Available online at www.sciencedirect.com
SCIENCE DIRECT®
Coordination Chemistry Reviews 248 (2004) 2165–2192
COORDINATION CHEMISTRY REVIEWS
www.elsevier.com/locate/ccr

Review

Carbohydrate derivative ligands in asymmetric catalysis

Montserrat Diéguez [b], Oscar Pàmies [b], Aurora Ruiz [b], Yolanda Díaz [b], Sergio Castillón [b], Carmen Claver [a,*]

[a] *Departament de Química Física i Inorgànica, Universitat Rovira i Virgili, Plaça Imperial Tàrraco 1, E-43005 Tarragona, Spain*
[b] *Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili, Plaça Imperial Tàrraco 1, E-43005 Tarragona, Spain*

Received 24 November 2003; accepted 30 April 2004
Available online 6 August 2004

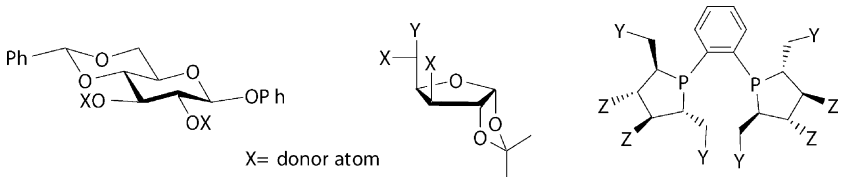
Contents

Abbreviations: BINAP, 2,2-bis(diphenylphosphino)-1,1′-binaphthyl; BSA, *N,O*-bis(trimethylsilyl)acetamide; COD, 1,5-cyclooctadiene; DEGUPHOS, 1-benzyl-3,4-bis(phenylsulphanyl)pyrrolidine; DIOP, *trans*-4,5-bis[(diphenylphosphonayl)methyl]-2,2-dimethyl-1,3-dioxolane; DIPAMP, 1,2-ethanediyl-bis(2-methoxyphenyl-phenyl)phosphine; DUPHOS, 1,2-bis((2,5-dimethylphospholano)benzene; ee , enantiomeric excess; MOM, methoxy-ethoxy-methylene; NBD, 2,5-norbornadiene; TADDOL, α,α,α′,α′-tetraphenyl-2,2′-dimethyl-1,3-dioxolane-4,5-dimethanol

* Corresponding author. Tel.: +34 977559574; fax: +34 077559563.
E-mail address: claver@quimica.urv.es (C. Claver).

doi:10.1016/j.ccr.2004.04.009

Carbohydrates are readily available and highly functionalized compounds with several stereogenic centers. The application of carbohydrate derivatives as ligands in asymmetric catalysis in different catalytic processes is discussed. The systematic modification of the carbohydrate ligands leads to high activity and selectivity in many metal-catalyzed processes.



Abstract

This review describes how carbohydrates have been applied as ligands in transition metal asymmetric catalysis. In general, carbohydrates are functionalized with donor atoms such as P, N or S so that they can be coordinated to transition metals. The review deals with all the different types of ligands in turn. After an introduction describing their general features and advantages in asymmetric catalysis, the carbohydrate phosphorus ligands, diphosphines, diphosphites, diphosphinites, and related phosphorus ligands are reviewed. Heterodonor carbohydrate or hemilabile ligands such as N,P-, N,S-, P,S-, S,O- as well as N,N-, S,S- and O,O-ligands are also discussed. Other related ligands are included because of their importance in asymmetric catalysis. In all cases the most important results of their application in asymmetric catalysis are highlighted and the intermediates are studied.

Keywords: Catalysis; Asymmetric; Enantioselectivity; Carbohydrate ligands

1. Introduction

Carbohydrates are naturally enantiomeric pure compounds which have an interesting stereochemical diversity. Apart from their biological role, they are important chiral auxiliaries for enantioselective organic syntheses. The carbohydrate-metal interactions are of interest in metal-assisted or metal-catalyzed enantioselective syntheses. Because homogeneous catalysis is one of the most important approaches for preparing enantiomeric pure compounds carbohydrate derivatives have been increasingly used as chiral ligands in the last decade. Carbohydrates generally contain several weak donor sites. Since many of the catalytic precursors in homogeneous catalysis are coordination complexes of the platinum-group metals, the required ligands should contain such donor atoms as N, S and P which can form stable complexes with practically all transition metals. Carbohydrates are particularly useful for this purpose. They are readily available and highly functionalized compounds with several stereogenic centers. From the point of view of coordination chemistry, the carbohydrate complexes of platinum-group metals have recently been reviewed in an extensive work that deals with the chemical aspects of isolated and well characterized complexes including catalytic applications [1]. Other reviews describing carbohydrate complexes and their properties have been published [2–5]. The present review deals with the application of carbohydrate derivatives as ligands in asymmetric catalysis and discusses the most important activity and enantioselectivity results obtained in several catalytic processes as well as the efficiency of the catalytic systems formed with these ligands. Carbohydrate ligands can be modified which means that the steric and electronic factors can be systematically varied by introducing different functionalities in the synthesis of series of chiral ligands. These series can be screened in the search for high activities and enantioselectivities in many asymmetric processes and in some cases the activities and selectivities are excellent, as will be shown here. At the same time, they can provide useful information about the origin of the stereoselectivity of the reaction. The review covers the catalytic systems based on transition metals and carbohydrate phosphorus, nitrogen, oxygen, sulphur and heterodonor or hemilabile N,P-, N,S-, P,S-, S,O-ligands. In all cases the most important results of their application in asymmetric catalysis are highlighted and the intermediates are studied. Tartrate derivatives and related ligands are included because of their relevance to asymmetric catalysis. Although in many cases the catalytic precursor is not an isolated coordination complex but a catalytic system based on a metallic complex with an added ligand, it is important to note that the intermediate species involved in the catalytic cycle are coordination complexes of transition metals, which are included in this review if they have been characterized and reported.

2. Carbohydrate ligand types in asymmetric catalysis

Because of the diversity of backbone structures and the fact that the carbohydrates which are used as ligands in transition metal catalytic precursors can be functionalised and modified, several types of ligands have been prepared in re-

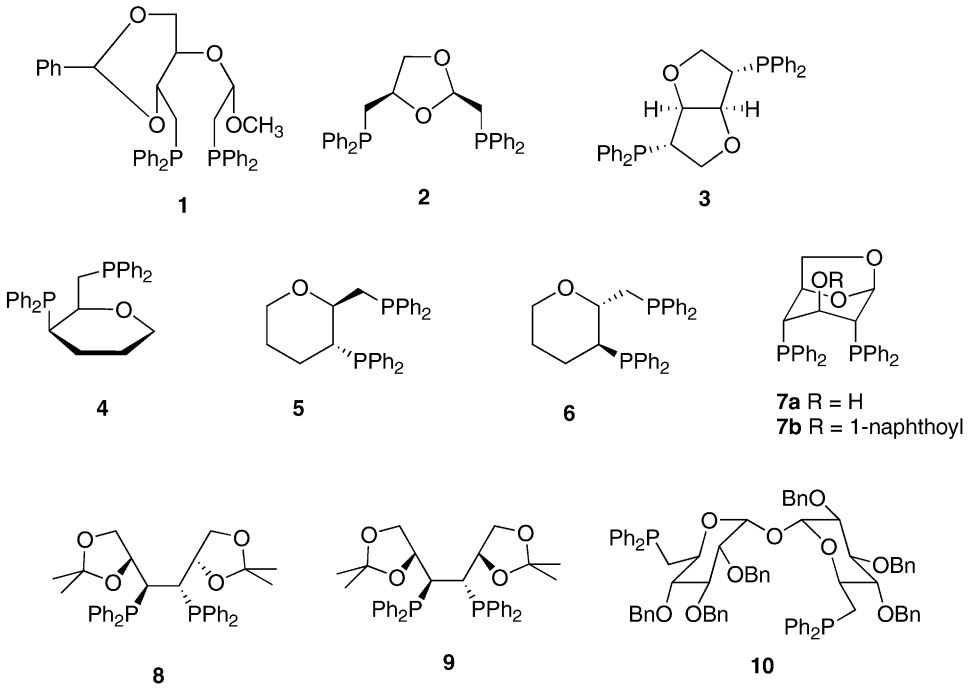


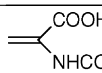
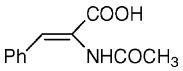
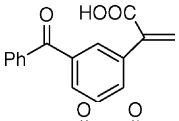
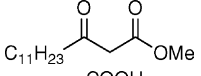
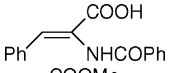
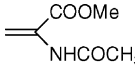
Fig. 1. Diphosphines with sugar backbones between 1979 and 1995.

cent decades. This review is organized according to the type of ligands studied, and takes into account first the nature of the donor atom (P, N, S, O) and second the functionalization of the ligand.

2.1. Carbohydrate bidentate phosphorus ligands

Bidentate ligands, in particular bidentate diphosphines have been considered the best ligands for transition metal asymmetric catalysis [6]. With the introduction of Kagan's DIOP, the first chiral diphosphane, the research on ligands for asymmetric catalysis focussed on bidentate ligands. Knowles et al. showed that DIPAMP as chelate diphosphine is superior to the corresponding monodentate species in rhodium catalyzed hydrogenation reaction. The use of bidentate ligands such as BINAP and DUPHOS have also led to extremely high enantiomeric excess values. These chelating compounds are supposed to be superior

Table 1
Metal-catalyzed asymmetric hydrogenation using ligands **1**–**10**

Entry	Substrate	Precursor	e.e. (%)[a]	Ref.
1		[Rh(COD)(**1**)]ClO_4 + NEt_3	20 (*R*)	[11]
2		[Rh(COD)(**2**)]ClO_4 + NEt_3	86 (*S*)	[11]
3		[Rh(COD)(**1**)]ClO_4 + Net_3	18 (*R*)	[11]
4		[Rh(COD)(**2**)]ClO_4 + NEt_3	78 (*S*)	[11]
5		[Rh(NBD)Cl]$_2$ + **3**	58[b]	[12]
6		[Rh(NBDd)$_2$]ClO_4 + **4**	73 (*S*)	[13]
7		[Rh(NBD)$_2$]ClO_4 + **5**	25 (*S*)	[14]
8		[Rh(NBD)$_2$]ClO_4 + **6**	6 (*S*)	[14]
9		[$Ru_2Cl(\mu\text{-}Cl)_3(COD)_2(CH_3CN)$] + **7a**	54[b]	[15]
10		[$Ru_2Cl(\mu\text{-}Cl)_3(COD)_2(CH_3CN)$] + **7b**	49[b]	[15]
11		[Rh(COD)$_2$]BF_4 + **8**	59[b]	[16]
12		[Rh(COD)$_2$]BF_4 + **9**	50[b]	[16]
13		Rh(I) + **10**	23[b], 82[b,c]	[17]

[a] Reaction carried out at 25 °C.
[b] Absolute configuration not determined.
[c] Reaction carried out at −10 °C.

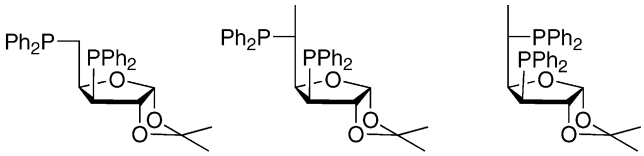
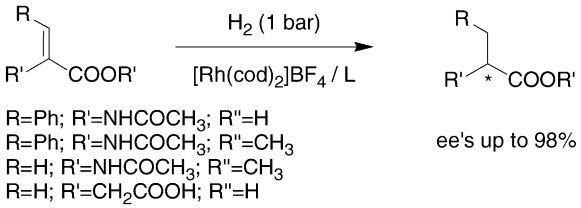


Fig. 2. Diphosphine ligands with a furanoside backbone derived from D-(+)-xylose and D-(+)-glucose.



Scheme 1. Rh-catalyzed asymmetric hydrogenation of dehydroamino acid derivatives using diphosphines **11**–**13**.

because of the resulting rigid catalysts which favor effective chiral induction [7]. Chiral diphosphites have been the subject of growing interest in asymmetric catalysis. In addition to their well known application in hydroformylation reaction [8], they have also been applied in other asymmetric processes, mainly in hydrogenation reactions [9]. Phosphine–phosphite, diphosphonites, diphosphinites, phosphoroamidites and other related ligands have been also applied in asymmetric catalysis and their scope has been expanded greatly in the last years [10].

2.1.1. Diphosphines

Initially, diphosphines derived from carbohydrates (Fig. 1) were used in the metal-catalyzed asymmetric hydrogenation of several prochiral olefins. In general, enantioselectivities were low to moderate (Table 1) [11–17]. Enantioselectivites were best with ligands **2** [11] and **4** [13] in the Rh-catalyzed asymmetric hydrogenation of acetamidoacrylic acid and *Z*-α-acetamidocinnamic acid, respectively (entries **2** and **6**).

Claver and co-workers made an important breakthrough in the use of diphosphine ligands with sugar backbones in asymmetric hydrogenation [18,19] They developed a series of C_1-derivative ligands from D-(+)-xylose and D-(+)-glucose (Fig. 2). Ligands **11** and **12** were efficiently applied in the Rh-catalyzed hydrogenation of α,β-unsaturated carboxylic acid derivatives (Scheme 1, e.e.'s as high as 98%). The results indicated that introducing methyl substituents at C-5 in ligand **11** significantly increased activity. Moreover, the configuration of C-5 strongly influences the enantioselectivity. Thus, results were better with ligand **12** than with ligand **13**.

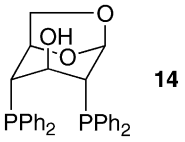
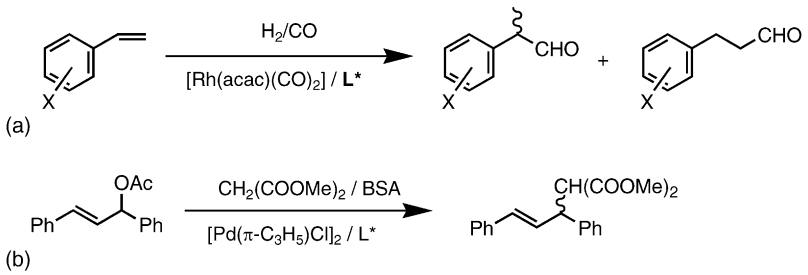


Fig. 3. Disphosphine developed by Liu et al. [23].

Ligands **11**–**13** were also applied in the Rh-catalyzed asymmetric hydroformylation of styrene derivatives [20] (Scheme 2a) and in Pd-catalyzed asymmetric allylic substitution reactions [21,22] (Scheme 2b). In general, activity was good and enantioselectivities moderate. As in the hydrogenation reaction, activities improved when a methyl substituent was introduced at C-5 of the sugar residue. It should be noted that in the hydroformylation reaction there is a cooperative effect between stereocenters C-3 and C-5, which results in a matched combination for ligand **12** (e.e.'s up to 58%). However, for the allylic alkylation, the configuration of C-5 has no relevant influence on the enantiodiscrimination. Also, for ligand **11** there is an important solvent effect which results in enantioselectivities as high as 78% when THF is used [21].

In 2000, Liu et al. designed a new diphosphine ligand **14** related to **7a** with a pyranoside backbone for the Rh-catalyzed asymmetric hydroformylation of olefins (Fig. 3) [23]. This ligand has shown excellent enantioselectivities in the hydroformylation of vinyl acetate (e.e.'s as high as 93%) while e.e.'s were moderate to low for styrene (e.e.'s as high as 68%) and norbornene (e.e.'s up to 25%). The rather high enantioselectivity in the hydroformylation of vinyl acetate is explained by the hydrogen bonding between the OH group in the ligand and the carbonyl group of the vinyl acetate.



Scheme 2. (a) Rh-catalyzed asymmetric hydroformylation of styrene derivatives and (b) Pd-catalyzed asymmetric allylic alkylation.

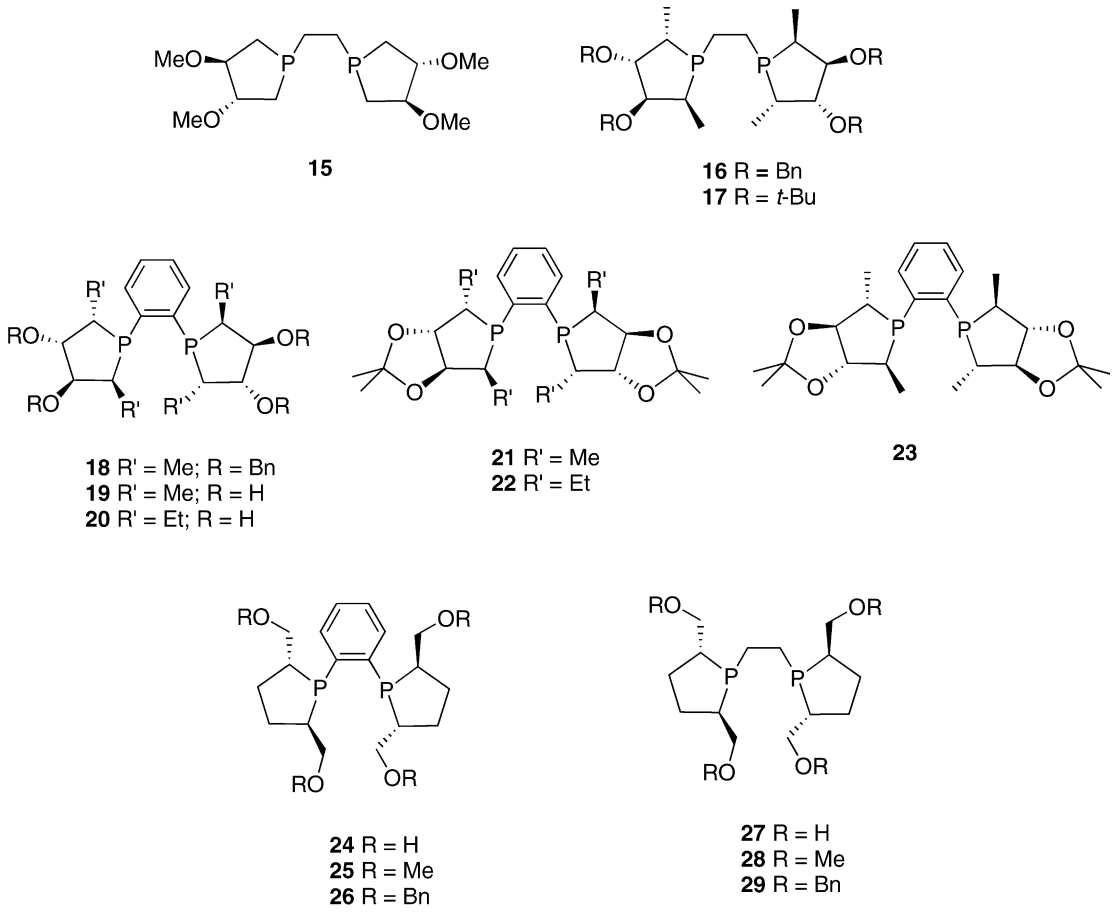


Fig. 4. Diphospholane ligands **15**–**29**.

