DOI: 10.1002/ejoc.200700082

Recent Progress in Asymmetric Catalysis Using Chiral Carbohydrate-Based Ligands

Montserrat Diéguez,*[a] Carmen Claver,[a] and Oscar Pàmies*[a]

Keywords: Asymmetric catalysis / Enantioselectivity / Carbohydrate ligands

This review describes the use of the most representative carbohydrate derivative ligands in asymmetric catalysis between 1972 and 2006 (approximately). Particular emphasis is placed on the latest results published in the most active period of this area of research (1998 to January 2007). In the first sections we cover the results obtained using homodonor ligands, such as phosphanes, phosphinites, phosphites and dithioethers. In the next sections, we present the results of using heterodonor ligands, such as P–P′, P–S, P–N and N–S ligands.

[a] Departament de Química Física i Inorgànica, Universitat Rovira i Virgili
C/Marcel·li Domingo s/n. 43007 Tarragona, Spain

Montserrat Diéguez studied chemistry at the Rovira i Virgili University in Tarragona (Spain), where she received her Ph.D. in 1997 working in the group of Prof. C. Claver. After a year as postdoctoral fellow with Prof. R. H. Crabtree at Yale University, in New Haven (USA), she returned to Tarragona in 1999. She is currently working as an associated professor at the Rovira i Virgili University. Her present research is focused on organometallic chemistry, mainly the synthesis of chiral ligands and asymmetric catalysis using a combinatorial approach.

Carmen Claver is Professor of Inorganic Chemistry at the Rovira i Virgili University in Tarragona (Spain), a position she has held since 1991. She received her Ph.D. in 1978 from the University of Zaragoza (Spain) working in the field of organometallic chemistry with Prof. Luis A. Oro. Her research is focused on fundamental aspects of homogeneous catalysis with transition metals, especially in asymmetric catalysis and polymerization processes.

Oscar Pamies studied chemistry at the Rovira i Virgili University in Tarragona (Spain), where he received his Ph.D. in 1999 working in the group of Prof. C. Claver. Then, he spent three years as a postdoc in the group of Prof. J.-E. Bäckvall at the Department of Organic Chemistry (Stockholm University), where he was involved in the study of the mechanism of hydrogen transfer reactions and in the development of new protocols for chemoenzymatic dynamic kinetic resolution. He is currently working at the Universitat Rovira i Virgili towards his habilitation. His research interests are asymmetric catalysis, organometallic chemistry and combinatorial synthesis.

1. Introduction

The growing demand for enantiomerically pure compounds for the development of pharmaceuticals, agrochemicals and flavours has captured the interest of chemists in recent decades. Of the various methods for producing enantiopure compounds, enantioselective homogeneous metal catalysis is particularly attractive, as is reflected by the many publications in this field and in the award of the 2001 Nobel Prize to W. S. Knowles, R. Noyori and K. B. Sharpless.[1] One of the main advantages of asymmetric catalysis over other methods used in asymmetric synthesis is that products can be selectively synthesised from cheap, commercially available prochiral starting materials without undesirable products being formed. Usually with this strategy, a transition metal complex containing a chiral ligand catalyses the transformation of a prochiral substrate into one enantiomer as major product.[1]

To reach the highest levels of reactivity and selectivity in catalytic enantioselective reactions, several reaction parameters must be explored and adjusted. In this optimisation process, careful selection and design of the chiral ligand is perhaps the most crucial step, since the best ligand strongly depends on each particular reaction. One of the simplest ways of obtaining chiral ligands is to transform or derivatise natural chiral compounds, thus making tedious resolution procedures unnecessary. In the last few years, impressive results have been obtained using carbohydrate derivative ligands in a wide range of catalytic asymmetric reactions.[2] Carbohydrates have many advantages: they are readily available, are highly functionalised and have several stereogenic centres. This enables series of chiral ligands to be synthesised and screened in the search for high activities and selectivities for each particular reaction. This tuning of the ligand structure allows for rational design of ligands, which provides valuable information about the origin of the selectivity. One of the main limitations of using natural products as precursors for ligands is that often only one of the enantiomers (in the case of carbohydrates, the D series) is readily available. However, this limitation can be overcome by using pseudo-enantiomer ligands or by suitable ligand tuning, as we show in this review.

Few reviews of the use of carbohydrate ligands in catalysis have been published.[2a,2b] The most recent cover the application of all published carbohydrate ligands. The scope of this review is narrower, and focuses on the use of the most representative carbohydrate derivative ligands in asymmetric catalysis between 1972 and 2006 (approximately). Particular emphasis is given to the results published in the latest and most active period for this area of research (1998 to January 2007). Therefore, this review provides a global overview of the research done and the possibilities for future research. In the first sections we cover the results obtained using homodonor ligands, such as phosphanes, phosphinites, phosphites, diphosphoroamidites, dithioethers and bis(oxazolines). In the next sections, we present the results of using heterodonor ligands, such as P–P′, P–S, P–N and N–S ligands. In the last section, we summarise the steps involved in the synthesis of the most important types of ligand groups.

2. Application of Carbohydrate Ligand Types in Asymmetric Catalysis

2.1. Phosphane Ligands

The successful early application in 1972 of the diphosphane DIOP (**1**, derived from tartaric acid, Figure 1)[3] in Rh-catalysed asymmetric hydrogenation (*ee*s up to 80%) led to the development of several types of carbohydrate-derived phosphane ligands (mainly diphosphanes) for asymmetric catalysis.[4] A review of the most successful carbohydrate phosphane ligands reveals three main trends: ligands derived from tartaric acid (DEGUPHOS and DIOP derivatives), phospholane ligands derived from mannitol, and bis(phosphanylamides) derived from glucose and mannose.

In the 1980s, ligand **2** (Figure 1), also derived from tartaric acid (with a more rigid five-membered chelate ring and the two stereocenters closer to the metal atom), provided better results than DIOP in the Rh-catalysed asymmetric hydrogenation of several dehydroamino acid derivatives (*ee*s up to >99%).[5]

More recently, RajanBabu's and Zhang's groups have developed several efficient diphosphane ligands (**3**–**6**) incorporating tartrate-derived 1,4-dioxane backbones for asymmetric hydrogenation (Figure 1). These modifications of DIOP improved enantioselectivities (up to 99%) by increasing the rigidity of the otherwise conformationally flexible seven-membered chelate ring. Two different strategies were applied: (a) a conformationally rigid 1,4-dioxane backbone was introduced, which gave rise to ligands **3** and **4**,[6] and (b) a methyl substituent was introduced in the α positions of the phosphane groups, which gave rise to ligands **5** and **6**.[7]

The last two successful modifications of DIOP ligands were made in 2004, with ligands **7a** and **7b**. These ligands were successfully applied in the metal-catalysed asymmetric hydrogenation of electron-rich enamides (Rh) and cyclic imines (Ir), providing better results than related ligands **5** and **6** (*ee*s up to >99.9% and 85%, respectively).[8]

The successful application of the DUPHOS ligand [1,2-bis(2,5-dimethylphospholanyl)benzene] in Rh-catalysed asymmetric hydrogenation led to the emergence of several related phospholane ligands as a powerful new class of compounds for asymmetric catalysis (Figure 2).[4] In general, this type of ligand maintains the high efficiency of DUPHOS in Rh-catalysed hydrogenation. Some of them have also been successfully applied in other asymmetric processes. In particular, Börner's, Holz's, Rieger's, Zhang's and RajanBabu's groups developed diphospholane ligands **8**–**12** and monophospholane ligand **13**, derived from D-mannitol, which have chiral information on both the α and β positions relative to the phosphorus atoms (Figure 2).[9] The families of ligands **8**, **9** and **12** were successfully applied in the Rh-catalysed hydrogenation of itaconic acid deriva-

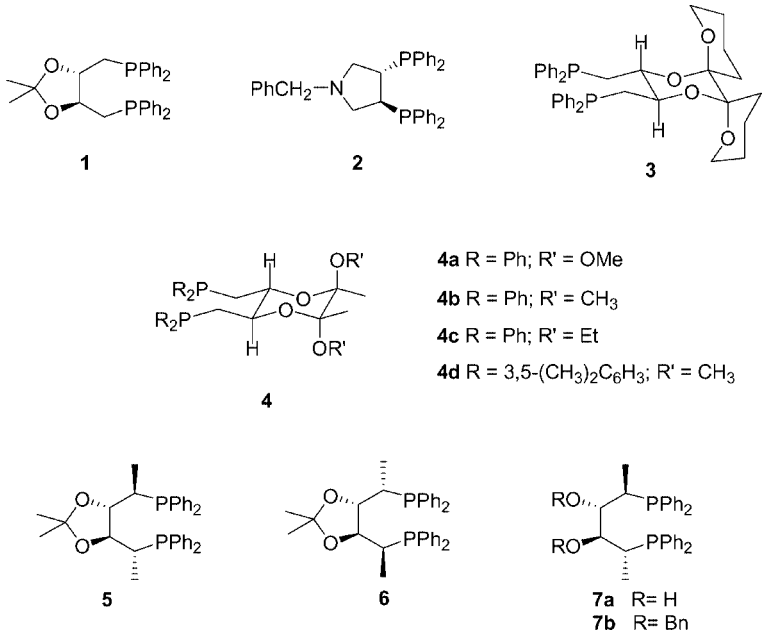


Figure 1. Diphosphane ligands derived from tartaric acid.

tives, enamides and enol acetates (*ee*s up to 99%).[9a–9g] Ligands **10**, **11** and **13** were applied in the Pd-catalysed allylic alkylation of dimethyl malonate onto (*E*)-1,3-diphenylprop-2-enyl acetate with high enantioselectivities using bidentate ligands **10** and **11** (*ee*s up to 99%).[9h,9i] Interestingly, the sense of asymmetric inductions appears to be dictated by the absolute stereochemistry of the P-carrying carbon atoms. Both enantiomers of the product can therefore be obtained.

