Synthesis of novel BINOL-derived chiral bisphosphorus ligands and their application in catalytic asymmetric hydrogenation

Yong-Gui Zhou and Xumu Zhang*
Department of Chemistry, The Pennsylvania State University, University Park, PA 16802, USA.
E-mail: xumu@chem.psu.edu

First published as an Advance Article on the web 19th April 2002
Received (in Cambridge, UK) 19th February 2002, Accepted 1st April 2002

Some novel ortho-substituted BINOL-derived bisphosphorus ligands (α-BINAP and α-NAPHOS) were synthesized from readily available (S)-BINOL; these ligands showed excellent enantioselectivities (up to 99% ee) in Rh(II)-frequently used chiral chelating ligands (Scheme 1) are BINAP4–moiety in BINAPO and the C of functionalized olefins.

Our synthetic routes are shown in Scheme 2, three 3,3(ortho)-disubstituted BINOL derivatives 1 were synthesized from commercially available (S)-BINOL according to the known literature methods.9 Chiral bisphosphinite ligands L1, L2, L3 and L4 (abbreviated as α-BINAPO) were prepared through reaction of chlorodiarylphosphine with the corresponding chiral diols in high yields. C2-symmetry chiral bisphosphine ligand L5 (abbreviated as α-NAPHOS) was synthesized from the known compound (S)-3,3'-diphenyl-2,2'-dibromomethyl-1,1'-binaphthyl 210 in two steps (Scheme 2).

In our previous work on synthesis of a ligand called binaplane,11 we found that less reactive 2,2'-dichloromethyl-1,1'-binaphthyl is more desirable for making chiral phosphines than 2,2'-dibromomethyl-1,1'-binaphthyl. We tried the known compound 210 for the synthesis of L5, no desired product was obtained. A simple anion exchange of compound 2 with lithium chloride in DMF afforded (S)-3,3'-diphenyl-2,2'-dichloromethyl-1,1'-binaphthyl 3 in 95% yield. Nucleophilic attack of compound 3 with lithium diphenylphosphinide in THF produced the desired bisphosphine ligands L5. The product was further purified by a short silica gel column eluted with hexane–DCM–EtOAc (80:20:1) in a glove box to give a white solid in 33% yield.

With these new ligands in hand, catalytic asymmetric hydrogenation of α-dehydroamino acid derivatives 4 and enamides 5 have been examined. Methyl (Z)-2-aminocaproate 4a and N-acetyl-1-phenylethamide 5a were used as standard substrates. The optimized results were shown in Table

![Scheme 1](image1)

![Scheme 2](image2)
1. We found that 3,3′-disubstituted bisphosphine ligands o-BINAPO are better than nonsubstituted BINAPO. For substrate 4a, ee increased from 73.2 to 99.9%. For substrate 5a, ee changed from 28.3 to 94.3%. A 3,3′-disubstituted bisphosphine ligand L5 (o-NAPHS) is also more effective for asymmetric hydrogenation than the corresponding NAPHS ligand, enantioselectivity increased from 54.0 to 98.7% for hydrogenation of 4a by changing ligand NAPHS to L5. These results supported our hypothesis of the importance of conformational rigidity in asymmetric catalysis. With o-BINAPO ligands, our hydrogenation results are comparable with those obtained with other chiral phosphorus-rhodium catalysts. For example, the ee values (%) of 6a reported in the literature12 are as follows: DIPAMP, 94; DIOP, 73; Chiraphos, 91; BBP, 98.5; BINAP, 67; BICP, 97.5; Ef-DuPhos, 99.4; SpiRIP, 99.9.

A variety of α-dehydroamino acid derivatives 4 were employed as substrates for the Rh-catalyzed hydrogenation reaction using L5 as ligand, the result was shown in Table 2 (entries 1–6). High enantiomeric excesses have been achieved. There is no major electronic effect on the substitution pattern of 4. However, for an o-BINAPO ligand L2, the ees were substrate-dependent (entries 7–11).

To expand the utility of o-BINAPO ligands system, we have examined Rh(i)-catalyzed enantioselective hydrogenation of simple enamides 5 using L2 as ligand (entries 12–15). High enantioselectivities (94.1–96.3% ee) have also been achieved. In conclusion, we have developed a novel, highly effective chiral bisphosphorus ligands based on a chiral binaphthyl backbone for catalytic asymmetric hydrogenation of enamides and α-dehydroamino acids. The 9-membered ring chelation with transition metals is still effective for asymmetric catalysis, and these ligands are likely to be effective for other catalytic reactions due to the big P–M–P bite angle. Further studies of other transition metal complexes of these ligands and their applications are in progress.

This work was supported by grants from National Institutes of Health. We acknowledge a generous loan of precious metals from Johnson Matthey Inc. XZ thanks Supelco for a gift of chiral GC column.

### Notes and references


