ORGANIC LETTERS

2001
Vol. 3, No. 2
243−245

General Synthetic Route to Chiral Flexible Biphenylphosphine Ligands: The Use of a Chiral Additive Enables the Preparation and Observation of Metal Complexes Incorporating the Enantiopure Form†

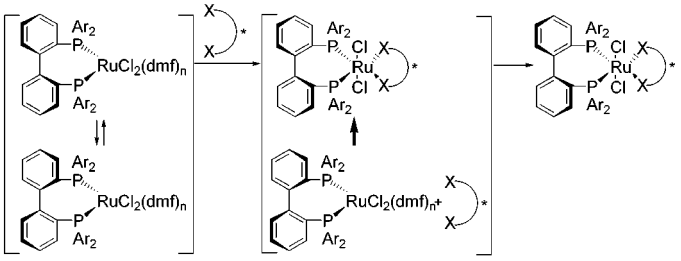
Koichi Mikami,* Kohsuke Aikawa, and Toshinobu Korenaga

Department of Applied Chemistry, Tokyo Institute of Technology, Tokyo 152-8552, Japan

kmikami@o.cc.titech.ac.jp

Received November 18, 2000

ABSTRACT



The enantio- and diastereomerically pure metal complex of a chirally flexible BIPHEP ligand is obtained through enantiomer-selective coordination of a BIPHEP–Ru complex with enantiopure 3,3′-dimethyldiaminobinaphthyl, DM-DBN, followed by epimerization of the remaining BIPHEP–Ru enantiomer to complex with DM-DABN. Thus, an efficient and general synthetic route to a variety of substituted BIPHEP ligands from biphenol and observation of the enantiomerically pure BIPHEP ligands in their Ru(II) complexes are described.

In an asymmetric catalysis,[1] the choice of a chiral ligand is a key factor in attaining a certain level of asymmetric induction and increasing the catalytic activity from the achiral precatalyst ("ligand accelerated catalysis" [2]). However, asymmetric synthesis or resolution is generally required to obtain enantiopure forms of chirally rigid ligands. By contrast, we have reported the use of chirally flexible biphenylphosphine (BIPHEP) ligands[3] (Figure 1) in the Ru-catalyzed asymmetric hydrogenation, instead of the enantiopure, chirally rigid BINAP counterparts.[4] Inherently, the BIPHEP ligands cannot be isolated in enantiopure forms without a substituent at the

† Paper by T. Korenaga, M. Terada, and K. Mikami presented at the 45th Symposium on Organometallic Chemistry, Japan, 1998.

(1) (a) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis, Vol. 1−3*; Springer: Berlin, 1999. (b) *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Ed.; VCH: Weiheim, 1998. (c) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994. (d) Brunner, H.; Zettlmeier, W. *Handbook of Enantioselective Catalysis*; VCH: Weiheim, 1993. (e) *Catalytic Asymmetric Synthesis, Vol. I* and *II*; Ojima, I., Ed.; VCH: New York, 1993; p 2000. (f) Kagan, H. B. *Comprehensive Organic Chemistry, Vol. 8*; Pergamon: Oxford, 1992. (g) *Asymmetric Catalysis*; Bosnich, B., Ed.; Martinus Nijhoff Publishers: Dordrecht, 1986.

(2) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059.

(3) BIPHEP was named after 6,6′-substituted MeO-BIPHEP. (a) Schmid, R.; Broger, E.; A. Cereghetti, M.; Crameri, Y.; Foricher, J.; Lalonde, M.; Müller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. *Pure Appl. Chem.* **1996**, *68*, 131−138. (b) Trabesinger, G.; Albinati, A.; Feiken, N.; Kunz, R. W.; Pregosin, P. S.; Tschoerner, M. *J. Am. Chem. Soc.* **1997**, *119*, 6315−6323, and references therein.

(4) (a) Mikami, K.; Korenaga, T.; Terada, M.; Ohkuma, T.; Pham, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 495−497. (b) Review on asymmetric activation : Mikami, K.; Terada, M.; Korenaga, T.; Matsumoto, Y.; Ueki, M.; Angelaud, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 3532−3556. Also see highlights of conformational control of ligand: Muñiz, K.; Bolm, C. *Chem. Eur. J.* **2000**, *6*, 2309−2316.

10.1021/ol0068896 CCC: $20.00 © 2001 American Chemical Society
Published on Web 12/15/2000

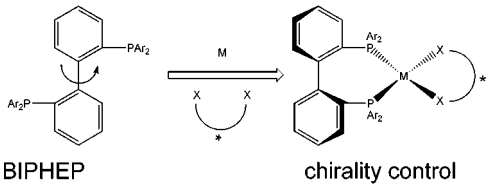


Figure 1.

