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Preface

Chiral phosphorus ligands

Chiral ligands are the foundation upon which metal-catalyzed asymmetric reactions are based. Searching the key words 'chiral ligand' in SciFinder indicates the increasing activity in this exciting field over the last 10 years (Fig. 1). A number of new concepts has been introduced, and major breakthroughs have been achieved by many research groups, both academic and industrial. Chiral phosphorus-based ligands are the most common and useful in organic syntheses. This special issue of *Tetrahedron*: *Asymmetry* features work by many key players in the field and reflects the growing excitement in the area.

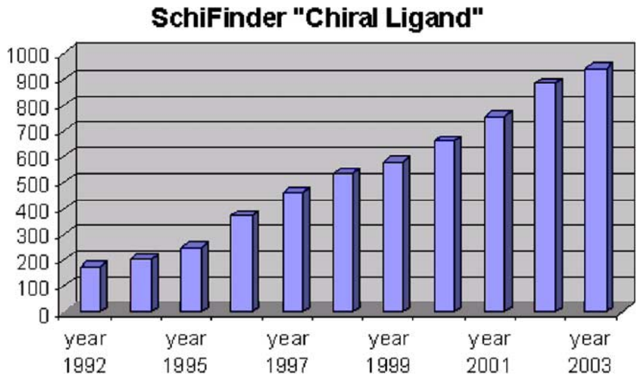

Figure 1.

There are no universal ligands and catalysts for asymmetric transformations. Many reactions are substrate-dependent and hence there are compelling reasons to develop new ligands tailor-made to specific reaction types. For practical reasons, ligands have to be able to be prepared easily, preferably in both enantiomeric forms. Catalysts derived from them should be both active and enantioselective.

The pioneering work in asymmetric hydrogenation by Knowles, Kagan and Noyori has been recognized with the Nobel and Wolf Prizes. Introduction of chiral phosphorus ligands is the key for their work. Many pharma companies (Aventis, Merck, Roche, and Pfizer), a variety of fine chemical companies (Bayer, BASF, Chemi, Degussa, Dow, DSM, Eastman, Great Lake, PPG-sipsy, Rhodia, and Takasago), several technology-service and metal companies (Chiral Quest, DHC-a division of Degussa, Johnson Matthey, Solvias, and Umicore) have developed commercial chiral phosphorus ligands or use them for practical applications. Several of these companies are represented in the special issue.

This special issue begins with several excellent reviews that summarize the state of the arts in the field in select areas. Development of chiral monodentate phosphorus ligands is discussed by Renaud and Bruneau. There is a strong demand and great reward in making effective ligands for asymmetric hydroformylation and Dieguez's review suggests many good directions. Landis' scholarly investigations on the development of chiral phospholane chemistry surely will inspire further interest in the community. Finally, Heller has examined structural information of metal–ligand complexes and relates them to asymmetric catalysis.

Alexakis et al. describe biphenol-based ligands for asymmetric conjugate addition. Boaz outlines more applications of the BoPhoz ligands. Consiglio's group highlight a novel approach for asymmetric Pauson–Khand reactions. Hoge's *P*-chirogenic bisphospholane represents a small portion of Pfizer's efforts on developing practical phosphine ligands for making pharmaceutical products. Lee has found a route to homoproline derivatives. Imamoto, reports a new set of chiral *P*-cyclic phosphines that are effective in asymmetric hydrogenations. Lemaire's special BINAP analog has been used for hydrogenations in ionic liquids. Minnaard, Feringa and de Vries's joint efforts on using chiral secondary phosphine oxides ligands are also communicated. Agbossou–Niedercorn's describes some *P*,*N*-ligands that have been used for hydrogenation of imines, a challenging area in asymmetric hydrogenation chemistry. Reetz, an original player in developing chiral monodentate phosphites, has applied a combinatorial approach for asymmetric hydrogenation and insightful results have been achieved. Saito and colleagues at Takasago have mapped the location of the key enantiodetermining space-filling groups and this has helped them to design ligands. In Zhang's three papers, conformational rigidity and metal–ligand conformations have been investigated. *ortho*-Substituted ligands have been prepared. Zhou has made a major contribution by introducing the spiro motif in chiral phosphorus ligands and highly

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enantioselectivity has been achieved in asymmetric hydrosilylation. Zhaoguo Zhang created several useful biaryl phosphines and high enantioselectivities are reported for asymmetric hydrogenation.

Cozzi has investigated the HetPhox, a modular chiral ligands, for the transfer hydrogenation and allylic alkylation. Also in the area of asymmetric hydrogenation, Hii reports the use of aminohydroxy phosphine oxide ligands containing stereogenic centers on carbon and phosphorus. Dieguez and Ruiz report asymmetric hydrogenation with furanoside diphosphinites. Genet and Marinetti have systematically explored heterotopic atropisomeric diphosphines and their applications in asymmetric hydrogenation and conjugate addition. Hou has created a new set of *P*,*N*-ligands and applied them for asymmetric Heck reaction. Ito and Kuwano have used TRAP ligands for asymmetric reductions. Li, Yeung and Chan introduce sets of phosphine–phosphinites, phosphoramidites, and phosphite ligands. Chan's group leads the way of chiral ligand development for asymmetric hydrogenation. Knochel, the father of MandyPhos and Taniaphos, continues his focused effort for making practical ligands from pinene-derivatives. Mezzitti et al. have found an efficient way for asymmetric cyclopropanation of alkenes using Ru-monodentate phosphoramidite complexes. Sannicolo's process work on chiral γ-lactones with his biaryl ligands is very practical. Splindler's paper on profiling of the Mandyphos and Taniaphos ligand families sets high standards in the field. Tongi and Pugin's work on silicagel-supported chiral biaryl-bisphosphine ligands addresses some of the problems in catalyst-immobilization, a remaining challenge in the field.

In conclusion, the development of effective chiral phosphorus ligands is challenging, requires imaginative approaches, and can be a rewarding intellectual exercise. I hope that this special issue conveys these thoughts.

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