Available online at www.sciencedirect.com
SCIENCE DIRECT®
Coordination Chemistry Reviews 242 (2003) 59–72
COORDINATION CHEMISTRY REVIEWS
www.elsevier.com/locate/ccr

Chiral mono- and bidentate ligands derived from chromium arene complexes—synthesis, structure and catalytic applications

Albrecht Salzer *

Institute of Inorganic Chemistry, RWTH Aachen, Aachen 52056, Germany

Received 6 November 2002; accepted 14 March 2003

Contents

Abstract

A general and versatile method to prepare optically active mono- and bidentate ligands based on arene chromium complexes has been developed, starting from commercially available (*R*)- or (*S*)-phenylethylamine and its derivatives. Various ligand functions can be introduced into the side chain as well as the *ortho*-position on the ring in a modular fashion creating a library of compounds suitable for application in homogeneous catalysis. The complexes have been successfully employed for enantioselective C–C coupling reactions as well as isomerization, hydrogenation, allylic sulfonation, hydrosilylation and hydroamination.

Keywords: Arene-π-complexes; Planar chirality; Phosphorus ligands; Asymmetric catalysis

1. Introduction

Enantioselective homogeneous catalysis remains one of the most challenging topics in organic and organometallic research. Continuous improvements are made, largely due to the development of new families of ligands. The Nobel committee recognized this by awarding the 2001 Nobel prizes in Chemistry for achievements in this field.

While searching for novel catalysts and ligands, chemists have used all types of organic building blocks, natural as well as unnatural. While earlier research focused on ligands derived from the "chiral pool", e.g. tartaric acid, terpenes, amino acids and sugars, the focus has shifted somewhat towards other ligand systems not derived from natural sources. This is largely due to the enormous success of such ligand families as BINAP and its derivatives, the DUPHOS ligands [1,2] as well as the "Josiphos" family of ligands [3,4]. It should be noted

* Tel.: +49-241-8094646; fax: +49-241-8092288.
E-mail address: albrecht.salzer@ac.rwth-aachen.de (A. Salzer).

0010-8545/03/$ - see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S0010-8545(03)00059-6

that these ligands contain unusual elements of chirality, such as planar and axial chirality. The Josiphos ligands are also special in that they incorporate a transition metal-containing unit as the central core around which the ligand framework is constructed. This transition metal itself is not involved in the catalysis, but is part of the scaffold to which the ligand functions are attached. The function of the metal is to create a chiral environment whose spatial and dynamic properties could not be achieved by an organic framework alone. In a few cases, the redox properties of the metal have been used to vary the electronic properties of the ligands as well as its solubility [5,6].

The reactivity of metal-containing bidentate ligands other than ferrocene has recently been reviewed [7]. We are interested in the chemistry of ligands derived from arenetricarbonylchromium complexes. Earlier work in this area has also been reviewed by Bolm and Muñiz [8] and recently by Gibson and Ibrahim [9]. The current article will summarize our own research in this field and will present synthetic, structural and catalytic work done in the recent past, including as yet unpublished work.

2. Synthesis and structural studies

2.1. Monodentate ligands

(*R*)- and (*S*)-phenylethylamine and its derivatives (Fig. 1) are commercially available and are produced on an industrial scale by a lipase-catalyzed resolution process by BASF [10].

After protection of the amino group by alkylation, the synthesis of chromium complexes is quite simple, following the general method outlined in Ref. [11]. The unsubstituted derivative (*R*)-tricarbonyl[{(α-dimethylamino)ethyl}η^6-benzene]chromium (**1**) can be easily prepared on a 25 g scale in almost quantitative yield [12,13]. The same is true for the *para*-substituted derivatives (R = Me, OMe and Cl), although the yield

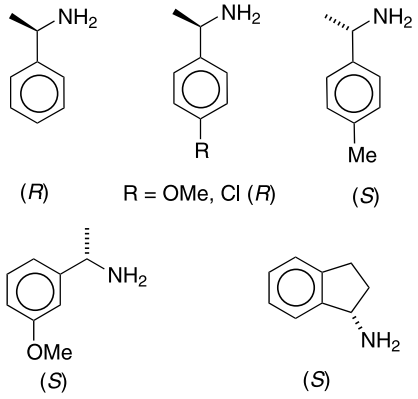
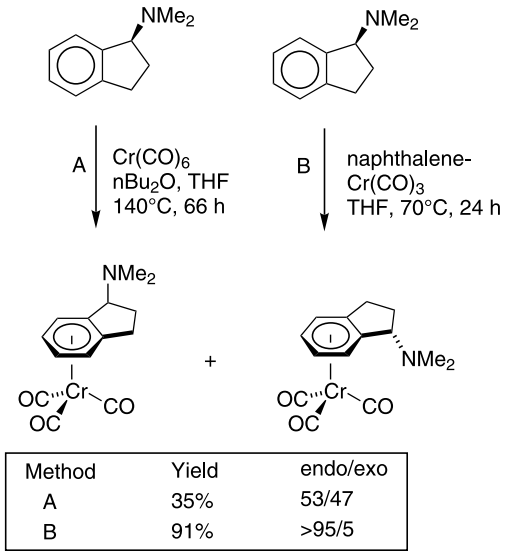


Fig. 1. Commercially available optically active amines used in this study.