Another important breakthrough came with a new class of bidentate ligands, the diphospholanes, derived mainly from D-mannitol, and related to DUPHOS. In recent years, they have emerged as a powerful ligands for asymmetric catalysis (Fig. 4) [24–28]. In 1987, Brunner and co-workers reported the synthesis of bisphospholane **15** derived from tartaric acid. However, due to the remote position of the chiral centers (β-position from the P-atom) from the metal center, the asymmetric induction in the Rh-catalytic hydrogenation of prochiral olefins was disappointingly low [24]. Recently, many modifications based on D-mannitol have been introduced, which result in highly efficient ligands for asymmetric catalysis.

In particular, Holz et al. developed novel diphospholanes **16**–**18** derived from D-mannitol. They have chiral information at both the α- and β-position of the phosphorus atom [25]. These ligands were tested in the Rh-catalyzed hydrogenation of a range of functionalized olefins. In all cases enantioselectivities were high (between 92.6 and 99.1% e.e.).

In this context, the groups of Zhang and co-workers [26] and Yan and RajanBabu [27] independently developed new diphospholanes **19**–**23**. These ligands have been extensively applied in the Rh-catalyzed asymmetric hydrogenation of dehydroamino acids and their derivatives, itaconic acid and its derivatives, enamides and enolacetates (Scheme 1). Surprisingly, the isopropylidene-protected bisphopholanes **21** and **22** did not work in this process. However, the rhodium complexes with ligands **19** and **20** are highly effective hydrogenation catalysts (e.e.'s usually >99%) [26]. Ligands **21** and **23** have also been applied in Pd-catalyzed allylic alkylation of dimethyl malonate to (*E*)-1,3-diphenylprop-2-enyl acetate. Enantioselectivies were high: 94% (*S*) (using ligand **21**) and >99% (*R*) (using ligand **23**) [27]. Interestingly, the sense of asymmetric induction appears to be dictated by the absolute stereochemistry of the P-carrying carbons.

Another recent series of diphospholane ligands **24**–**29** was efficiently used in the Rh-catalyzed asymmetric hydrogenation of α- and β-amino acid derivatives, itaconates and an unsaturated phosphonate. The enantioselectivities, ranging from 8 to 99% e.e., were strongly dependent on the type of substituent on the oxymethyl group as well on the bridge connecting the phospholane units. Thus, enantioselectivities were best with ligand. In the hydrogenation of prochiral β-oxo esters, e.e.'s as high as 98.8% were achieved with the Ru-**25** catalyst [28].

Brown and co-workers developed some interesting phospholane ligands in which a phospholane moiety (**30**–**31**),

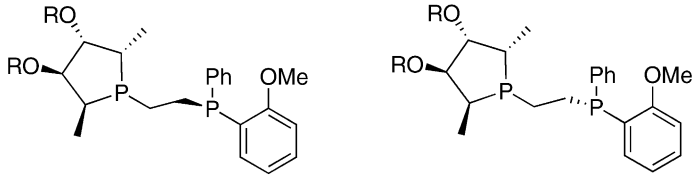


Fig. 5. Diphosphine ligands developed by Brown and co-workers.

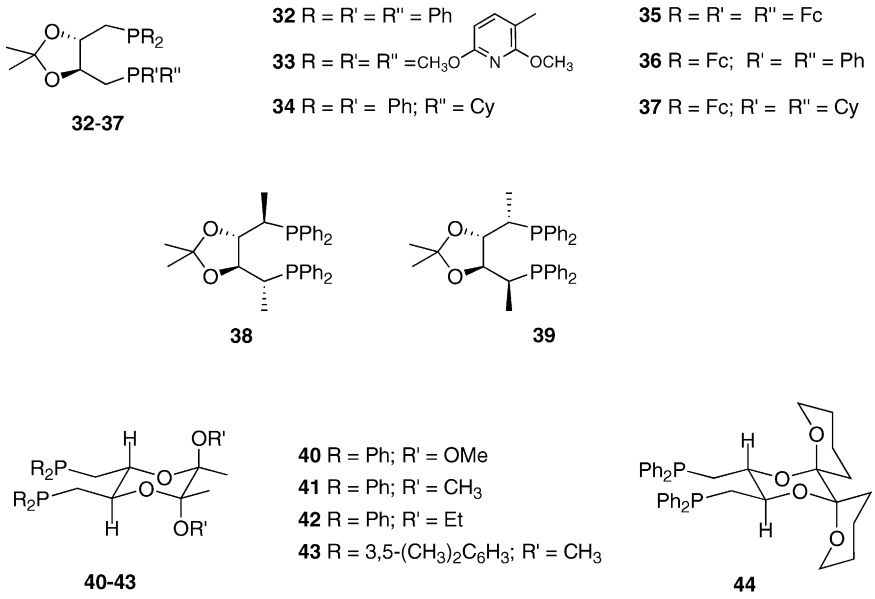


Fig. 6. C_2-symmetric diphosphine ligands derived from tartaric acid.

derived from D-mannitol, is combined with a DIPAMP type phosphine through an ethylene bridge (Fig. 5). These ligands were applied in the Rh-catalyzed hydrogenation of several itaconates with e.e.'s ranging between 80 and 95% [29].

The early successful application of the diphosphine DIOP (derived from tartaric acid) in Rh-catalyzed asymmetric hydrogenation [30] has recently resulted in the synthesis of several types of modified DIOP ligands (Fig. 6) [31–36]. In this context, the use of ligand **33** in the Rh-catalyzed asymmetric hydrogenation of amidoacrylic acids, enols and itaconic acids resulted in similar enantioselectivities but reversed absolute configuration to that obtained with DIOP ligand **32** [31]. However, the use of DIOP derivative ligands **34**–**37** led to lower enantioselectivites than those of the Rh-DIOP catalytic system in the asymmetric hydrogenation of dehydroamino acid derivatives [32,33].

The DIOP ligand was efficiently modified by introducing a methyl substituent in the α-positions of the phosphine groups. Thus, for the asymmetric hydrogenation of aryl enamides, ligand **38** resulted in better enantioselectivities (as high as 99%) than the DIOP ligand **32** [34,35]. Ligand **39** also improved the enantioselectivity of the Pd-catalyzed alkylation of dimethyl malonate to 1,3-diphenylprop-2-enyl acetate from 0 to 63% e.e. [27].

Another efficient modification by Zhang and co-workers resulted in ligands **40**–**44**, which contain a conformationally rigid 1,4-dioxane backbone. These ligands provide excellent enantioselectivities(as high as 99% e.e.) in the asymmetric hydrogenation of aryl enamides and MOM-protected β-hydroxyl enamides [36].

Another type of efficient diphosphine ligand derived from tartaric acid is the DEGUPHOS (**45**) and its derivatives **46**–**48** (Fig. 7) [37,38]. These ligands have also proven to be excellent for the Rh-catalyzed asymmetric hydrogenation of dehydroamino acid derivatives (Scheme 1) (e.e.'s as high as >99%).

2.1.2. Diphosphinites

The first examples of using diphosphinite ligands with a carbohydrate backbone in asymmetric catalysis were reported by the groups of Cullen [39], Jackson and Thompson

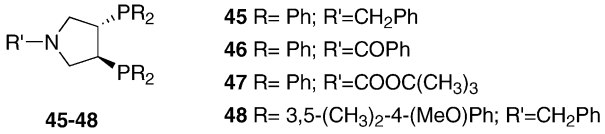


Fig. 7. Related DEGUPHOS ligands derived from tartaric acid.

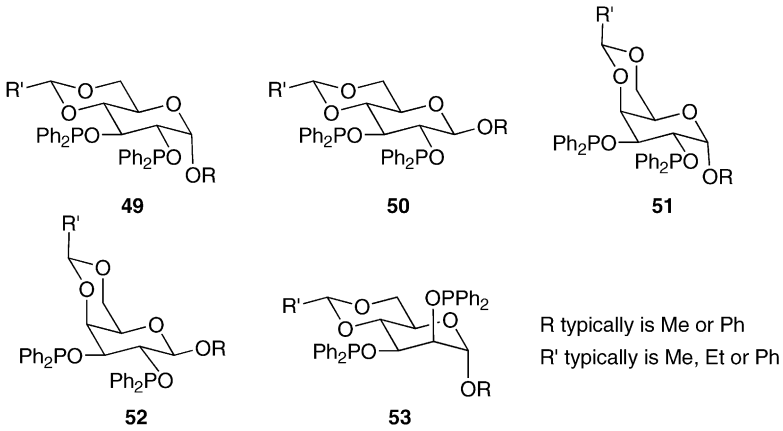


Fig. 8. Series of 2,3-diphenylphosphinite pyranoside ligands.

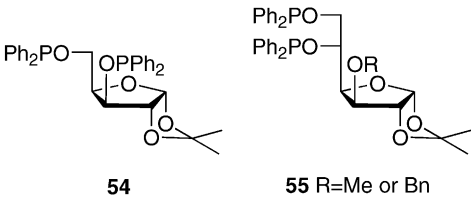


Fig. 9. Diphosphinite ligands with a furanoside backbone.

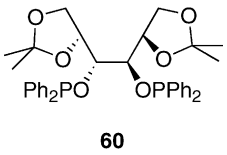


Fig. 11. Diphosphinite ligand 60 derived from D-mannitol.

[40], Selke [41] and Sinou and Descotes [42]. They studied a wide variety of 2,3-diphenylphosphinite pyranoside ligands (Fig. 8) in the asymmetric hydrogenation of dehydroamino acid derivatives (Scheme 1). In particular, enantioselecitivities (e.e.'s as high as 96.6%) were best with a series of β-glucopyranoside 2,3-diphosphinite ligands **50**, mainly developed by Selke and co-workers [39–41,43–47].

More recently, Börner and co-workers have used diphosphinite ligands **50** for the Rh-catalyzed asymmetric hydrogenation of imines with low enantioselecitivity [48].

In the 1980s, diphosphinite ligands with furanoside backbone derived from D-(+)-xylose **54** [49] and D-(+)-glucose **55** [50,51] (Fig. 9) were applied in the Rh-catalyzed asymmetric hydrogenation of α-acetamidocinnamic acid and in the asymmetric Grignard cross-coupling reaction, respectively. Enantioselectivities were low to moderate.

Ligand **54** was recently applied in the Ir-catalyzed hydrogenation of imines and provided moderate enantioselectivity (e.e.'s as high as 57%) [52]. Independently, the same ligand has been applied in the Ir-catalyzed hydrogenation of methyl α-acetamidoacrylate with e.e.'s as high as 83% [53].

In the late 1980s, Sunjic and co-workers developed a series of diphosphinite ligands with a pyranoside backbone (**56**–**59**) (Fig. 10) for the Rh-catalyzed asymmetric hydrogenation of *Z*-acetylaminocinnamic acid. Enantioselectivities (as high as 90.4% e.e.) were best with ligand **56** [54,55].

In 1989, Yamashita et al. prepared a diphosphinite ligand derived from D-mannitol **60** (Fig. 11). Enantioselectivites as high as 78% were obtained in the Rh-catalyzed hydrogenation of itaconic acid [56]. In 1999, Chan and co-workers used the same ligand for the Rh-catalyzed hydrogenation of α-acetamidoacrylic acid, which provided e.e.'s of up to 96.7% [57].

Recently, RajanBabu and co-workers have studied further modifications in the previously mentioned β-glucopyranoside 2,3-diphosphinite type ligand **50** and their use in the Ni-catalyzed asymmetric hydrocyanation and cross-coupling reaction, Rh-catalyzed asymmetric hydroformylation and hydrogenation of olefins and in the Pd-catalyzed asymmetric allylic alkylation reactions [7,58]. They systematically

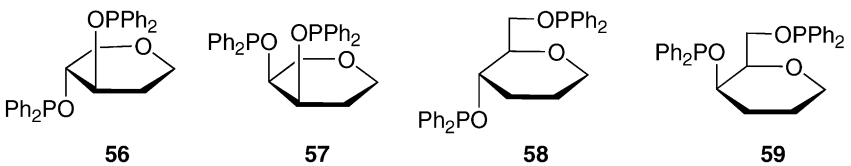


Fig. 10. Diphosphinite ligands with a pyranoside backbone.

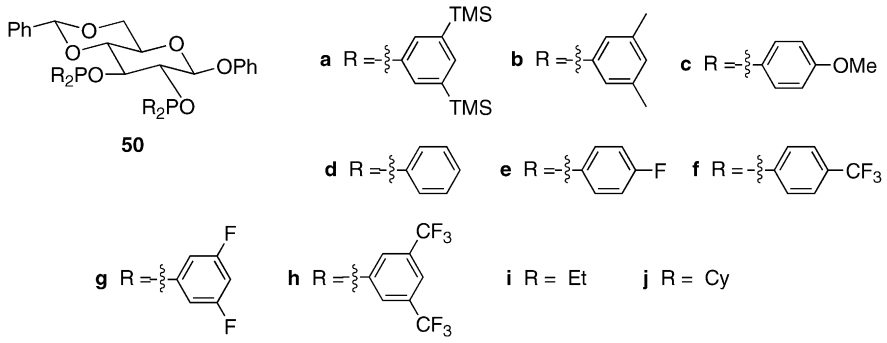
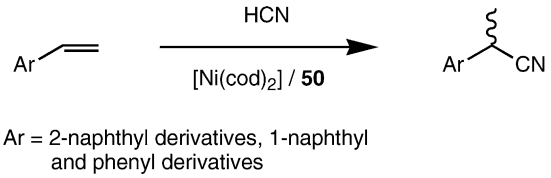


Fig. 12. Modifications of diphosphinite ligand **50** developed by RajanBabu.



Scheme 3. Ni-catalyzed asymmetric hydrocyanation reaction.

studied the electronic and steric properties of the diphosphinite ligands by introducing different phosphinite groups (**a**–**h**) in the basic ligand framework **50** (Fig. 12).

The results of the hydrocyanation [59–62] and hydroformylation [63] of various vinylarenes indicate that diphosphinite ligands with electron-withdrawing aryl substituent groups on the phosphorus give the best enantioselectivity. Thus, for the first process, ligands **50g** and **50h** provided e.e.'s of up to 91% (Scheme 3), whereas for the latter, e.e.'s were as high as 72% with ligand **50h**.

Ligands **50** were also used in the Ni-catalyzed cross coupling reaction of Grignard reagents and allylic phenyl ethers with moderate enantioselectivity (e.e.'s as high as 62% in the (*S*) isomer) [58].

For the asymmetric hydrogenation of several α,β-dehydroamino acid derivatives enantioselectivities were best with diphosphinite ligands with electron-donating aryl substituent groups on the phosphorus. Thus, e.e.'s as high as 99% were obtained with ligands **50a** and **50b** [64,65].

In general, the Pd-catalyzed alkylation of diethyl malonate to 1,3-diphenylprop-2-enyl acetate with ligands **50** proceeded with low to moderate enantioselectivities (e.e.'s as high as 59%). Interestingly, electron-withdrawing and electronic-rich diphosphinite ligands give products with opposite stereochemistries. Sterically bulky substituents have the same effect as electron-rich ones [66,67].

RajanBabu and co-workers have also developed new 3,4-diarylphosphinite ligands with a pyranoside backbone **61** and **65** and with a fructofuranoside backbone **66** (Fig. 13). These ligands have been applied in the Ni-catalyzed asymmetric hydrocyanation and in the Ni-catalyzed cross coupling reaction, and in the Rh-catalyzed asymmetric hydrogenation of alkenes [7b,58,60,62,65]. Ligands **61** and **62** were successfully applied in the hydrogenation reaction (e.e.'s as high as 98.3%). Interestingly, the sense of enantioselecitvity is reversed to that obtained with ligand **50**. And in this case also, the enantioselectivity was best with electron-donating substituents in the phosphinite moiety [65]. Ligand **66b**, with a diphenylphosphinite in C-3 and a bis(3,5-ditrifluromethylphenyl)phosphinite in C-4, provided excellent enantioselectivities (as high as 94%) in the asymmetric hydrocyanation of vinylarenes [62]. Ligands **61**–**65** were applied in the coupling reaction of Grignard reagents and allylic phenyl ethers with moderate enantioselectivity, but, interestingly, the sense of enantioselecitvity is reversed to that obtained with ligand **50** [58].