6-position.[5] However, the BIPHEP−Ru(II) complexes can be obtained in diastereomerically enriched forms, after complexation with a chiral diamine activator (1) to control the chirality through epimerization of BIPHEPs and (2) to increase the catalytic activity ("asymmetric activation") of the BIPHEP−Ru(II) complexes in the enantioselective hydrogenation of ketones.[4a]

The chirality control of BIPHEP−metal complexes can, in principle, be classified into two extremes. There is a continuum between the two. One is selective complexation of the chiral molecule (X−*−X) with one enantiomer of a racemic BIPHEP−metal complex along with the remaining BIPHEP−metal enantiomer which eventually epimerizes in order to complex with the chiral molecule (Figure 2a). The

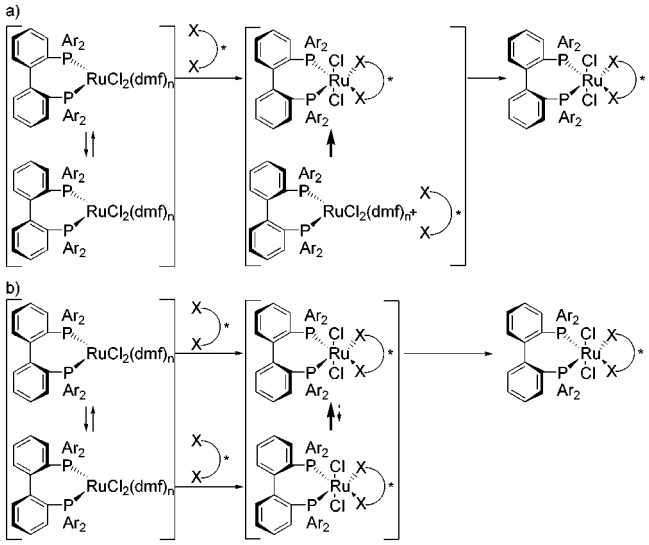
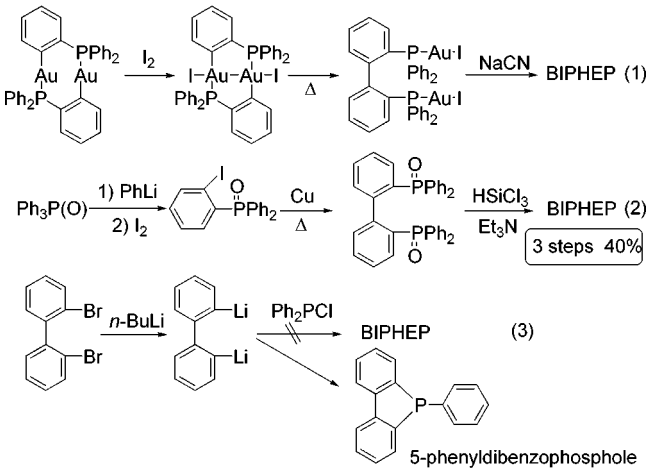


Figure 2.

other is nonselective complexation of the chiral molecule with both enantiomers of racemic BIPHEP−metal complex followed by epimerization of the less favorable diastereomeric BIPHEP−metal complex with the chiral molecule to the favorable diastereomer (Figure 2b).

Unfortunately, the BIPHEP ligand had been synthesized starting particularly from triphenylphosphine or its oxide (Scheme 1 (1) and (2)). Therefore, a variety of BIPHEPs bearing substituted diarylphosphine (PAr_2) groups could not

Scheme 1



be synthesized according to this method. Furthermore, the use of dibromobiphenyl was found to give, after dilithiation followed by treatment with diphenylphosphine chloride, 5-phenyldibenzophospholane instead of BIPHEP as previously reported (BPBP (2,2′-bis(diphenylphosphanyl)-1,1′-biphenyl): originally named)[5a] (Scheme 1 (3)). Herein, we wish to report an efficient and general synthetic route to a variety of substituted BIPHEP ligands from biphenol and observation of the enantiomerically pure BIPHEP ligands in their Ru(II) complexes with 3,3′-dimethyldiaminobinaphthyl, DM-DABN (named after DABN: diaminobinaphthyl).