Method	Yield	endo/exo
A	35%	53/47
B	91%	>95/5

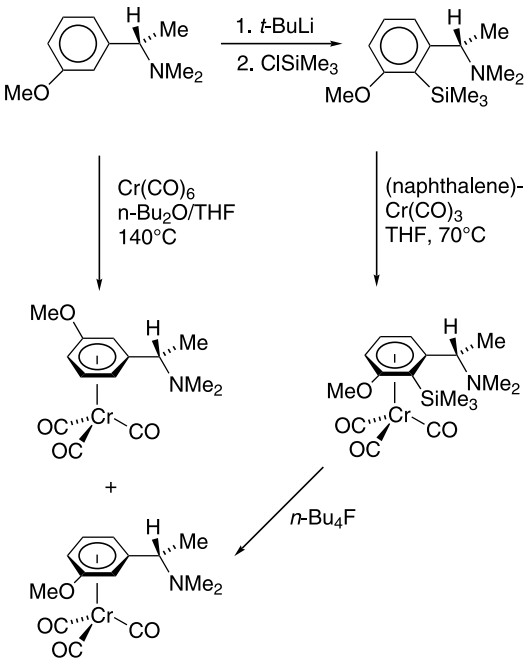
Scheme 1.

for the chloro compound is somewhat lower (69, 85 and 43%, respectively) [14]. It is advantageous to use an excess of hexacarbonylchromium, as this is easily removed from the product than an excess of the ligand.

Using the 3-methoxy-substituted arene or starting from dimethylaminoindane, this method produces a mixture of two diastereomers in a 1:1 ratio as, in addition to tetrahedral chirality in the side chains, these complexes exhibit planar chirality. These diastereomers are difficult to separate and we sought a diastereoselective route. Starting from Kündig's reagent, tricarbonyl(naphthalene)chromium [15], ligand exchange is easily achieved under mild conditions, giving the *endo*-isomer of the aminoindane derivative in excellent yield and high purity [14] (Scheme 1). The stereochemistry was confirmed by an X-ray structure analysis of a derivative (vide infra). Most likely, the preference for the *endo*-complex is due to weak prior coordination of the $Cr(CO)_3$ fragment to the amino group before complexation to the arene ring.

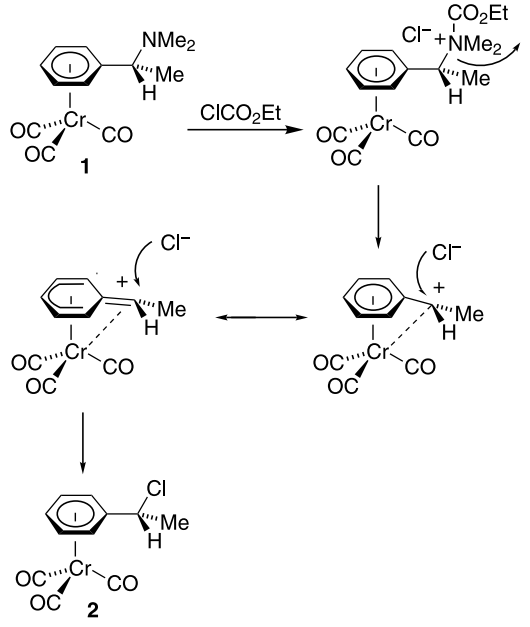
For 3-methoxyphenylethylamine, the direct complexation with $Cr(CO)_6$ gave 77% yield with an approximate 1:1 ratio and even the naphthalene $Cr(CO)_3$ method still gave two diastereomers so that we modified the starting material by regiospecifically introducing a trimethylsilylgroup into the 2-position. This strategy for the synthesis of planar-chiral arene complexes had been suggested by Uemura et al. [16]. The modified starting material now gave mainly one of the two possible diastereomers (de = 86% by NMR) in 71% yield (Scheme 2) [17]. Diastereomerically pure material was obtained after chromatographic separation (de > 98%). The absolute configuration of this isomer was again determined on a derivative (vide infra).

For the synthesis of further compounds, it was necessary to exchange the dimethylamino group for



Scheme 2.

other nucleophiles. We achieved this through a chance discovery: on treating (*R*)-tricarbonyl[{(α-dimethylamino)ethyl}η^6-benzene]chromium (**1**) with either ethyl chloroformate or chloroethyl chloroformate (ACE-Cl), a clean conversion was observed, leading to (*R*)-tricarbonyl[{(α-chloro)ethyl}η^6-benzene]chromium (**2**) in 93% yield [18]. This method is quite established for the conversion of tertiary amines into secondary amines, benzyl being the best leaving group [19]. Interestingly enough, the fate of the leaving group had never been fully established before and it was not known whether



Scheme 3.

this reaction proceeded enantioselectively in organic compounds. We have performed a similar reaction on uncomplexed (*R*)-phenylethylamine and have isolated as the major aromatic product styrene, but only a minimum amount of (α-chloro)ethylbenzene, which was shown to be mainly of the (*S*)-configuration [20]. Compound **2** was found to be 96% enantiomerically pure by HPLC which was identical to the enantiomeric purity of the starting (*R*)-phenylethylamine.

A possible mechanism for this conversion is shown in Scheme 3. This assumes that there is a stabilization of the benzylic carbocation through interaction with suitable metal orbitals, similar to the ferrocene moiety. Distortion of the benzyl ligand away from planarity and shifting the chromium away from the center of the aromatic ring increases the spatial overlap between the metal orbital and the empty p-orbital of carbon, leading to further stabilization. In order to still correspond to formal 18-electron species, the bonding between the metal and the arene should become η^7. From this bonding picture it should be expected that these cations incorporate a substantial amount of exocyclic double bond character [21a]. The computed energy barrier around the C_{ipso}–CH_2 bond in the unsubstituted benzylic cation is 45.4 kcal mol^{-1}, higher than in the corresponding benzylic anion [21b]. A benzylic carbocation coordinated to $Cr(CO)_3$ should therefore be configurationally stable. If the leaving group was expulsed while positioned anti to the chromium center and the subsequent nucleophilic attack occurs from the *exo*-face (the *endo*-side being protected by the $Cr(CO)_3$ moiety) a double inversion mechanism takes place resulting in overall retention of configuration. This seems to happen with the chloride ion in our case. Possibly, the chloride anion remains as an ion pair with the ammonium cation close to the benzylic position throughout the elimination of the carbamate ester.