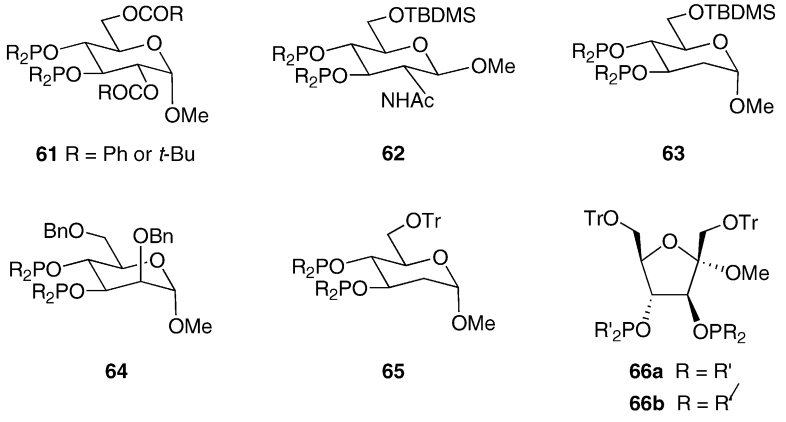
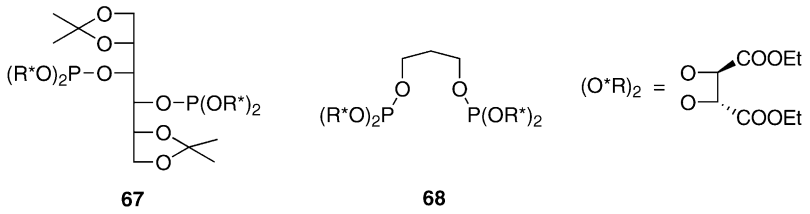
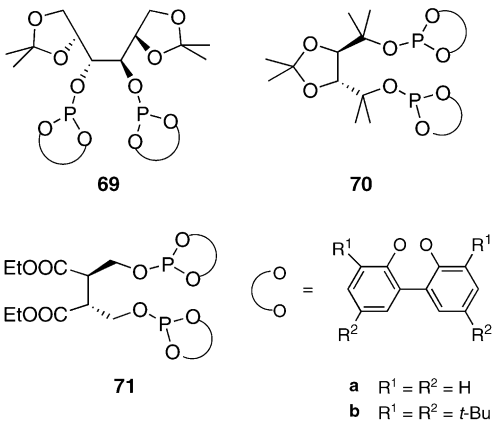


Fig. 13. 3,4-Diarylphosphinite ligands with a pyranoside backbone **61**–**66**.



67 68

Fig. 14. Diphosphite ligands **67** and **68**.



69 70 71

Fig. 15. Diphosphite ligands developed by van Leeuwen and co-workers.

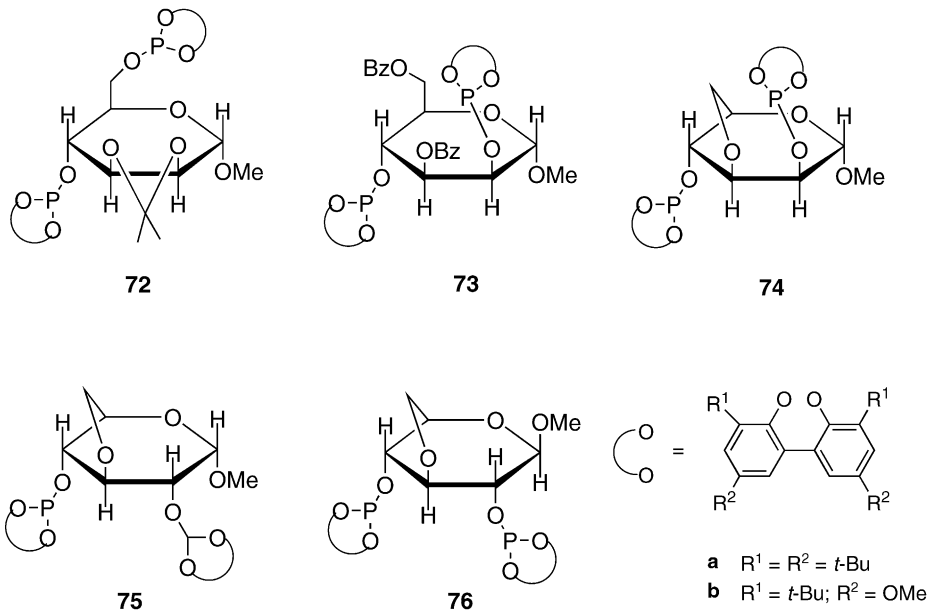
2.1.3. Diphosphites

The first reports on diphosphite ligands in asymmetric hydrogenation were made by Brunner and Pieronczyk [68] and Wink et al. [69]. They used diphosphite ligands based on mannitol (**67**) and tartaric acid derivatives (**68**) in the Rh-catalyzed hydrogenation of enamides and obtained low enantioselectivies (1–34% e.e.) (Fig. 14).

In 1993, van Leeuwen and co-workers developed a series of chiral C_2-symmetric diphosphites derived from 1,2:5,6-diisopropylidene-D-mannitol (**69**), α,α,α,α,-tetramethyl-1,3-dioxolan-4,5-dimethanol (**70**) and L-diethyl tartrate (**71**) for the Rh-catalyzed asymmetric hydroformylation of styrene (Fig. 15) [70]. The catalytic activity strongly depended on the bulkiness of the ligand. The enantioselectivity was best (20% e.e.) with ligand **71b**.

van Leuwen's group also synthesized a series of diphosphite ligands with a pyranoside backbone (**72**–**76**) for the asymmetric hydroformylation of styrene (Fig. 16). In general, good regioselecitivies in favor to the branched isomer and enantiolectivity was moderate. The enantioselectivity was best (64% e.e.) with ligand **72b** [71].

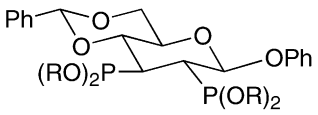
More recently, Selke and co-workers also reported the use of diphosphite ligands with a glucopyranoside backbone (**77**) (Fig. 17) in the Rh-catalyzed hydroformylation of vinyl acetate, allyl acetate and *p*-methoxystyrene [72]. In general, regioselectivities in the branched product were good and enantioselectivities were low to moderate (e.e.'s as high as 36%). These ligands were also tested in the Rh-catalyzed hydrogenation of methyl (*Z*)-2-*N*-acetamidocinnamate [72] and *N*-(1-phenylethylidene)benzylamine [48] and showed rather low enantioselectivities.



72 73 74

75 76

Fig. 16. Pyranoside diphosphite ligands **72**–**76**.



77

Fig. 17. Glucopyranoside diphosphite ligand **77**.

The groups of van Leeuwen and Claver have recently developed a series of diphosphite ligands with a furanoside backbone derived from D-(+)-xylose and D-(+)-glucose (Fig. 18) [71,73]. The modular construction of these ligands means that there is sufficient flexibility to fine-tune (a) the various configurations of the carbohydrate backbone and (b) the steric and electronic properties of the diphosphite substituents. This set of ligands has been applied in the Rh-catalyzed asymmetric hydroformylation of vinyl arenes, metal-catalyzed asymmetric hydrogenation of olefins, Pd-catalyzed asymmetric allylic alkylation reactions and in the Cu-catalyzed 1,4-addition.

For the Rh-catalyzed hydroformylation of vinyl arenes, this set of ligands not only shows excellent enantioselectivities (as high as 93%) but also regioselectivities (as high as 98.8%) under mild conditions [71,74–77]. The hydroformylation results show that the absolute configuration of the product is governed by the configuration at the stereogenic center C-3, while the level of enantioselectivity is influenced by a cooperative effect between stereocenters C-3 and C-5. Thus, both the *S* and *R* enantiomer of the product can be obtained with excellent enantioselectivity by using ligands with the basic framework **81** and **82**, respectively. Moreover, there is an influence on the substituents in the biaryl phosphite moieties. Thus, ligands **79c**, **79d** and **82c**, **82d**, with either methoxy substituents and trimethylsilyl groups, always produced the best enantioselectivity.

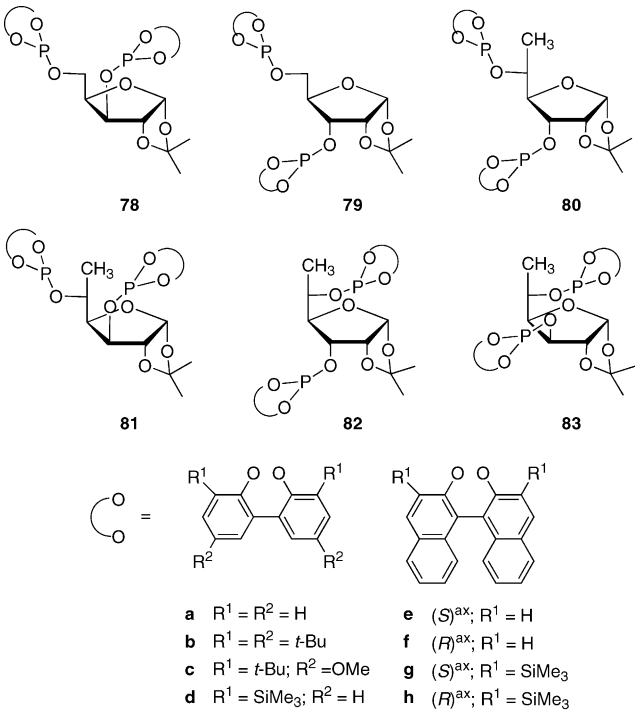


Fig. 18. Furanoside diphosphite ligands **78**–**83** derived from D-(+)-xylose and D-(+)-glucose.

For the Rh-catalyzed hydrogenation of several benchmark dehydroamino acid derivatives enantioselectivities (e.e. as high as >99%) and activities were excellent [74,78,79]. The results revealed that enantiomeric excesses depend strongly on the absolute configuration of C-3 and only slightly on the configuration of the stereocenter carbon C-5. Therefore, enantioselectivities were best with ligands **80** with *R* configuration on both C-3 and C-5 stereocenters. The presence of bulky substituents at the *ortho*-positions of the biaryl diphosphite moieties has a positive effect on enantioselectivity. The highest enantiomeric excess (e.e. >99%) was found for allofuranoside ligand **80d**, which has *o*-trimethylsilyl substituents in the biphenyl moieties. It was also found that the presence of a methyl substituent on the carbon C-5 significantly increased the activity and enantioselectivity.

Diphosphite ligands **78a** and **78b** have also been applied in the Ir-catalyzed asymmetric reduction of *N*-(phenylethylidene)aniline and enantioselectivities were poor to moderate (as high as 46%) [52].

Ligands **78**–**83** were also applied in the Pd-catalyzed alkylation of dimethyl malonate to 1,3-diphenylprop-2-enyl acetate [22,80] and in the Cu-catalyzed 1,4-addition of diethylzinc to 2-cyclohexenone [81–83]. The results indicated that enantiomeric excesses depend strongly on the absolute configuration of the stereocenter carbon C-3 of the carbohydrate backbone. Thus, the best ligands for asymmetric allylic alkylation are **78c** and **81c**, which provided e.e.'s of up to 95%. For the Cu-catalyzed 1,4-addition, enantioselectivites were best with ligands **78h**, **81g** (81% (*R*) and 84% (*S*)), respectively. Note that introducing a stereogenic center in C-5 had a positive effect on activity, although the enantioselectivity was unaffected.

Reetz and co-workers developed a series of C_2 derivative ligands derived from D-mannitol with different phosphite substituents (Fig. 19). These ligands were efficiently applied in the Rh-catalyzed hydrogenation of dimethyl itaconate and methyl *N*-acetamidoacrylate [84]. The results indicated that the sense of enantiodiscrimination is predominantly controlled by the configuration of the binaphthyl moiety. Moreover, they observed a cooperative effect between the stereogenic centers of the ligand backbone and the stereogenic binaphthyl phosphite moieties. This results in a matched combination for ligand **84e**, which provides e.e.'s of up to 94.5%.

2.1.4. Mixed P–P′ ligands

In 1996, Börner and co-workers developed a series of chiral phosphine–phosphite ligands with axial and central chirality (**85**–**89**), for the Rh-catalyzed asymmetric hydroformylation of allyl acetate (Fig. 20) [85]. The results clearly

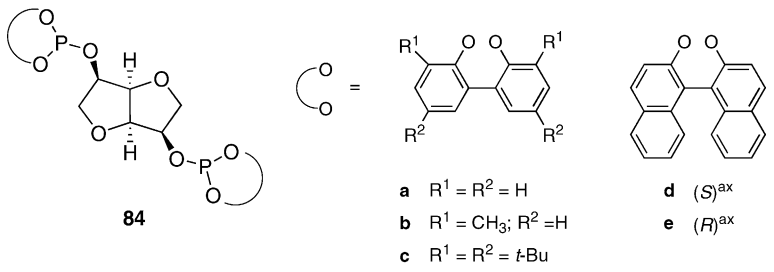


Fig. 19. D-Mannitol derived diphosphite ligands developed by Reetz et al.

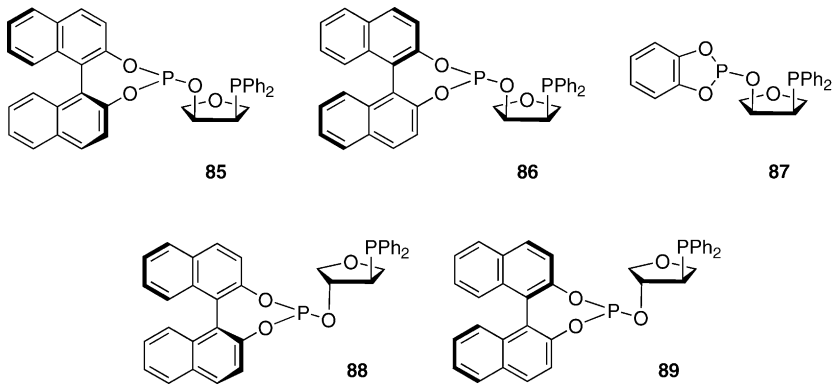


Fig. 20. Furanoside phosphine–phosphite ligands **85**–**89**.

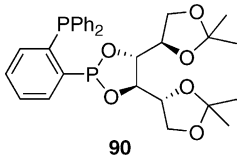


Fig. 21. Phosphine–phosphonite ligands derived from D-mannitol.

indicated that both central and axial chirality are responsible for the stereochemical outcome of this reaction. Thus, enantioselectivities of up to 44% e.e. were obtained using ligand **88**.

In 1999, Reetz and co-workers reported phosphine–phosphonite ligand **90** derived from D-mannitol (Fig. 21) [86]. This ligand was tested in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate with moderate enantioselectivities (e.e.'s as high as 60%).

Recently, Claver and co-workers developed a series of phosphine–phosphite ligands with a furanoside backbone (**91**) derived from D-(+)-xylose (Fig. 22) and applied them in the Rh-catalyzed asymmetric hydrogenation [87,88] and hydroformylation [89] of alkenes, in Pd-catalyzed allylic alkylation [80] and in the Cu-catalyzed 1,4-addition reaction [90].

For the asymmetric hydrogenation of several α,β-unsaturated carboxylic acid derivatives, enantioselectivities were excellent (up to >99%) under very mild reaction conditions. Varying the biphenyl substituents in the phosphite moiety greatly affected the enantioselectivity in the hydrogenation reactions. The enantioselectivity was best with ligand **91b**, which contains bulky *tert*-butyl groups in the *ortho*- and *para*-positions of the biphenyl moiety. The results also indicate that the sense of enantioselectivity is mainly controlled by the configuration of the phosphite moiety.

In general, enantioselectivities were low to moderate with these ligands in the Rh-catalyzed asymmetric hydroformylation of styrene (e.e.'s as high as 49%), in Pd-catalyzed allylic alkylation (e.e.'s as high as 42%) and in the Cu-catalyzed

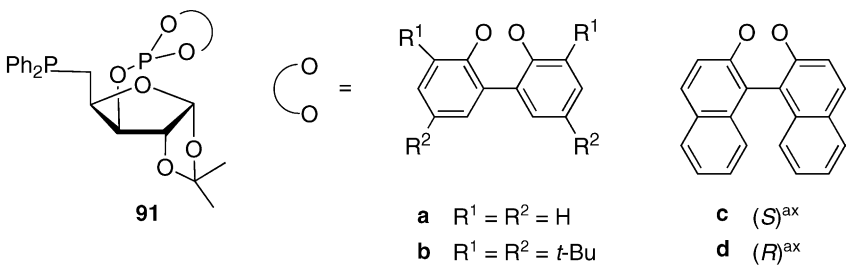


Fig. 22. Phosphine–phosphite ligands derived from D-(+)-xylose.

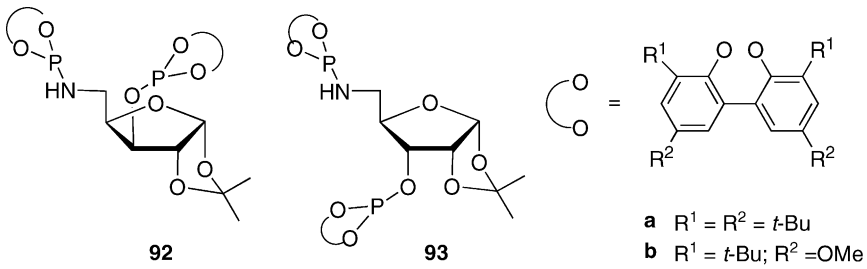


Fig. 23. Phosphite–phosphoroamidite ligands derived from D-(+)-xylose.

1,4-addition of diethylzinc to 2-cyclohexenone (e.e.'s as high as 19%).

Very recently, a series of phosphite–phosphoroamidite ligands with a furanoside backbone (**92**, **93**) (Fig. 23) were efficiently used in the Rh-catalyzed asymmetric hydrogenation of α,β-unsaturated carboxylic acid derivatives [91]. The results clearly show that the enantiomeric excesses and activities depend strongly on the absolute configuration of the C-3 stereocenter of the carbohydrate backbone and the substituents in the biphenyl moieties. Therefore, enantioselectivities and activities were best (e.e.'s as high as >99%) with ligand **92a**, which has *tert*-butyl groups in the *ortho*- and *para*-positions of the biphenyl moieties and an *R* configuration of C-3.

Ligands **92** and **93** were also applied in the Rh-catalyzed asymmetric hydroformylation of styrene [92] and in the Cu-catalyzed asymmetric 1,4-addition of diethylzinc to 2-cyclohexenone [93]. In both reactions, e.e.'s were moderate (as high as 65%).

2.2. Carbohydrate monodentate phosphorus ligands

With rare exceptions, monodentate phosphanes perform poorly in early transition-metal enantioselective catalysis. The introduction of DIOP, BINAP and other diphosphines meant that research focused on bidentate ligands [7]. The use of monodentate ligands in asymmetric catalysis, then, was neglected until quite recently when excellent enantioselectivities were reported in such transition metal-catalyzed reactions as hydrogenation [94], 1,4-addition to enones [95], hydrovinylation [96], the intramolecular Heck reaction and other C–C bond reactions [97]. A variety of monodentate phosphorus ligands have been used: for instance, phosphines [94g], phosphites [94a-c], phosphoroamidites [94d,e,97],

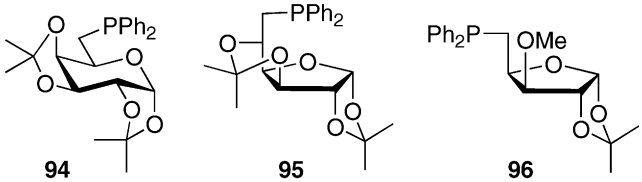


Fig. 24. Monophosphines used in rhodium asymmetric hydrogenation.

aminophoshinites [94f] and phosphonites [95a]. The use of chiral monodentate phosphines as ligands in transition metal asymmetric catalyzed reactions has been reviewed [98]. Many of these ligands are binaphthyl derivatives with biaryl axial chirality.

