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PEER REVIEWED

Synthesis of homochiral mono- and bis-phosphine ligands for homogeneous catalysis

KEYWORDS: Asymmetric synthesis, phosphine, ligand, DIPAMP, homogeneous catalysis, (S)-2,6-dimethyltyrosine.

Abstract The number of commercially available chiral bisphosphine ligands has grown substantially in the last decade, which has resulted in an increased range of applications in asymmetric chemocatalysis, together with improved enantioselectivity, higher S/C ratio's and milder reaction conditions. However, the majority of new ligands introduced are variations of the C2 axially symmetrical BINAP or DIOP, which contain a chiral backbone. In comparison, the synthesis of new P-chiral bisphosphines, based on the pioneering DIPAMP ligand, is noteworthy because fewer new examples of this structural class have been introduced and utilised.

Key contributors agree that this is undoubtedly a consequence of the lack of general synthetic methodology. This paper reviews the approach introduced by Jugé, Kagan and Brown that is referred to herein as the "nucleophilic displacement route." It involves the use of (*l*)-ephedrine as a chiral auxiliary in the formation of optically pure chloro-, alkyl- or aryl-oxazaphospholidine oxides or borane adducts, from which successive enantiospecific nucleophilic displacements can be made to afford a wide range of homochiral phosphines. The route offers substantial scope for new ligands with a more extensive range of substitution patterns at both phosphorus and the backbone.

INTRODUCTION

The success of homogeneous asymmetric catalysis has been attributed to the structure and stereochemistry of the coordinated ligand(s), which can be classified into three general structural types (Figure 1): (i) axial C2-symmetrical bisphosphines that contain a rigid chiral backbone linking two PPh_2 units such as BINAP and SEGPHOS, (ii) C2-symmetrical bisphosphines that contain a chiral backbone linking two PPh_2 or PR_2 units such as DIOP and DuPHOS, or (iii) P-chiral bisphosphines such DIPAMP and BisP* that contain two chiral phosphine units linked by an achiral backbone. However, despite the landmark discovery and success of DIPAMP, relatively little attention has been paid to this class of P-chiral phosphine ligands for more than 20 years, mainly because of the synthetic difficulty of their preparation and apprehension about possible stereomutation at the phosphorus atom(s)(1).

HISTORICAL PERSPECTIVE

DIPAMP (Figure 1) was conceived and developed by Knowles *et al.* at Monsanto Corporation in 1975, and subsequently stimulated the rapid development of asymmetric catalysis (2). Its rhodium catalyst derivative was employed in the first industrial scale catalytic asymmetric hydrogenation for the production of the Parkinson's disease drug;

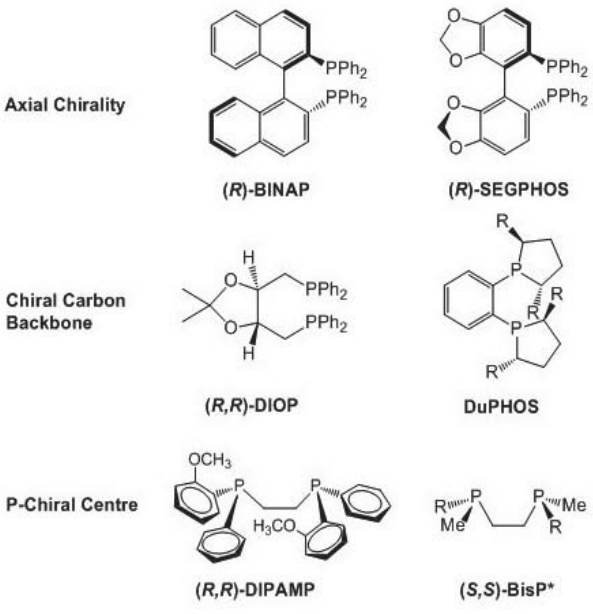
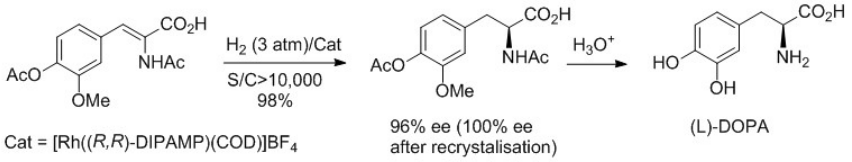


Figure 1. Classification of Chiral Bisphosphine Ligands.



Scheme 1. Original Knowles Asymmetric Synthesis of (L)-DOPA.