Recently, Kesselgruber and co-workers used the phospholane triflate salt of ligand **10** (compound **14**, Figure 2) with success in the Rh-catalysed hydrogenation of dimethyl

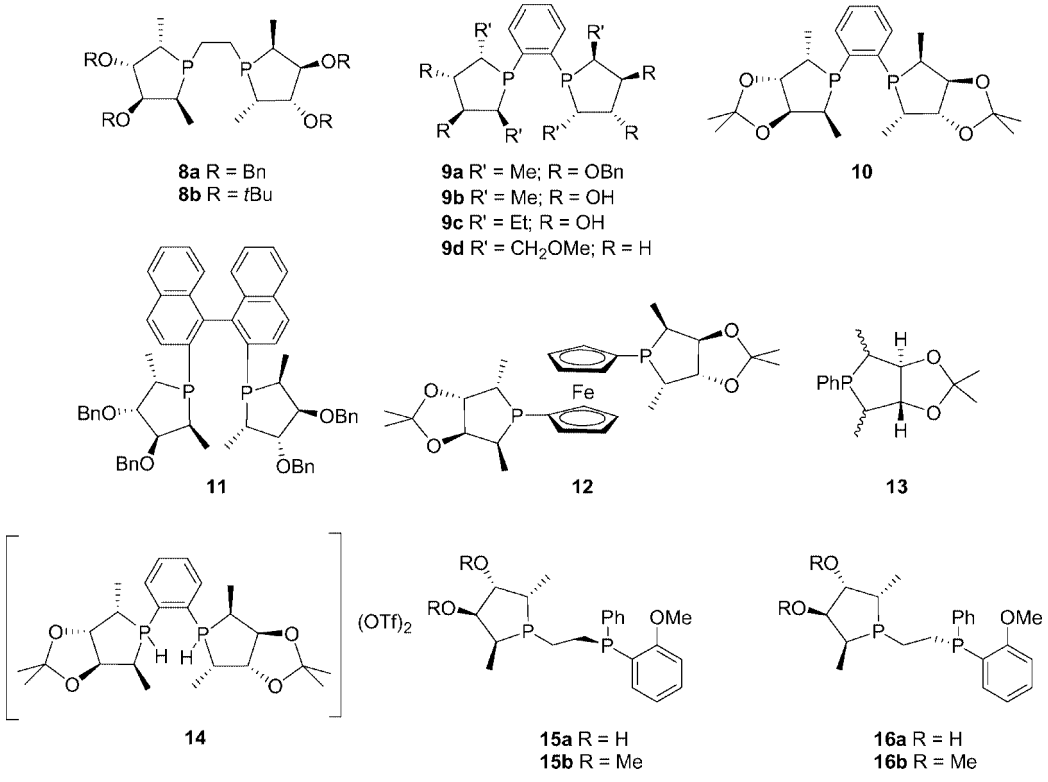
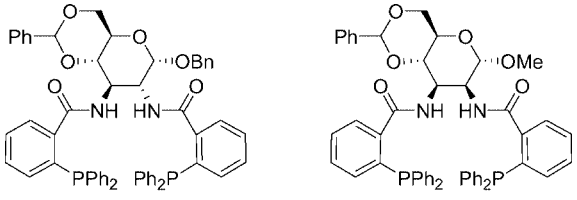


Figure 2. Selected phospholane ligands **8**–**16**.

itaconate (*ee*s up to >99%). This represents an important contribution, since the formation of the salt stabilises the diphospholane ligands, allowing them to be stored and transported without decomposition problems.[10]

Another efficient structural variation of DUPHOS combined a phospholane moiety, derived from D-mannitol, with a DIPAMP {bis[(2-methoxyphenyl)(phenyl)phosphanyl] ethane} chiral phosphane through an ethylene bridge with ligands **15** and **16** (Figure 2). These ligands were applied in the Rh-catalysed hydrogenation of several itaconates with *ee*s up to 95%.[11]

In 2006, Ruffo and co-workers developed a modification of the Trost bis(phosphanylamide) ligands[12] using diamines based on glucose and mannose as chiral auxiliaries (Figure 3, ligands **17** and **18**) for the highly enantioselective Pd-catalysed desymmetrisation of *meso*-cyclopent-2-ene-1,4-diol bis(carbamate) (*ee*s up to 97%). Interestingly, both enantiomers of the product can be obtained with high enantioselectivities by switching from glucose (**17**) to mannose (**18**) derivative ligands.[13]



17 (97% (-)) **18** (97% (+))

Figure 3. Bis(phosphanylamides) **17** and **18** developed by Ruffo and co-workers.

2.2. Phosphinite Ligands

Diphosphinites soon appeared as an alternative successful type of ligand in asymmetric catalysis, because they are more easily synthesised than phosphanes. In this context, the first important family of diphosphinite ligands applied to asymmetric catalysis are the pyranoside diphosphinite ligands **19** derived from D-glucose (Figure 4).[14,15] These were applied in several metal-catalysed asymmetric reactions and the results were best in the Rh-catalysed hydrogenation of dehydroamino acids [*ee*s up to 99% (*S*)][15a–15c] and Ni-catalysed asymmetric hydrocyanation of vinylarenes (*ee*s up to 91%)[15d,15e] reactions. The authors systematically studied the electronic and steric properties of the diphosphinite ligands by introducing several phosphinite groups in the basic ligand framework (**a**–**h**). They found that these phosphinite groups had an important effect on the catalytic performance. For the hydrogenation reaction, enantioselectivity was best with ligand **19a**, which contains electron-rich diphosphinite moieties, while for the hydrocyanation reaction the results were best with ligand **19h**, which contains electron-withdrawing aryl substituent groups on the phosphorus atom.

In the search for the (*R*) enantiomers of the hydrogenation products (D-amino acids), RajanBabu and co-workers developed diphosphinite ligands that were pseudo-enantiomeric to **19** in the form of the corresponding 3,4-diphosphinite ligands **20**, also derived from D-glucose (Figure 4). Ligand **20a** provided the highest enantioselectivities for the (*R*) enantiomers. In summary, the sugar-diphosphinite ligand systems developed by RajanBabu appear to be among the most practical ligands for the synthesis of (*S*)- and (*R*)-aromatic and heteroaromatic alanine derivatives.[15b]

RajanBabu and co-workers have also developed new 3,4-bis(diarylphosphinite) ligands **21** with furanoside backbones derived from D-fructose (Figure 4). These ligands were applied in different catalytic processes and the results were best in the Ni-catalysed asymmetric hydrocyanation of vinylarenes, with enantioselectivities up to 94% when ligand **21h** was used.[16]

In 1998, Uemura and co-workers developed a novel water-soluble disaccharide diphosphinite ligand **22**, derived from α,α-trehalose (Figure 5) for the highly enantioselective Rh-catalysed asymmetric hydrogenation of enamides and itaconic acid (*ee*s up to 99%).[17]

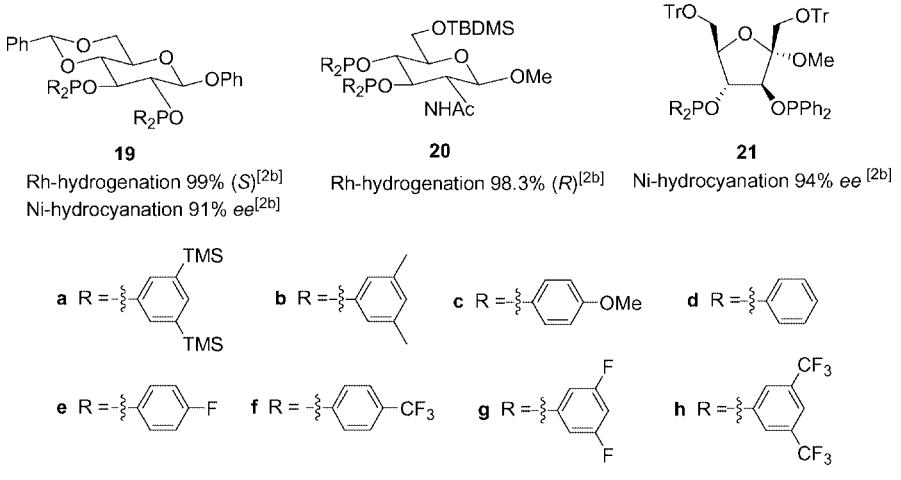
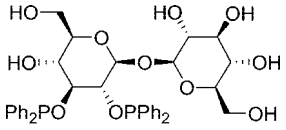


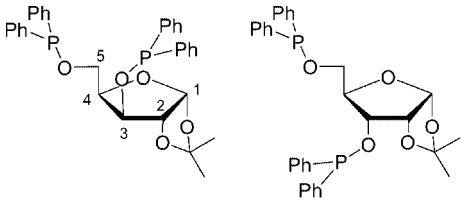
Figure 4. Diphosphinite ligands **19**–**21**.



22

Figure 5. Water-soluble diphosphinite ligand **22**.

In recent years, two new families of furanoside diphosphinite ligands have been designed and successfully applied in the asymmetric hydrogenation processes.[18,19] The first family is that of the furanoside ligands **23** and **24**, derived from D-xylose, which were applied in several metal-catalysed asymmetric reactions[20] with the best results in the metal-catalysed hydrogenation of several dehydroamino acids and itaconates (*ee*s up to 81%)[18b] (Figure 6). The results indicated that the metal source and the absolute configuration of the C-3 stereocenter of the carbohydrate backbone had important effects. The catalytic Rh-**23** and Ir-**24** diphosphinite system therefore provide *ee*s of up to 81%, while the other combinations provide *ee*s of up to 15%.[18]



23 (1*R*,2*R*,3*S*,4*R*) **24** (1*R*,2*R*,3*R*,4*R*)

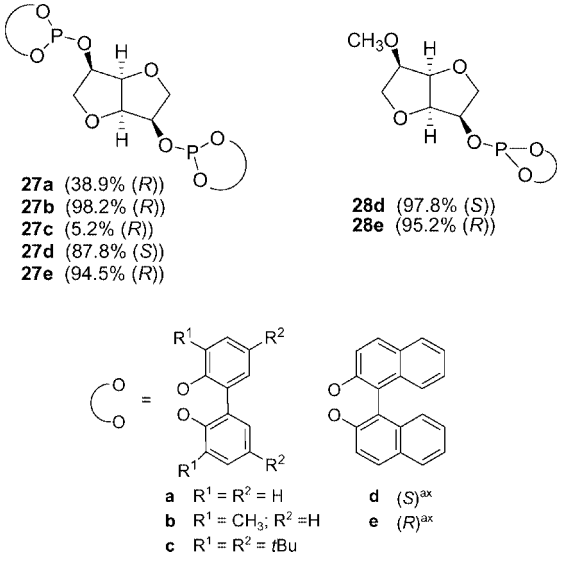
Figure 6. Diphosphinite ligands derived from D-xylose.