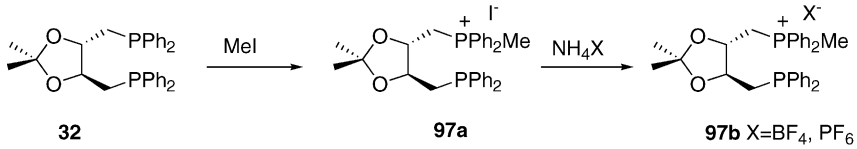
2.2.1. Monodentate phosphines

Initially, cationic rhodium complexes with monophosphines derived from sugars **92**–**94** (Fig. 24) were used in rhodium-catalyzed asymmetric reduction of α-amino acid precursors. They behaved like active catalytic precursors in the hydrogenation of several α-amino acid precursors, although the e.e. were low to moderate. The e.e.'s were best with phosphine **94** (as high as 54%) in the reduction of the α-acetylaminoacrylic acid [11].

The chiral diphenylphosphine **94** was also used in the Pd- and Ni-catalyzed asymmetric Grignard cross-coupling reaction of *sec*-butylmagnesium bromide with bromobenzene [51] (Scheme 4). Conversions were 99 and 77% for the Ni and Pd catalytic systems, respectively. The non-isomerized product *s*-BuPh was obtained in 99% (*S*) e.e. and 5% (*R*) e.e., respectively.

Later a phosphonium–phosphine derived from (*R*,*R*)-DIOP ('methyldiopium') **97** (Scheme 5) was prepared and used as a monophosphine ligand in the Rh-catalyzed hydro-

Scheme 4. Asymmetric Grignard cross-coupling reaction.



Scheme 5. *R*,*R* Methyldiopium salts from (*R*,*R*)-diop.

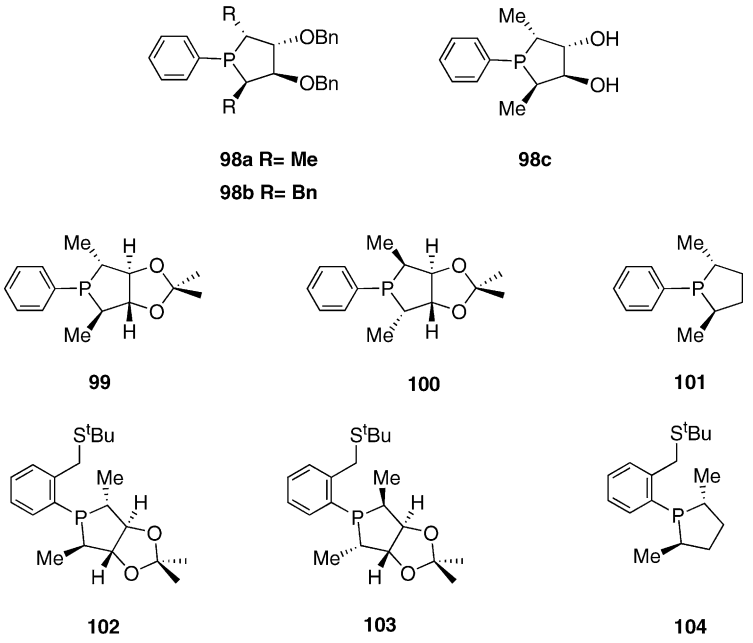


Fig. 25. Monodentate phospholes **98a**–**98c** and **99**–**104**.

genation of (*Z*)-α-acetamidocinnamic acid. The conversion (63%) and enantioselectivity (5% e.e.) were low. This system was also applied in the hydrogen transfer reaction using an azeotropic mixture of formic acid-triethylamine of several olefins, for which the corresponding diop-Rh system was not active. However, in all cases enantioselectivities were low [99].

2.2.2. Monodentate phospholes

Chiral phospholanes have been synthesized from readily available D-mannitol in high yields and some of them have shown to be excellent ligands in asymmetric catalytic reactions (Fig. 25) [26,27].

Thus, chiral hydroxyl monophosphane ligands **98a**–**98c** were tested in the Baylis–Hillman reaction using 4-pyridinecarboaldehyde and methylacrylate as reactants (Scheme 6). The highest enantioselectivity was 19% e.e. with ligand **98a**. Although in this case phospholane is the catalyst and it is not a transition metal catalytic reaction we shall briefly discuss the results. With the hydroxylphospholane **98c** as the catalyst, the reaction accelerated significantly (83% isolated yield in **9h** for **98c** versus 29% isolated yield in **70h** for **98a**). This acceleration has been attributed to the hydrogen-bonding interaction between a hydroxyl and an enolate **105** formed during the reaction (Fig. 26) [26].

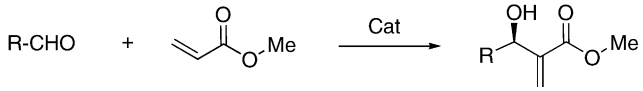
Functionalized C_2 symmetric monophospholanes **99**–**101** and monophospholanes with a pendant StBu group **102**–**104** (Fig. 25), prepared from D-mannitol were used in the Pd(0)-catalyzed allylation of dimethyl malonate (Scheme 2b). The yields of isolated products were greater than 95% in most cases. The enantioselectivity depends on the substitution pattern of the phospholane ring and to some extent on the reaction conditions and e.e.'s were between 29 and 94%. The chirality of C-3 and C-5 oxygen seems to play a crucial role in the asymmetric induction [27]. Enantioselectivity was best with ligand **99** (94% *R*) and its enantiomer **100** (93% *S*).

2.2.3. Monodentate phosphinites

Many monodentate phosphinites prepared from carbohydrate have been used in asymmetric catalytic reactions (Fig. 27).

Chiral diphenylphosphinite derived from D-galactose, L-rhamnose and D-glucose **106**–**113** were prepared and used in the metal-catalyzed asymmetric Grignard cross-coupling reaction (Scheme 4). *sec*-Butylmagnesium bromide was coupled with bromobenzene in the presence of nickel or palladium chloride. The optical yields were low to moderate. The highest yield was obtained with ligand **106**, with e.e. up to 53% [51].

It has been reported that monodentate or hemilabile ligands are required for the asymmetric hydrovinylation of



Scheme 6. Baylis–Hillman asymmetric reaction.

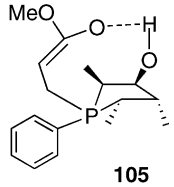


Fig. 26. Enolate formed during the Baylis–Hillman reaction.

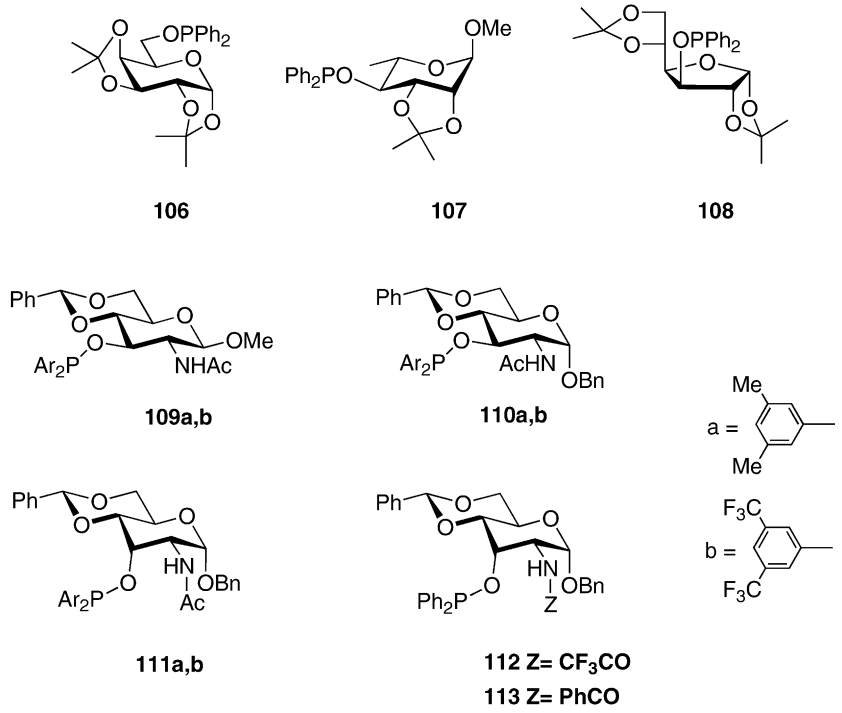


Fig. 27. Monodentate phosphinites **106**–**113**.

olefins (Scheme 7) [96]. Thus, carbohydrate-derived diarylphosphinite ligands **109**–**113** were successfully applied in the Ni-catalyzed asymmetric hydrovinylation reaction [100].

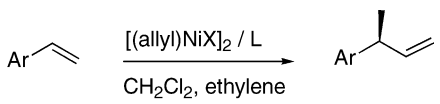
Diarylphosphinites prepared from readily available carbohydrates **109**–**113** in conjunction with a highly dissociated counterion ($[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4B^-$ or SbF_6^-) effect the hydrovinylation of 4-bromostyrene or 4-isobutylstyrene under ambient pressure of ethylene. Selectivity was best with ligand **112** (e.e. as high as 87%).

This hydrovinylation procedure has been applied for the synthesis of a 2-arylpropionic acid, a widely used antiinflammatory drugs. Thus, 3-(4-bromophenyl)-1-butene (prepared in a 98% isolated yield and 89% e.e. from 4-bromostyrene using catalyst Ni/**111a**) has been transformed into (*R*)-ibuprofen by cross-coupling with *i*-BuMgBr, ozonolysis, and subsequent oxidation of the resulting aldehyde [100].

2.2.4. Monodentate phosphonites

Cyclic monophosphonite ligands **114a**–**114e** and **115a**–**115d** derived from TADDOL [101] (Fig. 28) were tested in such Rh(I)- and Pd(0)-catalyzed reactions as hydrocarbonylations, hydroborations, and hydrosilylations of olefins. While the resulting catalysts were highly active and regioselective, they did not lead to useful enantiomer enrichment of the products in any of the processes studied. In contrast, the rhodium catalyzed hydrosilylation of ketones gave the corresponding secondary alcohols of (*R*)-configuration with up to 87% e.e. when phosphonite **115d** was used as ligand. The X-ray crystal structure of one representative, phosphonite **114b**, was determined [101].

Later, Rh(I) complexes [RhCl(NBD)**116**–**118a**–**118d**] (**119**–**121**)[RhCl(NBD)**117**] (**120**) and [RhCl(NBD)**118**] (**121**) were synthesized via the corresponding borane-phosphonite adducts. Isolating ligands **1163**–**118** was difficult



Scheme 7. Asymmetric hydrovinylation of olefins.

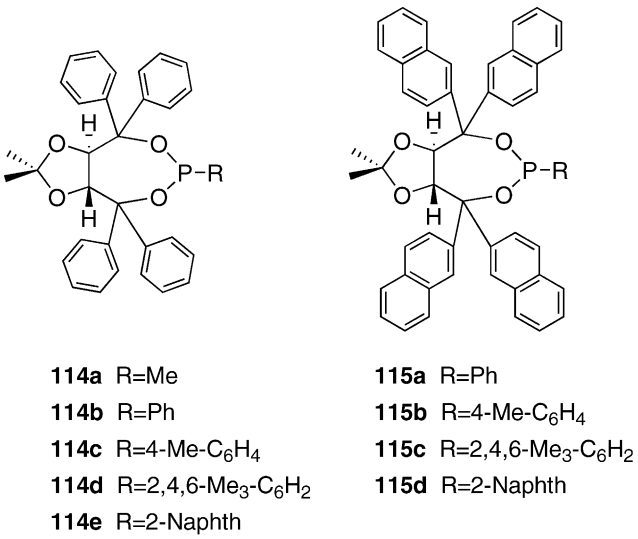


Fig. 28. Monophosphonites **114** and **115** used in asymmetric catalysis.

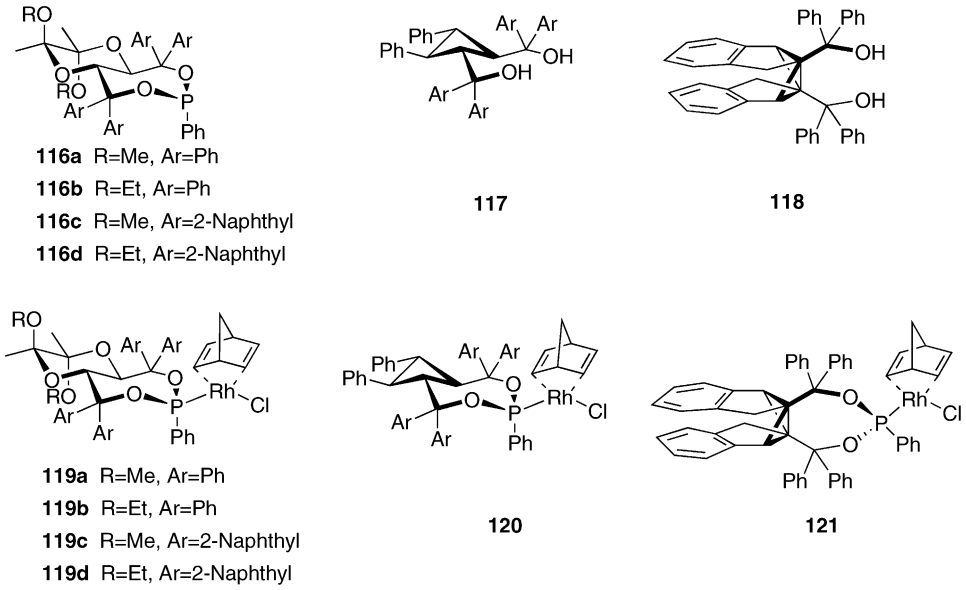
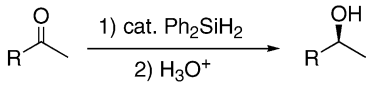


Fig. 29. Rhodium complexes with phosphonite ligands **116**–**121** (not isolated ligands).

because they are oxygen sensitive and their formation was accompanied by competitive formation of the corresponding tetrahydrofuran. The rhodium complexes were synthesised best in a one-pot procedure consisting of the cleavage of the borane phosphinite adducts followed by immediate addition of $[RhCl(NBD)]_2$. The rhodium complexes **120** and **121** were stable to oxygen and exceptionally thermally stable (Fig. 29). They turned out to be highly active catalysts in the asymmetric hydrosilylation of ketones in a broad temperature range. The conformational properties of the ligand backbone were revealed to be a crucial feature, which determined not only the extent but also the direction of the chirality transfer. Therefore, by choosing appropriate ligand backbones and temperatures, the enantioselectivities in the hydrosilylation of such different ketones as acetophenone (82% e.e.) and pivalophenone (86% e.e.) can be fairly good [102].

2.2.5. Monodentate phosphites

In the early eighties, the phosphite ligand **122** (Fig. 30), reported by Brunner, was used in the rhodium-catalyzed hydrogenation of (*Z*)-α-acetamidocinnamic acid with low enantioselectivity (e.e.'s as high as 25%) [103]. Later, monodentate phosphites **123** derived from D-glucofuranose were prepared and applied as ligands in the rhodium-catalyzed enantioselective hydrosilylation of acetophenone (Scheme 8).



Scheme 8. Enantioselective hydrosilylation of acetophenone.

The e.e. values varied substantially, from racemic to 58% e.e., depending on the nature of the phosphite ligand and the ligand to metal ratio. The reactivity of the selected phosphite **123** towards $[Rh(\mu\text{-}Cl)(COD)]_2$ and $[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$ allowed the synthesis of monosubstituted [Rh(Cl)(COD)**123**] and $[Rh(\mu\text{-}Cl)(C_2H_4)\mathbf{123}]_2$ complexes, and disubstituted complexes such as $[Rh(Cl)(C_2H_4)\mathbf{123}_2]$. This study indicated that the disubstituted compounds give better enantioselectivities than the monosubstituted ones [104].

A breakthrough in the use of monophosphite ligands in asymmetric catalysis came with the work of Reetz and Mehler [105]. They developed monophosphite ligands **124** derived from D-mannitol (Fig. 31) for the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate. These

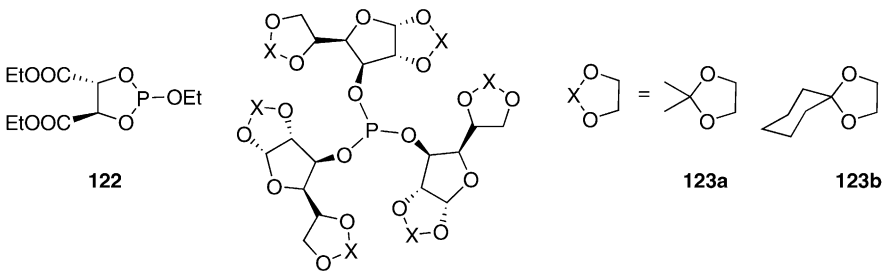


Fig. 30. Phosphites used in hydrogenation and hydrosylilation.

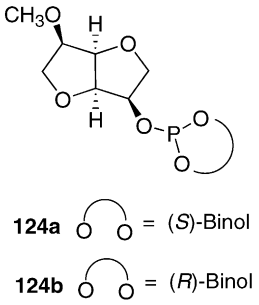


Fig. 31. Monophosphite ligands developed by Reetz and co-workers.

