Recent Advances in the Synthesis of P(III)-Chirogenic Compounds

M. J. Johansson and N. C. Kann*

Dept. of Chemistry and Bioscience, Chalmers University of Technology, SE-41296 Göteborg, Sweden

Abstract: Chiral phosphorus(III) ligands with chirality residing on the phosphorus atom have seen a renaissance upon the discovery that coordination to boron stabilises the phosphorus atom towards both oxidation and racemization. In this review we describe the newer methods that are available for the preparation of P-chirogenic ligands and discuss their advantages and limitations.

Keywords: Phosphorus, ligand, P-chirogenic, borane, chiral, asymmetric synthesis.

1. INTRODUCTION

Since it was discovered by Horner [1] that phosphorus with non-equivalent substituents can be chiral in its (III), (IV) and (V) oxidation states, much effort has been made towards developing procedures for the preparation of P-chirogenic phosphorus compounds. During the last decade the development of chiral phosphorus-containing ligands has been enormous, mainly because of the great breakthrough in developing new methods to prepare such compounds, but also due to the growing demand from the pharmaceutical, agrochemical and fine chemicals industry to be able to produce enantioenriched compounds in both a cost as well as atom efficient way [2]. There are excellent reviews dealing with ligands in asymmetric synthesis, [3-5] but only a few have emphasised the actual preparation of P-chirogenic compounds [6-8]. The development of P-chirogenic ligands, in particular, has emerged as an important task due to the great effectiveness of these ligands in homogenous asymmetric catalysis [9-11]. Historically, however, the chirogenic centre has in most cases been situated on the carbon skeleton surrounding phosphorus. Knowles [12-14] and Horner [15] changed and pioneered the work of P-chirogenicity by their early reports on asymmetric hydrogenation using P-chirogenic ligands.

Oxidation has been a major obstacle when working with trivalent phosphorus. Alkyl-substituted phosphines oxidise readily in air, making elaboration and handling of such compounds tedious. Formerly, this was solved by performing the steps needed to induce asymmetry at the pentavalent state and then, towards the end of the sequence, reducing the phosphorus atom back to its trivalent state. The major problem with the above mentioned strategy is partial or complete racemisation during the reductive step. Therefore, other ways of protecting phosphorus from oxidation had to be considered. The development started with Schmidbaur [16] in the early 1980s, who used P-borane complexes to both protect as well as activate the phosphorus atom. Borane complexed with phosphorus meets most demands one can require from a protecting group, i.e. the borane-phosphorus complex is easy to form and borane is easily removed under specific basic or acidic conditions. The normal hydroborating activity of BH_3 is lost while complexed to phosphorus. The P-borane complex is compatible with a great variety of reaction conditions, thus allowing the development of many new synthetic procedures for P-chirogenic phosphines. Moreover, since Imamoto and coworkers showed the potential of P-borane complexes as valuable precursors in phosphorus chemistry [17], the number of publications involving trivalent phosphorus has increased steadily. The use of strong acids to form P-chirogenic trialkylphosphonium [18] salts has been published recently; this will form a complement to already established protecting groups.

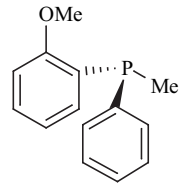
In this review, we describe how P-chirogenic phosphines can be obtained. Focus is on optically active phosphorus compounds with non-equivalent carbon substituents, but also heteroatom-substituted phosphines are briefly considered. The different methodologies are evaluated considering scope and limitations. Literature from 1997 to 2003 is considered, but earlier fundamental papers are also summarised and included.

2. CHIRAL AUXILIARIES

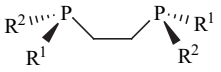
One of the most cited methods for preparing P-chirogenic phosphines is that developed by Jugé *et al*. using (-)-ephedrine [19] as a chiral auxiliary, in combination with the use of borane as a protecting group [20-24]. Bis(diethylamino)phenylphosphine was treated with (-)-ephedrine (**1**) and borane-dimethylsulfide to form a stable crystalline oxazaphospholidine borane (**2**), which could be used as a precursor for a number of different chiral phosphines (Scheme **1**). Treatment of (**2**) with one equivalent of an alkyl or aryl lithium reagent displaced the oxygen of the (-)-ephedrine-moiety with retention of configuration yielding (**3**). Acidic methanolysis gave phosphinite (**4**) with inversion, and treatment with another equivalent of lithium reagent introduced a second alkyl or aryl group also with inversion of configuration, with the formation of the desired borane-protected phosphine (**5**). Instead of methanolysis, treatment with hydrogen chloride can also be used, resulting in the corresponding

*Address correspondence to this author at the Dept. of Chemistry and Bioscience, Chalmers University of Technology, SE-41296 Göteborg, Sweden; Tel.: +46-31-7728212; Fax: +46-31-7723657; E-mail: kann@chembio.chalmers.se

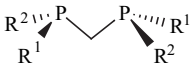
1570-193X/04 $45.00+.00



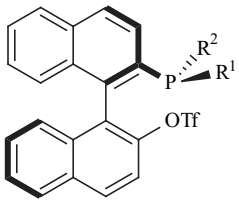
J. Chem. Soc., Chem. Commun. **1972**, 10



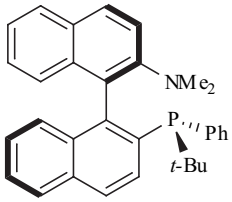
J. Am. Chem. Soc. **1998**, 1635



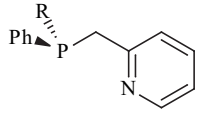
J. Org. Chem. **1999**, 2988



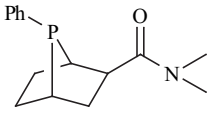
Tetrahedron Lett. **2003**, 8461



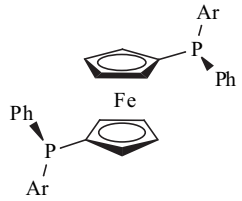
Org. Lett. **2002**, 999



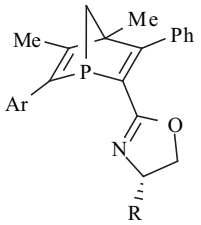
Organometallics **1997**, 2089



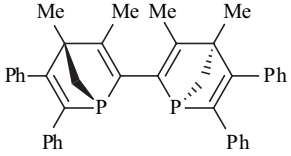
Chem. Commun. **1996**, 591



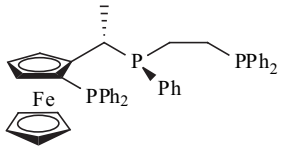
Tetrahedron: Asymmetry **1997**, 3185



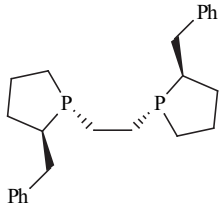
Org. Lett. **2000**, 2885



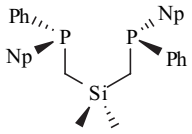
Chem. Eur. J. **1997**, 1365



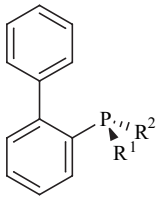
Chem. Commun. **2002**, 2672



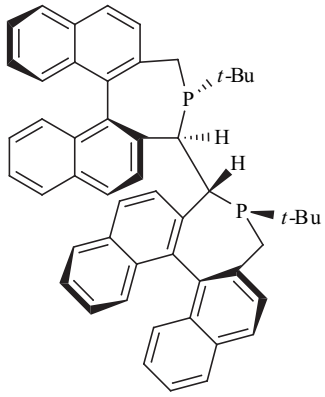
J. Am. Chem. Soc. **2003**, 10219



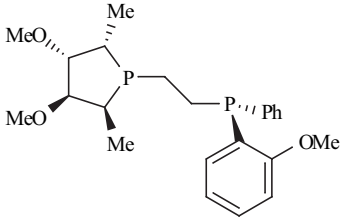
Organometallics **1998**, 668



Synlett. **2001**, 999



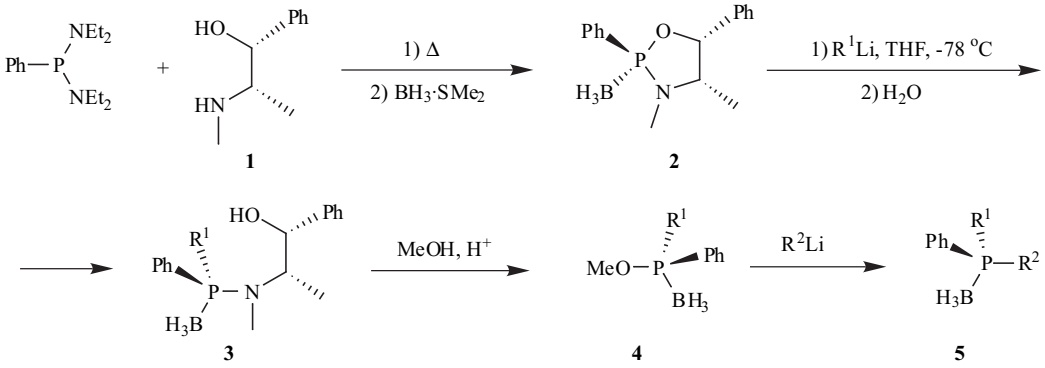
Angew. Chem. Int. Ed. **2002**, 1612



Chem. Commun. **1999**, 261

Angew. Chem. Int. Ed. **2003**, 3509

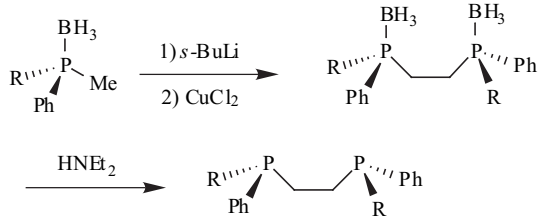
Fig. (1). A selection of P-chirogenic ligands.



Scheme 1. Preparation of P-chirogenic phosphines using (-)-ephedrine as a chiral auxiliary.

chlorophosphine borane, which can be reacted in the same way with lithium reagents [25, 26]. Grignard reagents can be used instead of organolithium reagents.

One advantage with this method is that the other enantiomer of the phosphine can be accessed simply by changing the order of addition of the two lithium reagents. This was demonstrated in the preparation of both (*R*)- and (*S*)-PAMP. Several chiral diphosphines were also prepared by deprotonation followed by oxidative coupling with $CuCl_2$ and subsequent removal of the borane group with diethylamine (Scheme **2**) [22].



Scheme 2. Cu(II)-mediated dimerisation of P-chirogenic monophosphines.

The ephedrine-based methodology has subsequently been applied by many research groups in the preparation of a number of different chiral phosphines. Brown and coworkers prepared both enantiomers of diphosphine (**6**) [27], as well as bulky monophosphines of the type (**7**) [28]. In the latter case, best results were achieved if the bulky substitutent was introduced late in the synthetic sequence. Yang *et al.* [29] explored the bonding properties of P-chirogenic bidentate ligands (**8**) towards rhodium, where the ligand was prepared using ephedrine.

Mezzetti and coworkers obtained chiral diphosphines with a silyl-backbone (**10**) *via* the reaction of (**2**) with organolithium reagents, followed by treatment with dimethylsilyldichloride (Scheme **3**) [30]. They also prepared diphosphines with bulky substituents, (**9**), using (-)-ephedrine as a chiral auxiliary [31].