The second recently developed family is that of the modular ligands **25** and **26**, with C_2 symmetry, systematically modified at positions 2 and 5 and in the bis(diarylphosphinite) ligands, and prepared from D-glucosamine, D-glucitol and tartaric acid (Figure 7). The application of these ligands in the metal-catalysed hydrogenation of dehydroamino acid derivatives and imines showed that the configuration and the substituents at positions 2 and 5 of the tetrahydrofuran backbone and the electronic properties of the diarylphosphinite moieties have a strong influence on the enantioselectivity of the processes. Therefore, in the Rh-catalysed hydrogenation of dehydroamino acid derivatives the enantioselectivities were best when ligands **25d** and **25e** were used (*ee*s up to 93%), whereas the best results in the Ir-catalysed hydrogenation of imines were provided with ligand **25f** (*ee*s up to 70%).[19]

2.3. Phosphite Ligands

Unlike phosphane and phosphinite ligands, which have a long history in several enantioselective catalytic processes, phosphites have emerged more recently as suitable ligands for asymmetric catalysis. Their highly modular construction, facile synthesis from readily available chiral alcohols and their π-acceptor capacity have proved to be highly advantageous. In this context, several carbohydrate phosphite ligands have now been developed and successfully applied in several asymmetric catalytic processes. The first successful families of carbohydrate phosphite ligands were developed by Reetz's and Alexakis' groups.

Reetz and co-workers developed the first phosphite ligand to be successfully applied in Rh-catalysed asymmetric hydrogenation. They synthesised a series of C_2-symmetric diphosphite ligands **27**[21] and monophosphite ligands **28**,[22] derived from D-mannitol, with different phosphite substituents (Figure 8). This family of ligands was applied in the Rh-catalysed hydrogenation of dimethyl itaconate and methyl *N*-acetamidoacrylate with high enantioselectivities (*ee*s up 98.2%). The results indicated that the sense of enantiodiscrimination is predominantly controlled by the configuration of the binaphthyl moiety. Both enantiomers of the product can therefore be obtained. Moreover, they observed a cooperative effect between the stereogenic centres of the ligand backbone and the stereogenic binaphthyl moieties. Interestingly, Reetz and co-

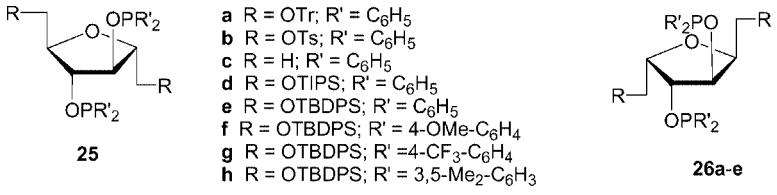


27a (38.9% (*R*))
27b (98.2% (*R*))
27c (5.2% (*R*))
27d (87.8% (*S*))
27e (94.5% (*R*))

28d (97.8% (*S*))
28e (95.2% (*R*))

a $R^1 = R^2 = H$
b $R^1 = CH_3$; $R^2 = H$
c $R^1 = R^2 = t$Bu
d $(S)^{ax}$
e $(R)^{ax}$

Figure 8. Phosphite ligands developed by Reetz and co-workers.



25

a R = OTr; R' = C_6H_5
b R = OTs; R' = C_6H_5
c R = H; R' = C_6H_5
d R = OTIPS; R' = C_6H_5
e R = OTBDPS; R' = C_6H_5
f R = OTBDPS; R' = 4-OMe-C_6H_4
g R = OTBDPS; R' = 4-CF_3-C_6H_4
h R = OTBDPS; R' = 3,5-Me_2-C_6H_3

26a-e

Figure 7. C_2-Diphosphinite ligands **25** and **26**.

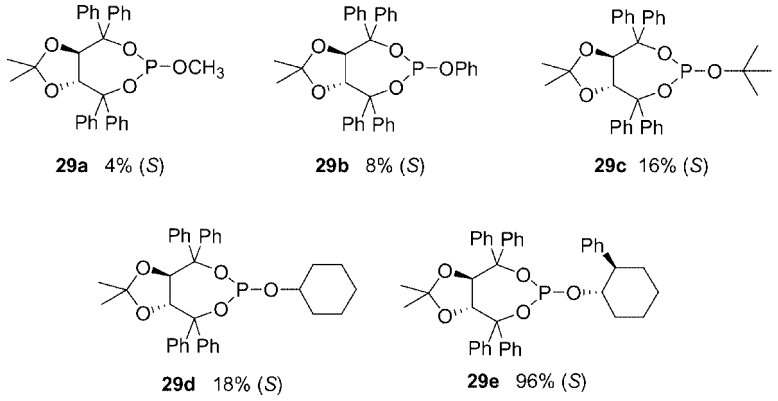


Figure 9. Selected phosphite ligands **29** used in the Cu-catalysed asymmetric addition of diethylzinc to cyclohexenone.

workers also found that ligand **27b**, with conformational flexibility in readily epimerizing biphenyl moieties, was superior to ligands with fixed binaphthyl chirality.[21]

Alexakis and co-workers developed a series of monophosphite ligands derived from TADDOL with several exocyclic alcohols (Figure 9). They found that ligand **29e** provided the highest enantioselectivities (*ee*s up to 96%) in Cu-catalysed 1,4-additions of diethylzinc to cyclic enones.[23]

These excellent results have led to the recent development of three main families of carbohydrate phosphite ligands.

In this context, an important series of diphosphite compounds – furanoside ligands **30**–**36a**–**h**, derived from D-(+)-xylose and D-(+)-glucose (Figure 10) – have been successfully applied in several asymmetric catalytic processes.[24–27] The highly modular construction of these ligands allows sufficient flexibility to fine-tune (a) the various configurations of the carbohydrate backbone, (b) the substituents at C-5 in the carbohydrate backbone (R = H, Me, OTBDPS), and (c) the steric and electronic properties of the diphosphite substituents (**a**–**h**). The many combinations they provide are the key to finding the most suitable ligands for each particular process. Therefore, this set of ligands has been successfully applied in the Rh-catalysed asymmetric hydroformylation of vinylarenes and dihydrofurans, metal-catalysed asymmetric hydrogenation of olefins, Pd-catalysed asymmetric allylic substitution reactions and in Cu-catalysed 1,4-additions. The authors found that the effects of the ligand parameters could be completely different for the same series of ligands, depending on the reaction studied. A suitable catalyst, that provided enantioselectivities comparable to those of the best catalysts reported in these processes, was found for each particular reaction.

For the Rh-catalysed hydroformylation of vinylarenes, this set of ligands shows not only excellent enantioselectivities (as high as 93%) but also excellent regioselectivities (as high as 98.8%) under mild conditions. The results show that the absolute configuration of the product is governed by the configuration at the stereogenic centre C-3 of the ligand backbone, while the level of enantioselectivity is influenced by a cooperative effect between stereocenters C-3 and C-5. Thus, both the (*S*) and the (*R*) enantiomers of the product can be obtained by using ligands with the basic frameworks

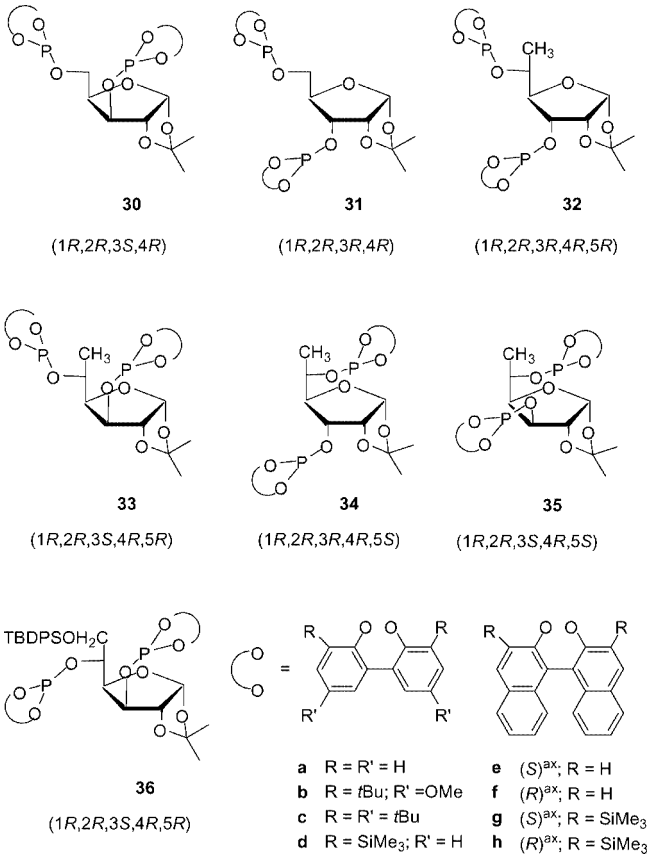


Figure 10. Furanoside diphosphite ligands **30**–**36**.