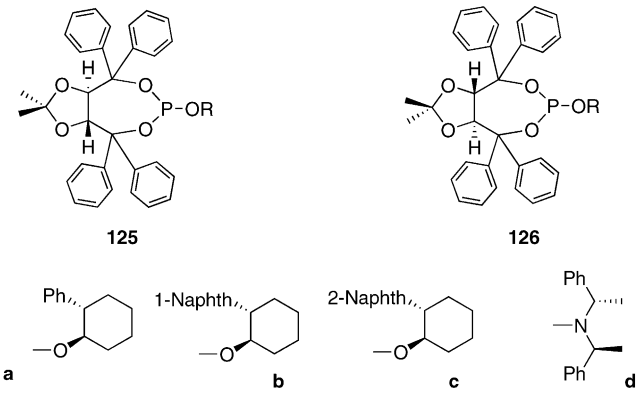
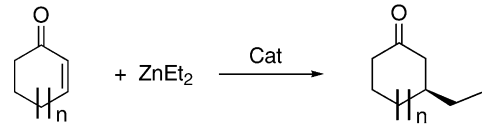


Fig. 32. Monophosphites **125** and **126** derived from TADDOL.

ligands provided excellent enantioselectivities of up to 99%.

On the other hand, TADDOL-derived cyclic phosphites have been reported and used in asymmetric catalysis (Fig. 32) [101,106,107].



Scheme 9. Addition of diethylzinc to cyclic enones.

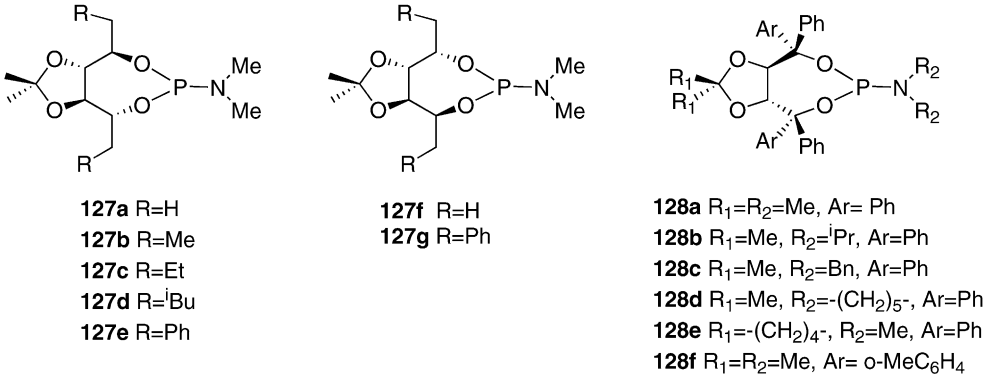
The asymmetric copper-conjugate addition of diethylzinc to acyclic enones using phosphite ligands **125** and **126** (Fig. 32) provided enantiomeric excesses as high as 92%. Interestingly, the addition of dimethylzinc to a macrocyclic 15-membered ring enone led to the optically active *R*-(muscone) in a 53% yield and a 79% enantiomeric excess [107]. These phosphites were also tested as ligands in rhodium hydroformylation of but-2-ene, but enantioselectivity was very low [101].

2.2.6. Monodentate phosphoroamidites

Several chiral monodentate phosphoramidites have been efficiently applied in asymmetric catalysis (Fig. 33).

Ligands **127a**–**127e**, prepared from D-mannitol, were efficiently applied in rhodium-catalyzed asymmetric hydrogenation. Enantioselectivities in the asymmetric hydrogenation of itaconic acid (94% e.e.) and α-acetamidocinnamic acid (89% e.e.) were high when Rh-complexes with two monodentate phosphoramidite ligands were used [108].

Phosphoroamidite ligands **128a**–**128f**, easily prepared from TADDOL were tested in the copper(II) catalyzed enantioselective addition of diethylzinc to cyclic enones (Scheme 9). Enantioselectivities of e.e. as high as 71% for cyclohexanone and as high as 62% for cyclopentanone were obtained. Enantioselectivity was considerably enhanced



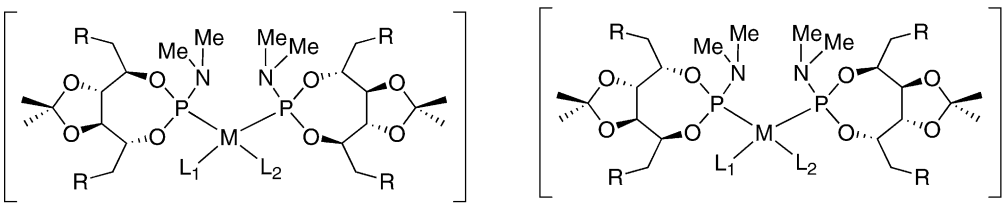


Fig. 33. Phosphoroamidite ligands **127** and **128**. Rhodium and palladium complexes **129** and **130** (M = Rh, L_1–L_2 = COD, M = Pd $L_1 = L_2$ = Cl) with ligands **127**.

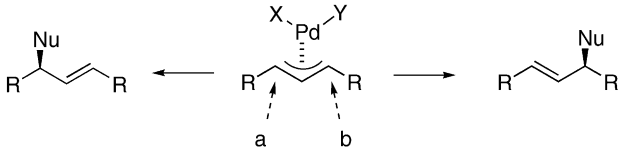
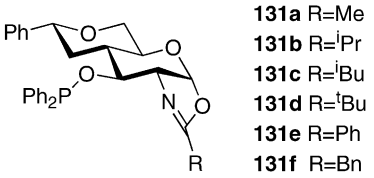


Fig. 34. Palladium metal-catalyzed allylic alkylation via allyl complexes.



131a R=Me
131b R=^{i}Pr
131c R=^{i}Bu
131d R=^{t}Bu
131e R=Ph
131f R=Bn

Fig. 35. Chiral phosphinite–oxazoline ligands **131a**–**131f**.

when powdered molecular sieves were added to the reaction mixture (for instance, from 24 to 48% e.e.) [109].

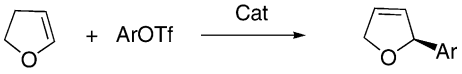
2.3. Carbohydrate P,E-bidentate ligands (E = N, S)

C_2-symmetrical ligands have dominated asymmetric catalysis for a long time. However for certain reactions, enantiocontrol could be more effective with nonsymmetrical ligands with two different coordinating heteroatoms than C_2-symmetric ligands. Transition metal-catalyzed allylic alkylation via allyl complexes is a good example (Fig. 34). In such reactions the regioselectivity of the nucleophilic attack determines the ratio of the two enantiomeric products. If the metal center is coordinated to two electronically different groups *X* and *Y*, the two allylic termini become electronically nonequivalent and are expected to have different reactivities.

However, it is important to consider that P, E-bidentate ligands can coordinate either as chelates or monodentates (probably through a P-atom) which would clearly affect their chiral induction. This is discussed in some of the works reviewed. Several groups have studied such P,N chiral ligands as chiralphosphinooxazolines [110] and the coordination chemistry and application of P,N-ligands have been reviewed [111]. Recently a review of chiral thioether ligands included the coordination chemistry and asymmetric catalysis of many P,S- and N,S-ligands [112].

2.3.1. P,N-ligands

Chiral phosphinite–oxazoline ligands **131a**–**131f** were synthesized from D-glucosamine hydrochloride (Fig. 35).



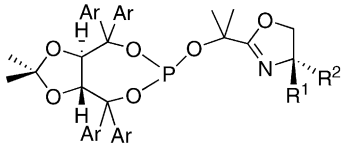
Scheme 10. Arylation of 2,3-dihydrofuran.

They behave effectively as chiral ligands and provide high enantiomeric excesses in Pd-catalyzed allylic alkylation, amination and arylation reactions [113–115].

The allylic alkylation of 1,3-diphenyl-3-acetoxyprop-1-ene with dimethyl malonate (Scheme 2b) proceeds smoothly in the presence of 0.25 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$. The substituent group R had a dramatic effect on the enantioselectivity excess. Ligands **131f** (R = Bn) or **131d** (R = Bu) gave lower enantioselectivities (80–90%) than ligands **131b** (R = Ph) or **131c** (R = *i*-Bu) (up to 94%). The enantiomeric excess (96%) was highest with ligand **131a** (R = Me) [113,114], which is also effective for the Pd-catalyzed amination of 1,3-diphenylprop-2-enyl carbonate, leading to the corresponding allylic amine in 94% e.e. [114]. These chiral phosphinite–oxazolines **131a**–**131f** also proved to be effective P,N-bidentate ligands in the palladium-catalyzed enantioselective arylation of 2,3-dihydrofuran. They gave 2-aryl-2,5-dihydrofuran (Scheme 10) selectively in high yields and with enantioselectivities between 86 and 96%. In this case e.e. was highest with ligand **131f**.

The complex $[PdCl_2(\mathbf{131b})]$ was prepared and its structure was characterized by X-ray crystallography. Structures of the complex $[(p\text{-}MeO_2CC_6H_4)PdI(\mathbf{131a})]$ and its cationic complex $[(p\text{-}MeO_2CC_6H_4)Pd(\mathbf{131a})]^+OTf^-$ were also elucidated on the basis of ^1H, ^{13}C, and ^{31}P NMR spectra, the $p\text{-}MeO_2CC_6H_4$ moiety on the palladium being located *trans* to the nitrogen of **131a**. This configuration might be responsible for an enantiofacial discrimination of 2,3-dihydrofuran that predominantly produces (*R*) isomer. The stoichiometric reaction of $[PhPd(\mathbf{131f})]^+OTf^-$ with 2,3-dihydrofuran has provided information about the mechanistic aspects of the arylation when P,N-ligands are used. The base-promoted deprotonation in the β-position leading to an alkene (2-aryl-2,5-dihydrofuran)-palladium(0) complex has been shown to be an important step for the selective formation of the product [115].

TADDOL-based ligands containing an oxazoline unit have been reported to be efficient at the rhodium enantioselective sylilation of ketones [116], palladium-catalyzed allylic alkylation and iridium catalyzed hydrogenation of olefins [117] (Fig. 36). "In situ" catalytic systems prepared



132a Ar=Ph, R^1=H, R^2=Ph
132b Ar=Ph, R^1=Ph, R^2=H
132c Ar=Ph, R^1=H, R^2=^{i}Pr
132d Ar=Ph, R^1=^{i}Pr, R^2=H
132e Ar=2-naphthyl, R^1=^{i}Pr, R^2=H
132f Ar=Ph, R^1=H, R^2=^{t}Bu

Fig. 36. TADDOL derivatives phosphite–oxazoline.

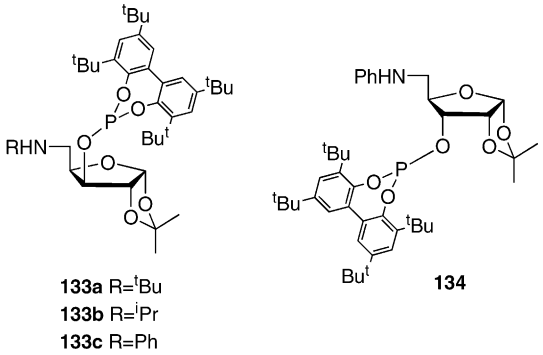


Fig. 37. Amino-phosphite ligands **133a**–**133c**, **134** derived from D-(+)-xylose.

from $[RhCl(COD)]_2$ and the ligands **132b** and **132d** were applied in the enantioselective hydrosilylation of acetophenone. The ligand **132d** with an *i*-Pr substituent on the dihydrooxazole ring gave a slightly better enantioselectivity (94%) than did **132b** which bears a Ph substituent (91%). The configuration of the product is mainly determined by the configuration of the dihydrooxazole moiety. The TADDOL-derived phosphite oxazoline **132c** was used in the palladium-catalyzed allylic alkylation of various substrates and generally provided enantioselectivities that were similar to or lower than other related P,N-ligands containing oxazoline (46–87%) [117]. As far as the iridium-catalyzed hydrogenation of olefins is concerned, the [Ir(COD)(**132c**)]TFBP (TFBP = tetrakis [3,5-bis(trifluoromethyl)(phenyl)] borate, was prepared and used as the catalytic precursor of several substrates. The conversions were higher than the ones obtained for related P,N-ligands containing oxazoline and the enantioselectivity was best in the hydrogenation of (*Z*)-2-(4-methoxyphenyl) but-2-ene (90%) [117].

Chiral amino-phosphite ligands have been used for the copper-catalyzed asymmetric 1,4-addition of diethylzinc to cyclohexenone (Scheme 9). A series of amino-phosphite ligands **133a**–**133c**, **134** (Fig. 37) derived from D-(+)-xylose were prepared and screened in the Cu-catalyzed asymmetric 1,4-addition of diethylzinc to cyclohexenone. Reaction rates were high (TOF > 1200 h^{-1}) and enantioselectivities moderate (up to 63% e.e.).

The results showed that the configuration of the stereogenic carbon atom C-3 at the ligand backbone and the different substituents at the amino group had considerable

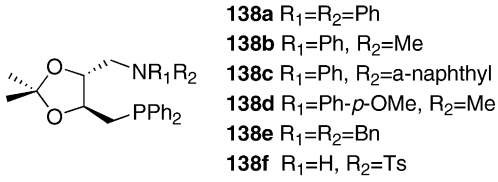


Fig. 39. P,N-ligands **138a**–**138f** derived from tartaric acid.

effects on the activity and enantioselectivity. The enantioselectivity was best with ligand **133c** which has (*R*) configuration at C-3 and a phenyl substituent on the amino group. Rhodium(I) and palladium(0) complexes containing chiral P,N-ligands derived from D-glucose and D-mannose have been prepared and applied as catalyst precursors in hydroboration and allylic alkylation (Fig. 38). These chiral P,N-chelates **135**–**137** were prepared and characterized for use in the synthesis of palladium(0) and rhodium(I) complexes of formula [Pd(P,N-chelate)(fumarodinitrile)] and [Rh(1,5-cyclooctadiene)(P,N-chelate)]BF_4. Coordination of fumarodinitrile to the palladium complex gives rise to two diastereomers. The diastereomeric ratio determined by RMN measurements shows that the ligands effectively discriminate between the enantioface of fumarodinitrile in the Pd(0) species, leading to a diastereomeric excess of 100% when the 2,3,4-tri-*O*-acetylated glucoside moiety linked to N through C6 (ligand **133**).

Given that **135** is effective at selectively distinguishing on the enantioface of fumarodinitrile, it was used as the chiral auxiliary in the palladium-catalyzed allylic alkylation. Although the reaction gives a good chemical yield, the enantioselectivity was only 20% e.e. (*S*). Results were better with ligand **137**, which gave 45% e.e. in the (*S*) enantiomer. It is interesting to note that the diastereomeric ratio found in the model fumarodinitrile Pd(0) complex for this ligand is in keeping with this value. The catalytic activity of the rhodium complex was tested in the asymmetric hydroboration/oxidation of styrene and derivatives with low enantioselectivities (e.e.'s up to 20%) [118].

A series of P,N-ligands **138a**–**138f** derived from tartaric acid have been used in palladium asymmetric allylic alkylation [119], rhodium-catalyzed hydrogenation [120] and hydroformylation [121] (Fig. 39). Chiral 1-(diphenylphosphino)-4-(dialkylamino) ligands, **8a**, **8b** (R = Ph, 1-naphthyl), were easily prepared from tartaric acid. Palla-

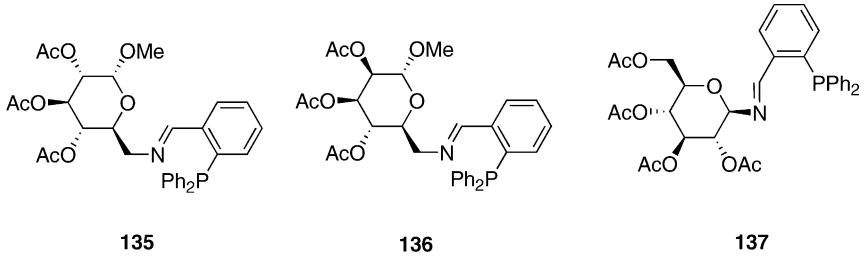


Fig. 38. P,N-ligands derived from D-glucose and D-mannose.

dium complexes of these ligands gave enantioselectivities as high as 75% in the alkylation of 1,3-diphenylprop-2-enyl acetate with di-Me malonate [119].

Chiral rhodium complexes, prepared from $[Rh(COD)_2]PF_6$ and ligands **138a**–**138f** have been used as catalysts in the hydrogenation of unsaturated amino acids. The rhodium-catalyzed hydrogenation of α-amino acid precursors shows that enantioselectivity is higher (enantiomeric excess values as high as 60%) in water with sodium dodecyl sulfate than in methanol [120]. These P,N-ligands have also been used in the rhodium-catalyzed hydroformylation of vinylstyrenes (*p*-F, *p*-MeO) and 2-vinylnaphthalene. The systems were active in mild conditions and the aldehyde regioselectivity was as high as 95% when CO/H_2 in a ratio of 1/1 was used. The highest e.e. was 23%. To elucidate the coordination mode of the P,N-ligands, NMR studies were performed under catalytic conditions. Although the NMR technique requires higher concentrations of complexes than catalytic experiments, it can provide valuable information about the species present during the catalytic cycle. In this case, it showed that species with monodentate ligands were present in the catalytic solution although there is no evidence to suggest that chelated P,N-species are also present. The P-coordinated species may be responsible for the low enantioselectivities.

2.3.2. P,S-ligands

Different combinations of carbohydrate P, S donor ligands have been studied, for example, phosphine-thioethers and phosphite–thioethers (Fig. 40). Carbohydrate phosphine-thioether ligands have proven to be effective in enantioselective Pd-catalyzed allylic substitution. Carbohydrate phosphite–thioether ligands have also been tested in enantioselective hydrogenation, hydroformylation and 1,4-addition of organometallic reagent to cyclohexenone.

2.3.2.1. Phosphine-thioethers. The ferrocene-based chiral phosphine thioglucose ligand **139** (Fig. 40) with one stereogenic C-atom in the P-S backbone affords an e.e. of 88% in the palladium allylic alkylation of the racemic test substrate PhCH = CHCH(OAc)Ph using the $CH\text{-}(CO_2Me)_2$ anion (Scheme 2b) [122].