Chiral ferrocenyl mono- and diphosphines have been prepared both by Jugé and others using variations of the ephedrine method [32-36]. In a representative example from the work of Nettekoven *et al*. [34], five different P-chirogenic methoxyphosphine boranes were reacted with 1,1'-dilithioferrocene, followed by treatment with

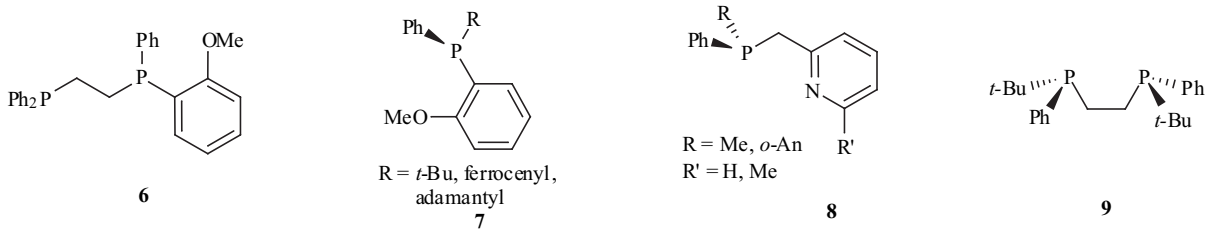
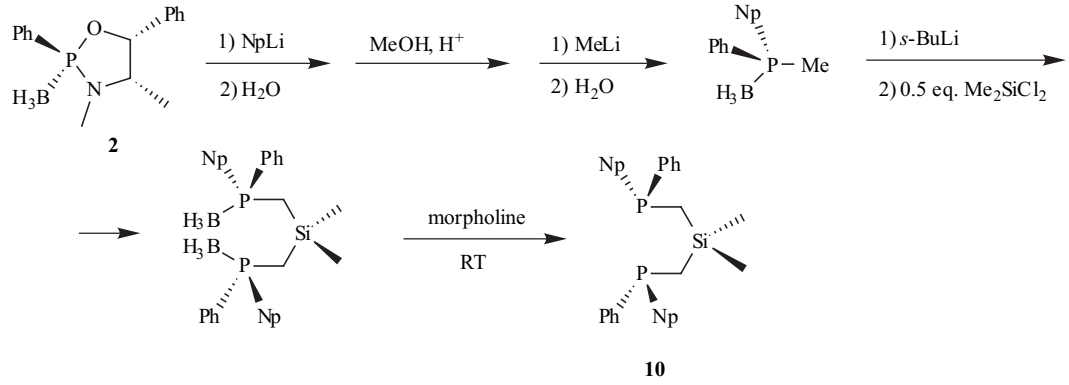
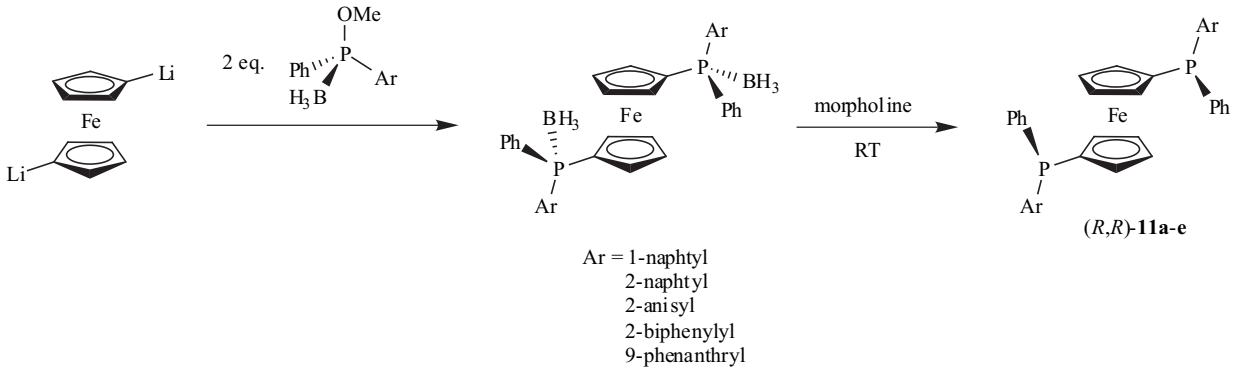


Fig. (2). P-chirogenic phosphines obtained *via* ephedrine-methodology.



Scheme 3. Preparation of diphosphines with a silyl backbone.



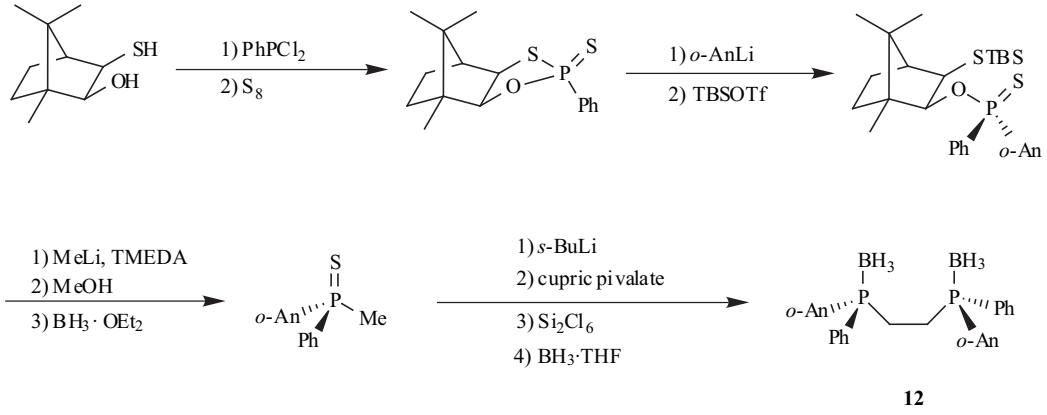
Scheme 4. Ferrocenyl diphosphines.

morpholine to remove the borane groups, forming chiral (*R*,*R*)-ferrocenyl diphosphines of the type (**11**) (Scheme **4**). These ligands were applied in rhodium-catalysed hydrogenation of olefins, as well as in the hydroformylation of alkenes.

Using the same strategy, Mezzetti also prepared two corresponding (*S*,*S*)-ferrocenyl diphosphines, and applied these in the asymmetric hydrogenation of alkenes with good results, although they were found less useful in the asymmetric hydrogenation of ketones [33].

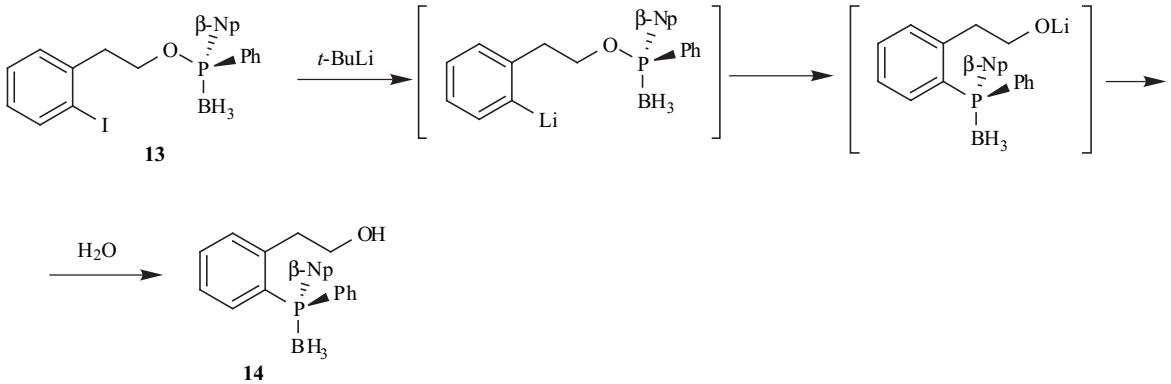
Corey *et al.* have prepared borane-protected (-)-(*R*,*R*)-DIPAMP (**12**) in >99% ee using a camphor-derivative instead of ephedrine as the chiral auxiliary (Scheme **5**) [37].

Two slightly different approaches to P-chirogenic phosphines using chiral auxiliaries have also been reported. Beak and coworkers prepared chiral phosphinite (**13**) using ephedrine methodology (Scheme **6**) [38]. Upon lithiation, phosphinite (**13**) rearranged to phosphine (**14**) with retention of configuration. Jugé has also used a similar rearrangement of phosphinites to make analogues of PAMP [39].

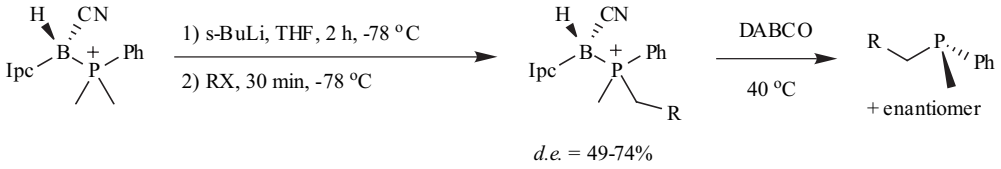


Scheme 5. Preparation of diphosphines using a camphor-based chiral auxiliary.

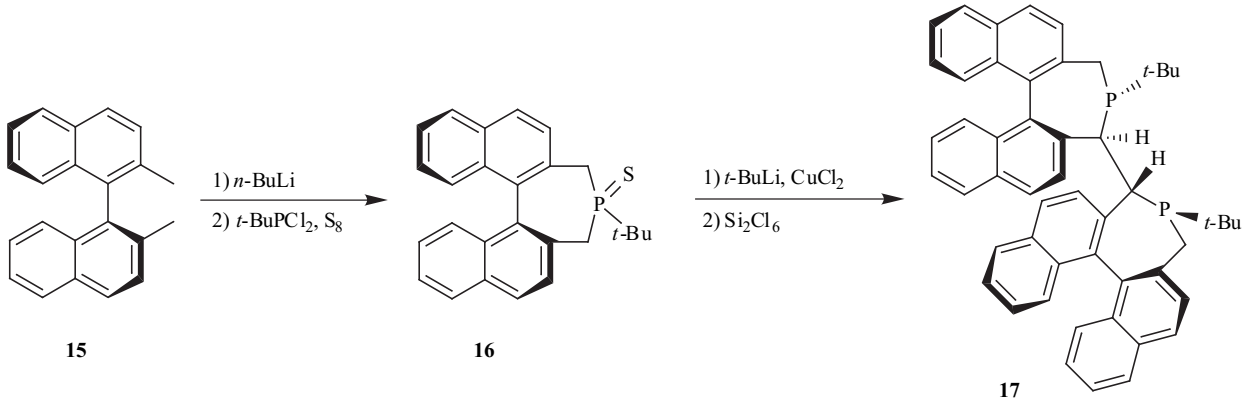
Vedrenne *et al.* used a chiral borane moiety to induce chirality onto phosphorus [40]. Dimethylphenylphosphine, protected with monoisopinocampheylcyanoborane, was treated with base, followed by different electrophiles, yielding diastereomeric products with a diastereomeric excess of up to 74% (Scheme **7**).



Scheme 6. A rearrangement approach to P-chirogenic phosphines.



Scheme 7. Use of a chiral borane to form P-chirogenic phosphines.



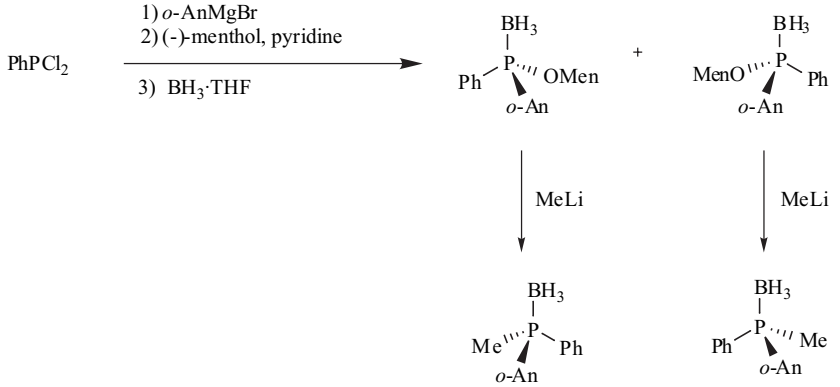
Scheme 8. Preparation of a binapine-ligand.

