*S*,*R*)-**1a** in 70% yield. For the oxazolines **1b** and **1c**, derived from (*S*)-2-amino-3-methylbutanol ((*S*)-valinol) (*S*)-**3b** and (*S*)-2-amino-2-phenylethanol ((*S*)-phenylglycinol) (*S*)-**3c**, respectively, the diastereomeric isomers were conveniently separated after the oxazoline ring formation.[9,10,11]

The 2,2'-bis(oxazolyl)-1,1'-binaphthyl ligands **1** were used for the copper-catalyzed cyclopropanation of styrene with diazoacetates which is the reaction most often examined with chiral oxazolyl ligands.[2,12,13] The asymmetric cyclopropanation was carried out in chloroform in the presence of 2 mol % of copper(I) catalyst generated in situ by mixing CuOTf•0.5C_6H_6 and the bis(oxazolyl)binaphthyl ligand to give 2-phenylcyclopropane-1-carboxylates **6** as a mixture of *trans* and *cis* isomers (Scheme 2).[14] The ratio of *trans*/*cis* isomers was determined by ^1H NMR and GC analysis, and their enantiomeric excess was determined by GC analysis using a chiral stationary phase column (Cyclodex β236M). The representative results are summarized in Table 1. Comparing a pair of diastereoisomeric bis(oxazolyl)binaphthyl ligands (*S*,*S*)-**1** and (*S*,*R*)-**1**, both of which possess *S* configuration on their oxazoline rings, the ligands with *S* axial chirality were found to be much more enantioselective than those with *R* axial chirality in the present asymmetric cyclopropanation. Thus, (*S*,*S*)-**1a**, which contains (*S*)-binaphthyl skeleton and (*S*)-(*t*-butyl)oxazoline, gave 87% ee of *trans*-**6a** and 86% ee of *cis*-**6a** (*trans*/*cis* = 59/41) in the reaction with ethyl diazoacetate **5a**, while (*S*,*R*)-**1a** gave 3% ee of the products under the same reaction conditions (Table 1, entries 1 and 2). The low enantioselectivity of (*S*,*R*) isomer was also observed with ligand **1b** (entry 4). Of the (*S*,*S*)-bis(oxazolyl)binaphthyls, the ligand containing the *t*-butyl substituent on its oxazoline rings turned out to be the best ligand giving the highest enantiomeric excess of



a: R = Et
b: R = *t*-Bu
c: R = *d*-menthyl
d: R = *l*-menthyl



Scheme 2

Table 1. Asymmetric Cyclopropanation of Styrene with Diazoacetates Catalyzed by Copper(I)-Bis(oxazolyl)binaphthyls[a]

entry	ligand **1** (X)	diazoacetate **5** (R)	yield[b] (%) of **6**	ratio[c] of *trans*/*cis*	% ee[d] (config)[e] *trans*	*cis*
1	(*S*,*S*)-**1a** (*t*-Bu)	**5a** (Et)	59	59/41	87 (1*R*,2*R*)	86 (1*R*,2*S*)
2	(*S*,*R*)-**1a** (*t*-Bu)	**5a** (Et)	52	70/30	3 (1*S*,2*S*)	3 (1*S*,2*R*)
3	(*S*,*S*)-**1b** (*i*-Pr)	**5a** (Et)	58	60/40	62 (1*R*,2*R*)	61 (1*R*,2*S*)
4	(*S*,*R*)-**1b** (*i*-Pr)	**5a** (Et)	38	64/36	4 (1*S*,2*S*)	4 (1*S*,2*R*)
5	(*S*,*S*)-**1c** (Ph)	**5a** (Et)	43	67/33	55 (1*R*,2*R*)	57 (1*R*,2*S*)
6	(*S*,*S*)-**1d** (CH_2Ph)	**5a** (Et)	59	68/32	16 (1*R*,2*R*)	8 (1*R*,2*S*)
7	(*S*,*S*)-**1a** (*t*-Bu)	**5b** (*t*-Bu)	67	72/28	89 (1*R*,2*R*)	92 (1*R*,2*S*)
8		**5c** (*d*-menthyl)	68	86/14	90 (1*R*,2*R*)	87 (1*R*,2*S*)
9		**5d** (*l*-menthyl)	60	68/32	95 (1*R*,2*R*)	97 (1*R*,2*S*)
10	(*S*,*S*)-**1b** (*i*-Pr)	**5b** (*t*-Bu)	48	72/28	72 (1*R*,2*R*)	71 (1*R*,2*S*)
11		**5c** (*d*-menthyl)	51	84/16	75 (1*R*,2*R*)	52 (1*R*,2*S*)
12		**5d** (*l*-menthyl)	50	68/32	87 (1*R*,2*R*)	91 (1*R*,2*S*)