(*S*)-3,4-dihydroxyphenylalanine (L-DOPA) by reduction of the *a*-(acylamino)acrylic acid substrate (Scheme 1).
Even given the excellent enantioselectivity and high S/C ratio of this reaction, (L)-DOPA is now commercially manufactured enzymatically using tyrosine phenol-lyase (TPL), obtained from *Erwinia herbicola* or by chemical synthesis using vanillin as the starting material (3). Undoubtedly the asymmetric hydrogenation *a*-(acylamino)acrylic acid substrate cost and its economics at commercial scale are the most substantive drivers for this shift.

CONTROL FACTORS IN HOMOGENOUS CATALYSIS

Various reviews focused on ligand design, catalysis performance and synthesis have been the subject of a number of excellent publications by, amongst others, Liu and Zhang (4), Tang and Zhang (5), Imamoto and co-workers (6), Zhou (7) and, more recently a comprehensive publication entitled "*P-Stereogenic Ligands in Enantioselective Catalysis*," published by Grabulosa (8). The key challenge in homogeneous asymmetric catalysis involves matching the steric and electronic properties of the coordinated ligand with the target substrate (Figure 2). Conceptually the variables in catalyst design are relatively straightforward (9).

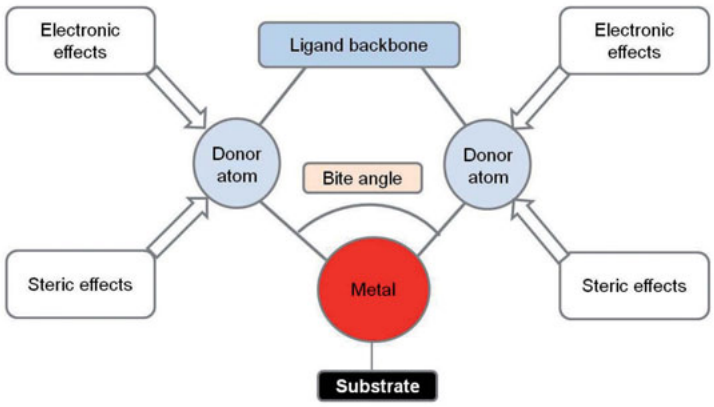


Figure 2. Design variables in homogeneous asymmetric catalysis.

As intimated by Imamoto (10), direct contact between the chiral centre and the transition-metal (i.e. the reaction site) facilitates exceedingly high levels of enantioselectivity. He further demonstrated that electron-rich metal catalysts bearing trialkylated P-chiral phosphine ligands exhibit a greater affinity for hydrogen, thereby enabling higher catalyst turnover numbers. These factors are considered to be the main advantages in using P-chiral ligands. This sentiment was somewhat shared by Knowles, who in his 2001 Nobel Lecture stated, "*We felt strongly that, if one wanted to get high ee values, the asymmetry would have to be directly on the phosphorus. That is where the action is*."

SYNTHETIC APPROACHES TO DIPAMP AND ANALOGUES

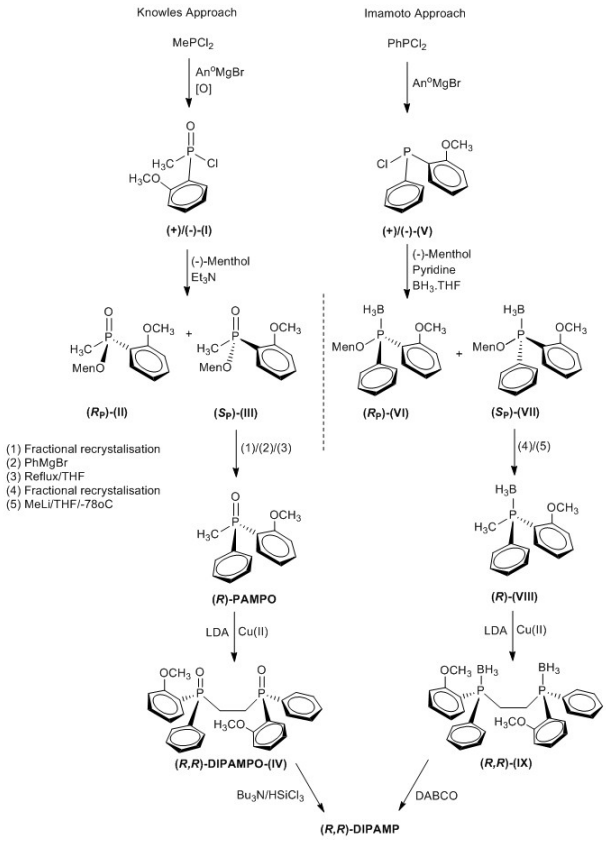
DIPAMP continues to be an effective ligand in homogeneous catalysis, given its utilisation in new synthetic and commercial applications. This is not surprising given its advantages (Table 1). Indeed, the substantive disadvantages mostly relate to its preparation.