Recently Tang *et al*. reported the preparation of a bisphosphepine ligand, abbreviated (*S*,*S*,*S*)-binapine, with chirality both on phosphorus and carbon, as well as axial chirality (Scheme **8**) [41]. (*S*)-2,2'-dimethylbinaphthyl (**15**) was converted to (**16**) and then oxidatively coupled with $CuCl_2$ after deprotonation with *t*-BuLi/TMEDA. Desulfurisation was effected with Si_2Cl_6, yielding diphosphine (**17**), which was found to be stable towards oxidation even after exposure to air for several days. Both isomers of binapine could be prepared using this route.

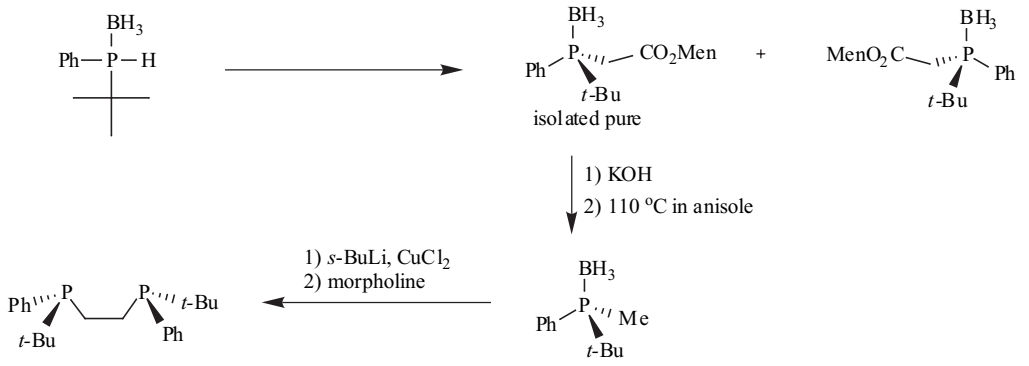
3. SEPARATION OF DIASTEREOMERIC PAIRS

Mislow and coworkers at the end of the 1960's, invented a new route to P-chirogenic phosphine oxides that made P-chirogenic compounds much more accessible. The method is based on the introduction of (-)-menthol as chiral moiety, thus forming a diastereomeric pair of phosphinites [42-44] with different physiochemical properties. Another similar route was subsequently developed by Nudelman [45] wherein both cholesterol and (-)-menthol were used as chiral auxiliaries. Cholesterol, however, does not seem to have the same generality. These fundamental contributions were the basis of more recent phosphorus-borane complex chemistry aimed at P-chirogenity, developed mainly by Imamoto *et al*. In an early paper, they introduced new procedures using (-)-menthol [17]. Phenyldichlorophosphine was sequentially treated with *o*-anisylmagnesium bromide, BH_3·THF and (-)-menthol/pyridine. The diastereomers formed were separated by preparative TLC and obtained in excellent diastereoselectivities (Scheme **9**). Substitution of the menthyloxy-group occurs with inversion of configuration to give the P-chirogenic phosphines.

Another route based on menthol, comprising derivatisation of a secondary racemic phosphine-borane to give methyl-substituted phosphines as final products, was also demonstrated in the same paper. A secondary phosphine-borane was alkylated with (-)-menthyl chloroacetate and the obtained diastereomeric pair was separated by crystallisation. One diastereomer was isolated in stereochemically pure form, hydrolysed and decarboxylated. The resulting methyl-substituted phosphine was then oxidatively dimerised using $CuCl_2$ and *sec*-BuLi to obtain a P-chirogenic diphosphine (Scheme **10**).

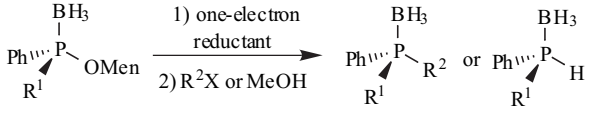


Scheme 9. P-chirogenic phosphines *via* diastereomeric menthoxy-phosphinites.



Scheme 10. Synthesis of diphosphines using menthyl-esters.

In a following paper Imamoto and coworkers describe an investigation of one-electron reducing agents acting on menthyloxy phosphine-boranes [46]. The reduction of the P-O bond in the phosphinite-borane complexes could be accomplished using several different one-electron reducing agents such as lithium naphthalenide, Li-NH_3, lithium 4,4'-di-*tert*-butylbiphenylide (LDBB) and lithium biphenylide (LB).

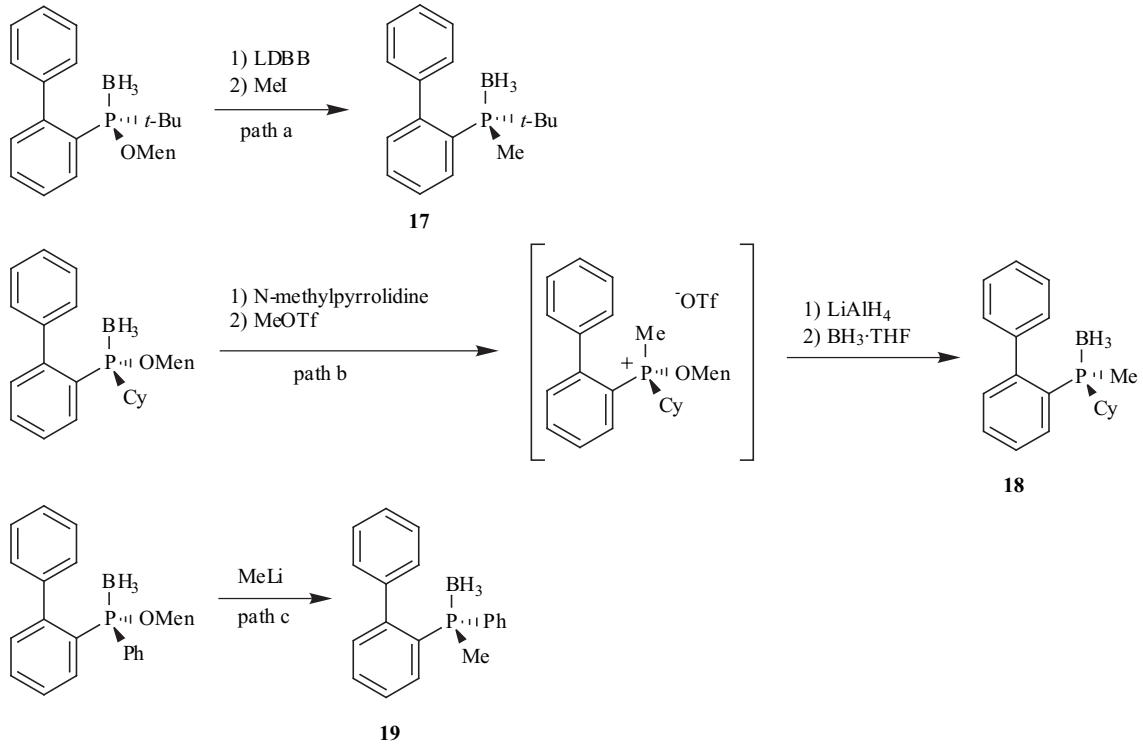


(1)

The tricoordinate phosphorus anion was generated within minutes at -78°C and reacted with an electrophile (BnBr, MeI and MeOH) at the same temperature. Yields were quantitative and all the above mentioned reductants reacted with retention of configuration. Lithium naphthalenide and Li-NH_3 gave a slightly higher ee than LDBB and lithium biphenylide (LB). The phosphorus anion is believed to racemise through pyramidal inversion, and elevated temperatures deteriorate the enantioselectivity.

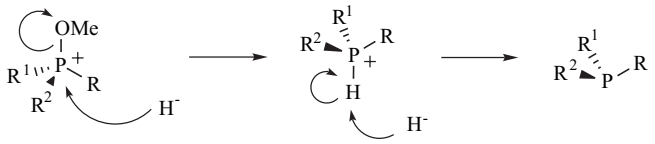
Phosphine ligands bearing a 2-biphenyl group have more recently shown great potential in a variety of reactions [47]. Tsuruta *et al.* reported a procedure whereby P-chirogenic monophosphines bearing a 2-biphenyl group were synthesised utilising the combined menthol and one-electron reduction methodologies (Scheme **11**) [48].

After preparation and separation of the three diastereoisomeric pairs of phosphinites with different substituents (*t*-Bu, Cy and Phe), a different way of introducing the methyl group had to be used in each case. In the *t*-Bu case (Scheme **11**, path a), a one-electron reduction followed by alkylation using methyl iodide, afforded the desired phosphine (**17**) in moderate ee, but after recrystallisation enantiopure material was obtained (72%, 75% ee, >99% after recrystallisation). Surprisingly, the analogous cyclohexyl derivative gave almost complete racemisation using the route outlined above, probably due to



Scheme 11. Biphenyl-substituted monophosphines.

stereomutation in the reductive step. Instead another route was employed (Scheme **11**, path b), where the starting phosphonite was deboranated and quaternised using MeOTf. The tetravalent species was reduced using $LiAlH_4$ and reprotected with BH_3·THF to facilitate the isolation of the P-chirogenic phosphine (**18**) in good yield and excellent enantioselectivity (73%, 97% ee). The procedure above originates from a paper by Imamoto and coworkers [49] where phosphine oxides are reduced stereospecifically by the use of a methylating reagent followed by reduction using $LiAlH_4$. The mechanism of the reduction is outlined below.

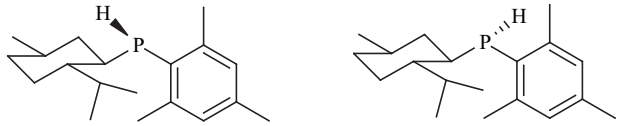


Scheme 12. Mechanism of the reduction with $LiAlH_4$.

To form ligand (**19**), a third route was employed (Scheme **11**, path c). The phosphinite was treated with methyl lithium to give the protected phosphine directly in excellent yield and selectivity (90%, 94% ee, >99% ee after recrystallisation). In this case, the reaction proceeds at 40 °C with complete inversion of configuration. As this route was superior in the case of a phenyl substituent, it was also evaluated for the alkylsubstituted phosphinites but with minor success as the substrates did not react or gave several products at reflux in THF.

Bader *et al.* used a somewhat modified menthol procedure to make (**20a**) and (**20b**) (Fig. (**3**)) [50]. Instead of using menthol as a temporary chiral auxiliary, (-)-menthylmag-nesium chloride was added to mesityldichlorophosphine. The resulting reaction mixture of diastereomers, epimeric at phosphorus was then treated with $LiAlH_4$ to give menthylmesitylphosphine in 48% overall yield after seven recrystallisations, using Na(acac) in acetonitrile. However, upon liberation of the free phosphine, epimerisation at the phosphorus centre occurred. The focus was then turned to the corresponding borane complex, which turned out to be more amenable to separation. Fractional crystallisation afforded one of the diastereomers in 97% de, which could be deboranated with diethylamine. The secondary phosphine was reported to be stable towards epimerisation for at least a week at room temperature.