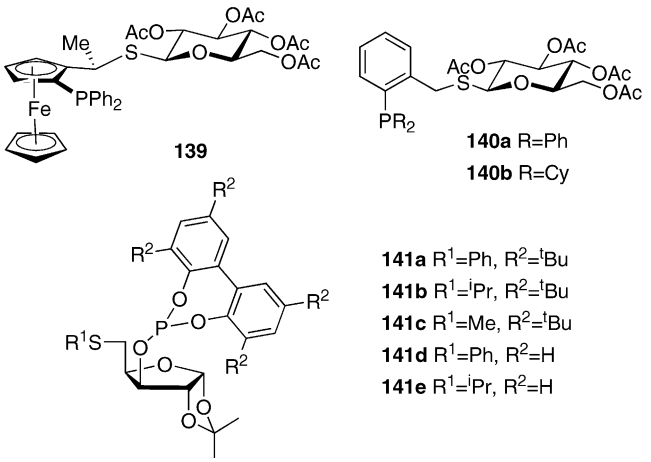
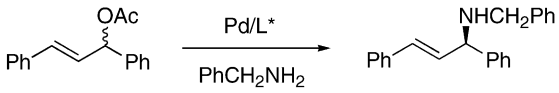


Fig. 40. Carbohydrate phosphine-thioether and phosphite–thioether ligands.

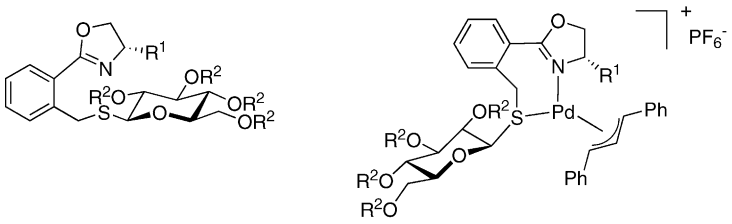
Compound **139** is an auxiliary with interesting structural cooperativity. Pregrosin and col. suggest that the combination of the two stereogenic fragments leads to a better e.e. A multinuclear NMR study has been made of the solution structure of the palladium allyl sugar-based ferrocenylphosphine complex of **139** in relation to enantioselective allylic alkylation catalysis. The ratio of the two isomers does not correlate with the experimental e.e. of 88%, which means that there are differences in the rates of attack of the nucleophile and/or uncharacterized equilibria [123]. When the thioglucose moiety was the only stereogenic unit on P, S ligands **140a**, **140b** containing phenyl and cyclohexyl phosphorus substituents (Fig. 40) enantioselectivities were only moderate (about 64 and 53%) [124]. Detailed NMR measurements for the 1,3-diphenylallylpalladium cationic complexes $[Pd(\eta^3\text{-}PhCHCHCHPh)(\mathbf{140})]PF_6$ reveal that there is an electronic *cis*-effect when the PPh_2 moiety is changed for the PCy_2 moiety and there is not necessarily a correlation between the observed enantiomeric excess and the diastereomer population in solution.

2.3.2.2. Phosphite–thioethers. Xylofuranoside phosphite–thiother ligands **141a**, **141b** (Fig. 40) have been used in palladium-catalyzed allylic alkylation (Scheme 2b). The substituents in the thioether moiety have a considerable effect on the activity, but not on the enantiodiscrimination (e.e. around 55% e.e.) [80]. The enantioselectivity is mainly controlled by the phosphite moiety. Therefore, it is assumed that the nucleophile attack takes place trans toward the thioether moiety. Ligand **141a** has also been used in palladium-catalyzed asymmetric allylic amination (Scheme 11) affording 67% e.e. The higher e.e. in the allylic amination can be explained by a later transition state, which results in larger ligand-allyl interaction.

Ligands **141a**–**141c** were tested in the rhodium-catalyzed asymmetric hydroformylation of styrene (Scheme 2a). Conversions were good (>99% in 5 h) and regioselectivities excellent in 2-phenylpropanal (94%) but enantiomeric excesses were practically null for all ligands [125]. To obtain information about the intermediate species formed during the hydroformylation process, a spectroscopic study was made under hydroformylation conditions. HP NMR results show that under hydroformylation conditions the thioether moiety is not coordinated to rhodium in the mononuclear active hydride-rhodium complexes.



Scheme 11. Palladium-catalyzed asymmetric allylic amination.



142a R^1= Ph, R^2= COMe
142b R^1= ^{i}Pr, R^2= COMe
142c R^1= Ph, R^2= CO^{t}Bu
142d R^1= ^{i}Pr, R^2= CO^{t}Bu

143a R^1= Ph, R^2= COMe
143b R^1= ^{i}Pr, R^2= COMe
143c R^1= Ph, R^2= CO^{t}Bu
143d R^1= ^{i}Pr, R^2= CO^{t}Bu

Fig. 41. Carbohydrate S,N-ligands and 1,3-diphenylallyl-Pd(II) complexes.

Cationic iridium complexes containing the phosphite–thioether ligands **141a**–**141c** were tested in the asymmetric hydrogenation of itaconic acid at 1 bar of H_2 and 40 °C (Scheme 1) [125]. The catalytic system was generated in situ from $[Ir(COD)_2]BF_4$ and the corresponding ligand. Conversions were good (100% in 12 h). Enantioselectivities were higher when the catalyst precursors containing R = *i*-Pr and Ph were used (51 and 47%, respectively).

Phosphite–thioether ligands **141a**–**141e** have been tested in the copper-catalyzed asymmetric 1,4-addition of organometallic reagents to 2-cyclohexenone (Scheme 8) [90]. In all the cases, reaction rates were excellent (TOF > 1200 h^{-1}) and the chemo- and regioselectivities in the 1,4-product were high, while enantioselectivities were moderate. Enantioselectivity was best with the catalyst precursor containing thioether-phosphite ligand **141d**, which has a phenyl substituent in the thioether moiety and a non-substituted biphenyl phosphite moiety (e.e. up to 41%).

2.4. Carbohydrate S,E-ligands (E = N, O, S)

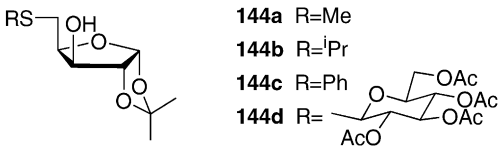
2.4.1. S,N-ligands

Bidentate ligands containing both chiral oxazoline and thiosugar elements **142a**–**142d** and their 1,3-diphenylallyl Pd(II) complexes **143a**–**143d** (Fig. 41) have been prepared by Pregosin and co-workers [126].

These N,S-oxazoline-thioglucose ligands afford excellent e.e.'s (90.2–96.9%) in the model enantioselective allylic alkylation reaction (Scheme 2b) when the 1,3-diphenylallyl Pd(II) complexes **143a**–**143d** are used as catalytic precursors. NMR studies of the Pd compounds show that they exist in solution as a mixture of *exo* and *endo* diastereomeric complexes. It is suggested that the dimethyl malonate nucleophile attack pseudo-*trans* to the thioether donor is preferred for electronic reasons, whereas the selective attack on the *endo* diastereomer, as opposed to the *exo* isomer, is because of steric effects in combination with allyl rotation. The organic product is formed by preferential reaction of a minor component.

2.4.2. S,O-ligands

Thioether hydroxy compounds **144a**–**144d** (Fig. 42) which were easily prepared from D-(+)-xylose, were used



144a R=Me
144b R=^{i}Pr
144c R=Ph
144d R=

Fig. 42. Carbohydrate S,O-ligands.

in the copper-catalyzed enantioselective 1,4-addition reaction of $ZnEt_2$ to cyclohexenone (Scheme 9) and $AlMe_3$ to *E*-non-3-en-2-one (Scheme 12) [127].

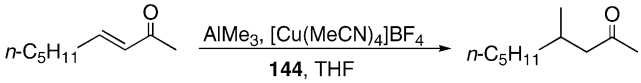
In the conjugate addition of cyclohexenone, the substituent of the thioeter moiety has an important effect on the rate and stereoselectivities. Conversions are higher for the catalyst precursor containing the electron-rich ligand **144b** (98% in 1 h) while enantioselectivity (62%) was better with the catalyst precursor containing ligand **144c**. The presence of a bulky substituent **144d** has a detrimental effect on conversion and enantioselectivity (41% conversion and 20% e.e.). The formation of ligand-free copper aggregates may be responsible for this. When these compounds were applied in the 1,4-addition of $AlMe_3$ to *E*-non-3-en-2-one (Scheme 12), the conversions (up to 73%) and enantioselectivities (up to 34%) were promising. In all the cases, the regioselectivity in the 1,4-product ranged from 70 to >90%.

2.4.3. S,S-ligands

Sugar dithioether ligands derived from tartaric acid **145**–**147** and from D-ribofuranose **149** (Fig. 43) have been tested in the asymmetric hydrogenation of prochiral olefins. Tartaric acid derivatives **145**, **146** and **148** have also been used in allylic alkylation.

Sugar disulfoxide ligands from L-(+)-tartaric acid **151** and **152** (Fig. 44) have been tested in the asymmetric hydrogenation of prochiral olefins.

2.4.3.1. Dithioethers. Sugar dithioether compounds **145a**–**145c** coordinated to iridium provide cationic com-



Scheme 12. Catalytic conjugate addition of $AlMe_3$ to E-non-3-en-2-one.

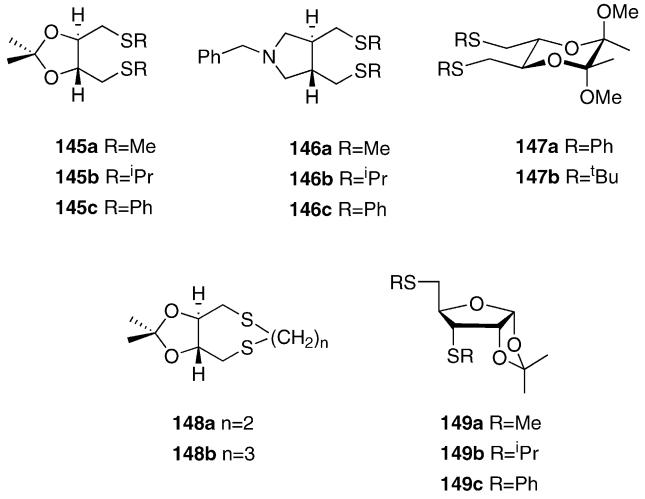


Fig. 43. Ditihioether ligands **145**–**149**.

plexes [Ir(COD)**145**]BF_4. These complexes lead to active systems for the asymmetric hydrogenation of several prochiral dehydroamino acid and itaconic acid derivatives (Scheme 1) [128]. In general, although hydrogenation takes place at room temperature and atmospheric pressure of H_2, the e.e. are low. The e.e. obtained with the [Ir(COD)**145b**]BF_4 catalytic system is higher than those with [Ir(COD)**145a**]BF_4 and [Ir(COD)**145c**]BF_4. The highest enantiomeric excess obtained was 47%.

Other sugar dithioether compounds prepared from (+)-L-tartaric acid **146a**–**146c** react with [Ir(COD)$_2$]BF_4 to give cationic complexes [Ir(COD)**146**]BF_4 which are active systems for the hydrogenation of prochiral dehydroamino acid and itaconic acid derivatives (Scheme 1) at room temperature under atmospheric pressure of H_2 [129]. In general the e.e.'s are low. The e.e. is highest when itaconic acid is hydrogenated with a precursor containing **146c** (68% *R*). Those catalytic systems in which the chiral ligand forms a five-membered ring with the metal center are more active and [Ir(COD)**146c**]BF_4 is more enantioselective than the related seven-membered ring iridium-chiral dithioethers **145a**–**145c** [128].

Dithioethers **147a** and **147b** (Fig. 43) have recently been synthesized from tartrates having the 1,4-dioxane backbone [36]. The enantioselectivities of these ligands were low (around 20% e.e.) when rhodium-based catalysts were used in the hydrogenation of a 2:1 *E*/*Z* mixture of the α-aryl enamide with a β-methyl group **150** (Scheme 13).

Sugar derivative dithioethers **149a**–**149c** (Fig. 43) from α-D-(+)-ribofuranose have been used in the iridium asymmetric hydrogenation of prochiral dehydroamino acid and itaconic acid derivatives at room temperature under 1 atm of H_2 [130]. The catalytic system was generated in situ from [Ir(COD)$_2$]BF_4 and the corresponding dithioether ligand in dichloromethane. Changing the substituent of the dithioethers has an important effect on the rate and optical induction. Thus, the conversions and optical inductions are higher for the precursor containing the bulky and electron-rich ligand **149b**. The highest enantiomeric excess obtained was 62% in the hydrogenation of itaconic acid. These results, using a C_1 dithioether with a six-membered chelate ring, are of the same order as the best e.e. values reported for the same substrates when a C_2 symmetrical dithioethers **146a**–**146c** with a more rigid five-membered chelate ring was used and they are much better than for C_2 symmetrical dithioethers **145a**–**145c** with a seven-membered chelated ring.

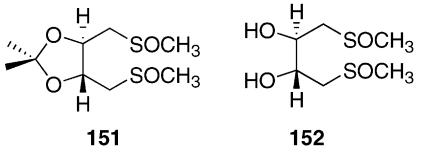
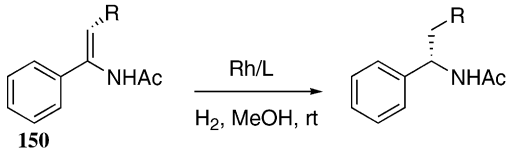


Fig. 44. Disulfoxide ligands derived from tartaric acid.



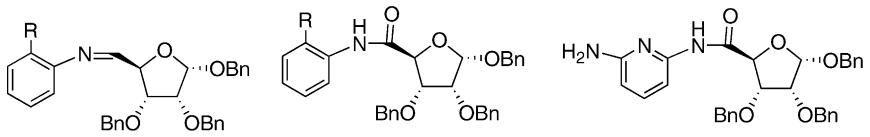
Scheme 13. Hydrogenation of **150** by Rh/**147**.

Chiral dithioether ligands **145b**, **145c**, **146b**, **146c** and **148a**, **148b** have been tested in the model Pd-catalyzed allylic alkylation reaction of *rac*-3-acetoxy-1,3-diphenyl-1-propene (Scheme 2b). They provide low to good enantioselectivities [131]. The best enantioselectivity (81%) was obtained with the compound **146c**.

2.4.3.2. Disulfoxides. Chiral disulfoxide ligands **151** (dios) and **152** (ddios) were prepared from tartaric in 1977 by James and McMillan (Fig. 44) [132]. Ruthenium complexes with S-bonded sulfoxide are precursors that are active in the asymmetric hydrogenation of prochiral acrylic acids but the e.e. obtained are low. The best e.e. is 25% in the hydrogenation of itaconic acid with the precursor dicloro(dios)(ddios)ruthenium(II) at 44 psi of H_2 and 55 °C.

2.5. Carbohydrate N and N–N ligands

There are not many examples of carbohydrate derivative nitrogen monodentate ligands. An easy, diastereoselective strategy has been reported for synthesizing a new tetrahydrofuranic chiral aldehyde and a new tetrahydrofuranic acid derived from D-ribose which were then converted into a new class of iminic- and amidic-carbohydrate-based chiral ligands **153a**–**153d** and **154a**–**154d** (Fig. 45). These ligands are characterized by the presence of a stereogenic center α to the iminic or amidic bond. The results of applying these chiral ligands in the conjugate addition of Et_2Zn to cyclohexenone led to good reaction rates, but the enantiomeric excesses were low (10–15%) [133].

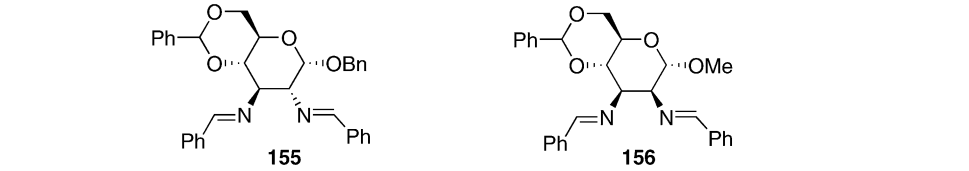


153a R=NH_2
153b R=SH
153c R=OH
153d R=OMe

154a R=NH_2
154b R=PPh_2
154c R=SMe

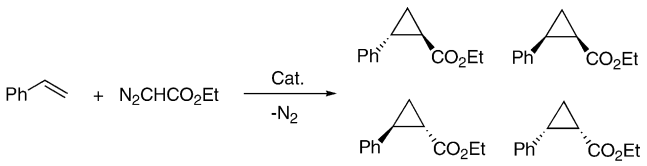
154d

Fig. 45. Iminic- and amidic-carbohydrate-based chiral ligands **153** and **154**.

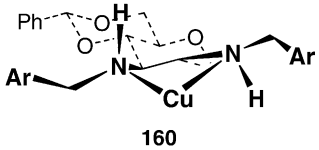


155 **156** **157** **158** **159**

Fig. 46. Diimino and diamino ligands, derived from α-D-glucose and α-D-mannose.



Scheme 14. Cyclopropanation of styrene.



160

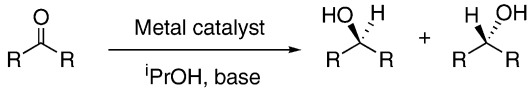
Fig. 47. Chiral pocket formed with coordinated C_2 symmetrical diamines.

As far as N–N carbohydrate derivatives are concerned, chiral diimino and diamino ligands, **155**, **157** and **159**, α-D-glucose and **156** and **158** derived from α-D-mannose (Fig. 46) were obtained by introducing the appropriate nitrogen functions at C-2 and C-3 of the sugar rings.

The ability of the new chelates to promote the asymmetric copper(I)-catalyzed cyclopropanation of styrene has been assessed and e.e.'s of up to 55% were obtained (Scheme 14).

The nature of both sugars and the chelates is crucial in determining the enantioselectivity of the reaction: Diimines and diamines derived from α-D-glucose were found to favour different enantiomers. When the activities of diimines derived from different sugars were compared, an analogous reverse effect was observed [134]. In the case of diamines based on glucose, a chiral pocket with C_2 symmetry **160** is responsible for promoting the formation of the enantiomer (*S*) (Fig. 47). A hydrophilic chiral diamine derived from D-glucose **159** has been used in the Rh(I)-catalyzed asymmetric hydrogenation of acetophenone by using isopropanol and ethanol as hydrogen sources (Scheme 14). The secondary alcohols were obtained with low or moderate e.e. achieving 50% with isopropanol at 25 °C [135] (Scheme 15).