Advantages	Disadvantages
High enantioselectivity for various aromatic enamides	Lower enantioselectivities of alkyl enamides
Rapid rates	Ligand synthesis a challenge
High catalyst turnovers	Low yield in ligand synthesis
Low hydrogen pressures	Free ligand susceptible to racemisation
Air stable catalyst precursors	

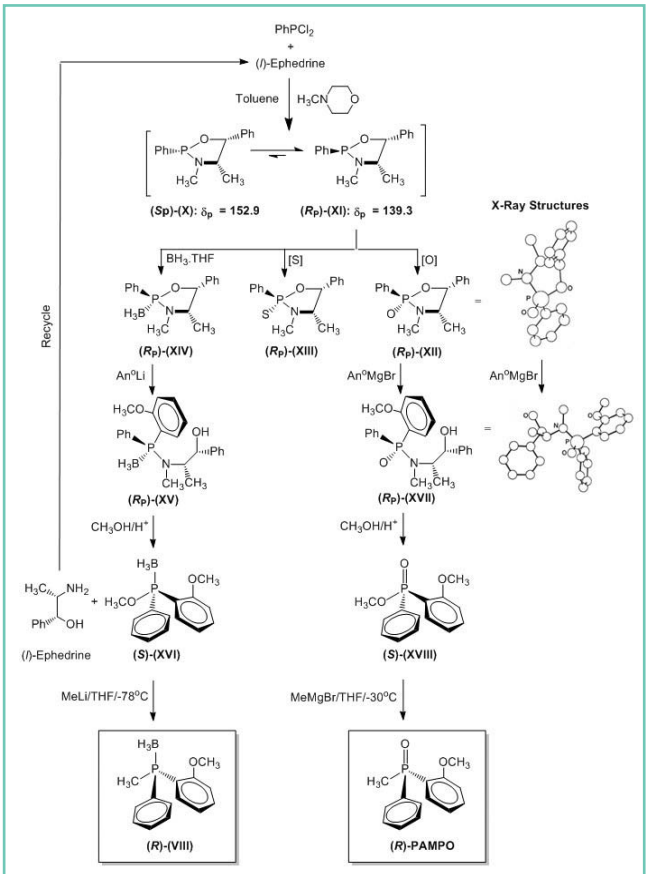
Table 1. Advantages and disadvantages of DIPAMP.

THE USE OF (-)-MENTHOL AS A RESOLVING AGENT

The use of (-)-menthol as a resolving agent in the formation of corresponding menthol ester diastereoisomers was first explored by Cram (11) and Mislow (12) in the late 1960's. Knowles subsequently improved this approach through the utilisation of racemic chloro methyl(*ortho*-anisyl)phosphine oxide-(I) in the synthesis of (R_P)-methyl menthyl(*ortho*-anisyl) phosphinates-(II) and its (S_P)-(III) diastereoisomer, the latter of which is the more soluble, allowing ease of isolation (2). It also has the required stereochemistry for subsequent manipulation (Scheme 2). Nucleophilic displacement of (-)-menthol using phenylmagnesium bromide under somewhat forcing conditions proceeds with inversion of configuration to yield (*R*)-methyl (*ortho*-anisyl) phenylphosphine oxide, typically referred to as (*R*)-PAMPO. Formation of the lithium carbanion and subsequent Cu(II) promoted oxidative coupling affords the bisphosphine oxide-(IV), which is reduced by $HSiCl_3$ in the presence of base to yield the desired bisphosphine, (*R,R*)-DIPAMP (Scheme 2).
Tricoordinate phosphorus compounds in low oxidation states are usually air-sensitive, making their handling and storage difficult. Chiral phosphines are additionally prone to racemisation, especially at high temperature. However, derivative phosphine-borane adducts are air-stable compounds, and can be conveniently isolated, purified, and stored. Consequently, they have emerged as indispensable intermediates for the preparation of P-chiral phosphines (13). Besides its protective function with respect to the labile phosphine group, BH_3 activates adjacent substituents



Scheme 2. Comparison of the Knowles and Imamoto approaches to DIPAMP.