Another elegant approach was taken by Vedejs *et al*. who synthesised a menthyl substituted tertiary phosphine, 9-fluorenylmenthylphenylphosphine (**21**), epimeric at phosphorus [51]. The diastereomeric pair was then subjected to a crystallisation-induced asymmetric transformation, i.e. the crystallisation was carried out by heating the mixture at reflux in heptane and slowly evaporating the solvent. This procedure resulted in a final diastereomeric ratio of 20:1. After borane protection of the phosphine, the fluorenyl substituent was removed in a stereospecific fashion, using lithium naphthalenide. The resulting anion was reacted with electrophiles to give tertiary phosphine-boranes (**22**) with total stereospecificity (>99% de) (Scheme **13**).

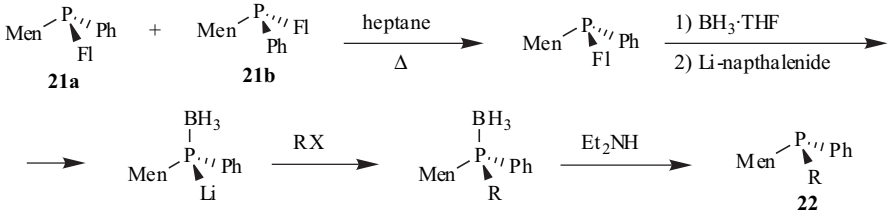


20a **20b**

Fig. (3). Menthyl-based P-chirogenic ligands.

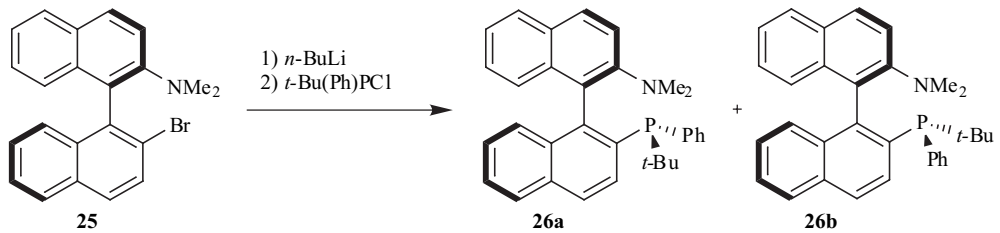
Yet another approach was taken by Brown and coworkers [52] who wanted to combine the best of two worlds. Knowles' PAMP [53], combined with Burk's BPE or DuPHOS [54-56] would together form an interesting bidentate ligand, where the phosphorus moiety would potentially have different functions in a hydrogenation reaction [43, 47]. Starting from a racemic anisylphenyl-phosphine-borane complex, performing a conjugate addition with diethylvinylphosphate followed by an alane reduction (aluminium hydride) afforded the corresponding primary phosphine (**23**) (Scheme **14**). Phosphine (**23**) was then reacted with a cyclic sulphate to form the diphosphines (**24**) using the procedure of Burk *et al.* [56]. The diastereomeric diphosphines obtained were then separated using MPLC to give the pure diastereomers. The hybrid ligands were used in the asymmetric hydrogenation of itaconate esters with good results.

In all earlier examples, auxiliaries with stereogenic carbon centres have been utilised. In a recent example by Hamada and Buchwald, axial asymmetry was employed in order to obtain a separable diastereomeric pair [57]. In Reaction (2), the synthetic route is outlined to the hybrid bidentate ligand comprising both axial as well as P-chirogenicity. In the synthesis, (**25**) is treated with

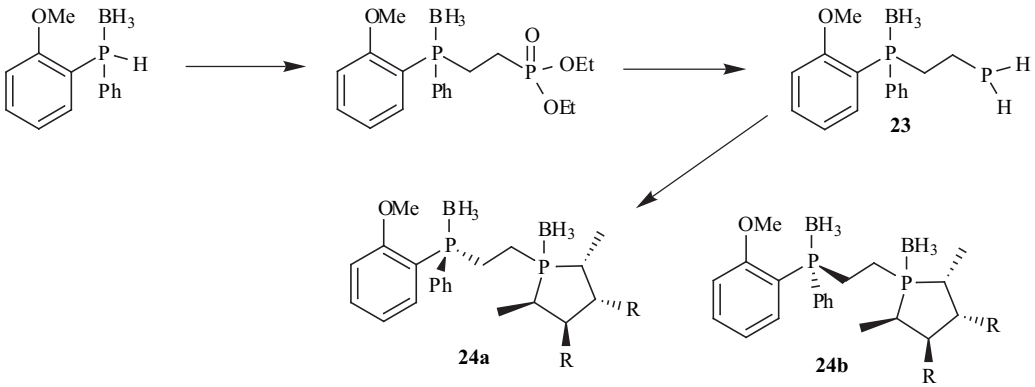


21a **21b** **22**

Scheme 13. Crystallisation-induced asymmetric synthesis of phosphines.



25 **26a** **26b** (**2**)

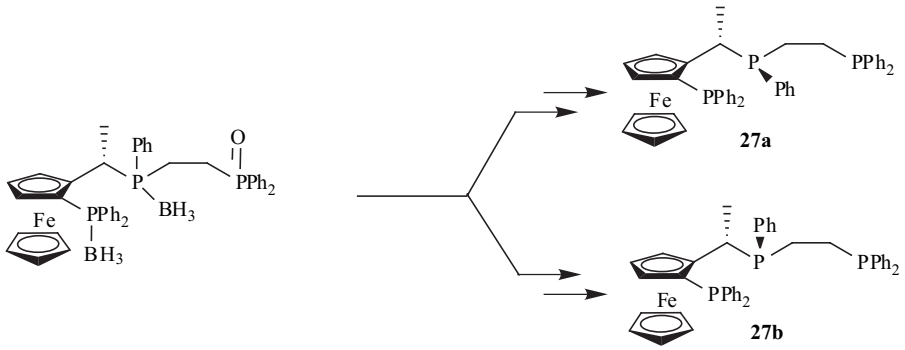


Scheme 14. Preparation of P-chirogenic diphosphines for asymmetric hydrogenation.

butyllithium whereafter the formed aryllithium is trapped with racemic *tert*-butylphenylchlorophosphine to give the diastereomeric pair of phosphines (**26**). The R_P enantiomer was isolated stereochemically pure after crystallisation in 12% yield. The residual solution containing both R_P and S_P was subsequently treated with BH_3·THF to furnish the corresponding phosphine-boranes, and the diastereomers were separated by chromatography. Deprotection was accomplished using triflic acid followed by KOH. The Noteworthy is that all attempts to use any silane derivative for the reduction resulted in P-epimerisation.

4. CHEMICAL RESOLUTION AND RESOLUTION *VIA* CHROMATOGRAPHY

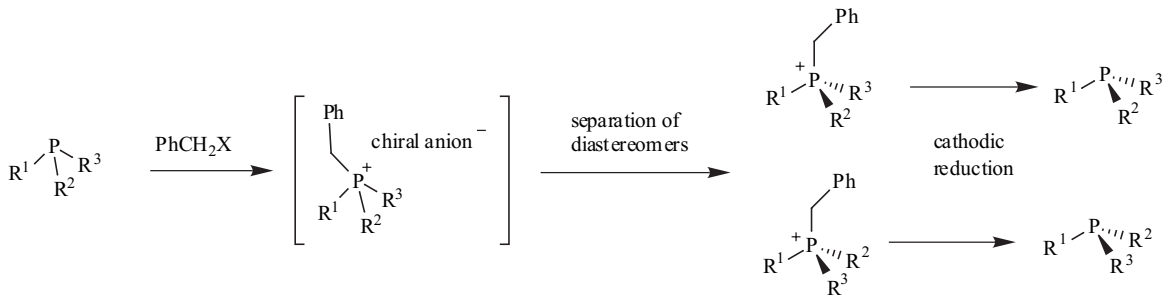
The use of resolving techniques for the preparation of P-chirogenic compounds has a long history, dating back to



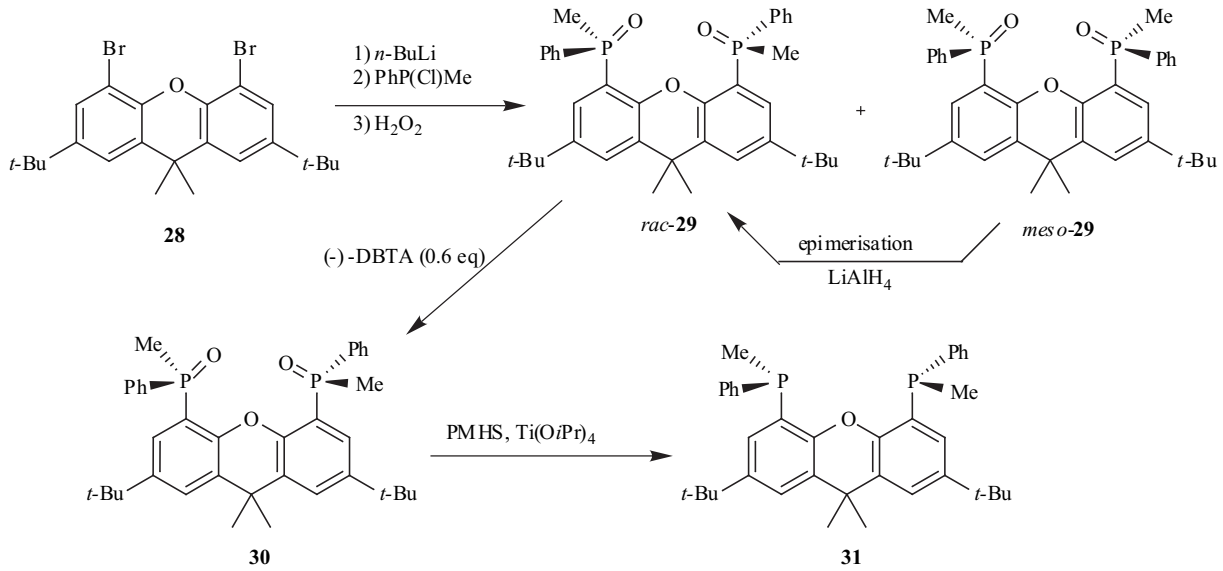
Scheme 15. Tridentate phosphine ligands.

phosphines were used in Pd-catalysed asymmetric enolate vinylation and arylation reactions.

Tridentate ligands for a long time have been stated as interesting compounds for homogeneous catalysis [58-60]. Barbaro *et al.* have in an elegant way shown a route to highly functionalised tridentate phosphines (**27**), where phosphorus, carbon and planar chirality exist in the same ligand (Scheme **15**) [61]. The approach is again based on the preparation and separation of a diastereomeric pair. The phosphine oxide is reduced using $CeCl_3/NaBH_4$, $LiAlH_4$ in THF, followed by deboranation using morpholine. 1911, when Meisenheimer resolved a racemic mixture of a phosphine oxide [62]. Almost fifty years later, Kumli *et al.* prepared the first P-chirogenic diastereomeric phosphonium salt using silver *d*-(-)-dibenzoyl hydrogen tartrate and *l*-(+)-dibenzoyl hydrogen tartrate respectively [63]. Another complementary method used benzylbromide to quaternise a tertiary phosphine, followed by the formation of diastereomeric pair using tartaric acid [43]. After separation, the chiral quaternary benzyl phosphonium salts could be reduced using a mercury cathode yielding tertiary phosphines in good yields, and with retention of configuration (Scheme **16**).



Scheme 16. P-chirogenic phosphines *via* resolution.