Palladium complexes containing N-chelates **161a** (R = H, Me) and **162** (Fig. 48) (R = H or Me; R′ = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose residue, Fig. 48) have been reported and used in mild hydrogenation of olefins in water. In these ligands, the N donor atom is directly linked to a chiral C: for instance, the C_1 atom of the sugar ring. The ability of the ligands to induce enantioselective coordination of prochiral olefins was assessed by preparing Pd(0) complexes [Pd(N, N-chelate)(olefin)]. Hydrophilic complexes were obtained by deprotecting the hydroxy groups of the sugar residue and used for hydrogenating alkenes in H_2O. The course of the reaction is



Scheme 15. Hydrogenation of acetophenone.

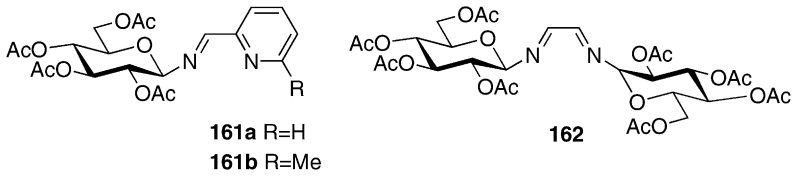


Fig. 48. N-chelate ligands used in hydrogenation of olefins in water.

strongly influenced by pH, and homogeneous hydrogenation of the double bond takes place only under basic conditions. An attempt to enantioselectively reduce the double bond of α-ethylacrilonitrile was unsuccessful [136].

2.6. Carbohydrate O,E-ligands (E = N, O)

2.6.1. N,O-ligands

Copper(II) catalysts bearing Schiff-base ligands derived from salicylaldehyde or pyridine-2-carboxaldehyde and naturally occurring amino-sugars (**163**–**166**) have been applied to the synthesis of cyclopropane carboxylates by means of a catalytic asymmetric cyclopropanation of haloalkenes (Fig. 49). The reaction, which can lead to four isomeric cyclopropane carboxylates described by the 1R and 1S forms and which have two geometric isomers each (*cis* and *trans*), gives low to moderate yields and low geometric control and enantioselectivity. Just in one case, the catalyst formed by pyridine-2-carboxaldehyde and an α-alloderivative afforded 58% of the insecticidally most desirable cis-1R-isomer [137].

Monosaccharide derived catalysts have also been developed for the catalytic enantioselective addition of diethylzinc to aldehydes (Fig. 50) [138]. D-xylose derivatives **167** and **168** were tested as ligands in the addition of diethylzinc to aldehydes. 5-Deoxy-1,2-*O*-isopropylidene-5-morpholino-α-D-xylofuranose (**167**, R_2N = morpholino) provided high enantioselectivity for aromatic and relatively hindered aliphatic aldehydes (benzaldehyde, 90% yield, 96% e.e. in 1-phenylpropan-1-ol (*R*)), and 5-deoxy-5-hexahydroazepinyl-1,2-isopropylidene-α-D-xylofuranose (**168**, R_2N = hexahydroazepinyl) was highly effective for unhindered aliphatic aldehydes (heptanal, 75% yield, 83% e.e. in 3-nonanol (*R*)).

A series of new chiral ligands derived from D-fructose were synthesized and also applied in the enantioselective addition of diethylzinc to aldehydes [139]. Comparison of the enantioselectivities obtained with these ligands demonstrated that their catalytic properties are highly dependent upon the length of the backbone between the coordinating nitrogen and oxygen atoms in the ligands. Ligands having bigger backbones (**171**, **172**) induce higher enantioselectivity and activity than the ligands with shorter backbones (**169**, **170**). In terms of reactivity and enantioselectivity, acetone-protected ligand **170** (R_1 = –CH_3 and R_2 = H) and cyclohexanone-protected ligand **171** (R_1 = –$(CH_2)_5$–) are the best catalysts (96% yield, 82% e.e. (*R*) and 99% yield, 83% e.e. (*R*) in 1-phenyl-propanol, respectively).

2.6.2. O and O,O-ligands

Complex **174** has proved to be a potent chiral template for enantioselective reactions. Exchange of the Cl-atom for

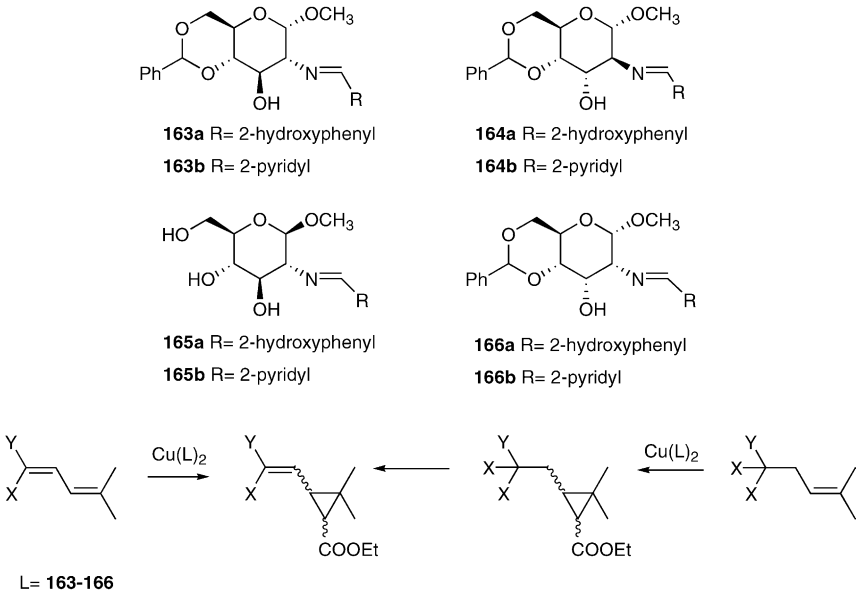


Fig. 49. Ligands **163**–**166** for copper catalyzed cyclopropanation of haloalkenes.

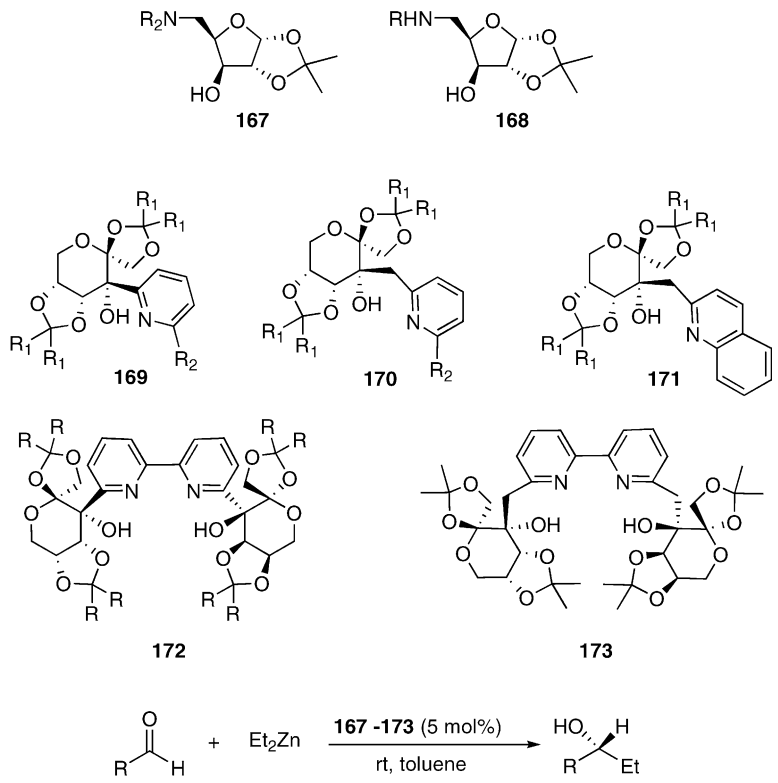


Fig. 50. D-Xylose (**167**–**168**) and D-fructose ligands (**169**–**173**) for the diethylzinc addition to aldehydes.

allyl [140], ester enolates [141] or glycine enolates [142] and reaction with aldehydes gives homoallyl alcohols, β-hydroxy-esters, and threo-β-hydroxy-α-amino acids, respectively, with high enantio- and diastereoselectivity (Fig. 51).

Complex **175**, which has a bidentate threitol ligand derived from *R*,*R*-(+)-tartaric acid (TADDOL) [143], was also tested in the same reactions (Fig. 52). It was found to be a good auxiliary for allyl transfer (for recent applications see [144]) but less stereoselective in the aldol reactions than the bis-diacetoneglucose analog. The reaction is more successful on a stoichiometric basis, although it can be catalytic when activated aldehydes are used (Fig. 53).

Complex **176** is used as a Lewis acid [145] catalyst in asymmetric processes such as cycloaddition reactions, Diels–Alder and [2 + 2] cycloaddition reactions, Sharpless oxidation, sulfoxidation and Baeyer–Villiger oxidations, and cyclopropanation.

Chiral(acyloxy)borane (CAB) (**177**, **178**) is also derived from tartaric acid and is used above all as a Lewis acid in catalytic asymmetric Diels–Alder cycloaddition reactions. It gives optimal selectivities when α-substituted α,β-unsaturated aldehydes are used as dienophiles [146].

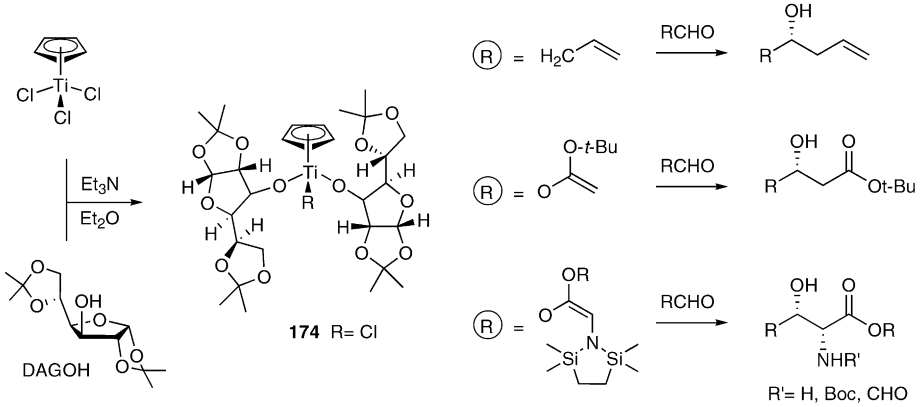


Fig. 51. Titanium complex containing two diacetonglucose units.

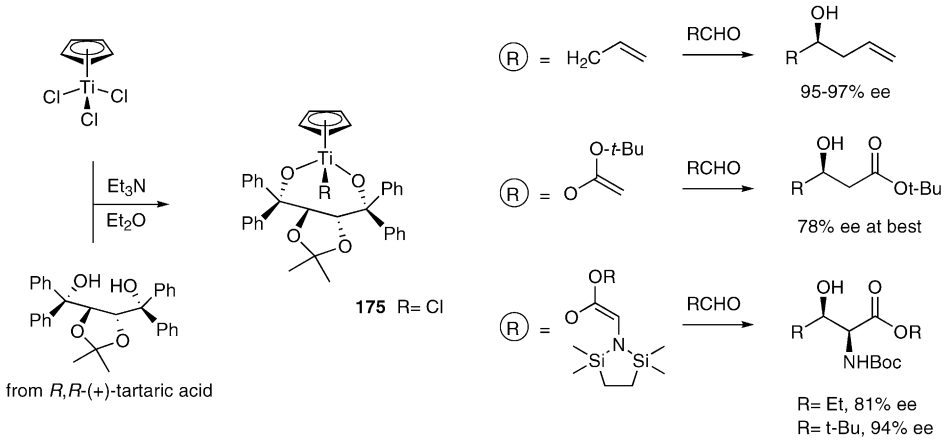


Fig. 52. Titanium complex containing TADDOL as ligand.

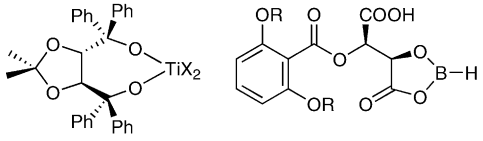


Fig. 53. Ti-TADDOL complexes (**176**) and tartaric acid-borane derivatives (**177**–**178**).

3. Concluding remarks

Carbohydrate derivatives are widely used as ligands for asymmetric transition metal processes. Carbohydrates have been functionalized and modified in many ways to behave as chiral ligands. From the previous sections it can be concluded that the use of carbohydrates derivatives from D-xylose, D-mannose, D-glucose, D-galactose, L-rhamnose, D-fructose, etc. has increased in the last years leading to a considerable number of ligands with a variety of different backbones. Moreover, systematic variation of stereogenic centers and the introduction of substituents with different electronic and steric properties has enlarged the structural diversity of these ligands. Although carbohydrates occur in only one enantiomeric form, interestingly, in some cases the selection of appropriate combinations of stereogenic centers in the carbohydrate backbone allows, in the metal catalyzed reaction, to obtain both enantiomers in enantioselective way, thus behaving as what it is called pseudo-enantiomers. The degree of enantiocontrol has been shown to depend on the functionalization of the donor atoms and also on the sugar chiral backbone. For instance, in the hydrogenation of dehydro aminoacids, itaconic acids and related susbtrates, diphosphines, diphosphites and phosphine–phosphite provide high enantioselectivity. Among the array of chiral structures with these coordinating functionalities, however, only some C_1 diphosphines derived from D-(+)-xylose and D-(+)-glucose give e.e.'s as high as 98%, while C_2 diphospholanes derived from D-mannitol incorporated into DUPHOS are highly effective in hydrogenation reactions (e.e. >99%) and allows the reaction to be performed in water. DIOP related ligands having a methyl substituent in the α-position to the P-atoms (derived from mannitol), or a conformationally rigid 1,4-dioxane backbone instead of the isopropylidene acetal, provide 99% e.e. Interestingly, diphosphite ligands derived from D-(+)-xylose and D-(+)-glucose provide e.e. >99% e.e., in particular those structures where a methyl substituent was introduced at C-5. This result is particularly relevant since only a few catalysts achieve high enantioselectivity in hydroformylation of styrene. Many of these diphosphorus ligands are also effective in palladium allylic alkylation.

Although in general less effective that the bidentate phosphorus ligands, monodentate ligands have been successfully applied to several reactions, for instance, cross-coupling reaction, where a monodentate phoshine provide 99% e.e., or hydrogenation of dimethyl itaconate where monophosphites derived from D-mannitol provide excellent enantioselectivities of up 99%. Monodentate phoshinites are particular useful in hydrovinylation of olefins where e.e. as high as 90% are obtained. Monodentate phosphoroamidites lead to high e.e. (96%) in hydrogenation reactions. Mixed or hemilabile N–P or N–S ligands are particularly effective for allylic alkylation where interesting spectroscopic studies have been developed. In other cases, as for hydroformylation reaction, the characterization of intermediates in reaction conditions show that for both P,N- or P,S-ligands, the ligand behave as monodentate, coordinated through the P-atom. Nitrogen and sulfur ligands, although effective in hydrogenation, allylic alkylations, cyclopropanation, conjugate addition and other reaction provide in general moderate enantioselectivity. Oxygen ligands derived from D-fructose induce high enantioselectivity in the addition of diethylzinc to aldehydes. TADDOL derivatives coordinated to Ti complexes have proved to be interesting chiral templates for providing enantio- and diastereoselectivity in several reactions.