33 and **34**, respectively. Moreover, the substituents in the biaryl phosphite moieties have an influence. Thus, ligands **33b/d** and **34b/d**, with either methoxy substituents or trimethylsilyl groups, always produced the best enantioselectivity.[24a–24e] Ligand **33b** has also recently been successfully applied in the asymmetric hydroformylation of 2,3- and 2,5-dihydrofurans (*ee*s up to 75% and regioselectivities up to 99%).[24f]

Ligands **30**–**36** were also successfully applied in the Pd-catalysed allylic substitution of several disubstituted linear (*ee*s up to 99%) and cyclic (*ee*s up to 96%) substrates.[26]

The results indicated that enantioselectivities were affected by the substituents both at C-5 and on the phosphite moieties, by the configurations of carbon atoms C-3 and C-5, and the configurations of the biaryl moieties. The enantioselectivities were best with ligand **33b**, which has a glucofuranoside backbone and bulky *tert*-butyl substituents at both the *ortho* and the *para* positions of the biphenyl moieties. It should be noted that this ligand family also provides high activity (because of the strong π-acceptor capacity of the phosphite moieties) and enantioselectivities in several substrate types, which overcomes the most important limitations of the most successful catalytic systems for the Pd-asymmetric allylic alkylation reaction, such as low reaction rates and the high substrate specificity.[26c]

Ligand **30b** was also used to stabilise Pd nanoparticles. These particles catalysed the allylic alkylation of *rac*-3-acetoxy-1,3-diphenylprop-1-ene with dimethyl malonate, leading to almost total conversion of the (*R*) enantiomer and almost no reaction with the (*S*) form.[26d] This gave rise to 97% *ee* for the alkylation product and a kinetic resolution of the substrate recovered with ca. 90% *ee*.

Ligands **30**–**35** were also successfully applied in the Rh-catalysed hydrogenation of several benchmark dehydroamino acid derivatives and itaconates[25] and in the Cu-catalysed 1,4-addition of diethylzinc to cyclohex-2-enone.[27] In contrast with hydroformylation and allylic substitution reactions, the enantiomeric excesses depend strongly on the absolute configuration at C-3 and only slightly on the configuration at the carbon stereocenter C-5. However, the ligand that provides the best enantioselectivity is different for each process. Therefore, for Rh-catalysed hydrogenations, the enantioselectivities were best with ligand **32d**, with the (*R*) configuration at both C-3 and C-5 stereocenters (*ee*s up to 99%), while for Cu-catalysed 1,4-additions enantioselectivities were best with ligands **30h** and **33g** [81% (*R*) and 84% (*S*), respectively]. These results, together with those for hydroformylation, clearly show the importance of using modular scaffolds in the ligand design. For both processes, it was also found that the presence of a methyl substituent on the carbon atom C-5 significantly increased the activity and enantioselectivity.

Recently, Chan and co-workers reported the synthesis of chiral pyranoside diphosphites **37** and **38**, derived from D-glucose and D-galactose, for application in Cu-catalysed 1,4-additions to cyclic enones (Figure 11).[28] The enantioselectivities depend on the absolute configurations at the C-4 stereogenic centres in the ligand backbones, while the stereogenic binol units control the preferential enantiomer configurations. Therefore, the results were best with ligand **37b** (*ee*s up to 88%).

The pioneering work by Alexakis,[23,29] Feringa[30] and Reetz[22] on monodentate ligands for asymmetric catalysis has opened up a new frontier in design and synthesis: a simple route for efficient new monophosphorous ligands. Therefore, the successful use of monophosphite ligands **28** and **29** in asymmetric catalysis (see above) has led to the more recent synthesis of several other monophosphite carbohydrate ligands. In this context, a wide range of new

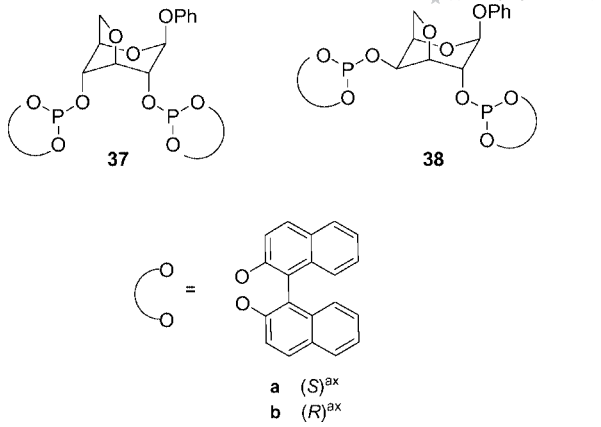


Figure 11. Pyranoside diphosphite ligands **37** and **38**.

and efficient monophosphite ligands **39**–**48** (Figure 12) have been developed for the Rh-catalysed hydrogenation of vinyl carboxylates, dehydroamino acids and enamides[31,32] and for the Ni-catalysed trialkylaluminium addition to aryl aldehydes.[33] These ligands contain different biaryl moieties and were synthesised from various sugars, including fructose, galactose, glucose, mannitol and mannose. This leads to a wide range of sugar backbones and ligands with different steric and electronic properties.

In particular, Reetz and co-workers reported the use of ligands **39**–**43e**–**f** in the Rh-catalysed hydrogenation of vinyl carboxylates.[31] The results show that there is a cooperative effect between the configuration of the binaphthyl moieties and the configuration of the sugar backbone. Therefore, enantioselectivities were best with phosphite **39f**, prepared from (*R*)-binol and a D-(+)-glucose derivative (*ee*s up to 94%).

On the other hand, Zheng and co-workers have successfully used ligands **39**–**40e**–**g**, **44**–**45e**–**g**, **47** and **48** in the Rh-catalysed hydrogenation of dehydroamino acids (*ee*s up to 98.4%) and enamides (*ee*s up to 99.6%).[32] The hydrogenation results using ligands **39**, **40**, **44** and **45** indicate that the enantiomeric excess depends strongly on the configuration of carbon atom C-3. In general, therefore, ligands **40** and **45**, with (*R*) configurations, produced much higher enantioselectivities than ligands **39** and **44** with the opposite configurations. In this case, these results also suggest that there is a cooperative effect between the configuration of the binaphthyl moiety and the configuration of the carbohydrate backbone. The enantioselectivities (up to 99.6% *ee*) were therefore best with ligands **40f** and **45f**. Ligands **47** and **48** were also highly efficient in the hydrogenation of dehydroamino acids and enamides, providing high enantioselectivities (*ee*s up to 99.8%) and activities (TONs up to 5000).[32b,32c]

In 2006, Diéguez and co-workers successfully used ligands **39**–**40a**–**f**, **41c**, **44b**, **44c** and **46c** in Ni-catalysed asymmetric trialkylaluminium additions to several arenecarbaldehydes.[33] The results indicated that the sugar backbone, the configurations at C-3 and C-4 in the ligand backbone and the type of substituent/configuration in the biaryl

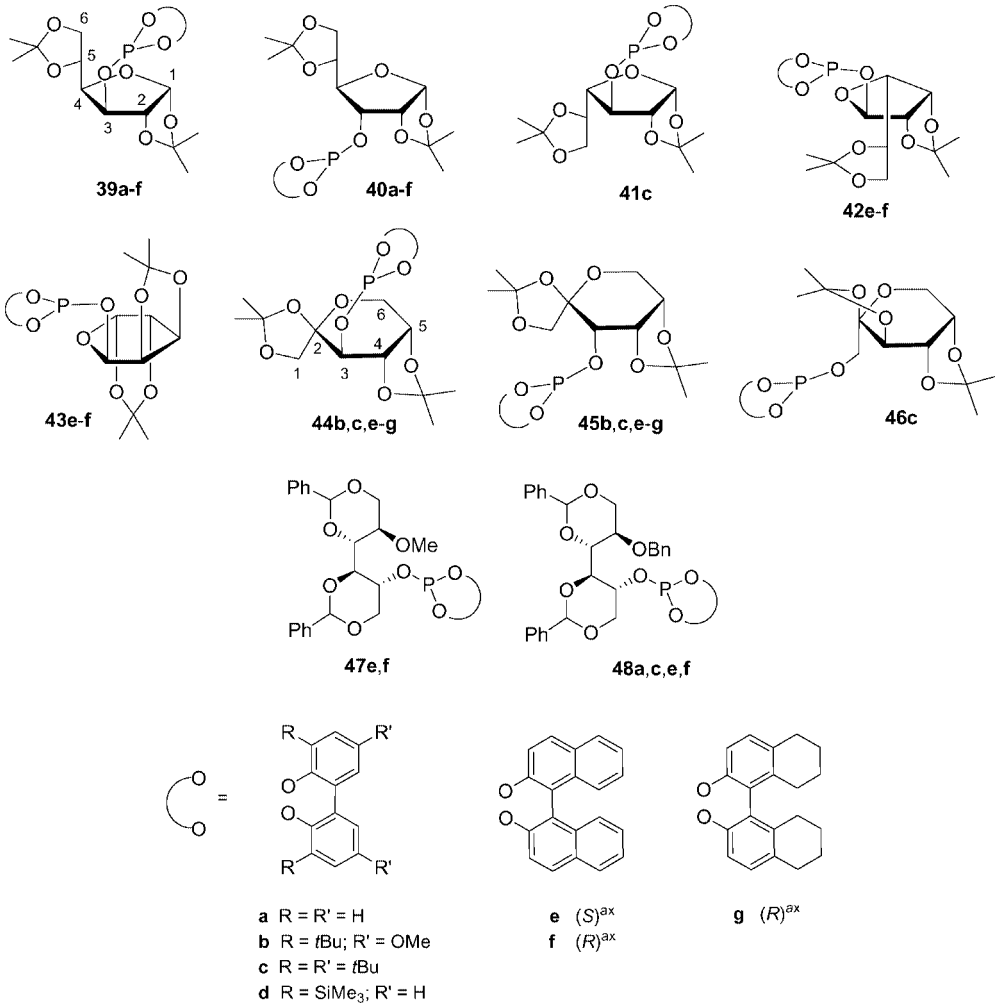


Figure 12. Monophosphite ligands **39**–**48**.

phosphite moiety had an important effect on the catalytic performance. Therefore, the enantioselectivities and activities were best with ligand **39c** (*ee*s up to 94%). These ligands represented the first phosphite ligands applied to this process.