[a] The reaction was carried out in chloroform in the presence of 2 mol % of the copper(I) catalyst at 20 ℃ for 5 hr under nitrogen: chloroform (0.8 mL), styrene (4.0 mmol), diazoacetate (0.5 mmol), $[Cu(OTf)]_2 \cdot C_6H_6$ (5 μmol), ligand (11 μmol). [b] Isolated yield of a mixture of *trans*-**6** and *cis*-**6**. [c] The ratio of *trans*-**6**/*cis*-**6** was determined by ^1H NMR and GC analysis. [d] Determined by GC analysis with Cyclodex β236M (25 m x 0.25 mm) for *trans*-**6a-d** and *cis*-**6a-c**, and with Chirasil-Val (25 m x 0.25 mm) for *cis*-**6d**. [e] Absolute configuration of *trans*-**6a** and *cis*-**6a** was determined by measurement of their specific rotation values (see text and ref 15), and that of *trans*- and *cis*-**6b-d** was determined by chemical correlation with **6a** (footnote 16).

cyclopropanes, and sterically less bulky substituents gave lower enantioselectivities. Thus, the enantiomeric excess of *trans*-**6a** obtained with (*S*,*S*)-**1a** was 87% ee (entry 1), while those obtained with (*S*,*S*)-**1b** (X = *i*-Pr), (*S*,*S*)-**1c** (X = Ph), and (*S*,*S*)-**1d** (X = CH_2Ph) were 62% ee, 55% ee, and 16% ee, respectively (entries 3, 5, and 6). The absolute configuration of the product was assigned to be (1*R*,2*R*) for *trans*-**6a** and (1*R*,2*S*) for *cis*-**6a** by measurement of the specific rotations (*trans*-**6a** (84% ee): $[\alpha]_D^{20}$ –247 (*c* 0.99, chloroform), *cis*-**6a** (85% ee): $[\alpha]_D^{20}$ –17 (*c* 2.02, chloroform)).[15]

The enantioselectivity in the asymmetric cyclopropanation was improved by use of sterically bulkier diazoacetate esters. The reaction of *t*-butyl diazoacetate **5b** in the presence of copper(I)/(*S*,*S*)-**1a** catalyst gave *trans*- and *cis*-*t*-butyl cyclopropanecarboxylates **6b** of around 90% ee (entry 7). The highest enantioselectivity was observed in the reaction of *l*-menthyl ester **5d**, which gave 95% ee for *trans*-cyclopropane **6d** and 97% ee for *cis*-**6d**, the *trans*/*cis* ratio being 68/32 (entry 9).

Acknowledgment:

We thank the Ministry of Education, Japan, for a Grant-in-Aid for Scientific Research, for partial financial support of this work. We gratefully acknowledge Prof. A. I. Meyers of Colorado State University for providing ^1H NMR data of compounds (*S*,*S*)-**1a-c** and (*S*,*R*)-**1a-c**.

References and Notes:

1 For a review up till 1985: Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837.

2 For recent reviews: (a) Togni, A.; Venanzi, L. M. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497. (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339.

3 (a) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005. (b) Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.* **1991**, *32*, 7373. (c) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta.* **1991**, *74*, 232. (d) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726. (e) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc.* **1991**, *113*, 728. (f) Helmchen, G.; Krotz, A.; Ganz, K. T.; Hans, D. *Synlett* **1991**, 257.

4 For reviews: (a) Nógrádi, M. *Stereoselective Synthesis*; 2nd Ed. Weinheim: New York, 1995. (b) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503. (c) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.