Substitutions at the benzylic position of chromium arene complexes normally do not proceed with full retention of configuration, unless the nucleophile is present in large excess, i.e. the nucleophile is the solvent [22] or the carbocation is part of an annelated ring, where rotation of the side chain is impossible and the

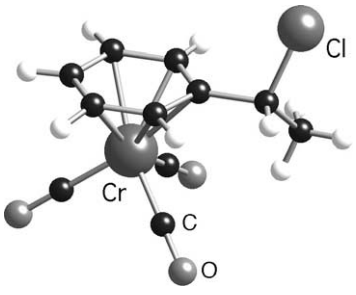
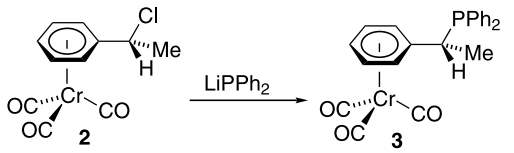


Fig. 2. X-ray structure of **2**.



Scheme 4.

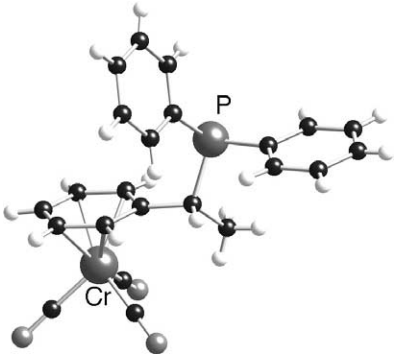


Fig. 3. X-ray structure of **3**.

nucleophile always attacks from the side opposite to the metal [23] (vide infra).

The absolute configuration was determined via X-ray structure analysis (Fig. 2). It was found to be (*R*), so the reaction proceeded with retention of configuration, in agreement with the proposed mechanism.

The chloride substituent was easily exchanged for other nucleophiles such as PPh_2 (Scheme 4).

The stereochemistry of the substitution of the chloride by $LiPPh_2$ was again ascertained by X-ray crystallography. The product tricarbonyl[{(α-diphenylphosphino)ethyl}η^6-benzene]chromium (**3**) was also formed via retention of configuration [18]. The X-ray structure of this product is shown in Fig. 3.

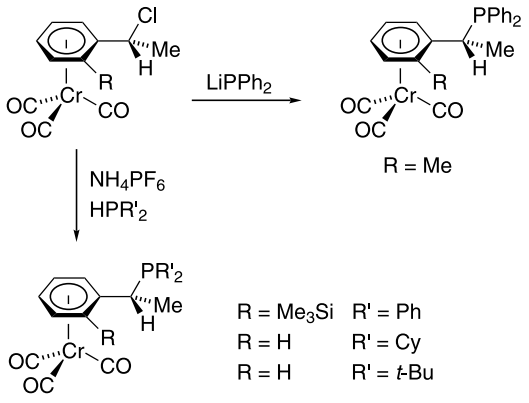
In order to ascertain that all substitution reactions performed on **2** with nucleophiles proceeded enantioselectively, we introduced a substituent into the 2-position of the ring via diastereoselective metalation and electrophilic addition of either MeI or $(CH_3)_3SiCl$ [12]. This introduces planar chirality into the compounds, so that the stereoselectivity of reactions in the benzylic position can be monitored through the second chiral element via NMR (Scheme 5). The reactions with R = Me or Me_3Si shown in Scheme 5 proceed with de > 98% [20].

When the 2-position was occupied by a bulky substituent, the exchange of chloride for phosphorus nucleophiles required the use of secondary phosphines in the presence of NH_4PF_6 or $TlPF_6$.

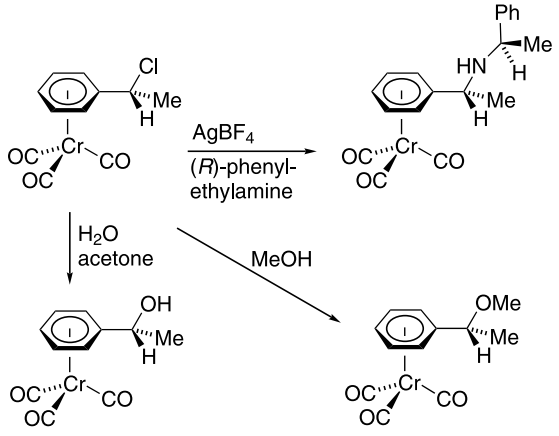
We also investigated the substitution of the chloride substituent for nitrogen, oxygen and carbon nucleophiles. Reaction of **2** with (*R*)-α-phenylethylamine in the presence of $AgBF_4$ generated the amino complex. The diastereomeric excess was determined by NMR to be between 89 and 92%, which is in the expected range considering that commercial (*R*)-α-phenylethylamine incorporated twice into the molecule has an ee of 96%.

We had noted during the syntheses that complex **2** and ist derivatives could be purified by chromatography over deactivated SiO_2 or Al_2O_3 without hydrolysis. This was in contrast to the analogous (α-chloroethyl)ferrocene, which we also prepared but which proved to be extremely sensitive to hydrolysis. Any reaction of the chromium complexes with oxygen nucleophiles was therefore expected to be very slow. This was confirmed by the reaction of **2** with methanol, which required 2 h reaction time in neat solution. (*R*)-[{(α-Methoxy)ethyl}-η^6-benzene]$Cr(CO)_3$ was formed in quantitative yield with complete retention of configuration. Similar reactions were performed on the substituted derivatives (Scheme 6).

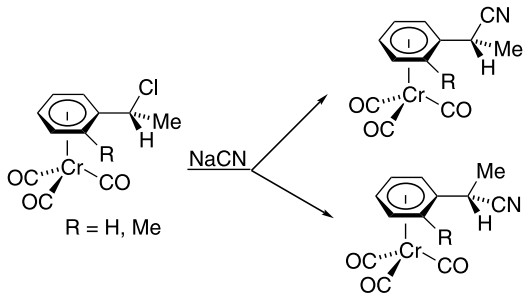
Jaouen and coworkers [22] had prepared the methoxy derivative by starting from optically active (*R*)-[{(α-hydroxy)ethyl}-η^6-benzene]$Cr(CO)_3$ which was protonated with H_2SO_4 in methanol as the solvent. This reaction proceeds with only 72% retention of configuration. This clearly demonstrates that nucleophilic substitution at the benzylic position of chromium arene complexes is not always as selective as in the corresponding ferrocenyl compounds.