Scheme 3. The Nucleophilic Route to DIPAMP and Analogues.

such as methyl groups or P-H bonds to deprotonation with a strong base. This methodology provides an efficient alternative to the difficult synthesis of a variety of optically active tertiary phosphine compounds.

The above approach was further improved by Imamoto (Scheme 2), who prepared the borane adduct equivalent of PAMPO in a different reaction sequence that uses racemic chloro (*ortho*-anisyl) phenylphosphine-(V) to prepare racemic menthyl(*ortho*-anisyl)phenyl phosphine boranes-(VI) & (VII). Following separation of the (R_P)-(VI) and (S_P)-(VII) diastereoisomers, the latter is utilised for subsequent reaction with MeLi to form (*R*)-methyl (*ortho*-anisyl)phenylphosphine borane-(VIII). Subsequent formation of the lithium anion using LDA in the presence of Cu(II), results in the formation of the diborane adduct: (*R,R*)-(IX, Scheme 2). This can be stored and used as required to directly prepare (*R,R*)-DIPAMP as required *via* deboration (*vide infra*).

BORANATION - DEBORONATION

Reaction of BH_3.THF complex with free phosphine occurs readily and quantitatively with complete preservation of stereochemical integrity at phosphorus (1). Liberation of the enantiomerically pure phosphine can be subsequently achieved in a stereospecific manner with retention of configuration, using either of two effective methods: (i) treatment with an excess of a strongly nucleophilic amine such as pyrrolidine, morpholine, or DABCO (14) and (ii) using strong acids such as CF_3SO_3H or HBF_4–OMe_2, followed by treatment with NaOH or $NaHCO_3$ (15). Both methods are carried out under mild conditions and maintain the stereochemical integrity of the phosphine.

Using the same approach, (*S,S*)-1,2-bis[cyclohexyl(*ortho*-methoxyphenyl)phosphino]ethane and (*S,S*)-1,2-bis[(*ortho*-ethylphenyl)phenylphosphino]ethane have been prepared by Imamoto. The latter is structurally similar to (*S,S*)-DIPAMP, but possesses no methoxy functional group. The application of the Rh-complex of this ligand in the asymmetric hydrogenations of *a*-(acylamino)acrylic acids was found to produce comparable results to those obtained with DIPAMP (opposite configuration was however, obtained). This finding ruled out the assumption that weak binding of the methoxy group borne on DIPAMP with the Rh-metal, plays a role in the stereoregulation of the asymmetric reduction. Accordingly, steric effects seem to be more important than coordinative interactions.

As intimated above, the synthetic challenge essentially relates to the preparation of homochiral phosphine oxides or borane adducts. By contrast, the subsequent methodology (i.e. the ease of formation of the lithium carbanion) is effective and well proven on a wide range of ligands and well exemplified by Imamoto and co-workers. The next section of this paper reviews the versatility of the "nucleophilic displacement route" to homochiral phosphines using (*I*)-ephedrine as a chiral auxiliary.

THE NUCLEOPHILIC DISPLACEMENT ROUTE TO HOMOCHIRAL PHOSPHINES USING (*I*)-EPHEDRINE AS A CHIRAL AUXILIARY

Oxazaphospholidine formation

Reaction of diclorophenylphosphine with (*I*)-ephedrine in toluene and *N*-methylmorpholine results in the formation of a pair of P(III) phenyloxazaphospholidines-(X & XI; Scheme 3) that can be monitored by ^{31}P NMR spectroscopy (Scheme 3).

Over time (ca 48 h) the thermodynamically preferred R_P (δ_P = 139.3 ppm) diastereoisomer-(XI) is formed exclusively. The base plays an essential role in this process, as alluded to by Grabulosa (8). A plausible mechanism is presented in Scheme 4. Attack of phosphorus by chloride ion on (S_P)-(X) causes P-O ring cleavage to afford the ring-opened alcohol species and regeneration of *N*-methylmorpholine. The ring-opened intermediate undergoes a pseudorotation followed by ring closure, together with the elimination of HCl to afford the (R_P)-phenyloxazaphospholidine-(XI).

The above approach can also be used to prepare other aryl- and alkyl-oxazaphospholidine analogues starting from $RPCl_2$ (where R = alkly or aryl). Alternatively the corresponding (2*R*, 4*S*, 5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine can be prepared from PCl_3 and (*I*)-ephedrine in the presence of *N*-methylmorpholine. Chloride. Displacement using Grignard reagents can then be used to generate the required alkyl- or aryl-oxazaphospholidine (Scheme 5).