2.4. Diphosphoroamidite Ligands

During recent decades there has been a huge advance in the use of phosphoroamidite ligands for several asymmetric processes.[34] However, to the best of our knowledge, only one family of diphosphoroamidite ligands based on carbohydrates – **49** (Figure 13) – has been successfully applied in asymmetric catalysis.[35] Good to excellent activities [TOFs up to 850 mol substrate × (mol Pd × h)$^{-1}$] and enantioselectivities (*ee*s up to 95%) in Pd-catalysed allylic alkylation were obtained for several di- and monosubstituted linear and cyclic substrates. The results indicate that the catalytic performance is strongly affected by the substituents and the axial chirality of the biaryl moieties of the ligand. The study of the 1,3-diphenyl- and cyclohexenyl-derived (π-allyl)Pd intermediates by NMR spectroscopy pro-

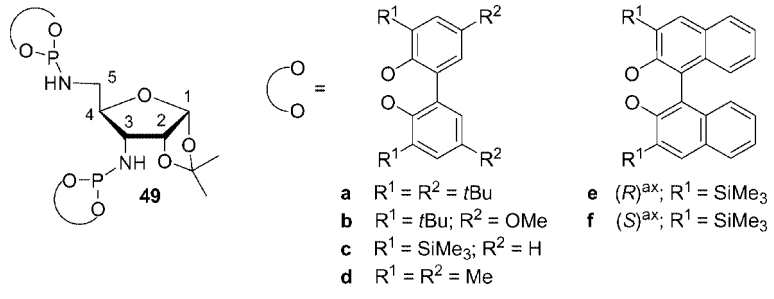


Figure 13. Diphosphoroamidite ligands **49**.

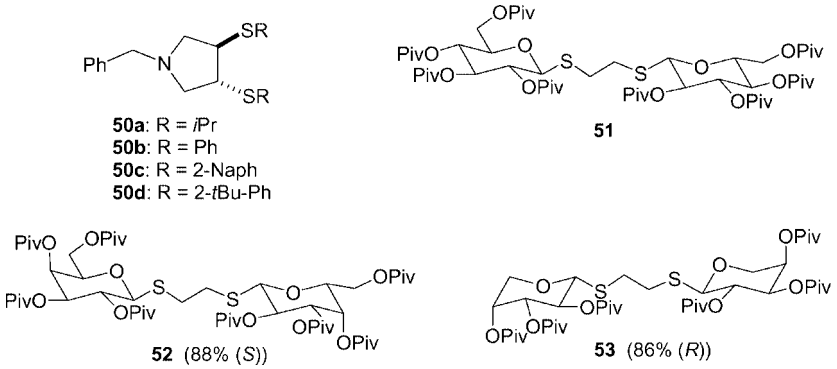


Figure 14. Successful carbohydrate dithioether ligands **50**–**53**.

vided an understanding of the catalytic behaviour observed. This study indicates that the nucleophilic attack takes place predominantly at the allylic terminal carbon atom located *trans* to the phosphoroamidite moiety attached to C-5.

2.5. Dithioether Ligands

Unlike phosphorus carbohydrate ligands, sulfur donor ligands have not been widely used in asymmetric catalysis, though some of them have provided high enantioselectivities.[36] However, in recent years, several dithioether ligands have been developed. Chiral dithioethers were first successfully used in Pd-catalysed allylic alkylations with DEGUS-type ligands **50** (Figure 14), derived from tartaric acid (*ee*s up to 81% with ligand **50b**).[37]

Recently, Khiar and co-workers used a combinatorial approach to find the best dithioether ligand **51** (Figure 14) from a library of 64 potential ligands (four linkers × four sugar residues × four protective groups) for the Pd-catalysed allylic alkylation of diethyl malonate to 1,3-diphenylprop-2-enyl acetate (*ee*s up to 90%).[38a] In the search for both enantiomers of the alkylation product, the authors successfully prepared pseudo-enantiomers **52** and **53** derived from D-galactose and D-arabinose, respectively (Figure 14).[38b]

2.6. Bis(oxazoline) Ligands

Although bis(oxazoline) ligands have emerged as one of the most versatile ligand classes for metal-catalysed asymmetric transformations, to the best of our knowledge only one bis(oxazoline) ligand – **54**, derived from D-glucosamine (Figure 15) – has been successfully applied in the enantioselective Cu-catalysed cyclopropanation of olefins (*ee*s up to 82%).[39]

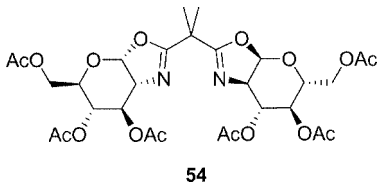


Figure 15. Successful carbohydrate bis(oxazoline) ligand **54**.

2.7. Heterodonor Ligands

Several types of heterodonor carbohydrate chiral ligands containing different donor atoms have been developed for asymmetric catalysis. In particular, mixed P–P′, P–S, P–N and, to a lesser extent, N–S donor ligands have provided excellent results.

2.7.1. Heterodonor P–P′ Ligands

The first successful family of P–P′ carbohydrate ligands were the phosphane–phosphite ligands **55** (Figure 16), derived from D-xylose.[40] They were successfully applied in Rh-catalysed asymmetric hydrogenations of several α,β-unsaturated carboxylic acid derivatives (*ee*s up to >99%) under very mild conditions. These ligands contain different phosphite substituents (**a**–**e**), which affect the catalytic performance. The enantioselectivity was best with ligand **55b**, which contains bulky *tert*-butyl groups in the *ortho* and *para* positions in the biphenyl moiety. The results also indicate that the stereogenic binol units control the preferential enantiomer configuration. Therefore, ligand **55d**, with the (*R*)-binaphthyl moiety, mainly provided the (*R*)-configured hydrogenation product (97.6% *ee*), while ligand **55e**, with the (*S*)-binaphthyl moiety, gave the opposite enantiomer in 98.3% *ee*. Both enantiomers of the product can therefore be obtained with high enantioselectivity.

The second successful family of P–P′ donor carbohydrate ligands were the phosphite–phosphoroamidite ligands **56** and **57**, also derived from D-xylose (Figure 16).[41] These ligands are related to diphosphite ligands **30**–**31** and phosphane–phosphite ligands **55** (mentioned above). The introduction of a phosphoroamidite moiety at C-5 in the ligand backbone is highly advantageous, leading to high enantioselectivities not only in Rh-catalysed hydrogenations of dehydroamino acids (*ee*s up to 99% using ligand **56b**)[41a] but also in Pd-catalysed allylic substitution reactions (*ee*s up to 98%).[41b] Interestingly, this ligand family also provides high activities (because of the high π-acceptor capacity of the phosphoroamidite moiety) and enantioselectivities in different substrate types (mono- and disubstituted linear and cyclic substrates), which overcomes the most important limitations of the most successful catalytic systems for Pd-asymmetric allylic alkylation, such as low reaction rates and the high substrate specificity. Therefore, ligand **56g** afforded

98% *ee* in the alkylation of hindered disubstituted linear substrates, while ligand **57f** gave the best enantioselectivity in the alkylation of monosubstituted linear substrates (90% *ee*). However, for disubstituted unhindered linear and cyclic substrates the best *ee*s were obtained with ligands **57g** (89% *ee*) and **57b** (91% *ee*), respectively.

The last family of mixed P–P′ donor carbohydrate ligands are the phosphinite–phosphite ligands **58**, related to **25**, in which a phosphinite moiety has been replaced by a phosphite group (Figure 16). Ligand **58d** proved to be effective in Ir-catalysed hydrogenations of ketimines (*ee*s up to 73%).[19b,42]

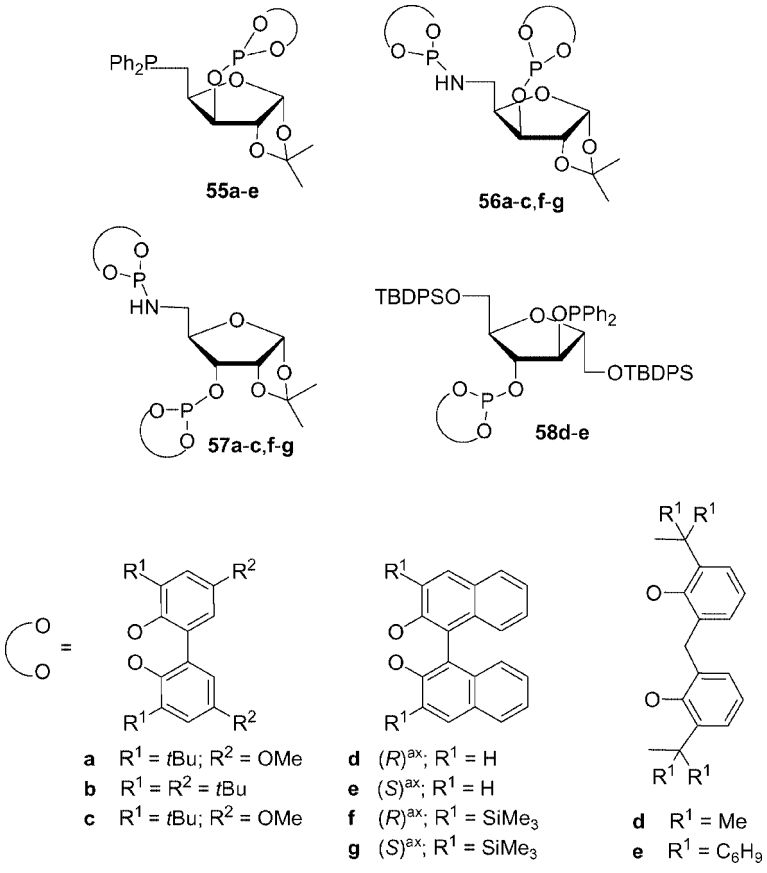


Figure 16. Heterodonor P–P′ ligands **55**–**58**.