Scheme 5.



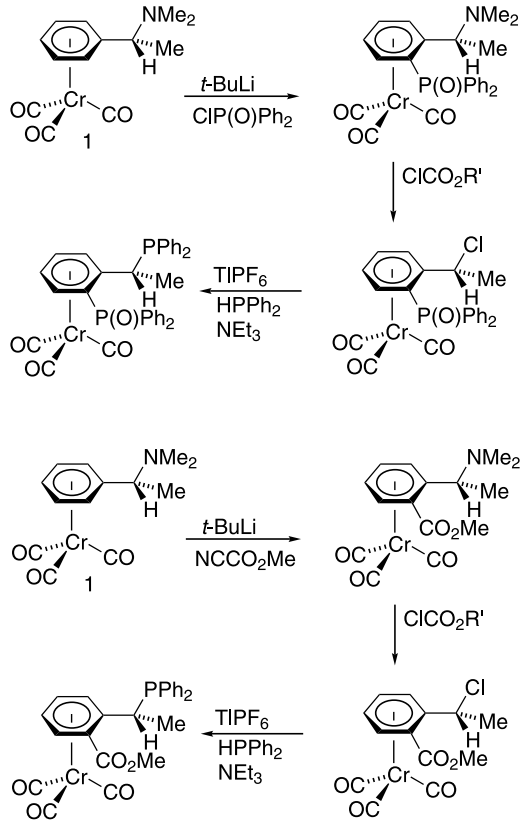
Scheme 6.



Scheme 7.

The hydrolysis of benzyl chloride coordinated to $Cr(CO)_3$ according to Pettit and coworkers [24] proceeds 10^4–10^5 times faster than that of the uncomplexed benzyl chloride. Hydrolysis of **2**, as remarked before, is quite slow compared to the corresponding ferrocene. On reaction with water in acetone solution, **2** is completely hydrolyzed after 12 h, again with complete retention of configuration [20].

Even more important than the stereoselective addition of O, N or P nucleophiles is the addition of C nucleophiles, as this opens the route to a large variety of chiral organic compounds. We have as yet only investigated the reaction with the cyanide ion. This reaction however was not diastereoselective and gave a racemic compound for reaction with **2** and a 1:1 mixture of diastereomers for the methyl-substituted derivative



Scheme 8.

(Scheme 7), which were, however, separable by chromatography [20].

2.2. Bidentate ligands

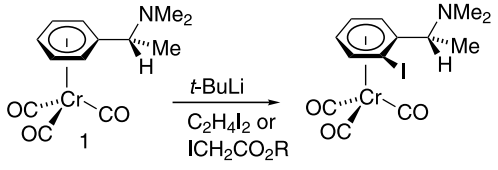
The diastereoselective metalation of **1** and subsequent electrophilic addition into the *ortho*-position had already been mentioned. Apart from CH_3I or $(CH_3)_3SiCl$, other electrophiles can be used as well. In order to prepare hemilabile bidentate ligands, we used $P(O)R_2Cl$ or methylcyanoformate ("Manders reagent"). Subsequent double exchange of the NMe_2 and chloride substituents gave bidentate ligands (Scheme 8).

We were even able to introduce a halide substituent into the *ortho*-position by reaction of the lithio intermediate with either methyl iodoacetate or diiodoethane. The previously known (p*S*,*R*)[(2-{α-*N*,*N*-dimethylamino)ethyl}-1-iodo-η^6-benzene]$Cr(CO)_3$ [25] was formed and may serve in future as a very useful starting material for further *ortho*-substituted derivatives (Scheme 9).

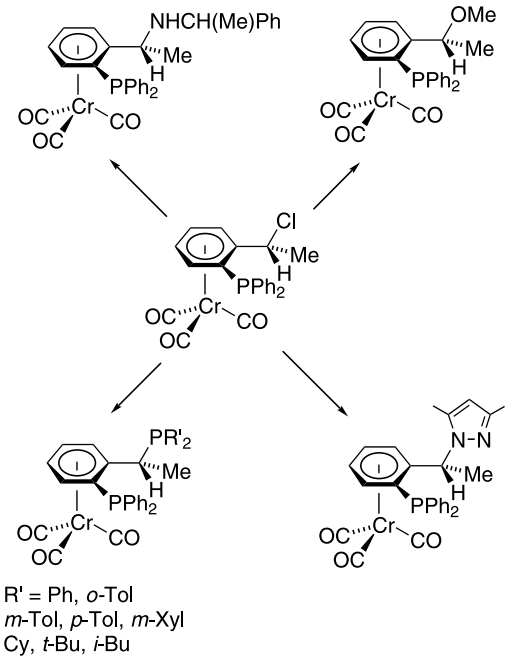
The major aim of our research was of course the synthesis of chelating diphosphines. Uemura and coworkers [26] had already prepared two derivatives, but through a somewhat elaborate route via chromium complexes derived from (*S*)-phenylethanol. Our method seems to be superior as it has considerably greater scope and higher overall yields, starting from commercially available, cheap (*R*)- or (*S*)-phenylethylamine. After metalation and electrophilic introduction of the PPh_2 moiety into the *ortho*-position, the amino group was replaced for a chloro substituent, which was easily dehalogenated with $TlPF_6$ in the presence of a secondary phosphine. We have performed this reaction with many different PR_2 groups, as shown in Scheme 10. In addition, we have prepared bidentate ligands with other amines, alcohols and pyrazoles [27].