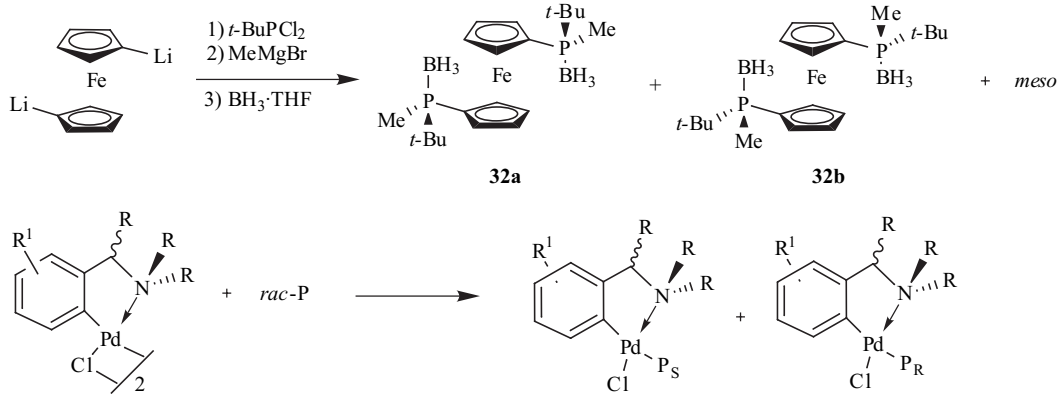
Scheme 17. Preparation of a P-chirogenic diphosphine *via* resolution.

Hamada *et al.* resolved a diphosphine obtained *via* transmetallation of aryl dibromide (**28**) using *n*-BuLi, followed by substitution using chloromethylphenylphosphine and oxidation to the corresponding phosphine oxide [64] (Scheme **17**). The obtained mixture contained *rac*-(**29**) and *meso*-(**29**). The latter, however, readily epimerised to the corresponding *rac*-(**29**) under reductive conditions, and the mixture was resolved using (*R*,*R*)-(-)-dibenzoyl-tartaric acid ((-)-DBTA, 0.6 eq), yielding (+)-(**30**) in 37% yield (99.6% ee). The enantioenriched mother liquor was then treated with ammonia, followed by salt formation using (+)-DBTA to afford (-)-(**30**)·(+)-DBTA in comparable yield and selectivity. The free phosphine oxides were liberated using ammonia and reduced with titanium tetraisopropoxide and polymethyl hydroxysilane (PMHS) with complete retention of configuration at phosphorus to form diphosphine (**31**).

Imamoto and coworkers used a similar approach in their synthesis of P-chirogenic 1,2-bis(isopropylmethylphosphino)benzene [65].

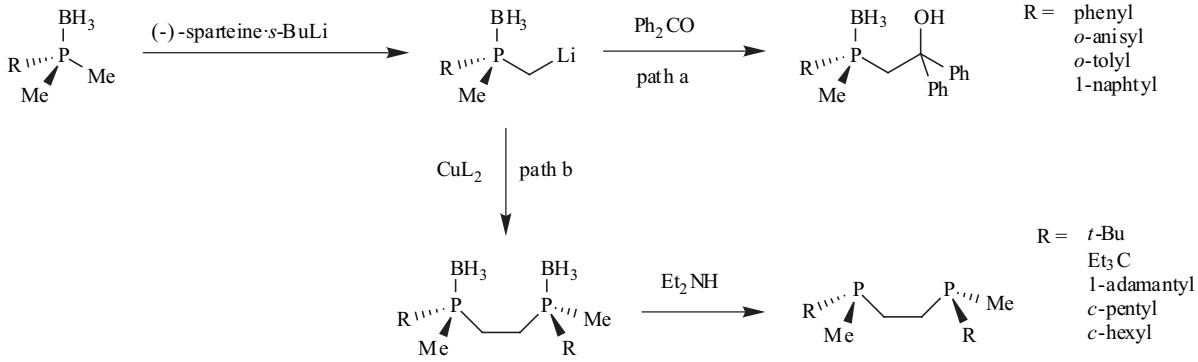
The use of a chiral stationary phase in a HPLC column is probably the most convenient and time-efficient method to resolve an enantiomeric pair of phosphine-boranes or phosphine oxides. Methods used for enantiomeric excess determinations using chiral stationary phases in HPLC can often be transferred directly to preparative scale. Tsuruta and Imamoto successfully used preparative chiral HPLC in order to resolve 1,1'-bis[(*t*-butyl)methyl-phosphino]ferrocene (Reaction **3**) [66]. After the first steps, *rac*-(**32**) was formed in 50% along with 10% of the *meso*-compound. The enantiomers were resolved and separated using a semi-preparative Daicel Chiralpak AD column.

By complexing a racemic mixture of a phosphine with an optically active metal-containing coordination complex, a diastereomeric pair is formed. The first reported resolution of a phosphine using a chiral metal complex dates back to 1968 [67], when a platinum/(+)-dehydroxyephedrine system was used to resolve *rac*-methylphenyl-*tert*-butyl phosphine into its two antipodes. The rationale behind this successful method has ever since gained a lot of interest. In this paper, however, it will be very briefly summarised due to the large number of publications in the area and we therefore refer to an excellent review on the subject [68]. In recent years mainly *ortho*-metallated metallacycles have been used to accomplish resolution and asymmetric synthesis. In Reaction (**4**), the principle of resolution using orthometalated metallacycles is shown [69-74]. The same type of metallacycle can also function as a chiral auxiliary in the enantioselective preparation of chiral phosphines [73, 75-81].



(**3**)

(**4**)



Scheme 18. Asymmetric deprotonation of prochiral phosphine boranes.

5. ENANTIOSELECTIVE DEPROTONATION

Enantioselective deprotonation using a chiral amine-alkyllithium complex can be used to differentiate between two prochiral sites in a *meso* compound or to selectively deprotonate only one enantiomer of a racemic mixture [82-84]. Muci *et al*. [85] were the first to apply this technique to the preparation of P-chirogenic phosphines. Dimethylaryl-phosphine-boranes were enantioselectively deprotonated using (-)-sparteine·*sec*-butyllithium and the anion subsequently trapped with benzophenone, yielding chiral borane-protected tertiary phosphines in high yield and 79-87% ee (Scheme **18**, path a). Oxidative coupling of the intermediate chiral anions with copper(II) pivalate, was also carried out, giving chiral diphosphines in 96-99% ee, contaminated with small amounts of the meso diastereomer. The latter could be removed by chromatographic purification and the diphosphines could be enriched to >99% ee by recrystallisation. Deprotection of the phosphine-borane complexes to afford the pure phosphines was effected by heating in diethylamine.

Using a similar technique Imamoto *et al.* prepared P-chirogenic dialkyl-substituted disphosphines, abbreviated BisP* (Scheme **18**, path b), and applied these to rhodium-catalysed enantioselective hydrogenation [11, 86]. Unsymmetrical BisP* ligands were also synthesised by Imamoto and coworkers and studied in detail in enantioselective hydrogenation [87, 88], and recently a symmetrical ferrocenyl-substituted diphosphine ligand was prepared by the same group giving good results in palladium-catalysed asymmetric allylic alkylation [89].

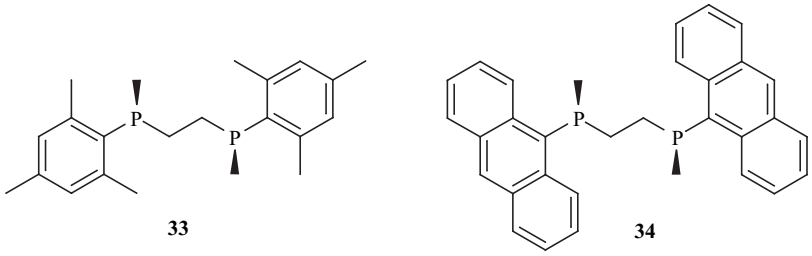
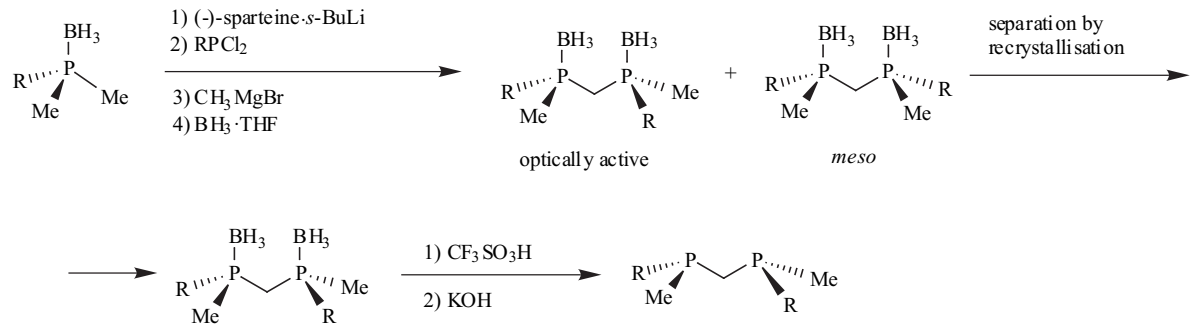


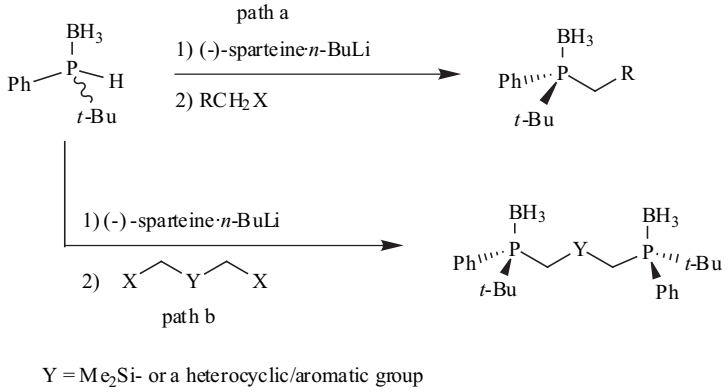
Fig. (4). BisP*-type diphosphine ligands with bulky substituents.

Mezzetti and coworkers prepared mixed aryl-alkyl diphosphines of the BisP*-type containing bulky aryl groups (Ar = mesityl, anthranyl), using the (-)-sparteine-*sec*-butyllithium methodology and yielding diphosphines (**33**) and (**34**) in 37% and 18% ee respectively (Fig. (**4**)) [31].

Imamoto and coworkers have also prepared methylene-bridged diphosphines, named MiniPHOS ligands, using a slightly different reaction sequence (Scheme **19**, R = *i*-Pr, *c*-C_6H_{11}, *t*-Bu, Ph) [90]. After the initial desymmetrisation step, the lithium anion intermediate was treated with an alkyl- or aryl phosphine dichloride, followed by MeMgBr



Scheme 19. Imamoto's MiniPHOS ligands.