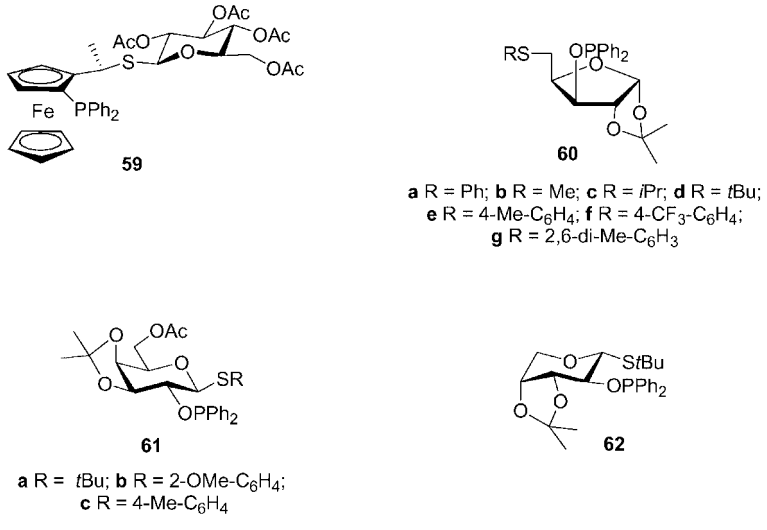


Figure 17. Heterodonor P–S ligands.

2.7.2. Heterodonor P–S Ligands

So far, only three carbohydrate-based catalytic systems have provided good results in asymmetric catalysis (Figure 17).

The ferrrocenylphosphane thiosugar **59** developed by Pregosin and co-workers afforded an *ee* of 88% in the palladium-catalysed allylic substitution of diethyl malonate onto 1,3-diphenylprop-2-enyl acetate.[43]

More recently, a series of thioether–phosphinite ligands **60a**–**g**, with furanoside backbones, were applied in Pd-catalysed allylic substitutions of mono- and disubstituted linear and cyclic substrates (*ee*s up to 95%),[44a,44b] Rh-catalysed hydrogenations of dehydroamino acids and itaconates (*ee*s up to 96%)[44c] and Cu-catalysed 1,4-additions to cyclohexenone (*ee*s up to 72%).[20b] These ligands contained several thioether substituents with different electronic and steric properties. The authors found that this group had an important effect on the catalytic performance, enantioselectivities being best when the bulkiest ligands **60c**–**d** were used.

At the same time, simple thioether–phosphinite ligands **61** and **62**, with pyranoside backbones, were successfully applied in Pd-catalysed allylic substitutions of 1,3-diphenylprop-2-enyl acetate (*ee*s up to 96%) and Rh-catalysed asymmetric hydrogenations of methyl cinnamate (*ee*s up to 92%). For both catalytic processes enantioselectivities were best when bulky *tert*-butyl substituents were present in the thioether moiety. Both enantiomers of the products were obtained by using pseudo-enantiomeric ligands **61a** and **62**.[45]

2.7.3. Heterodonor P–N Ligands

Kunz and Uemura made an important breakthrough in the use of P–N-donor carbohydrate ligands in asymmetric catalysis.[46,47] Kunz and co-workers developed the phosphane–oxazoline ligand **63**, derived from D-glucosamine (Figure 18), for the allylic alkylation of symmetrically and unsymmetrically substituted allyl acetates with high enantioselectivities (*ee*s up to 98%).[46] Uemura and co-workers synthesised a series of phosphinite–oxazoline ligands **64**, also derived from D-glucosamine (Figure 18). The enantioselectivity (*ee*s up to 96%) was best with ligand **64a**, which had a methyl substituent on the oxazoline moiety, in the allylic alkylation and amination of 1,3-diphenylprop-2-enyl acetate.[47a,47b] These ligands also proved to be effective in the Pd-catalysed Heck arylation of 2,3-dihydrofuran (*ee*s up to 96%).[47c]

Recently, the replacement of the phosphinite group in ligand **64** by a phosphite moiety has led to the formation of phosphite–oxazoline ligands **65**–**68a**–**g** (Figure 18).[48] The introduction of a biaryl phosphite moiety in the ligand design proved to be highly advantageous. The new ligands **65** provided higher enantioselectivities and reaction rates than related phosphinite–oxazoline ligands both in Pd-catalysed

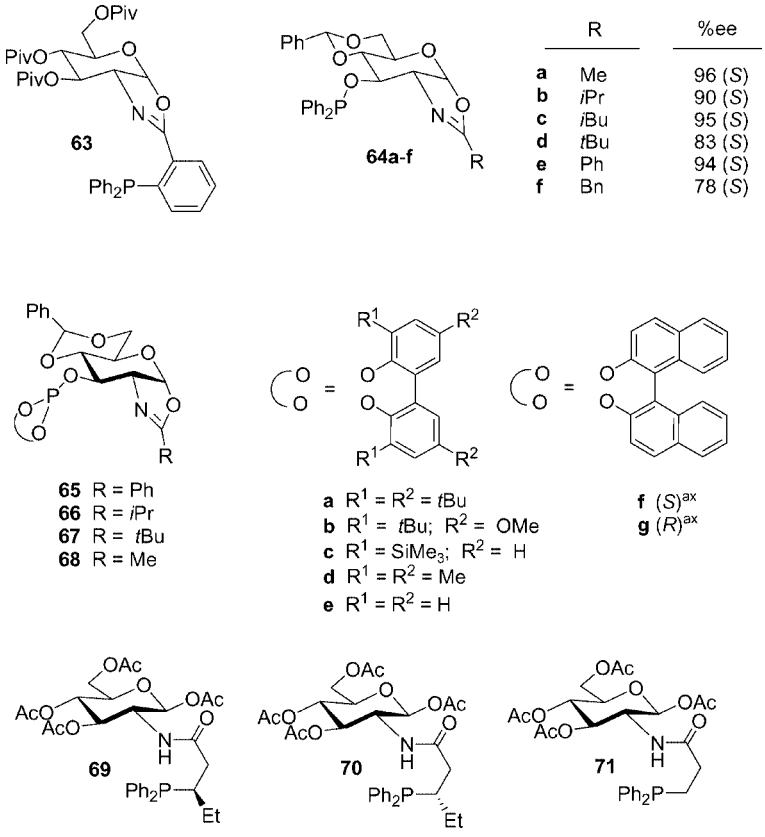


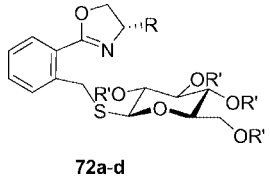
Figure 18. Heterodonor P–N ligands **63**–**71**.

allylic substitutions [*ee*s up to 99%, TOFs up to 400 mol substrate × (mol Pd × h)$^{-1}$][48a] and in Pd-catalysed Heck reactions (*ee*s up to 99%, total conversion in 10 min).[48b,48c] Moreover, the presence of a flexible phosphite moiety opens up the possibility of using the (phosphite–oxazoline)Pd catalytic systems with a wide range of different substrate types in both catalytic processes.

In 2005, Framery and co-workers developed phosphane–amide ligands **69**–**71** (Figure 18) derived from D-glucosamine for the Pd-catalysed allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate. The results clearly showed a cooperative effect between stereocenters that resulted in a matched combination for ligand **70** (*ee*s up to 86%).[49]

2.7.4. Heterodonor N–S Ligands

The thioglucose-derived compounds **72a**–**d**, each containing a chiral oxazoline moiety (Figure 19), that were used as chiral ligands in palladium-catalysed allylic alkylations of 1,3-diphenylprop-2-enyl acetate have proved to be some of the most successful mixed N–S donor ligands in this reaction. The effects of the thiosugar substituents on enantioselectivity were mild.[50]



72a-d

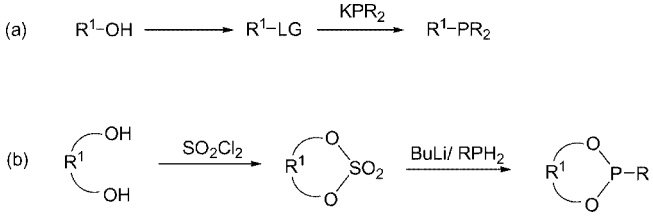
	R	R'	% ee
a	*i*Pr	C(O)Me	93 (*S*)
b	*i*Pr	C(O)*t*Bu	97 (*S*)
c	Ph	C(O)Me	90 (*S*)
d	Ph	C(O)*t*Bu	96 (*S*)

Figure 19. Heterodonor N–S ligands **72**.

3. General Synthesis of Carbohydrate-Based Ligand Types

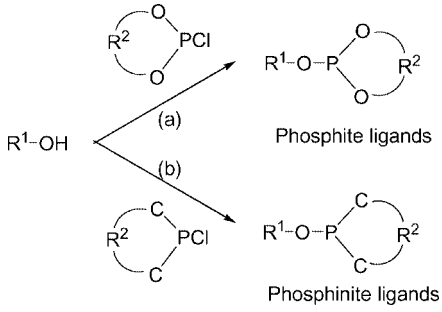
Most of the carbohydrate ligands dealt with in this review were synthesised from sugars or sugar derivatives such as xylose, fructose, glucose, mannitol and tartaric acid, among others. This has given rise to a wide range of sugar backbones with different electronic and steric properties. Most of the carbohydrate-based ligands developed for asymmetric catalysis are P-donors. Although phosphane sugar ligands played an early dominant role in several enantioselective catalytic processes, other types of ligands, such as phosphinite, phosphite, phosphoroamidite, oxazoline and thioether and their combinations have emerged more recently as suitable ligands for asymmetric catalysis. Their lower sensitivity to air and other oxidizing agents, easier synthesis (fewer steps) from readily available alcohols and easier modular construction have proved to be highly advantageous. We now summarise the steps involved in the synthesis of the most relevant types of ligand groups (phosphane, phosphite, phosphinite, thioether, oxazoline and their combinations).