(2*R*, 4*S*, 5*R*)-2-Phenyl-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine-(XI) undergoes stereospecific oxidation to readily form the corresponding (R_P)-oxide-(XII), (R_P)-sulphide-(XIII) and the (R_P)-borane-(XIV) adduct (Scheme 2). While much of the early work on these compounds focused on the oxazaphopsholidine oxides, subsequent effort has been directed on the borane adducts due to ease of deboronation (*vide supra*) and other advantages.

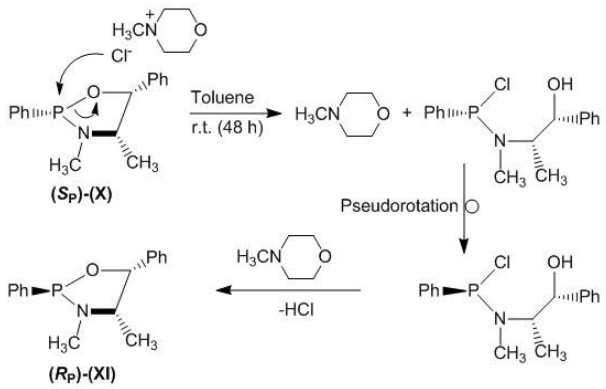
Oxazaphospholidine ring opening; formation of the second P-C bond

(2*R*, 4*S*, 5*R*)-2-Phenyl-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide-(XII) undergoes a stereospecific nucleophilic P-O ring opening with *ortho*-anisylmagnesium bromide to form the ring opened alcohol (R_P)-(XVII, Scheme 3). The generality of the reaction is broad and high yielding. The stereochemistry of the transformation was determined by X-ray crystallographic studies, which demonstrated that the reaction proceeds with retention of configuration at phosphorus (16).

The corresponding borane adducts undergo the same transformation with the corresponding organolithium reagents and with the same stereochemical outcome, exhibiting high enentioselectivity and isolated yield (17). Grabulosa has provided a comprehensive review of the scope of this reaction (8).

P-N bond cleavage by acid-catalysed methanolysis

The phosphinamide P-N residue in the ring opened (R_P)-alcohol-(XVII) is not easily displaced by organometallic reagents and has to be converted to the corresponding (*S*)-methylphosphinate-(XVIII, Scheme 3). This reaction is well precedented and occurs with inversion of configuration at phosphorus, per an S_N2 substitution. General conditions typically involve methanol in the presence of sulphuric acid and are enantiospecific.



Scheme 4. Proposed mechanism for the formation of the R_P phenyloxazaphospholidine diastereoisomer.

Formation of the third P-C bond

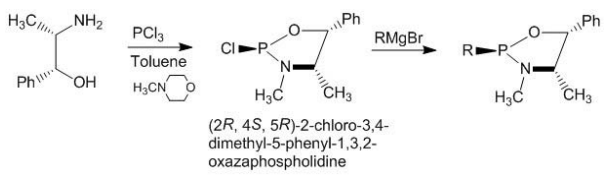
Nucleophilic displacement of the methoxy residue occurs readily to introduce a wide range of alkyl and aryl substituents, however, a methyl group is usually introduced in this step (8). As for formation of the second P-C bond, the oxazaphospholidine oxides react in high yields with Grignard reagents, while organolithium reagents are preferred for the corresponding borane adducts (Schemes 2 and 3).

The reaction proceeds with inversion of configuration at phosphorus. Utilisation of the borane series is the preferred approach to prepare (*R*)-(VIII); trivially referred to as PAMP.BH_3 (Schemes 2 & 3). The generality of the above approach allows both enantiomers to be readily prepared, either through the utilisation of (*d*)-ephedrine or changing the sequence of the nucleophilic substitution reactions.

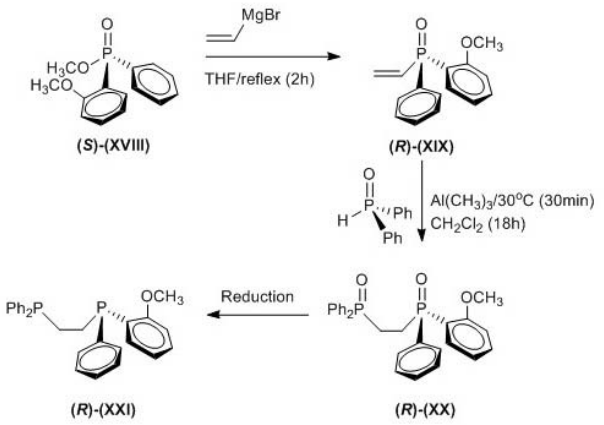
Synthesis of bisphosphines with chirality at one P-centre