References

[1] D. Steinborn, H. Junicke, Chem. Rev. 100 (2000) 4283.
[2] (a) S.J. Angyal, Chem. Soc. Rev. 9 (1980) 415;
(b) S.J. Angyal, Adv. Carbohydr. Chem. Biochem. 47 (1989) 1.
[3] U. Piarulli, C. Floriani, Prog. Inorg. Chem. 45 (1997) 393.
[4] J.F. Verchère, S. Chapelle, F. Xin, D.C. Crans, Prog. Inorg. Chem. 47 (1998) 837.
[5] (a) B. Gyurcsik, L. Nagy, Coord. Chem. Rev. 203 (2000) 81;
(b) L. Pellerito, L. Nagy, Coord. Chem. Rev. 224 (2002) 111;
(c) L. Nagy, A. Szorcsik, J. Inorg. Biochem. 89 (2002) 1.
[6] (a) R. Noyori (Ed.), Asymmetric Catalysis in Organic Synthesis, Wiley, New York, 1994;
(b) I. Ojima (Ed.), Catalytic Asymmetric Synthesis, Wiley, New York, 2000.
[7] (a) M.J. Burk, F. Bienewald, in: M. Beller, C. Bolm (Eds.), Transition Metal for Organic Synthesis, Wiley, New york, 1998;
(b) E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, Springer, Berlin, 1999.
[8] P.W.N.M. van Leeuwen, C. Claver (Eds.), Rhodium Catalyzed Hydroformylation, Kluwer, Dordrecht, 2000.
[9] (a) M.T. Reetz, T. Neugebauer, Angew. Chem. Int. Ed. 38 (1999) 179;
(b) D.G. Blackmond, T. Rosner, T. Neugebauer, M.T. Reetz, Angew. Chem. Int. Ed. 38 (1999) 2196.
[10] (a) M. Clochard, E. Mattmann, F. Mecier, L. Ricard, F. Matthey, Org. Lett. 5 (2003) 3093;
(b) V.I. Tararov, R. Kadyrov, T.H. Riermeier, J. Holz, A. Börner, Tetrahedron: Asymmetry 10 (1999) 4009.
[11] D. Lafont, D. Sinou, G. Descotes, J. Organomet. Chem. 169 (1979) 87.
[12] J. Bakos, B. Heil, L. Markó, J. Organomet. Chem. 253 (1983) 249.
[13] I. Habus, Z. Raza, V. Sunjic, Croatica Chim. Acta 61 (1988) 857.
[14] V. Sunjic, I. Habus, G. Comisso, F. Moimas, Gazz. Chim. It. 119 (1989) 229.
[15] C.B. Li, A. Bernet, E. Vasella, A. Broger, A. Meli, Carbohydr. Res. (1991) 149.
[16] B.M. Choudary, M.R. Sarma, A.D. Prasad, N. Narender, Indian J. Chem. 33B (1994) 152.
[17] S.R. Gilbertson, C.W.T. Chang, J. Org. Chem. 60 (1995) 6226.
[18] O. Pàmies, G. Net, A. Ruiz, C. Claver, Eur. J. Inorg. Chem. (2000) 2011.
[19] M. Diéguez, O. Pàmies, A. Ruiz, S. Castillón, C. Claver, Tetrahedron: Asymmetry 11 (2000) 4701.
[20] M. Diéguez, O. Pàmies, G. Net, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 12 (2001) 651.
[21] O. Pàmies, A. Ruiz, G. Net, C. Claver, H. Kalchhauser, M. Widhalm, Monatsh. Chem. 131 (2000) 1173.
[22] M. Diéguez, S. Jansat, M. Gomez, A. Ruiz, G. Muller, C. Claver, Chem. Commun. (2001) 1132.
[23] S. Liu, X. Li, A. Wang, Catal. Today 63 (2000) 531.
[24] H. Bruner, R. Sievi, J. Organomet. Chem. 328 (1987) 71.
[25] J. Holz, M. Quirmbach, U. Schmidt, D. Heller, R. Stürmer, A. Börner, J. Org. Chem. 63 (1998) 8031.
[26] W. Li, Z. Zhang, D. Xiao, X. Zhang, J. Org. Chem. 65 (2000) 3489.
[27] Y.Y. Yan, T.V. RajanBabu, Org. Lett. 2 (2000) 199.
[28] J. Holz, R. Stürmer, U. Schmidt, H.J. Drexler, D. Heller, H.P. Krimmer, A. Börner, Eur. J. Org. Chem. (2001) 4615.
[29] D. Carmichael, H. Doucet, J.M. Brown, Chem. Commun. (1999) 261.
[30] H.B. Kagan, T.P. Dang, J. Am. Chem. Soc. 94 (1972) 6429.
[31] W. Hu, C.C. Chen, G. Xue, A.S.C. Chan, Tetrahedron: Asymmetry 9 (1998) 4183.
[32] F. Robert, G. Oehme, D. Sinou, J. Mol. Catal. A 139 (1999) 105.
[33] D. Guillaneux, L. Martiny, H.B. Kagan, Collect. Czech. Chem. Commun. 65 (2000) 717.
[34] Y.Y. Yan, T.V. RajanBabu, Org. Lett. 2 (2000) 4137.
[35] W. Li, X. Zhang, J. Org. Chem. 65 (2000) 5871.
[36] W. Li, J.P. Waldkirch, X. Zhang, J. Org. Chem. 67 (2002) 7618.
[37] U. Nagel, E. Kinzel, J. Andrade, G. Prescher, Chem. Ber. 119 (1986) 3326.
[38] U. Nagel, B. Rieger, Organometallics 8 (1989) 1534.
[39] R.W. Cullen, Y. Sugi, Tetrahedron Lett. 19 (1978) 1635.
[40] R. Jackson, D.J. Thompson, J. Organomet. Chem. 159 (1798) C29.
[41] R. Selke, React. Kinet. Catal. Lett. 10 (1979) 135.
[42] D. Sinou, G. Descotes, React. Kinet. Catal. Lett. 14 (1980) 463.
[43] R. Selke, H. Pracejus, J. Mol. Catal. 37 (1986) 213.
[44] R. Selke, J. Prakt. Chem. 4 (1987) 717.
[45] R. Selke, J. Organomet. Chem. 370 (1989) 249.
[46] R. Selke, M. Scwarze, H. Baudish, I. Grassert, M. Michalik, G. Oehme, B. Costisella, J. Mol. Catal. 84 (1993) 223.
[47] R. Selke, M. Ohff, A. Riepe, Tetrahedron 52 (1996) 15079.
[48] V.I. Tatarov, R. Kadirov, T.H. Riermeier, J. Holz, A. Börner, Tetrahedron: Asymmetry 10 (1999) 4009.
[49] H. Brunner, W. Pieronczyk, J. Chem. Res. (S) (1980) 1275.
[50] T.H. Johnson, G. Rangarajan, J. Org. Chem. 45 (1980) 62.
[51] A. Iida, M. Yamashita, Bull. Chem. Soc. Jpn. 61 (1988) 2365.
[52] E. Guiu, B. Muñoz, S. Castillón, C. Claver, Adv. Synth. Catal. 345 (2003) 169.
[53] E. Guimet, M. Diéguez, A. Ruiz, C. Claver, Tetrahedron: Asymmetry, submitted for publication.
[54] I. Habus, Z. Raza, V. Sunjic, J. Mol. Catal. 42 (1987) 173.
[55] G. Snatzer, Z. Raza, I. Habus, V. Sunjic, Carbohydr. Res. 182 (1988) 179.
[56] M. Yamashita, M. Naoi, H. Imoto, T. Oshikawa, Bull. Chem. Soc. Jpn. 62 (1989) 942.
[57] Y. Chen, X. Li, S. Tong, M.C.K. Choi, A.S.C. Chan, Tetrahedron Lett. 40 (1999) 957.
[58] T.A. Ayers, T.V. RajanBabu, Process Chem. Pharm. Ind. (1999) 327.
[59] T.V. RajanBabu, A.L. Casalnuovo, J. Am. Chem. Soc. 114 (1992) 6265.
[60] T.V. RajanBabu, A.L. Casalnuovo, Pure Appl. Chem. 66 (1994) 1535.
[61] A.L. Casalnuovo, T.V. RajanBabu, T.A. Ayers, T.H. Warren, J. Am. Chem. Soc. 116 (1994) 9869.
[62] T.V. RajanBabu, A.L. Casalnuovo, J. Am. Chem. Soc. 118 (1996) 6325.
[63] T.V. RajanBabu, T.A. Ayers, Tetrahedron Lett. 35 (1994) 4295.
[64] T.V. RajanBabu, T.A. Ayers, A.L. Casalnuovo, J. Chem. Soc. 116 (1994) 4101.
[65] T.V. RajanBabu, T.A. Ayers, G.A. Halliday, K.K. You, J.C. Calabrese, J. Org. Chem. 62 (1997) 6012.
[66] N. Nomura, Y.C. Mermet-Bouvier, T.V. RajanBabu, Synlett (1996) 745.
[67] D.S. Clyne, Y.C. Mermet-Bouvier, N. Nomura, T.V. RajanBabu, J. Org. Chem. 64 (1999) 7601.
[68] H. Brunner, W. Pieronczyk, J. Chem. Res. (S) (1980) 76.
[69] D.J. Wink, T.J. Kwok, A. Yee, Inorg. Chem. 29 (1990) 5006.
[70] G.J.H. Buisman, P.C.J. Kamer, P.W.N.M. van Leeuwen, Tetrahedron: Asymmetry 4 (1993) 1625.
[71] G.J.H. Buisman, M.E. Martin, E.J. Vos, A. Klootwijk, P.C.J. Kamer, P.W.N.M. van Leeuwen, Tetrahedron: Asymmetry 6 (1995) 719.
[72] R. Kadyrov, D. Heller, R. Selke, Tetrahedron: Asymmetry 9 (1998) 329.
[73] M. Diéguez, A. Ruiz, C. Claver, J. Chem. Soc., Dalton Trans. (2003) 2957.
[74] O. Pàmies, G. Net, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 11 (2000) 1097.
[75] M. Diéguez, O. Pàmies, A. Ruiz, S. Castillón, C. Claver, Chem. Commun. (2000) 1607.
[76] M. Diéguez, O. Pàmies, A. Ruiz, S. Castillón, C. Claver, Chem. Eur. J. 7 (2001) 3086.

[77] M. Diéguez, O. Pàmies, A. Ruiz, C. Claver, New J. Chem. 26 (2002) 827.
[78] O. Pàmies, G. Net, A. Ruiz, C. Claver, Eur. J. Inorg. Chem. (2000) 1287.
[79] M. Diéguez, A. Ruiz, C. Claver, J. Org. Chem. 67 (2002) 3796.
[80] 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. 66 (2001) 8867.
[81] O. Pàmies, G. Net, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 10 (1999) 2007.
[82] O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 11 (2000) 4377.
[83] M. Diéguez, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 12 (2001) 2895.
[84] M.T. Reetz, T. Neugebauer, Angew. Chem. Int. Ed. 38 (1999) 179.
[85] A. Kless, J. Holz, D. Heller, R. Kadirov, R. Selke, C. Fischer, A. Börner, Tetrahedron: Asymmetry (1996) 33.
[86] M.T. Reetz, A. Gosberg, Tetrahedron: Asymmetry 10 (1999) 2129.
[87] O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, Chem. Commun. (2000) 2383.
[88] O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, J. Org. Chem. 66 (2001) 8364.
[89] O. Pàmies, G. Net, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 12 (2001) 3441.
[90] M. Diéguez, O. Pàmies, G. Net, A. Ruiz, C. Claver, J. Mol. Catal. A: Chem. 185 (2002) 11.
[91] M. Diéguez, A. Ruiz, C. Claver, Chem. Commun. (2001) 2702.
[92] M. Diéguez, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 12 (2001) 2827.
[93] M. Diéguez, A. Ruiz, C. Claver, Tetrahedron: Asymmetry 12 (2001) 2861.
[94] (a) M.T. Reetz, G. Mehler, A. Meiswinkel, T. Sell, Tetrahedron Lett. 43 (44) (2002) 7941;
(b) M.T. Reetz, T. Sell, A. Meiswinkel, G. Mehler, Angew. Chem. Int. Ed. (2003) 42;
(c) M.T. Reetz, L.J. Goossen, A. Meiswinkel, J. Paetzold, J. Feldthusen, Org. Lett. 5 (2003) 3099;
(d) D. Pena, A.J. Minnaard, A.H.M. de Vries, J.G. de Vries, B.L. Feringa, Org. Lett. 5 (2003) 5475;
(e) X. Jia, X. Li, L. Xu, O. Shi, X. Yao, A.S.C. Chan, J. Org. Chem. 68 (2003) 4539;
(f) K. Junge, G. Oehme, A. Monsees, T. Riermeier, U. Dingerdissen, M. Beller, J. Organometal. Chem. 675 (2003) 91;
(g) K. Junge, G. Oehme, A. Monsees, T. Riermeier, U. Dingerdissen, M. Beller, Tetrahedron Lett. 43 (2002) 4977.
[95] (a) A. Martorell, R. Naasz, B.L. Feringa, P.G. Pringle, Tetrahedron: Asymmetry 12 (2001) 2497;
(b) Y. Iguchi, R. Itooka, N. Miyaura, Synlett 7 (2003) 1040.
[96] T.V. RajanBabu, Chem. Rev. 103 (2003) 2845.
[97] (a) R. Imbos, A.J. Minnaard, B.L. Feringa, Dalton Trans. 10 (2003) 2017;
(b) A. Duursma, R. Hoen, J. Schuppan, R. Hulst, A.J. Minnaard, B.L. Feringa, Org. Lett. 5 (2003) 3111.
[98] (a) F. Lagasse, H. Kagan, Chem. Pharm. Bull. 48 (2000) 315;
(b) Hayashi, Acc. Chem. Res. 33 (2000) 354;
(c) H. Brunner, W. Zettlelmeie, Handbook of Enantioselective Catalysis, vols. I and II, VCH, 1993.
[99] L. Viau, R. Chauvin, J. Organomet. Chem. 654 (2002) 180.
[100] H. Park, T.V. RajanBabu, J. Am. Chem. Soc. 124 (2002) 734.
[101] J. Sakai, W.B. Schweizer, D. Seebach, Helv. Chim. Acta 76 (1993) 2654.
[102] D. Haag, J. Runsink, H.D. Scharf, Organometallics 17 (1998) 398.
[103] H. Brunner, P. Willigs, J. Chem. Res (S) 3 (1980) 76.
[104] A. Suarez, A. Pizzano, I. Fernandez, N. Khiar, Tetrahedron: Asymmetry 12 (2001) 633.
[105] M.T. Reetz, G. Mehler, Angew. Chem. Int. Ed. 39 (2000) 3889.
[106] D. Seebach, M. Hayakawa, J. Sakai, W.B. Schweizer, Tetrahedron 48 (1993) 1711.
[107] A. Alexakis, C. Benhaïm, X. Fournioux, A. Van der Heuvel, J.M. Levêque, S.P. March, S. Rosset, Synlett 11 (1999) 1811.
[108] A. Bayer, P. Murszat, U. Thewalt, B. Rieger, Eur. J. Inorg. Chem. 10 (2002) 2614.
[109] E. Kelle, J. Maurer, R. Naasz, T. Schader, A. Meetsma, B.L. Feringa, Tetrahedron: Asymmetry 9 (1998) 2409.
[110] G. Helmechen, A. Pfaltz, Acc. Chem. Res. 33 (2000) 336.
[111] K.N. Gavrilov, A.I. Polouskin, Russ. Chem. Rev. 8 (2000) 662.
[112] A. Masdeu-Bultó, M. Dieguez, E. Martín, M. Gomez, Coord. Chem. Rev. 242 (2003) 59.
[113] K. Yonehara, T. Hashizume, K. Mori, K. Ohe, S. Uemura, Chem. Commun. 5 (1999) 415.
[114] K. Yonehara, T. Hashizume, K. Mori, K. Ohe, S. Uemura, J. Org. Chem. 64 (1999) 9374.
[115] K. Yonehara, K. Mori, T. Hashizume, K.G. Chung, K. Ohe, S. Uemura, J. Organomet. Chem. 603 (2000) 40.
[116] D.K. Heldmann, D. Seebach, Helv. Chim. Acta 82 (1999) 1096.
[117] R. Hilgraf, A. Pfaltz, Synlett (1999) 1817.
[118] C. Borriello, M.E. Cucciolito, A. Panunzi, F. Ruffo, Inorg. Chim. Acta 353 (2003) 238.
[119] F. Robert, N. Gaillard, D. Sinou, J. Mol. Catal. A 144 (1999) 473.
[120] F. Robert, D. Sinou, J. Organomet. Chem. 604 (2000) 99.
[121] A. Aghmiz, A. Masdeu-Bulto, C. Claver, D. Sinou, J. Mol. Catal. A 184 (2002) 111.
[122] A. Albinati, P.S. Pregosin, K. Wick, Organometallics 15 (1996) 2419.
[123] K. Boog-Wick, P.S. Pregosin, G. Trabesinger, Mag. Res. Chem. 36 (1998) S189.
[124] P. Barbaro, A. Currao, J. Herrmann, R. Nesper, P.S. Pregosin, R. Salzmann, Organometallics 15 (1996) 1879.
[125] O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, Organometallics 19 (2000) 1488.
[126] K. Boog-Wick, P.S. Pregosin, G. Trabesinger, Organometallics 17 (1998) 3254.
[127] O. Pàmies, G. Net, A. Ruiz, C. Claver, S. Woodward, Tetrahedrom: Asymmetry 11 (2000) 871.
[128] M. Dieguez, A. Orejón, A.M. Masdeu-Bultó, R. Echarri, S. Castillón, C. Claver, A. Ruiz, J. Chem. Soc., Dalton Trans. (1997) 4611.
[129] M. Diéguez, A. Ruiz, C. Claver, M.M. Pereira, A.M.A. d'Rocha Gonsalves, J. Chem. Soc., Dalton Trans. (1998) 3517.
[130] O. Pàmies, M. Diéguez, G. Net, A. Ruiz, C. Claver, J. Chem. Soc., Dalton Trans. (1999) 3439.
[131] S. Jansat, M. Gómez, G. Muller, M. Diéguez, A. Aghmiz, C. Claver, A.M. Masdeu-Bultó, L. Flores-Santos, E. Martin, M.A. Maestro, J. Mahía, Tetrahedron: Asymmetry 12 (2001) 1469.
[132] B.R. James, R.S. McMillan, Can. J. Chem. 55 (1977) 3927.
[133] M.C. Pigro, G. Angiuoni, G. Piancatelli, Tetrahedron 58 (2002) 5459.
[134] C. Borriello, M.E. Cucciolito, A. Panunzi, F. Ruffo, Tetrahedron: Asymmetry 12 (2001) 2467.
[135] C. Borriello, M.E. Cucciolito, A. Panunzi, F. Ruffo, A. Saporito, Inorg. Chem. Commun. 6 (2003) 1081.
[136] C. Borriello, M.L. Ferrara, I. Orabona, A. Panunzi, F. Ruffo, Dalton Trans. (2000) 2545.
[137] D.A. Holland, D.J. Laidler, Milner, J. Mol. Catal. 11 (1981) 119.
[138] B.T. Cho, N.J. Kim, Chem. Soc., Perkin Trans. 1 (1996) 2901.
[139] H. Huang, H. Chen, X. Hu, C. Bai, Z. Zheng, Tetrahedron: Asymmetry 14 (2003) 297.
[140] M. Riediker, R.O. Duthaler, Angew. Chem. Int. Ed. Engl. 28 (1989) 494.
[141] (a) R.O. Duthaler, P. Herold, X. Lottenbach, K. Oertle, M. Riediker, Angew. Chem. Int. Ed. Engl. 28 (1989) 495;
(b) R.O. Duthaler, P. Herold, S. Wyler-Helfer, M. Riediker, Helv. Chim. Acta 73 (1990) 659.

[142] G. Bold, R.O. Duthaler, M. Riediker, Angew. Chem. Int. Ed. Engl. 28 (1989) 497.
[143] R.O. Duthaler, A. Hafner, M. Riediker, Pure Appl. Chem. 62 (1990) 631.
[144] (a) S. Bouz-Bouz, J. Cossy, Tetrahedron Lett. 44 (2003) 4471;
(b) S. Bouz-Bouz, J. Cossy, Org. Lett. 5 (2003) 3029;
(c) J. Cossy, C. Willis, B. Bellosta, S. Bouz-Bouz, J. Org. Chem. 67 (2002) 1982;
(d) J. Cossy, S. Bouz-Bouz, F. Pradaux, C. Willis, B. Bellosta, Synlett (2002) 1595;
(e) J. Cossy, C. Willis, L. Saint-James, Synthesis (2002) 951.
[145] K. Narasaka, Synthesis (1991) 1.
[146] (a) K. Furuta, A. Kanematsu, H. Yamamoto, S. Takaoka, Tetrahedron Lett. 30 (1989) 7231;
(b) K. Furuta, S. Shimizu, Y. Miwa, H. Yamamoto, J. Org. Chem. 54 (1989) 1483;
(c) K. Ishihara, Q. Gao, H. Yamamoto, J. Org. Chem. 58 (1993) 6917;
(d) K. Ishihara, Q. Gao, H. Yamamoto, J. Am. Chem. Soc. 115 (1993) 10412.