In general, the phosphane sugar ligands presented in this review are prepared in two main steps by using two different synthetic procedures: (a) conversion of the alcohol unit of the sugar backbone into a leaving group (usually a mesyl, tosyl or a triflate) and subsequent treatment with the desired diaryl- or dialkylphosphide salt [Scheme 1(a)], or (b) treatment of two alcohol units of the sugar with thionyl chloride to form the corresponding sulfate, which is then treated with the desired phosphanide salt to give the corresponding phosphane [Scheme 1(b)].



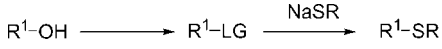
Scheme 1. Typical synthetic procedures for the preparation of phosphane ligands (LG = leaving group).

The most successful carbohydrate phosphite and phosphinite ligands are synthesised very efficiently in one step from the corresponding sugar alcohols (Scheme 2). Therefore, treatment of the corresponding phosphorochloridite [Scheme 2(a)] or chlorophosphane [Scheme 2(b)] with the appropriate sugar alcohol in basic media produce the desired phosphite or phosphinite ligand, respectively.



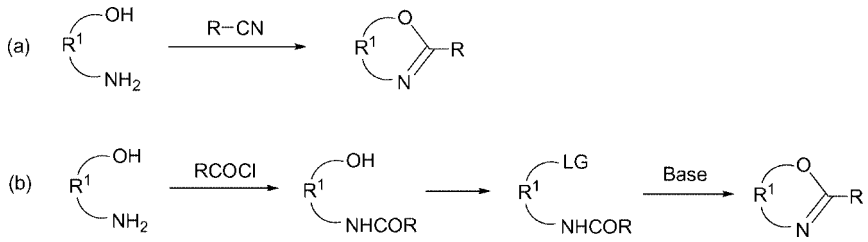
Scheme 2. Typical synthesis of phosphite and phosphinite ligands.

Thioether ligands are synthesised in two steps using an approach similar to method (a) described above for the phosphane ligands. The alcohol unit of the sugar backbone is first converted into a leaving group (usually a triflate) and then reacts with the corresponding thiolate salt (Scheme 3).



Scheme 3. Typical synthesis of thioether ligands.

Sugar oxazoline ligands are prepared mainly by two different synthetic procedures: (a) in one step by treatment of the appropriate 1,2-amino alcohol sugar unit with a nitrile compound in the presence of a Lewis acid [Scheme 4(a)], or (b) in three steps by treatment of the amino alcohol sugar compound with 1 equiv. of acyl chloride to form the corresponding amide, subsequent transformation of the hydroxy group of the resulting amide compound into a leaving group and finally the addition of a base to give rise to the formation of the oxazoline [Scheme 4(b)].



Scheme 4. Typical synthetic procedures for the preparation of oxazoline ligands (LG = leaving group).

4. Concluding Remarks

Carbohydrate ligands have undoubtedly become some of the most versatile ligands for enantioselective catalysis. They were mainly developed for asymmetric hydrogenations and allylic substitutions and, to a lesser extent, for hydroformylations, hydrocyanations, 1,4- and 1,2-additions and Heck reactions. However, the excellent results obtained in the later catalytic processes are expected to lead to new designs of carbohydrate ligands. Among these ligands, bidentate phosphorus donors have been widely used. These are mainly phosphanes, phosphinites and phosphites, but other donor atoms such as sulfur or nitrogen and monodentate ligands have recently also emerged as suitable carbohydrate ligands. All these ligands were synthesised from sugars or sugar derivatives such as xylose, fructose, glucose, mannitol and tartaric acid, among others. This has led to a wide range of sugar backbones with different electronic and steric properties. The properties of the ligand have proved to lead to excellent control of selectivity. This means that by appropriate ligand tuning (i) a ligand can be selected for each particular reaction, and (ii) both enantiomers of the product are accessible.

Acknowledgments

We thank the Spanish Government (Consolider Ingenio CSD2006-0003, CTQ2004-04412/BQU and the Ramon y Cajal fellowship for O. P.) and the Catalan Government (2005SGR007777 and Distinction to M. D. and C. C.) for financial support.

[1] See, for example: a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; b) I. Ojima, *Catalytic Asymmetric Synthesis*, Wiley, New York, **2000**; c) E. N. Jacobsen, A. Pfaltz, H. Yamamoto, *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**.

[2] See, for instance: a) M. Diéguez, O. Pàmies, C. Claver, *Chem. Rev.* **2004**, *104*, 3189–3215; b) M. Diéguez, O. Pàmies, A. Ruiz, Y. Díaz, S. Castillón, C. Claver, *Coord. Chem. Rev.* **2004**, *248*, 2165–2192; c) M. Diéguez, A. Ruiz, C. Claver, *Dalton Trans.* **2003**, 2957–2963; d) O. Pàmies, M. Diéguez, A. Ruiz, C. Claver, *Chim. Oggi* **2004**, *22*, 12–14.

[3] H. N. Kagan, T. P. Dang, *J. Am. Chem. Soc.* **1972**, *94*, 6429–6433.

[4] See, for instance: W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029–3070.

[5] a) U. Nagel, E. Kinzel, J. Andrade, G. Prescher, *Chem. Ber.* **1986**, *119*, 3326–3343; b) U. Nagel, B. Rieger, *Organometallics* **1989**, *8*, 1534–1538.

[6] W. Li, J. P. Waldkirch, X. Zhang, *J. Org. Chem.* **2002**, *67*, 7618–7623.

[7] a) Y. Y. Yan, T. V. RajanBabu, *Org. Lett.* **2000**, *2*, 4137–4140; b) W. Li, X. Zhang, *J. Org. Chem.* **2000**, *65*, 5871–5874; c) X. Zhang, US Patent WO 01/34612 A2, **2001**.

[8] D. Liu, W. Li, X. Zhang, *Tetrahedron: Asymmetry* **2004**, *15*, 2181–2184.

[9] a) J. Holz, M. Quirmbach, U. Schmidt, D. Heller, R. Stürmer, A. Börner, *J. Org. Chem.* **1998**, *63*, 8031–8034; b) W. Li, Z. Zhang, D. Xiao, X. Zhang, *J. Org. Chem.* **2000**, *65*, 3489–3496; c) D. Liu, W. Li, X. Zhang, *Org. Lett.* **2002**, *4*, 4471–4474; d) A. Bayer, P. Murszat, U. Thewalt, B. Rieger, *Eur. J. Inorg. Chem.* **2002**, 2614–2624; e) J. Holz, R. Stürmer, U. Schmidt, H. J. Drexler, D. Heller, H. P. Krimmer, A. Börner, *Eur. J. Org. Chem.* **2001**, 4615–4624; f) J. Holz, D. Heller, R. Stürmer, A. Börner, *Tetrahedron Lett.* **1999**, *40*, 7059–7062; g) T. V. RajanBabu, Y. Y. Yan, S. Shin, *J. Am. Chem. Soc.* **2001**, *123*, 10207–10213; h) Y. Y. Yan, T. V. RajanBabu, *Org. Lett.* **2000**, *2*, 199–202; i) X. Zhang, WO Patent 03/040149 A2, **2003**.

[10] M. Kessegruber, M. Thommen, WO Patent 2004098772 A2, **2004**.

[11] D. Carmichael, H. Doucet, J. M. Brown, *Chem. Commun.* **1999**, 261–262.

[12] See, for instance: B. M. Trost, D. L. van Vranken, *Chem. Rev.* **1996**, *96*, 395–422.

[13] F. Ruffo, R. Del Litto, A. De Roma, A. D'Errico, S. Magnolia, *Tetrahedron: Asymmetry* **2006**, *17*, 2265–2269.

[14] a) R. Jackson, D. J. Thompson, *J. Organomet. Chem.* **1978**, *159*, C29–C31; b) R. Selke, H. Pracejus, *J. Mol. Catal.* **1986**, *37*, 213–225; c) R. Selke, *J. Prakt. Chem.* **1987**, *329*, 717–724; d) R. Selke, *J. Organomet. Chem.* **1989**, *370*, 249–256; e) R. Selke, M. Schwarze, H. Baudisch, I. Grassert, M. Michalik, G. Oehme, N. Stoll, B. Costisella, *J. Mol. Catal.* **1993**, *84*, 223–237.

[15] a) T. V. RajanBabu, T. A. Ayers, A. L. Casalnuovo, *J. Am. Chem. Soc.* **1994**, *116*, 4101–4102; b) T. V. RajanBabu, T. A. Ayers, G. A. Halliday, K. K. You, J. C. Calabrese, *J. Org. Chem.* **1997**, *62*, 6012–6028; c) T. A. Ayers, T. V. RajanBabu, US Patent 5510507, 1996; d) T. V. RajanBabu, A. L. Casalnuovo, *J. Am. Chem. Soc.* **1992**, *114*, 6265–6266; e) A. L. Casalnuovo, T. V. RajanBabu, T. A. Ayers, T. H. Warren, *J. Am. Chem. Soc.* **1994**, *116*, 9869–9882.

[16] T. V. RajanBabu, A. L. Casalnuovo, *Pure Appl. Chem.* **1994**, *66*, 1535–1542.

[17] K. Yonehara, K. Ohe, S. Uemura, *J. Org. Chem.* **1999**, *64*, 9381–9385.

[18] a) H. Brunner, W. Pieronczyk, *J. Chem. Res. (S)* **1980**, 76–76; b) E. Guimet, M. Diéguez, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2004**, *15*, 2247–2251.

[19] a) M. Aghmiz, A. Aghmiz, Y. Díaz, A. M. Masdeu-Bultó, C. Claver, S. Castillón, *J. Org. Chem.* **2004**, *69*, 7502–7510; b) M. Meseguer, H.-C. Militzer, S. Castillón, C. Claver, Y. Díaz, M. Aghmiz, E. Guiu, A. Masdeu, DE Patent 10241256 A1, **2004**.

[20] a) E. Guimet, J. Parada, M. Diéguez, A. Ruiz, C. Claver, *Appl. Catal., A* **2005**, *282*, 215–220; b) E. Guimet, M. Diéguez, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2005**, *16*, 2161–2165; c) E. Guimet, M. Diéguez, A. Ruiz, C. Claver, *Inorg. Chim. Acta* **2005**, *358*, 3824–3828.