This method of course also allowed to vary the nature of the phosphane in *ortho*-position by using different electrophiles PR_2Cl. Again, a variety of complexes were prepared (Scheme 11) [27].

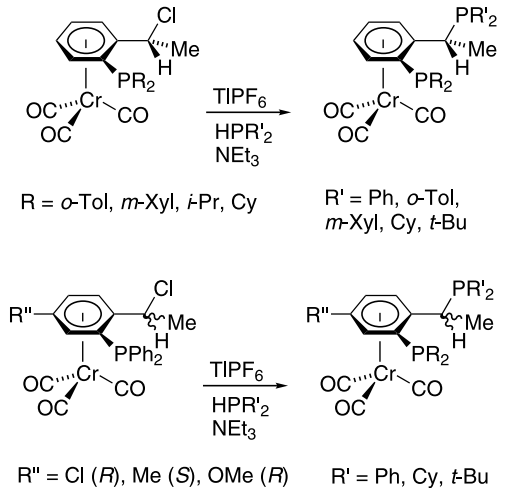
A particular noteworthy derivative was prepared by the addition of a secondary phospholane, derived from (*S*,*S*)-hexane-2,5-diol, into the α-position. As the phospholane has two chiral centers (*R*,*R*), the reaction normally gives one of two possible diastereomers. By starting also from (*S*)-phenylethylamine, we prepared the enantiomer of **1**, which after further reaction steps as



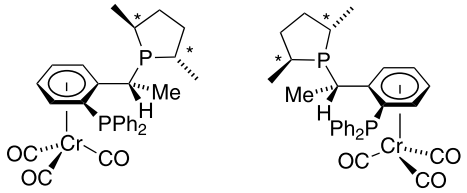
Scheme 9.



Scheme 10.



Scheme 11.



Scheme 12.

described before was converted into the other diastereomeric diphosphine (Scheme 12) [28].

These results show that the synthesis of bifunctional optically active ligands with symmetry C_1 starting from compound **1** or its enantiomer is easily done in three reaction steps allowing an almost "combinatorial"

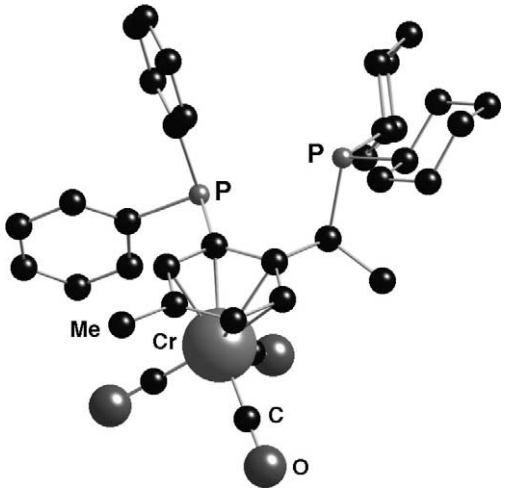


Fig. 4. X-ray structure of the bidentate chromium ligand **4**.

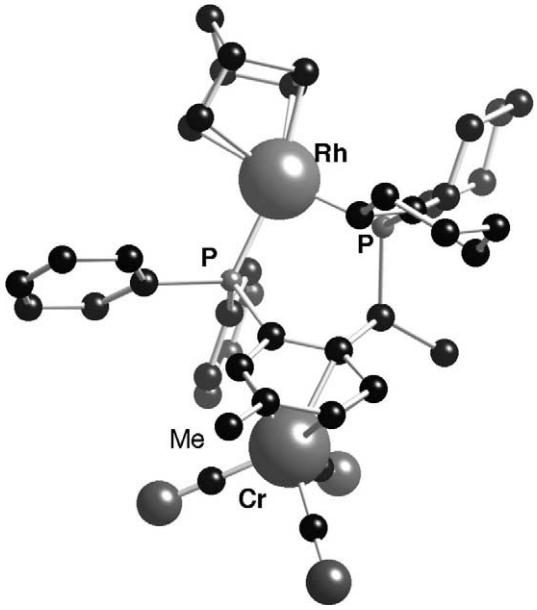


Fig. 5. X-ray structure of the norbornadiene rhodium cation **5** incorporating ligand **4**.

approach to a large variety of chelating planar-chiral ligands.

As functional derivatives of (*R*)- or (*S*)-phenylethylamine with different substituents in the 4-position are also available, we prepared a number of chelating diphosphines from these starting materials (Scheme 11). We structurally characterized the diphosphine (*S*)-[4-{α-(dicyclohexylphosphanyl)ethyl}-3-(diphenylphosphanyl)-η^6-toluene]$Cr(CO)_3$ (**4**), derived from the starting material (*S*)-4-(tolylethyl)amine (Fig. 4), and also its rhodium norbornadiene complex (**5**), which showed that the chromium complexes are suitable bidentate ligands with a bite angle of ca. 91°, making them suitable for coordination in octahedral, tetrahedral or trigonal-bipyramidal environment (Fig. 5) [29]. The correspond-