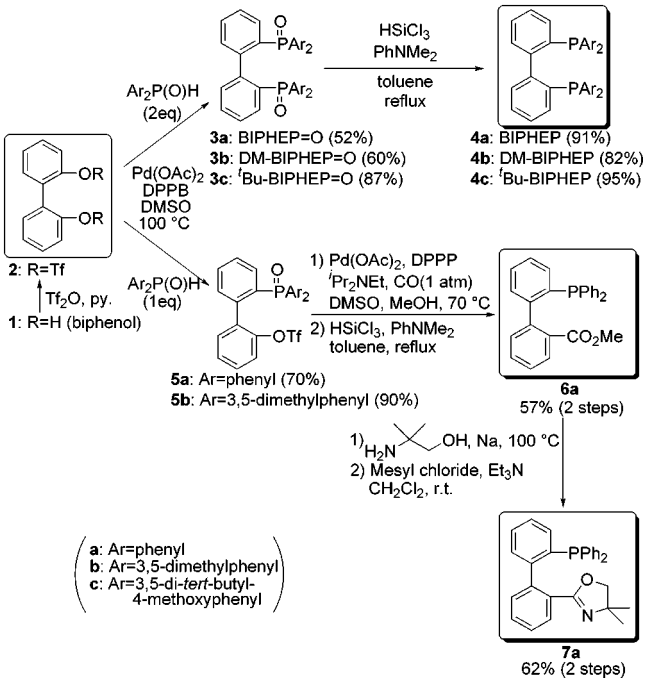
The present syntheses of BIPHEPs reflect their flexible nature in sharp contrast to the chiral rigidity of BINAPs. The synthesis of BINAP from binaphthyl ditriflate has been reported using Ni[6] and Pd[7] catalysts. Particularly, $NiCl_2$(dppe) is an excellent catalyst for the coupling reaction of Ph_2PH with binaphthyl ditriflate to give BINAP in one step.[6] However, the biphenyl ditriflate counterpart (**2**) with $NiCl_2$(dppe) and Ph_2PH gave a complex mixture of products. In the BINAP synthesis, $Pd(OAc)_2$ has been used for the coupling reaction of $Ph_2P(O)H$ with binaphthyl ditriflate, however, to give only binaphthyl monophosphine oxide.[6a,7] In sharp contrast, biphenyl ditriflate (**2**), with $Pd(OAc)_2$ and $Ph_2P(O)H$ in DMSO at 100 °C, was found to afford the diphosphine oxide, BIPHEP═O (**3**), presumably due to the flexibility of the biphenyl dihedral angle as compared to chirally rigid BINAPs (Scheme 2). The syntheses of substituted BIPHEPs, namely, the 3,5-dimethyl analogue, DM (i.e.,

(5) (a) BPBP was also termed for this bisphosphine ligand but synthesized unsuccessfully to give the monophosphine, 5-phenyldibenzophospholane: Uehara, A.; Bailar, J. C., Jr. *J. Organomet. Chem.* **1982**, *239*, 1−10. See also: Miyamoto, T. K.; Matsuura, Y.; Okude, K.; Ichida, H.; Sasaki, Y. *J. Organomet. Chem.* **1989**, *373*, C8−C12. (b) Bennett, M. A.; Bhargava, S. K.; Griffiths, K. D.; Robertson, G. B. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 260−261. (c) Desponds, O.; Schlosser, M. *J. Organomet. Chem.* **1996**, *507*, 257−261. (d) Desponds, O.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 47−48.

(6) (a) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180−7181. (b) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Org. Synth.* **1998**, 6−11.

(7) Synthesis of MOP ligand: Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945−1948.

Scheme 2



Xyl)-BIPHEP═O (**3b**) and 3,5-di-*tert*-butyl analogue **3c** were also achieved in 60% and 87% yields, respectively, using the corresponding $Ar_2P(O)Hs$ which were prepared from ArMgBr and $(EtO)_2P(O)H$. These BIPHEP═Os (**3a**−**c**) were easily converted to BIPHEPs (**4a**−**c**) by reduction with trichlorosilane in 91%, 82%, and 95% yields, respectively.

When 1 equiv of $Ar_2P(O)Hs$ were used for biphenyl ditriflate **2**, the monophosphine oxides (**5a** and **5b**) could be obtained in 70% and 90% yields, respectively. Furthermore, the biphenyl monophosphine oxide monotriflate (**5**) thus obtained could be utilized for the synthesis of other biphenyl phosphine ligands (**6** and **7**). The triflate group in **5a** was converted to a carbomethoxy group by treatment of CO/MeOH with Pd catalyst.[8] Reduction of phosphine oxide gave carbomethoxy phosphine **6a** in 57% yield (two steps). The carbomethoxy group in **6a** was easily converted to oxazoline. The carbomethoxy group in **6a** reacted with amino alcohol in the presence of Na.[9] Cyclization[9] gave phosphino oxazoline **7a** in 62% yield (two steps).