5 During the preparation of this manuscript, a study was reported describing asymmetric intramolecular cyclopropanation with a 2,2'-bis(oxazolyl)-6,6'-dimethyl-1,1'-biphenyl: Gant, T. G.; Noe, M. C.; Corey, E. J. *Tetrahedron Lett.* **1995**, *36*, 8745.

6 Compounds (*S*,*S*)-**1a-c** and (*S*,*R*)-**1a-c** have appeared as intermediates for synthesis of optically active binaphthyldicarboxylic acid, which were prepared by enantioselective Ullmann coupling of corresponding 1-bromo-2-(oxazolyl)naphthalenes: Nelson, T. D.; Meyers, A. I. *J. Org. Chem.* **1994**, *59*, 2655.

7 Binaphthyldicarboxylic acid **2** was prepared from 2,2'-dibromo-1,1'-binaphthyl by lithiation with *n*-BuLi and subsequent carboxylation with solid CO_2.

8 Vorbruggen, H.; Krolikiewicz, K. *Tetrahedron Lett.* **1981**, *22*, 4471.

9 The stereochemistry of (*S*,*S*)- and (*S*,*R*)-**1** was assigned by comparison of their ^{1}H NMR data with those reported by A. I. Meyers: Meyers, A. I. *private communication*. Also see ref 6.

10 Because of difficulty in separation of the diastereomers, isomerically pure (*S*,*S*)-**1d** was prepared from enantiomerically pure (*S*)-**2** according to the same synthetic sequences shown in Scheme 1.

11 Specific rotations for the bis(oxazolyl) compounds are as follows: (*S*,*S*)-**1a**: $[\alpha]_D^{20}$ –167 (*c* 0.59, chloroform). (*S*,*R*)-**1a**: $[\alpha]_D^{20}$ +36 (*c* 0.97, chloroform). (*S*,*S*)-**1b**: $[\alpha]_D^{20}$ –217 (*c* 0.52, chloroform). (*S*,*R*)-**1b**: $[\alpha]_D^{20}$ –31 (*c* 1.90, ethanol). (*S*,*S*)-**1c**: $[\alpha]_D^{20}$ –166 (*c* 0.71, chloroform). (*S*,*S*)-**1d**: $[\alpha]_D^{20}$ –91 (*c* 0.78, chloroform).

12 For a recent review on catalytic asymmetric cyclopropanations: Doyle, M. P. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; p 63.

13 For recent examples: (a) Evans, D. A.; Woerpel, K. A.; Scott, M. J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 430. (b) Piqué, C.; Fähndrich, B.: Pfaltz, A. *Synlett* **1995**, 491. (c) Tokunoh, R.; Tomiyama, H.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 2449. See also ref 3a-d.

14 A typical procedure is given for the reaction of styrene with *t*-butyl diazoacetate (**5b**) in the presence of Cu(I)/(*S*,*S*)-**1a** complex: A solution of Cu(OTf)•0.5C_6H_6 (0.01 mmol) and (*S*,*S*)-**1a** (1.1 equiv to Cu) in 0.3 mL of chloroform was stirred at ambient temperature for 60 min, and then 4.0 mmol of styrene was added to the solution. To the mixture was added a chloroform solution of *t*-butyl diazoacetate (**5b**) (0.5 mmol in 0.5 mL) as dropwise at 20 °C with the aid of syringe pump equipment over a period of 3.0 hr and the entire mixture was stirred for additional 2.0 hr, during which all of the diazoacetate was consumed. The reaction mixture was filtered through alumina plug to remove the catalyst and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel to give 67% yield of **6b** as a mixture of diastereomers. The mixture of *trans* and *cis*-**6b** was subjected to ^{1}H NMR and GC analysis to determine the diastereomeric ratio and the enantiomeric excess (see text).

15 The specific rotations for (1*S*,2*R*)-**6a** (99% ee) and (1*S*,2*S*)-**6a** (99% ee) have been reported to be $[\alpha]_D$ +18.6 (*c* 1.01, chloroform) and $[\alpha]_D$ +296 (*c* 0.88, chloroform), respectively. See ref 3d.

16 Transformation of **6b-d** to **6a** was carried out in refluxing ethanol in the presence of a trace amount of *conc*-H_2SO_4.

(*Received in Japan* 23 *April* 1996)