This methodology can also be used to produce bisphosphine ligands that contain only one chiral phosphorus centre. Reaction of (*S*)-methyl (*ortho*-anisyl)phenylphosphinate-(XVIII) with vinyl magnesium bromide affords the corresponding (*R*)-phenyl (*ortho*-anisyl)vinylphosphine oxide-(XIX) that can then undergo Michael additions with HPR_2 to afford the corresponding diphosphine oxide-(XX, Scheme 6). Reduction then affords the homochiral bisphosphine-(XXI). The analogous borane adducts can be similarly prepared using the corresponding organolithium reagents.

The above nucleophilic displacement approach using (*I*)-ephedrine as a chiral auxiliary affords access to a vast range of new P-chiral ligands that are free of intellectual property and patent restrictions, since the approach has now been widely reported in the open literature. One application, where DIPAMP and analogues are of interest, is the asymmetric synthesis of (*S*)-2,6-dimethyltyrosine, which is presented below as a case study.



Scheme 5. Formation and utilisation of (2*R*, 4*S*, 5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine.



Scheme 6. Synthesis of bisphosphines with chirality at one P-centre.

Ligand	S/C	Solvent	P (atm)	T (°C)	R.T (h)	e.e.	Ref'
(*S,S*)-DioxyBenzP*	100	AcOEt	4	60	18	68.0	19
(*S,S*)-DioxyBenzP*	200	THF	4	40	18	55.0	19
(*S,S*)-DioxyBenzP*	200	MeOH	20	r.t.	23	55.0	19
(*S,S*)-DioxyBenzP*	200	CH_2Cl_2	20	r.t.	18	98.2	19
(*S,S*)-BenzP*	200	CH_2Cl_2	20	r.t.	18	98.7	19
(*S,S*)-QuinoxP*	200	AcOEt	5	60	18	84.0	19
(*S,S*)-QuinoxP*	200	CH_2Cl_2	20	r.t.	18	99.2	19
(*S,S*)-QuinoxP*	1,000	CH_2Cl_2	20	r.t.	18	99.1	19
(*R,R*)-DIPAMP	100	AcOEt	5	60	24	92.0	19
(*S,S*)-FerroTANE	500	AcOEt	5	60	16	93.0	20
(*R,R,S,S*)-TangPhos	2,000	MeOH	15	30	N.R	98.0	21

Table 2. Variables in the Catalytic Asymmetric Synthesis of (*S*)-2,6-dimethyltyrosine

Key: S/C = Substrate/Catalyst ration; P = Pressure; T = Temperature; OP = Optical Purity; e.e. = enantiomeric excess; Ref = Reference (literature or other), NR = not reported.
(*S*)-2,6-Dimethyltyrosine HCl salt and other analogues are available commercially in gram and multi-Kg quantities (22).

Also noteworthy with respect to its broad utilisation, is the methyl group on phosphine-boranes (e.g. (*R*)-(VIII), Schemes 2 and 3). This can be easily deprotonated on treatment with a strong base such as *s*-BuLi, permitting the synthesis of a variety of functionalised chiral phosphine-boranes. The carbanion may be subjected to *C*-alkylation using various electrophiles such as allyl bromide, chlorotrimethylsilane, or carbonyl compounds, and high yields of the corresponding monophosphine-boranes are typical (18).