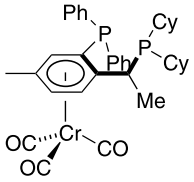
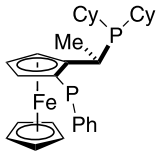
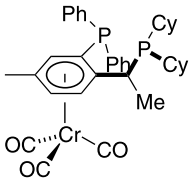
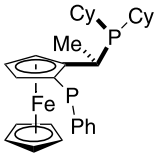
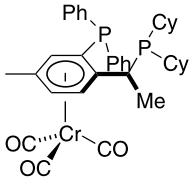
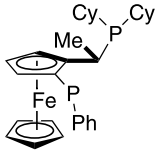
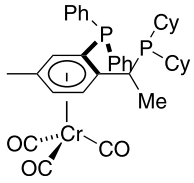
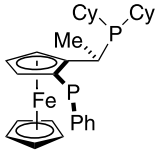
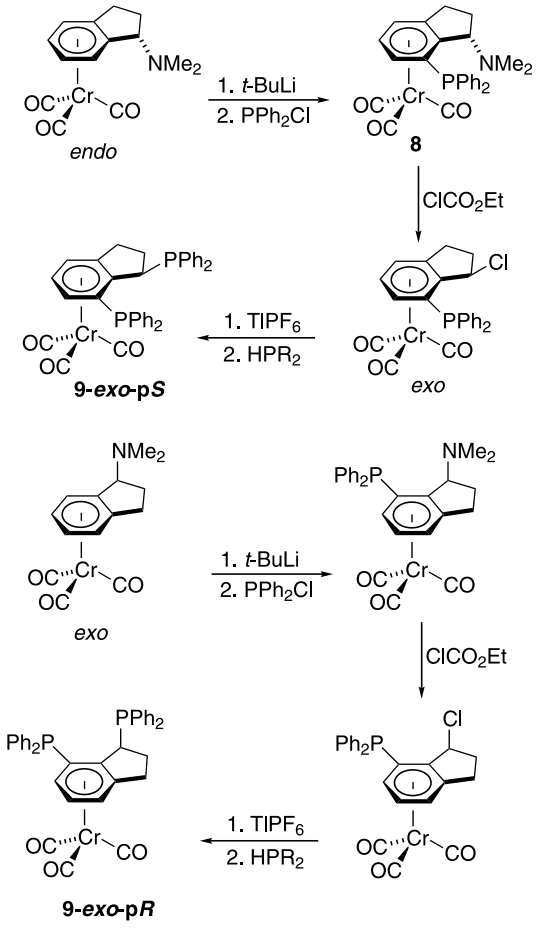
torsion angle	compound 4	5	6	7	torsion angle
	76	66	-70	-69	
	97	56	-64	-56	
	26	29	-24	-15	
	148	73	-145	-101	

Fig. 6. Relevant torsion angles in the structures of the (*S*,p*R*)-diphosphine **4** and its norbornadiene rhodium complex **5** and (*R*,p*S*)-Josiphos **6** and its norbornadiene rhodium complex **7**.

ing Josiphos–rhodium (**7**) complex has a bite angle of 93° [30].

Fig. 6 compares relevant torsion angles between the (*S*,p*R*)-diphosphine (**4**) and its norbornadiene rhodium complex (**5**) with (*R*,p*S*)-Josiphos (**6**) and ist norbornadiene rhodium complex (**7**) [30]. One can clearly see that the conformational changes due to complexation are more pronounced in the chromium complex than in the ferrocene derivative. This is probably due to the smaller bite angle of the two *ortho*-substituents on the arene ring compared to the cyclopentadienyl ring. Both phosphorous atoms have to rotate significantly to insure proper overlap of their lone pairs with rhodium, with 41° for the PCy_2 group and with 75° for the PPh_2 groups. This rotation is only 8° and 44°, respectively, for Josiphos.

The complexes derived from aminoindane and 3-methoxyphenylethylamine were already mentioned in Chapter 1.1. In the aminoindane complex, the *endo*-isomer was exclusively formed on reaction with Kündig's reagent. This compound also underwent *ortho*-lithiation and PPh_2 could be introduced via electrophilic addition with formation of complex **8**. Exchange of the amino group with ethylchloroformate gave the chloro complex as an intermediate and subsequent exchange with $TlPF_6$ and $HPPh_2$ gave the expected diphosphine **9**. Although in the starting complex **8** the amino group was *endo*, the PPh_2 group in **9** was *exo*, as nucleophilic attack at the benzylic carbon could in this case only occur with inversion, that is from opposite to the tricarbonylmetal unit (Scheme 13). The same reaction performed with the *exo*-aminoindane complex, separated from a mixture of the two diastereomeric PPh_2/NMe_2 complexes by flash chromatography, also gave the *exo*-phosphine compound as the enantiomer of **9**, so that the retention of configuration was observed [29].



Scheme 13.

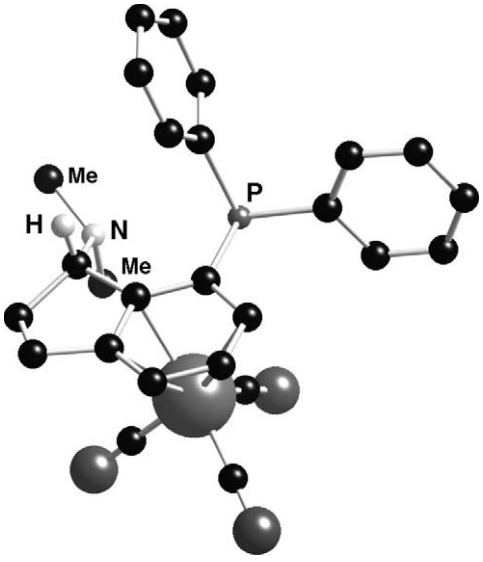


Fig. 7. X-ray structure of compound **8**.

Complex **8** and the enantiomer of complex **9** were both characterized by X-ray structure analysis (Figs. 7 and 8).

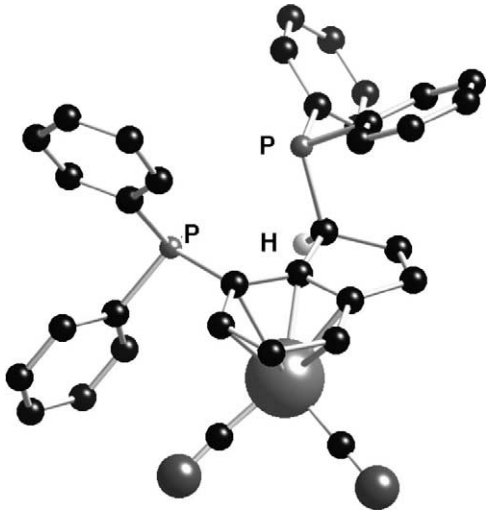
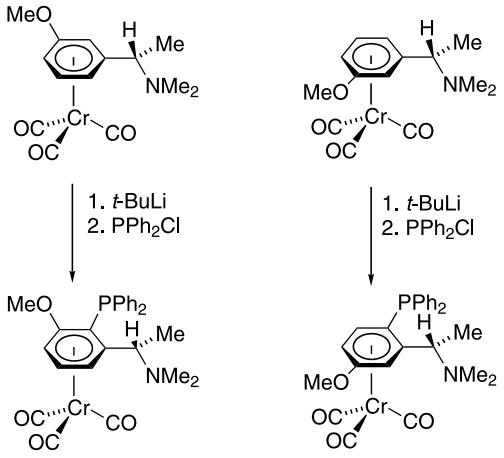