The BIPHEP ligands can be transformed to several metal complexes in racemic forms. However, the chirality control of the BIPHEP ligands in their metal complexes is feasible in two manners by the aid of a chiral molecule (X−*−X) (Figure 2).[4a] Complexation of BIPHEP ligand with $[RuCl_2(C_6H_6)]_2$ in DMF gave the racemic $RuCl_2(biphep)(dmf)_n$ (**8a**) (BIPHEP−Ru). A mixture of BIPHEP−Ru (**8a**) and (*R*)-DM-DABN (**9**) was found to provide only $RuCl_2$[(*R*)-biphep]-[(*R*)-dmdabn] ((*R*)-**8a**/(*R*)-**9**) in dichloromethane as observed by ^1H NMR analysis[10] (Figure 2a). The remaining (*S*)-BIPHEP−Ru (**8a**) complexed, only after epimerization to (*R*)-**8a**, with (*R*)-DM-DABN (**9**) in 2-propanol at 50 °C as detected in ^1H NMR spectra.[10] Indeed, the (*R*)/(*R*)-configuration of the BIPHEP−$RuCl_2$/DM-DABN diastereomer was determined by X-ray analysis of the single-crystal obtained from dichloromethane−ether−hexane (Figure 3).[11] Thus, (*R*)-

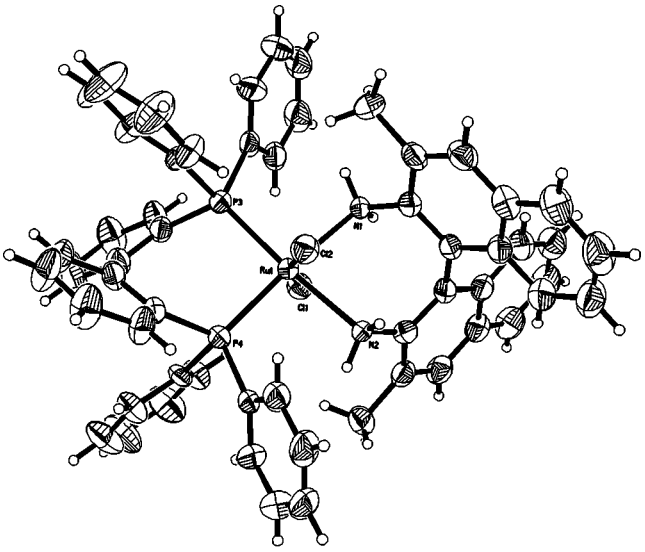


Figure 3.

8a/(*R*)-**9** was eventually obtained from the initial BIPHEP−Ru racemic complex (**8a**) quantitatively.

In summary, we have disclosed herein that the enantio- and diastereomerically pure metal complex of the BIPHEP ligand can be obtained quantitatively through enantiomer-selective coordination of BIPHEP−Ru complex with enantiopure DM-DABN, followed by epimerization of the remaining BIPHEP enantiomer in order to complex with DM-DABN. We have also reported an efficient and general synthetic route to a variety of substituted BIPHEP ligands from biphenol.

Acknowledgment. We are grateful to Drs. H. Kumobayashi and N. Sayo of Takasago International Corp. We also thank to Dr. Kenji Yoza in Nippon Brucker Co. for X-ray analysis of $RuCl_2$(biphep)(dmdabn) complex. This work was financially supported by the Ministry of Education, Science, Sports and Culture of Japan (Nos. 09238209 and 10208204) and the Research Fellowships of the Japan Society for the Promotion of Science for Dr. Toshinobu Korenaga.

OL0068896

(8) Ogasawara, M.; Yoshida, K.; Kamei, H.; Kato, K.; Uozumi, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1779−1787.

(9) Zhang, W.; Yoneda, Y.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron: Asymmetry* **1998**, *9*, 3371−3380.

(10) Only one diastereomer was observed in ^1H NMR spectra. (*R*)-**8a**/(*R*)-**9**: δ 4.04 (d, 9.3 Hz, 2H, amino proton), 4.78 (d, 9.3 Hz, 2H, amino proton).

(11) X-ray analysis of $RuCl_2$[(*R*)-binap][(*R*)-dmdabn]: Mikami, K.; Korenaga, T.; Ohkuma, T.; Noyori, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 3707−3710.