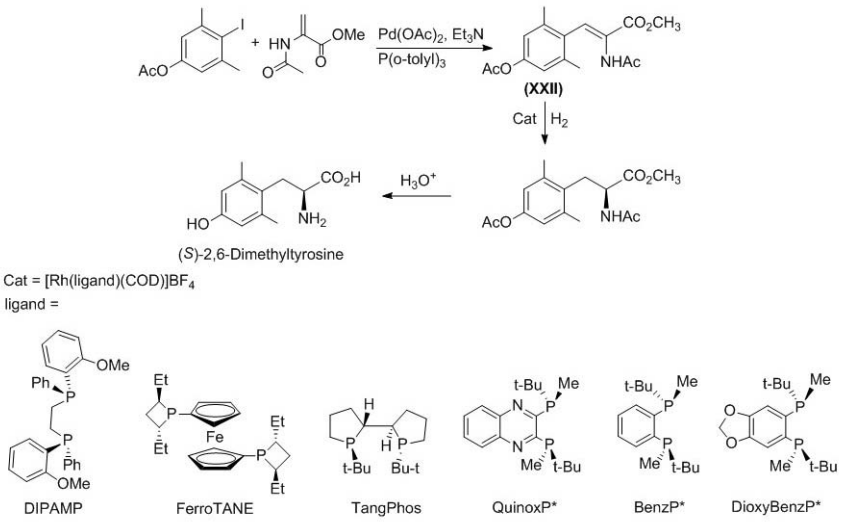
LIGAND SELECTIVITY IN THE ASYMMETRIC SYNTHESIS OF (*S*)-2,6-DIMETHYLTYROSINE

As a comparative case study, the synthesis of (*S*)-2,6-Dimethyltyrosine is reviewed below from a catalyst screening perspective and highlights the diversity of ligand classes that are reported in the literature and used within our own studies. (*S*)-2,6-Dimethyltyrosine is an unnatural amino acid that is used in the synthesis of the δ-opioid antagonist, Dmt-Tic pharmacophore and several other pre-clinical development candidates. Reported literature approaches involve the catalytic asymmetric hydrogenation of the pro-chiral dehydroaminoacid substrate; (*Z*)-2-acetamido-3-(4-acetoxy-2,6-dimethylphenyl)-prop-2-enoate-(XXII) that can be readily prepared at scale (Scheme 7).

There are now several reported asymmetric hydrogenations that all utilise different chiral bisphosphine ligands within their respective [Rh(chiral bisphosphine)(1,5-COD)]BF_4 catalysts. The ligands range from (*R,R*)-DIPAMP (Beck) to (*S,S*)-Et-FerroTANE (Praquin), (*R,R,S,S*)-TangPhos (Lennon), QuinoxP* (Imamoto), BenzP* (Imamoto), and DioxyBenzP* (Imamoto) and are shown in Scheme 7.

Imamoto reports the application of the three rhodium complexes of QuinoxP*, BenzP*, and DioxyBenzP* in the asymmetric hydrogenation of a range of α- and β-dehydroamino acid derivatives and enamides (19). The rhodium catalyzed asymmetric hydrogenations of methyl (*Z*)-2-acetamido-3-(4-acetoxy-2,6-dimethylphenyl)-2-propenoate-(XXII) are shown in Table 2, utlising the [Rh(ligand)(COD)]BF_4 systems shown in Scheme 7. Reactions using DioxyBenzP* in ethyl acetate, THF, or methanol resulted in full conversion, but the enantioselectivities were disappointingly low. By contrast, the reaction in dichloromethane remarkably improved the ee to 98.2%. BenzP* provided the desired product with similarly high ee (98.7%). Use of QuinoxP* in ethyl acetate gave the product with higher ee (84%) than the use of DioxyBenzP* (68% ee). The reaction using QuinoxP* with S/C = 200 in dichloromethane afforded the product with 99.2% ee. Lowering the catalyst loading to 0.1 mol % also enabled full conversion to product without any decrease in enantioselectivity.

We note that Praquin and co-workers abandoned the use of (*R,R*)-DIPAMP and instead resorted to FerroTANE, which afforded the product in 93% e.e. (20). Significantly, the S/C ratio could be improved five-fold to 500:1, significantly higher than the equivalent DIPAMP system, with reaction completion still within an acceptable timescale and without any loss in enantiomeric purity. The Rh catalyst derived from TangPhos has been reported to proceed with higher S/C ratios, presumably because it is optimised relative the other systems (21).



Scheme 7. Synthesis of (*S*)-2,6-dimethyltyrosine by catalytic asymmetric hydrogenation.

CONCLUSION

The nucleophilic displacement route is a versatile and powerful methodology for the synthesis of homochiral mono- and bis-phosphine ligands for asymmetric catalysis. Its wider application should facilitate the generation of new P-chiral ligands and thereby further increase the scope of asymmetric transformations that can be effected through the application of their derivative homogenous catalysts.