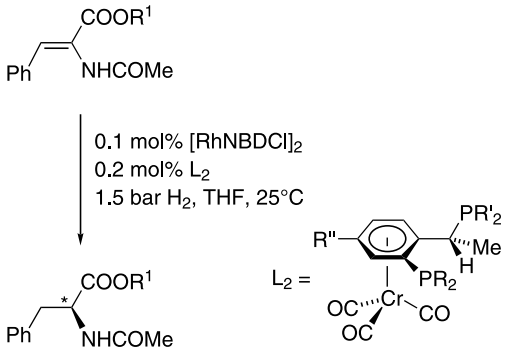
Fig. 8. X-ray structure of **9**-*exo*-p***R***.



Scheme 14.

It was already mentioned that reaction of 3-methoxyphenylethylamine gave two diastereomers on complexation with $Cr(CO)_6$, but only one isomer when introducing first a trimethylsilyl group into the 2-position (Scheme 2). After lithiation of the mixture of the two isomers and electrophilic addition of PPh_2, we were able to separate both diastereomers via flash chromatography. Independently, we isolated the single isomer from the trimethylsilyl-protected amine, removed the protecting group and then introduced the PPh_2 group (Schemes 14 and 15) [17].

In both cases, the diastereoselective lithiation proceeds in such a way that the methyl group of the side chain points away from the metal in the lithiated intermediate. In one diastereomer, the PPh_2 group therefore ends up in the 2-position, while in the other diastereomer, the PPh_2 group is directed to the 5-position. Both complexes are diastereomerically pure by NMR analysis. Both compounds could be crystal-



R	R'	R"	R^1	ee (%)
Ph	Cy	H	Me	81.5 (R)
Ph	Cy	H	H	66.2 (R)
Cy	Ph	H	H	31.1 (S)
Ph	t-Bu	H	Me	7 (S)
Ph	t-Bu	H	H	6.7 (S)
Ph	Cy	Me	Me	91 (S)
Ph	Cy	OMe	Me	89 (R)
Ph	Cy	Cl	Me	87 (R)
Ph	t-Bu	Me	Me	8 (R)
Ph	t-Bu	OMe	Me	4 (S)
Ph	t-Bu	Cl	Me	8(S)
Ph	Ph	Me	Me	4 (S)
Ph	Ph	OMe	Me	4 (R)
Ph	Ph	Cl	Me	12 (R)

Scheme 15.

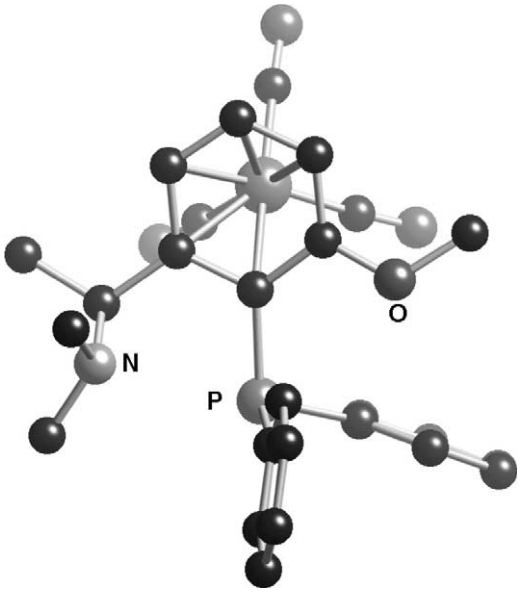


Fig. 9. X-ray structure of (*S*)-[1-{α-(dimethylamino)ethyl}-2-(diphenylphosphanyl)-3-methoxy-η^6-benzene]Cr(CO)$_3$.

lized and the assignments were confirmed by X-ray diffraction (Figs. 9 and 10) [17].

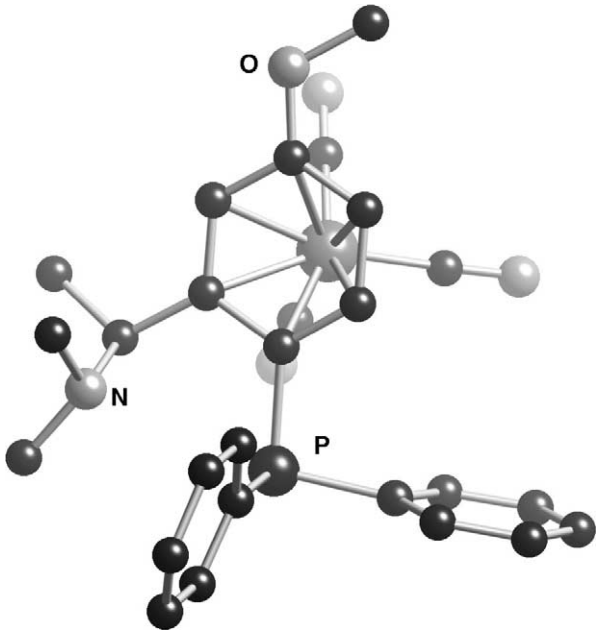


Fig. 10. X-ray structure of (*S*)-[1-{α-(dimethylamino)ethyl}-2-(diphenylphosphanyl)-5-methoxy-η^6-benzene]Cr(CO)$_3$.