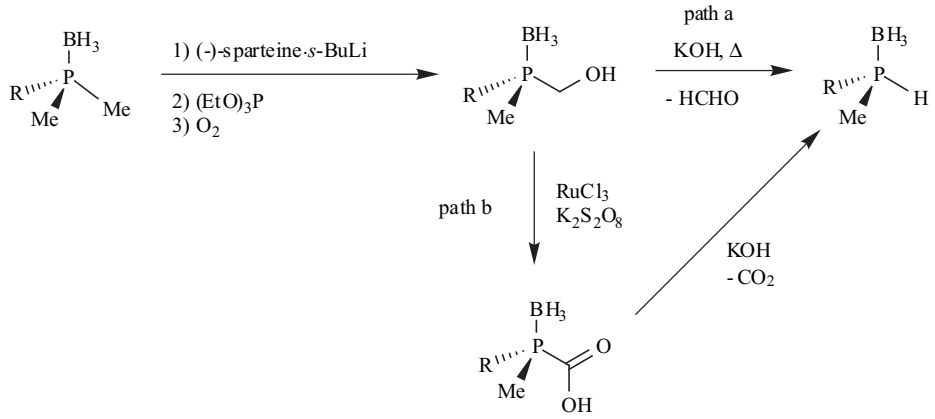
Scheme 20. Dynamic resolution of secondary phosphine boranes.

and BH_3·THF, forming a 1:1 mixture of the optically active diphosphine and the corresponding meso compound. Separation by recrystallisation, followed by deprotection using trifluoromethanesulfonic acid and potassium hydroxide in sequence, gave the desired MiniPHOS derivatives. These were tested in three different types of asymmetric organometallic transformations: Rh-catalysed hydrogenation of dehydroamino acids, hydrosilylation of ketones, as well as Michael reactions of diethylzinc with α,β-unsaturated ketones catalysed by copper, with good to excellent results. Hybrid phosphine sulfide ligands have also been prepared and applied in palladium-catalysed asymmetric allylic substitution [91].

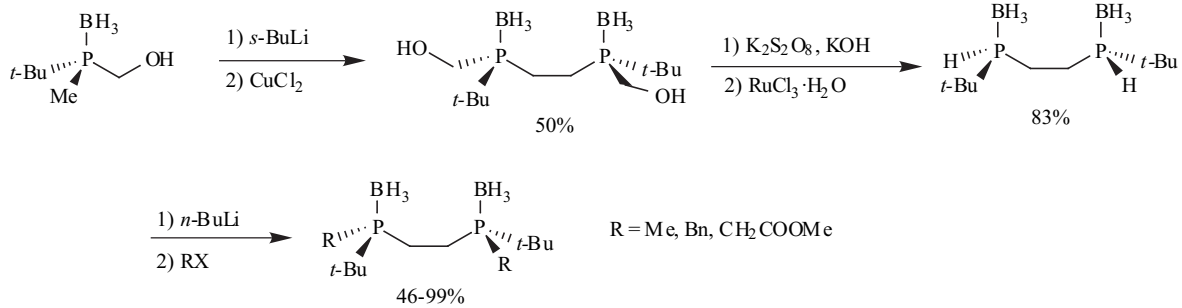
A somewhat different but related approach was taken by Livinghouse and coworkers, who used dynamic resolution of a racemic secondary borane with (-)-sparteine·*n*-butyllithium, followed by treatment with different electrophiles to form enantioenriched tertiary phosphines (Scheme **20**, path a) [92, 93]. By using difunctional electrophiles, bidentate ligands of different types could be prepared (Scheme **20**, path b).

Pincer ligands of this type (Y = *m*-C_6H_4) have been synthesised by both Lebel *et al.* [94] and by Spek and van Koten [95], and similar methodology was also used by Müller and Brand [96] to prepare P-chirogenic phosphine anions in order to study the complexation ability of the thus formed phosphides towards lithium and aluminium.

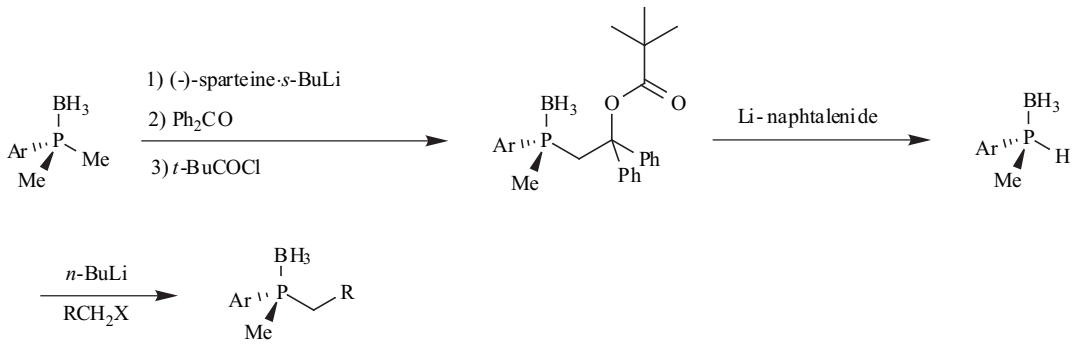
As an alternative to using racemic secondary phosphine-boranes as precursors, the corresponding enantiopure compounds can also be prepared using asymmetric deprotonation, and subsequently alkylated with retention of configuration to form tertiary phosphines. Two different methods for preparing P-chirogenic secondary phosphines have been described. Imamoto employed an oxidation-



Scheme 21. Preparation of P-chirogenic secondary phosphine boranes *via* elimination.



Scheme 22. Preparation of BisP*-type ligands.



Scheme 23. Formation of tertiary phosphines *via* P-chirogenic secondary phosphines.

elimination strategy to prepare secondary mono- and diphosphines in high enantiomeric excess [97]. Asymmetric deprotonation of alkyl/aryl dimethylphosphine-boranes with (-)-sparteine and *sec*-butyllithium, followed by oxidation of the intermediate chiral lithium anion, yielded the corresponding alcohol, which was subsequently deformylated with base (Scheme **21**, path a). This method however, gave either high yields but low stereospecificity or high ee but low yield. Further oxidation of the alcohol by $RuCl_3/K_2S_2O_8$ to form the carboxylic acid (Scheme **21**, path b), followed by elimination with potassium hydroxide in water/acetonitrile, was found to be a more successful method and afforded the desired secondary phosphines in high yield and excellent stereoselectivity.

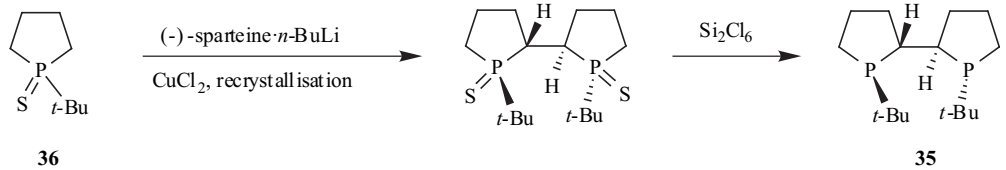
For preparing diphosphines, dimerisation with copper(II)chloride was carried out at the alcohol stage, and the product was then oxidised and decarbonylated in the same manner as earlier (Scheme **22**). Alkylation of the secondary diphosphine with *sec*-butyllithium and electrophiles completed the synthesis of the borane-protected chiral diphosphines [98].

Livinghouse used a somewhat different strategy, also starting with prochiral aryldimethylphosphine-boranes but trapping the intermediate chiral lithium anion with benzophenone, followed by esterification of the resulting alcohol with trimethylacetyl chloride (Scheme **23**) [93]. The intermediate esters were formed in 75-99% ee, but could all be recrystallised to >99% enantiomeric excess at this stage. Reduction with lithium naphthalenide followed by protonation with methanol gave enantiopure secondary phosphine boranes. These were alkylated using *n*-butyllithium and alkyl halides, forming tertiary mono- or diphosphine-boranes. After deprotection, the diphosphines were utilised in Rh(I)-catalysed [4+2] cycloadditions with modest to good results, depending on the substituents on the phosphine.

Several research groups have used the concept of asymmetric deprotonation in the synthesis of chiral phospholane ligands [99-106]. One of the more interesting members of this class is Tangphos (**35**), a chiral bisphospholane ligand, which has shown excellent results in asymmetric Rh-catalysed hydrogenation [101]. Tangphos is prepared *via* the phosphane sulfide (**36**), which is deprotonated with (-)-sparteine·*n*-butyllithium in the usual manner and subsequently dimerised using copper(II)chloride (Scheme **24**). Removal of the sulphur was effected with hexachlorodisilane.

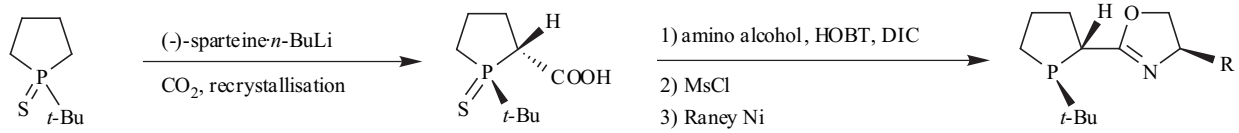
The same research group also developed a new catalyst suitable for Ir-catalysed asymmetric hydrogenation. Instead of a diphosphine, a mixed phosphine-oxazoline catalyst was prepared [102]. Phosphane sulfide (**36**) was again deprotonated and the chiral lithium anion was trapped with carbon dioxide (Scheme **25**). The intermediate chiral acid was coupled with different amino alcohols and subsequently cyclised to the oxazoline in the presence of MsCl. Removal of the thio-function with Raney Ni gave ligands (**37**), which, after coordination to $[Ir(COD)Cl]_2$, were applied in the asymmetric hydrogenation reactions with good to excellent enantioselectivity.

Hoge prepared bisphospholane (**38**), with a two-carbon spacer between the phosphorus atoms, *via* asymmetric



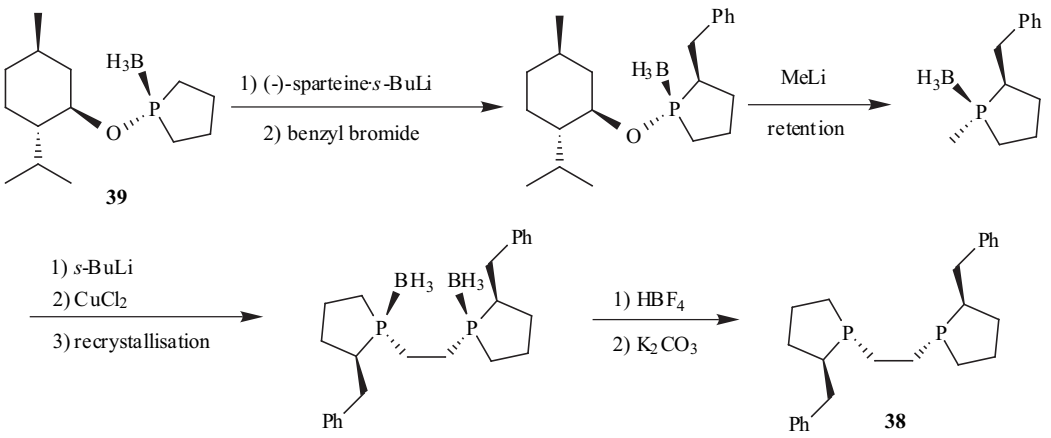
36 **35**

Scheme 24. Preparation of Tangphos.



36 **37**

Scheme 25. Mixed phospholane-oxazolidine ligands.

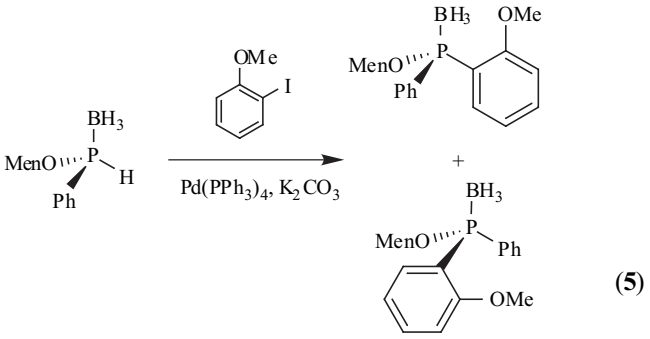


Scheme 26. Preparation of a P-chirogenic bisphospholane.

deprotonation of menthoxy-phosphinite (**39**) with (-)-sparteine and *s*-BuLi, followed by treatment with MeLi and dimerisation with copper(II)chloride (Scheme **26**) [104, 107]. The borane-protected diphosphine was initially formed in 96% ee but could be isolated in >99% ee after recrystallisation. Deprotection with HBF_4 followed by hydrolysis with K_2CO_3 gave the desired (*R*,*R*)-diphosphine enantiomer (**38**). The (*S*,*S*)-enantiomer was also prepared, but a substrate-based strategy was used in this case.