REFERENCES AND NOTES

1. T. Imamoto, *Asymmetric Hydrogenation*, Prof. Iyad Karamé (ed), (2012). ISBN: 978-953-51-0785-9, InTech, DOI: 10.5772/48584. Available from: http://www.intechopen.com/books/hydrogenation/asymmetric-hydrogenation.
2. W.S. Knowles, *Adv. Synth. Catal* **345**: 3-13 (2003).
3. T. Katayama, H. Kumagai, *L-DOPA, Microbial Production*, Encyclopedia of Industrial Biotechnology 1–4 (2010).
4. D. Liu, X. Zhang, *Eur. J. Org. Chem* 646–649 (2005).
5. W. Tang, X. Zhang, *Chem. Rev* **103**: 3029-3069 (2003).
6. T. Imamoto, K. Tamura, Z. Zhang, Y. Horiuchi, M. Sugiya, K. Yoshida, A. Yanagisawa, I.D. Gridnev, *J. Am. Chem.Soc* **134**: 1754–1769 (2012).
7. Q-Lin Zhou, *Privileged Chiral Ligands in Catalysis*, Wiley (2011).
8. A. Grabulosa, *P-Stereogenic Ligands in Enantioselective Catalysis*, RSC Catalysis Series (2011).
9. J.A. Gillespie, E. Zuidema, P.C.J. Kamer and P.W.N.M. van Leeuwen in Chapter 1, *Phosphorus(III) Ligands in Asymmetric Catalysis (Design & Synthesis)*, P.C.J. Kamer (ed) and P.W.N.M. van Leeuwen (ed)., Wiley (2012).
10. K.V.L. Crépy, T. Imamoto, *Top. Curr. Chem* **229**: 1–40 (2003).
11. A. Nudelman and D.J.Cram, *J. Am. Chem. Soc* **90**: 3869 (1968).
12. R.A. Lewis, K. Mislow. *J. Am. Chem. Soc* **91**: 7009 (1969).
13. T. Imamoto, Pure Appl. Chem **65**: 655 (1993).
14. H. Brisset, Y. Gourdel, P. Pellon, M. Le Corre. *Tetrahedron Lett* **34**: 4523 (1993).
15. L. McKinstry and T. Livinghouse, Tetrahedron Lett., **35**: 9319 (1994) and L. McKinstry and T. Livinghouse, *Tetrahedron* **50**: 6145 (1994).
16. J.V. Carey, M.D. Barker, J.M. Brown, M.J.H. Russell. *J. Chem. Soc., Perking Trans. I* 831-839 (1993).
17. C. Darcel, J. Uziel and S. Jugé in Phosphorus Ligands in Asymmetric Catalysis: Synthesis and Applications, A. Borner, (ed.), Wiley-VCH. Weinheim 1211 (2008).
18. K.V.L. Crépy, T. Imamoto. *Top Curr Chem* **229**: 1–40 (2003).
19. T. Imamoto, K. Tamura, Z. Zhang, Y. Horiuchi, M. Sugiya, K. Yoshida, A. Yanagisawa, I.D. Gridnev. *J. Am. Chem. Soc* **134**: 1754–1769 (2012).
20. C.F.B. Praquin, P.D. de Koning, P.J. Peach, R.M. Howard, S.L. Spencer. *Org. Process Res. Dev* **15**: 1124-1129 (2011).
21. I. Lennon, Presentation at Catalysis Development Conference, Newmarket, UK (2013).
22. http://shop.keyorganics.net

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JLL & DSM

JLL Partners (JLL), the middle-market private equity firm, and **Royal DSM**, the global Life Sciences and Materials Sciences company, have announced the successful closing of the transaction announced in November 2013 combining DSM Pharmaceutical Products (DPP) and Patheon Inc. into a new privately held company, named DPx Holdings B.V. (DPx).
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ADDIVANT ANNOUNCES COMPLETION OF PHASE 1 OF CAPACITY EXPANSION AT ITS PRODUCTION FACILITY IN PYONGTAEK, SOUTH KOREA

Addivant announced the completion of its first stage of a series of capacity expansions at its production facility at Pyongtaek, South Korea. The capacity of ALKANOX® 240, phosphite antioxidant has been increased by 40 percent. Further expansion is currently under progress and is scheduled to be completed by early 2015.
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i-CHIRAL 6

Chiral Technologies Worldwide has announced the availability of i-CHIRAL 6, a set of six Daicel 3-µm immobilised CSPs packed in columns of 4.6 mm internal diameter and 150 mm long. This combination of columns, which includes CHIRALPAK® IA, IB, IC, ID, IE and IF, raises method development success rates to greater than 93 percent. The company refers that the i-CHIRAL 6 set, which complements i-CHIRAL 4 set released in late 2013, is designed for high-speed, high-efficiency separations of enantiomers. It is the complementarity nature of the added CHIRALPAK IE and IF that allows scientists to achieve resolution of the most difficult-to-separate target compounds.
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