[21] M. T. Reetz, T. Neugebauer, *Angew. Chem. Int. Ed.* **1999**, *38*, 179–181.

[22] M. T. Reetz, G. Mehler, *Angew. Chem. Int. Ed.* **2000**, *39*, 3889–3893.
[23] a) A. Alexakis, J. Burton, J. Vastra, C. Benhaim, X. Fournioux, A. van den Heuvel, J. M. Levêque, F. Mazé, S. Rosset, *Eur. J. Org. Chem.* **2000**, 4011–4027; b) A. Alexakis, C. Benhaim, *Org. Lett.* **2000**, *2*, 2579–2581; c) A. Alexakis, J. Vastra, J. Burton, C. Benhaim, P. Mangeney, *Tetrahedron Lett.* **1998**, *39*, 7869–7872.
[24] a) G. J. H. Buisman, M. E. Martin, E. J. Vos, A. Klootwijk, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Tetrahedron: Asymmetry* **1995**, *6*, 719–738; b) M. Diéguez, O. Pàmies, A. Ruiz, S. Castillón, C. Claver, *Chem. Commun.* **2000**, 1607–1608; c) M. Diéguez, O. Pàmies, A. Ruiz, S. Castillón, C. Claver, *Chem. Eur. J.* **2001**, *7*, 3086–3094; d) M. Diéguez, O. Pàmies, A. Ruiz, C. Claver, *New J. Chem.* **2002**, *26*, 827–833; e) O. Pàmies, G. Net, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2001**, *12*, 3441–3445; f) M. Diéguez, O. Pàmies, C. Claver, *Chem. Commun.* **2005**, 1221–1223.
[25] a) O. Pàmies, G. Net, A. Ruiz, C. Claver, *Eur. J. Inorg. Chem.* **2000**, 1287–1294; b) M. Diéguez, A. Ruiz, C. Claver, *J. Org. Chem.* **2002**, *67*, 3796–3801.
[26] a) M. Diéguez, S. Jansat, M. Gomez, A. Ruiz, G. Muller, C. Claver, *Chem. Commun.* **2001**, 1132–1133; b) O. Pàmies, G. P. F. van Strijdonck, M. Diéguez, S. Deerenberg, G. Net, A. Ruiz, C. Claver, P. C. J. Kamer, P. W. N. M. van Leeuwen, *J. Org. Chem.* **2001**, *66*, 8867–8871; c) M. Diéguez, O. Pàmies, C. Claver, *Adv. Synth. Catal.* **2005**, *347*, 1257–1266; d) S. Jansat, M. Gómez, K. Philippot, G. Muller, E. Guiu, C. Claver, S. Castillón, B. Chaudret, *J. Am. Chem. Soc.* **2004**, *126*, 1592–1593.
[27] a) O. Pàmies, G. Net, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **1999**, *10*, 2007–2010; b) O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2000**, *11*, 4377–4383; c) M. Diéguez, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2001**, *12*, 2895–2900.
[28] L. Wang, Y.-M. Li, C.-W. Yip, L. Qiu, Z. Zhou, A. S. C. Chan, *Adv. Synth. Catal.* **2004**, *346*, 947–953.
[29] A. Alexakis, J. Vastra, J. Burton, P. Mangeney, *Tetrahedron: Asymmetry* **1997**, *8*, 3193–3196.
[30] M. van den Berg, A. J. Minnaard, E. P. Schudde, J. van Esch, J. G. de Vries, B. L. Feringa, *J. Am. Chem. Soc.* **2000**, *122*, 11539–11540.
[31] M. T. Reetz, L. J. Goosen, A. Meiswinkel, J. Paetzol, J. F. Jensen, *Org. Lett.* **2003**, *5*, 3099–3101.
[32] a) H. Huang, Z. Zheng, H. Luo, C. Bai, X. Hu, H. Chen, *Org. Lett.* **2003**, *5*, 4137–4139; b) H. Huang, Z. Zheng, H. Luo, C. Bai, X. Hu, H. Chen, *J. Org. Chem.* **2004**, *69*, 2335–2361; c) H. Huang, X. Liu, H. Chen, Z. Zheng, *Tetrahedron: Asymmetry* **2005**, *16*, 693–697; d) H. Huang, X. Liu, S. Chen, H. Chen, Z. Zheng, *Tetrahedron: Asymmetry* **2004**, *15*, 2011–2019.
[33] Y. Mata, M. Diéguez, O. Pàmies, S. Woodward, *J. Org. Chem.* **2006**, *71*, 8159–8165.
[34] See, for instance: a) B. L. Feringa, *Acc. Chem. Res.* **2000**, *33*, 346–353; b) R. B. C. Jagt, P. Y. Toullec, D. Geerdink, J. G. de Vries, B. L. Feringa, A. J. Minnaard, *Angew. Chem. Int. Ed.* **2006**, *45*, 2789–2791; c) K. Tissot-Croset, D. Polet, A. Alexakis, *Angew. Chem. Int. Ed.* **2004**, *43*, 2426–2428; d) D. Polet, A. Alexakis, K. Tissot-Croset, C. Corminboeuf, K. Ditrich, *Chem. Eur. J.* **2006**, *12*, 3596–3609; e) M. D. K. Boele, P. C. J. Kamer, M. Lutz, A. L. Spek, J. G. de Vries, P. W. N. M. van Leeuwen, G. P. F. van Strijdonck, *Chem. Eur. J.* **2004**, *10*, 6232–6246; f) K. Biswas, O. Prieto, P. J. Goldsmith, S. Woodward, *Angew. Chem. Int. Ed.* **2005**, *44*, 2232–2234; g) A. Alejakis, C. Benhaim, S. Rosset, M. Humam, *J. Am. Chem. Soc.* **2002**, *124*, 5262–5263.
[35] E. Raluy, M. Diéguez, O. Pàmies, *J. Org. Chem.* **2007**, *72*, 2842–2850.
[36] For a review on sulfur ligands, see: A. M. Masdeu-Bultó, M. Diéguez, E. Martin, M. Gómez, *Coord. Chem. Rev.* **2003**, *242*, 159–201.
[37] a) S. Jansat, M. Gómez, G. Müller, M. Diéguez, A. Aghmiz, C. Claver, A. M. Masdeu Bultó, L. Flores-Santos, E. Martin, M. A. Maestro, J. Mahía, *Tetrahedron: Asymmetry* **2001**, *12*, 1469–1474; b) F. Fernández, M. Gómez, S. Jansat, G. Müller, E. Martin, L. Flores-Santos, P. X. García, A. Aghmiz, M. Jiménez-Pedrós, A. M. Masdeu-Bultó, M. Diéguez, C. Claver, M. A. Maestro, *Organometallics* **2005**, *24*, 3946–3956.
[38] a) N. Khiar, C. S. Araújo, E. Alvarez, I. Fernández, *Tetrahedron Lett.* **2003**, *44*, 3401–3404; b) N. Khiar, C. S. Araújo, B. Suárez, I. Fernández, *Eur. J. Org. Chem.* **2006**, 1685–1700.
[39] M. Irmak, A. Groschner, M. M. K. Boysen, *Chem. Commun.* **2007**, 177–179.
[40] a) O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, *Chem. Commun.* **2000**, 2383–2384; b) O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, *J. Org. Chem.* **2001**, *66*, 8364–8369.
[41] a) M. Diéguez, A. Ruiz, C. Claver, *Chem. Commun.* **2001**, 2702–2703; b) E. Raluy, C. Claver, O. Pàmies, M. Diéguez, *Org. Lett.* **2007**, *9*, 49–52.
[42] E. Guiu, M. Aghmiz, Y. Díaz, C. Claver, B. Meseguer, C. Militzer, S. Castillón, *Eur. J. Org. Chem.* **2006**, 627–633.
[43] A. Albinati, P. S. Pregosin, K. Wick, *Organometallics* **1996**, *15*, 2419–2421.
[44] a) E. Guimet, M. Diéguez, A. Ruiz, C. Claver, *Tetrahedron: Asymmetry* **2005**, *16*, 959–963; b) M. Diéguez, O. Pàmies, C. Claver, *J. Organomet. Chem.* **2006**, *691*, 2257–2262; c) E. Guimet, M. Diéguez, A. Ruiz, C. Claver, *Dalton Trans.* **2005**, 2557–2562.
[45] a) N. Khiar, B. Suárez, M. Stiller, V. Valdivia, I. Fernández, *Phosphorus Sulfur Silicon Relat. Elem.* **2005**, *180*, 1253–1258; b) N. Khiar, B. Suárez, V. Valdivia, I. Fernández, *Synlett* **2005**, 2963–2967.
[46] B. Gläser, H. Kunz, *Synlett* **1998**, 53–54.
[47] a) K. Yonehara, T. Hashizume, K. Mori, K. Ohe, S. Uemura, *Chem. Commun.* **1999**, 415–416; b) K. Yonehara, T. Hashizume, K. Mori, K. Ohe, S. Uemura, *J. Org. Chem.* **1999**, *64*, 9374–9380; c) K. Yonehara, K. Mori, T. Hashizume, K. G. Chung, K. Ohe, S. Uemura, *J. Organomet. Chem.* **2000**, *603*, 40–49.
[48] a) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Adv. Synth. Catal.* **2005**, *347*, 1943–1947; b) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Org. Lett.* **2005**, *7*, 5597–5599; c) Y. Mata, M. Diéguez, O. Pàmies, *Chem. Eur. J.* **2007**, *13*, 3296–3304.
[49] A. Konovets, K. Glegola, A. Penciu, E. Framery, P. Jubault, C. Goux-Henry, K. M. Pietrusiewicz, J. C. Quirion, D. Sinou, *Tetrahedron: Asymmetry* **2005**, *16*, 3183–3187.
[50] K. Boog-Wick, P. S. Pregosin, G. Trabesinger, *Organometallics* **1998**, *17*, 3254–3264.

Received: January 31, 2007
Published Online: July 6, 2007