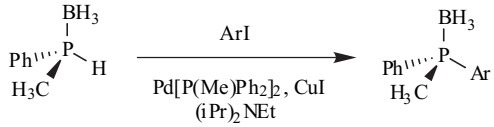
6. PALLADIUM-CATALYSED CARBON-PHOSPHORUS COUPLING REACTIONS

Another approach to P-chirogenic tertiary phosphines is *via* palladium catalysed coupling of secondary phosphines with aryl halides, triflates or nonaflates [108]. Imamoto applied this method in the reaction of menthyl phenylphosphinite-boranes with iodoanisol in the presence of 5 mol % of $Pd(PPh_3)_4$, finding that the reaction could be controlled to give either retention or inversion depending on the solvent used [109]. Using potassium carbonate in acetonitrile, the coupled product was afforded with retention of configuration in a 96% yield, while the same base in THF gave inversion of configuration in a somewhat lower yield (76%).



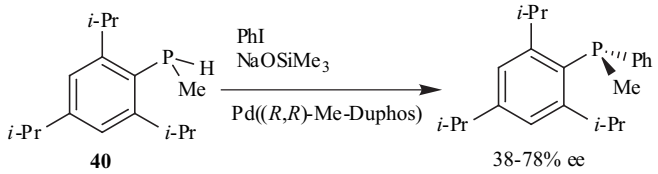
(**5**)

Livinghouse and coworkers used a Pd(0)-Cu(I) cocatalysed system to prepare P-chirogenic phosphines from enantiopure (*S*)-methylphenylphosphine-borane with retention of configuration, the optimum palladium catalyst being preformed $Pd[P(Me)Ph_2]_2$ [110]. One advantage of the cocatalysed system was that the reaction proceeded at much lower temperatures (-10 °C to 0 °C) than those reported earlier [111].



(**6**)

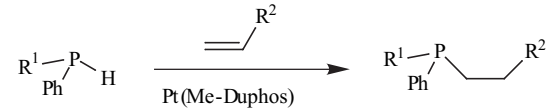
Glueck and coworkers used Pd(*R*,*R*)-Me-DuPHOS as the catalyst in the coupling of racemic (**40**) with phenyl iodide under different reaction conditions, and also used low-temperature ^{31}P NMR to study the mechanism of the reaction [112]. Further studies concerning the stereochemical nature of the reaction in a similar system were discussed in a later report, showing that both the transmetalation step and the reductive elimination proceeded with retention of configuration [113, 114].



40

(**7**)

Glueck and coworkers have also applied transition-metal catalysed methodology in the preparation of several different types of P-chirogenic phosphines. Pt(Me-DuPHOS)-catalysed hydrophosphination was used to prepare phosphines of the type (**41**) [115]. Although the enantioselectivity was rather low, this is an interesting new concept for the preparation of P-chiral phosphines.



rac

R = Is, Mes, *o*-An, Cy, *i*-Bu, Me

R' = CN, CO_2t-Bu

0-22% ee

41

(**8**)

7. CONCLUSIONS AND OUTLOOK

The use of borane as a protecting group has enabled the development of new methodology for the preparation of P-chirogenic phosphines, and many of the new ligands show great promise in different types of asymmetric

transformations. Considering the rapid development within the field, we anticipate a number of new exciting P-chirogenic phosphine ligands appearing the next few years, as well as novel methods for their preparation.

8. ACKNOWLEDGEMENT

The authors gratefully acknowledge the Swedish Foundation for Strategic Research for financial support.

ABBREVIATIONS

acac	=	Acetylacetonate
An	=	Anisyl
Cy	=	Cyclohexyl
BisP*	=	1,2-bis(alkylmethylphosphino)ethane
BPE	=	1,2-bis(phospholano)ethane
DABCO	=	1,4-diazabicyclo[2.2.2]octane
DBTA	=	Dibenzoyl-tartaric acid
DIC	=	Diisopropylcarbodiimide
DIPAMP	=	1,2-bis[(2-methoxyphenyl) phenylphosphine]ethane
DuPHOS	=	1,2-bis(phospholano)benzene
ee	=	Enantiomeric excess
Fl	=	Fluorenyl
HOBt	=	1-hydroxybenzotriazole
Is	=	2,4,6-triisopropylphenyl
LB	=	Lithium biphenylide
LDBB	=	Lithium 4,4'-di-*tert*-butylbiphenylide
Men	=	Menthyl
MeOTf	=	Methyl trifluoromethanesulfonate
Mes	=	Mesityl
MiniPHOS	=	Bis(alkylmethylphosphino)methane
MsCl	=	Methanesulfonyl chloride
Np	=	Neopentyl
o-An	=	*Ortho*-anisyl
OMen	=	Menthyloxy
PAMP	=	2-methoxyphenyl(methyl)phenylphosphine
PMHS	=	Polymethylhydroxysilane
TBSOTf	=	*Tert*-butyldimethylsilyl trifluoromethanesulfonate
TMEDA	=	*N*,*N*,*N*',*N*'-tetramethylethylenediamine

REFERENCES

[1] Horner, L.; Winkler, H.; Rapp, A.; Mentrup, A.; Hoffmann, H.; Beck, P. *Tetrahedron Lett.,* **1961**, 161.
[2] Blaser, H.U. *Chem. Commun.,* **2003**, 293.
[3] Yamanoi, Y.; Imamoto, T. *Rev. Heteroatom. Chem.,* **1999**, *20*, 227.
[4] Brunel, J.M.; Buono, G. *Top. Curr. Chem.,* **2002**, *220*, 79.
[5] Kolodiazhnyi, O.I. *Tetrahedron: Asymmetry,* **1998**, *9*, 1279.
[6] Ohff, M.; Holz, J.; Quirmbach, M.; Börner, A. *Synthesis,* **1998**, 1391.
[7] Quin, L.D. *A Guide To Organophosphorus Chemistry,* John Wiley & Sons: New York, **2000**.
[8] Crepy, K.V.L.; Imamoto, T. *Top. Curr. Chem.,* **2003**, *229*, 1.
[9] Crepy, K.V.L.; Imamoto, T. *Adv. Synth. Catal.,* **2003**, *345*, 79.
[10] Gridnev, I.D.; Higashi, N.; Imamoto, T. *J. Am. Chem. Soc.,* **2000**, *122*, 10486.
[11] Gridnev, I.D.; Yamanoi, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Cat.,* **2001**, *343*, 118.
[12] Knowles, W.S.; Sabacky, M.J. *J. Chem. Soc., Chem. Commun.,* **1968**, 1445.
[13] Knowles, W.S. *Angew. Chem. Int. Ed.,* **2002**, *41*, 1999.
[14] Knowles, W.S. *Adv. Synth. Catal.,* **2003**, *345*, 3.
[15] Horner, L.; Siegel, H.; Buthe, H. *Angew. Chem. Int. Ed. Engl.,* **1968**, *7*, 942.
[16] Schmidbaur, H. *J. Organomet. Chem.,* **1980**, *200*, 287.
[17] Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.,* **1990**, *112*, 5244.
[18] Danjo, H.; Sasaki, W.; Miyazaki, T.; Imamoto, T. *Tetrahedron Lett.,* **2003**, *44*, 3467.
[19] (-)-Ephedrine has earlier been used for the preparation of P-chirogenic pentavalent phosphorous compounds, see: Cooper, D.B.; Hall, C.R.; Harrison, J.M.; Inch, T.D. *J. Chem. Soc., Perkin Trans. 1,* **1977**, 1969.
[20] Jugé, S.; Genêt, J.-P. Organic Phosphorus Compounds Complexed to Boron, Their Preparation and Applications. US Patent 5,043,465, Aug. 27, 1991
[21] Jugé, S.; Stephan, M.; Achi, S.; Genêt, J.P. *Phosphorus Sulfur Silicon Relat. Elem.,* **1990**, *49-50*, 267.
[22] Jugé, S.; Stephan, M.; Laffitte, J.A.; Genêt, J.P. *Tetrahedron Lett.,* **1990**, *31*, 6357.
[23] Jugé, S.; Stephan, M.; Genêt, J.P.; Halutdesportes, S.; Jeannin, S. *Acta Crystallogr. Sect. C-Cryst. Struct. Commun.,* **1990**, *46*, 1869.
[24] Preparation of chiral phosphines using (-)-ephedrine, *via* the corresponding phosphine oxides, was earlier reported by the same research group, see: Jugé, S.; Genêt, J.P. *Tetrahedron Lett.,* **1989**, *30*, 2783.
[25] Moulin, D.; Darcel, C.; Jugé, S. *Tetrahedron: Asymmetry,* **1999**, *10*, 4729.
[26] Bauduin, C.; Moulin, D.; Kaloun, E.B.; Darcel, C.; Jugé, S. *J. Org. Chem.,* **2003**, *68*, 4293.
[27] Ramsden, J.A.; Brown, J.M.; Hursthouse, M.B.; Karalylov, A.I. *Tetrahedron: Asymmetry,* **1994**, *5*, 2033.
[28] Brown, J.M.; Laing, J.C.P. *J. Organomet. Chem.,* **1997**, *529*, 435.
[29] Yang, H.; Lugan, N.; Mathieu, R. *Organometallics,* **1997**, *16*, 2089.
[30] Stoop, R.M.; Mezzetti, A.; Spindler, F. *Organometallics,* **1998**, *17*, 668.
[31] Maienza, F.; Spindler, F.; Thommen, M.; Pugin, B.; Malan, C.; Mezzetti, A. *J. Org. Chem.,* **2002**, *67*, 5239.
[32] Kaloun, E.B.; Merdes, R.; Genêt, J.P.; Uziel, J.; Jugé, S. *J. Organomet. Chem.,* **1997**, *529*, 455.
[33] Maienza, F.; Worle, M.; Steffanut, P.; Mezzetti, A.; Spindler, F. *Organometallics,* **1999**, *18*, 1041.
[34] Nettekoven, U.; Kamer, P.C.J.; van Leeuwen, P.W.N.M.; Widhalm, M.; Spek, A.L.; Lutz, M. *J. Org. Chem.,* **1999**, *64*, 3996.
[35] Nettekoven, U.; Kamer, P.C.J.; Widhalm, M.; van Leeuwen, P.W.N.M. *Organometallics,* **2000**, *19*, 4596.
[36] Colby, E.A.; Jamison, T.F. *J. Org. Chem.,* **2003**, *68*, 156.
[37] Corey, E.J.; Chen, Z.L.; Tanoury, G.J. *J. Am. Chem. Soc.,* **1993**, *115*, 11000.
[38] Tollefson, M.B.; Li, J.J.; Beak, P. *J. Am. Chem. Soc.,* **1996**, *118*, 9052.
[39] Moulin, D.; Bago, S.; Bauduin, C.; Darcel, C.; Jugé, S. *Tetrahedron: Asymmetry,* **2000**, *11*, 3939.
[40] Vedrenne, P.; Le Guen, V.; Toupet, L.; Le Gall, T.; Mioskowski, C. *J. Am. Chem. Soc.,* **1999**, *121*, 1090.
[41] Tang, W.J.; Wang, W.M.; Chi, Y.X.; Zhang, X.M. *Angew. Chem. Int. Ed.,* **2003**, *42*, 3509.
[42] Korpium, O.; Mislow, K. *J. Am. Chem. Soc.,* **1967**, *89*, 4784.
[43] Andersen, N.G.; Ramsden, P.D.; Che, D.Q.; Parvez, M.; Keay, B.A. *Org. Lett.,* **1999**, *1*, 2009.
[44] Lewis, R.A.; Korpium, O.; Mislow, K. *J. Am. Chem. Soc.,* **1967**, *89*, 4786.

[45] Nudelman, A.; Cram, D.J. *J. Org. Chem.,* **1971**, *36*, 335.
[46] Oshiki, T.; Hikosaka, T.; Imamoto, T. *Tetrahedron Lett.,* **1991**, *32*, 3371.
[47] Andersen, N.G.; Ramsden, P.D.; Che, D.Q.; Parvez, M.; Keay, B.A. *J. Org. Chem.,* **2001**, *66*, 7478.
[48] Tsuruta, H.; Imamoto, T. *Synlett.,* **2001**, 999.
[49] Imamoto, T.; Kikuchi, S.-i.; Miura, T.; Wada, Y. *Org. Lett.,* **2001**, *3*, 87.
[50] Bader, A.; Pabel, M.; Willis, A.C.; Wild, S.B. *Inorg. Chem.,* **1996**, *35*, 3874.
[51] Vedejs, E.; Donde, Y. *J. Org. Chem.,* **2000**, *65*, 2337.
[52] Carmichael, D.; Doucet, H.; Brown, J.M. *Chem. Commun.,* **1999**, 261.
[53] Knowles, W.S.; Vineyard, B.D.; Sabacky, M.J. *J. Chem. Soc., Chem. Commun.,* **1972**, 10.
[54] Burk, M.J.; Feaster, J.E.; Harlow, R.L. *Organometallics,* **1990**, *9*, 2653.
[55] Burk, M.J. *J. Am. Chem. Soc.,* **1991**, *113*, 8518.
[56] Burk, M.J.; Feaster, J.E.; Nugent, W.A.; Harlow, R.L. *J. Am. Chem. Soc.,* **1993**, *115*, 10125.
[57] Hamada, T.; Buchwald, S.L. *Org. Lett.,* **2002**, *4*, 999.
[58] Johnson, C.R.; Imamoto, T. *J. Org. Chem.,* **1987**, *52*, 2170.
[59] Burk, M.J.; Feaster, J.E.; Harlow, R.L. *Tetrahedron: Asymmetry,* **1991**, *2*, 569.
[60] Burk, M.J.; Harlow, R.L. *Angew. Chem. Int. Ed. Engl.,* **1990**, *29*, 1462.
[61] Barbaro, P.; Bianchini, C.; Giambastiani, G.; Togni, A. *Chem. Commun.,* **2002**, 2672.
[62] Meisenheimer, J.; Lichtenstadt, L. *Ber.,* **1911**, *44*, 356.
[63] Kumli, K.F.; McEwen, W.E.; Vanderwerf, C.A. *J. Am. Chem. Soc.,* **1959**, *81*, 248.
[64] Hamada, Y.; Matsuura, F.; Oku, M.; Hatano, K.; Shioiri, T. *Tetrahedron Lett.,* **1997**, *38*, 8961.
[65] Miura, T.; Imamoto, T. *Tetrahedron Lett.,* **1999**, *40*, 4833.
[66] Tsuruta, H.; Imamoto, T. *Tetrahedron: Asymmetry,* **1999**, *10*, 877.
[67] Chan, T.H. *J. Chem. Soc., Chem. Commun.,* **1968**, 895.
[68] Wild, S.B. *Coord. Chem. Rev.,* **1997**, *166*, 291.
[69] Albert, J.; Bosque, R.; Cadena, J.M.; Delgado, S.; Granell, J. *J. Organomet. Chem.,* **2001**, *634*, 83.
[70] Albert, J.; Bosque, R.; Cadena, J.M.; Delgado, S.; Granell, J.; Muller, G.; Ordinas, J.I.; Bardia, M.F.; Solans, X. *Chem. Eur. J.,* **2002**, *8*, 2279.
[71] Albert, J.; Bosque, R.; Cadena, J.M.; Granell, J.R.; Muller, G.; Ordinas, J.I. *Tetrahedron: Asymmetry,* **2000**, *11*, 3335.
[72] Dunina, V.V.; Golovan, E.B. *Tetrahedron: Asymmetry,* **1995**, *6*, 2747.
[73] Dunina, V.V.; Kuz'mina, L.G.; Rubina, M.Y.; Grishin, Y.K.; Veits, Y.A.; Kazakova, E.I. *Tetrahedron: Asymmetry,* **1999**, *10*, 1483.
[74] Albert, J.; Cadena, J.M.; Granell, J.R.; Solans, X.; Font-Bardia, M. *Tetrahedron: Asymmetry,* **2000**, *11*, 1943.
[75] Aw, B.H.; Hor, T.S.A.; Selvaratnam, S.; Mok, K.F.; White, A.J.P.; Williams, D.J.; Rees, N.H.; McFarlane, W.; Leung, P.H. *Inorg. Chem.,* **1997**, *36*, 2138.
[76] Aw, B.H.; Leung, P.H.; White, A.J.P.; Williams, D.J. *Organometallics,* **1996**, *15*, 3640.
[77] Aw, B.H.; Selvaratnam, S.; Leung, P.H.; Rees, N.H.; McFarlane, W. *Tetrahedron: Asymmetry,* **1996**, *7*, 1753.
[78] Leung, P.H.; Lang, H.F.; White, A.J.P.; Williams, D.J. *Tetrahedron: Asymmetry,* **1998**, *9*, 2961.
[79] Leung, P.H.; Lang, H.F.; Zhang, X.W.; Selvaratnam, S.; Vittal, J.J. *Tetrahedron: Asymmetry,* **2000**, *11*, 2661.
[80] Leung, P.H.; Loh, S.K.; Vittal, J.J.; White, A.J.P.; Williams, D.J. *Chem. Commun.,* **1997**, 1987.
[81] Song, Y.C.; Vittal, J.J.; Chan, S.H.; Leung, P.H. *Organometallics,* **1999**, *18*, 650.
[82] Beak, P.; Basu, A.; Gallagher, D.J.; Park, Y.S.; Thayumanavan, S. *Acc. Chem. Res.,* **1996**, *29*, 552.
[83] Hoppe, D.; Hense, T. *Angew. Chem. Int. Edit. Engl.,* **1997**, *36*, 2283.
[84] Willis, M.C. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 1765.
[85] Muci, A.R.; Campos, K.R.; Evans, D.A. *J. Am. Chem. Soc.,* **1995**, *117*, 9075.
[86] Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.,* **1998**, *120*, 1635.
[87] Ohashi, A.; Imamoto, T. *Tetrahedron Lett.,* **2001**, *42*, 1099.
[88] Ohashi, A.; Kikuchi, S.-i.; Yasutake, M.; Imamoto, T. *Eur. J. Org. Chem.,* **2002**, 2535.
[89] Oohara, N.; Katagiri, K.; Imamoto, T. *Tetrahedron: Asymmetry,* **2003**, *14*, 2171.
[90] Yamanoi, Y.; Imamoto, T. *J. Org. Chem.,* **1999**, *64*, 2988.
[91] Sugama, H.; Saito, H.; Danjo, H.; Imamoto, T. *Synthesis,* **2001**, 2348.
[92] Wolfe, B.; Livinghouse, T. *J. Am. Chem. Soc.,* **1998**, *120*, 5116.
[93] Heath, H.; Wolfe, B.; Livinghouse, T.; Bae, S.K. *Synthesis,* **2001**, 2341.
[94] Lebel, H.; Berthod, M.; Belanger-Gariepy, F. *Acta Crystallogr. Sect. E., Struct Rep. Online,* **2001**, *57*, o282.
[95] Williams, B.S.; Dani, P.; Lutz, M.; Spek, A.L.; van Koten, G. *Helv. Chim. Acta,* **2001**, *84*, 3519.
[96] Müller, G.; Brand, J. *Organometallics,* **2003**, *22*, 1463.
[97] Nagata, K.; Matsukawa, S.; Imamoto, T. *J. Org. Chem.,* **2000**, *65*, 4185.
[98] Crepy, K.V.L.; Imamoto, T. *Tetrahedron Lett.,* **2002**, *43*, 7735.
[99] Hume, S.C.; Simpkins, N.S. *J. Org. Chem.,* **1998**, *63*, 912.
[100] Blake, A.J.; Hume, S.C.; Li, W.-S.; Simpkins, N.S. *Tetrahedron,* **2002**, *58*, 4589.
[101] Tang, W.; Zhang, X. *Angew. Chem. Int. Ed.,* **2002**, *41*, 1612.
[102] Tang, W.J.; Wang, W.M.; Zhang, X.M. *Angew. Chem. Int. Ed.,* **2003**, *42*, 943.
[103] Kobayashi, S.; Shiraishi, N.; Lam, W.W.L.; Manabe, K. *Tetrahedron Lett.,* **2001**, *42*, 7303.
[104] Hoge, G. *J. Am. Chem. Soc.,* **2003**, *125*, 10219.
[105] Pietrusiewicz, K.M.; Koprowski, M.; Pakulski, Z. *Tetrahedron: Asymmetry,* **2002**, *13*, 1017.
[106] Pakulski, Z.; Koprowski, M.; Pietrusiewicz, K.M. *Tetrahedron,* **2003**, *59*, 8219.
[107] For another P-chirogenic bisphospholane see: Shimizu, H.; Saito, T.; Kumobayashi, H. *Adv. Synth. Catal.,* **2003**, *345*, 185.
[108] Lipshutz, B.H.; Buzard, D.J.; Yun, C.S. *Tetrahedron Lett.,* **1999**, *40*, 201.
[109] Oshiki, T.; Imamoto, T. *J. Am. Chem. Soc.,* **1992**, *114*, 3975.
[110] Al-Masum, M.; Kumaraswamy, G.; Livinghouse, T. *J. Org. Chem.,* **2000**, *65*, 4776.
[111] Al-Masum, M.; Livinghouse, T. *Tetrahedron Lett.,* **1999**, *40*, 7731.
[112] Moncarz, J.R.; Laritcheva, N.F.; Glueck, D.S. *J. Am. Chem. Soc.,* **2002**, *124*, 13356.
[113] Moncarz, J.R.; Brunker, T.J.; Glueck, D.S.; Sommer, R.D.; Rheingold, A.L. *J. Am. Chem. Soc.,* **2003**, *125*, 1180.
[114] For a related study, see: Moncarz, J.R.; Brunker, T.J.; Jewett, J.C.; Orchowski, M.; Glueck, D.S.; Sommer, R.D.; Lam, K.C.; Incarvito, C.D.; Concolino, T.E.; Ceccarelli, C.; Zakharov, L.N.; Rheingold, A.L. *Organometallics,* **2003**, *22*, 3205.
[115] Kovacik, I.; Wicht, D.K.; Grewal, N.S.; Glueck, D.S.; Incarvito, C.D.; Guzei, I.A.; Rheingold, A.L. *Organometallics,* **2000**, *19*, 950.

Received: 6 November, 2003 **Accepted: 1 December, 2003**