In conclusion, we were able to prepare a large variety of mono- and bidentate ligands based on chromium arene compounds by a simple three-step procedure. The commercial availability of many derivatives of optically active phenylethylamine opens the route into a rich chemistry of functional derivatives.

3. Catalytic applications

3.1. Hydrogenation

We have investigated the rhodium-catalyzed enantioselective hydrogenation of C=C double bonds and C=N double bonds using various diphosphine ligands whose synthesis was described in the last chapter.

Thus, reaction of methyl acetamidoacrylate, under 100 bar pressure in methanol at 40 °C, in the presence of 0.2% catalyst, formed in situ from $[CODRhCl]_2$ and the "Daniphos" ligand **10** (R = Ph, R′ = Cy) [31], afforded a quantitative yield of the hydrogenation product in > 95% ee [27]. This result compares well with those obtained from the best C_2-symmetrical ligands [32] found in the literature as well as with Togni's Josiphos ligand (88% ee) [33]. On the other hand, when acetoaminocinnamic acid and its methyl ester were used as a substrate, lower enantioselectivities were observed. Hydrogenation of the methyl ester of acetamidocinnamic acid with "Daniphos" gave 53.7% ee in methanol, but 81.5% ee in THF. Again, this value compares well with 80.8% ee measured by us under the same conditions for Josiphos, although a value of 96% ee was reported in the

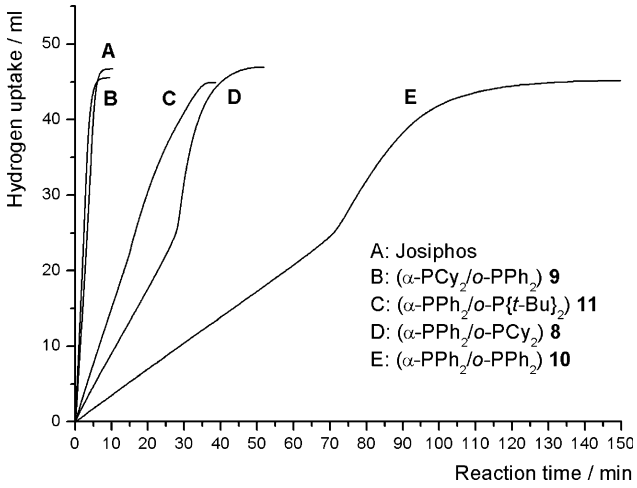
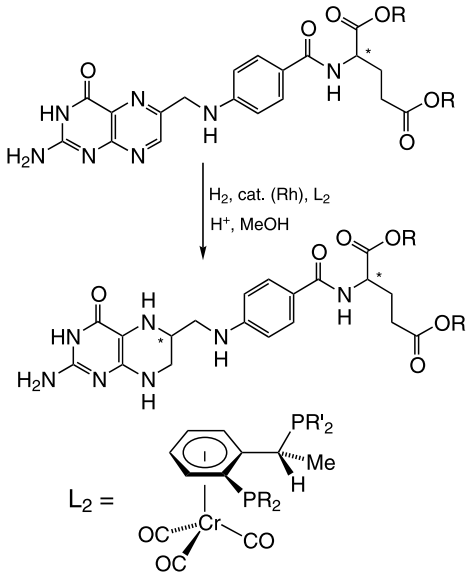


Fig. 11. Hydrogen uptake for the hydrogenation of norbornadiene with the rhodium complexes of **8**, **9**, **10** and **11**, and Josiphos.

literature [33]. When using an inverse "Daniphos" ligand **11** (R = Cy, R′ = Ph) the ee value was 31.1%, but with preference for the other enantiomer. The inverse Josiphos ligands are known, but to our knowledge this effect has not been noticed before [34]. Only the ligand with R = Cy gave acceptable ee values for these substrates.

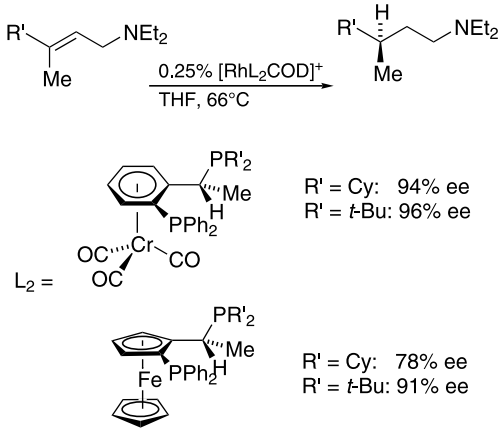
We have measured some rate constants for the hydrogenation of norbornadiene to obtain quantitative data on the reaction rate of the chromium ligands compared to Josiphos. The derivative **12** (R = Ph, R′ = Ph) proved to be considerably slower than the complexes with aliphatic phosphines in the side chain. Josiphos was considerably faster than the chromium complexes **10** (R = Ph, R′ = Cy), **12** and **13** (R = Ph, R′ = *t*-Bu) (Fig. 11). For some of the chromium complexes, there is a selectivity visible for the hydrogenation of the first and the second double bonds of the diene [35]. The inverse Daniphos ligand **11**, however, was faster than all others in this reaction.

In collaboration with the Swiss company Merck–Eprova, we have also investigated the hydrogenation of folic acid ester. Here, the pterine ring with two C=N double bonds can be hydrogenated. Overall, we tested 15 derivatives of the chromium complexes. The highest de value was obtained with another "inverse" Daniphos ligand (R = *i*-Pr, R′ = Ph), which again favored the opposite diastereomer in contrast to all other complexes (Scheme 16) [36].



R	R'	de
Ph	Cy	14
Ph	*o*-Tolyl	32
o-Tolyl	Ph	26
o-Tolyl	*o*-Tolyl	36
Ph	*m*-Xylyl	18
m-Xylyl	Ph	28
m-Xylyl	*m*-Xylyl	32
i-Pr	Ph	-42

Scheme 16.



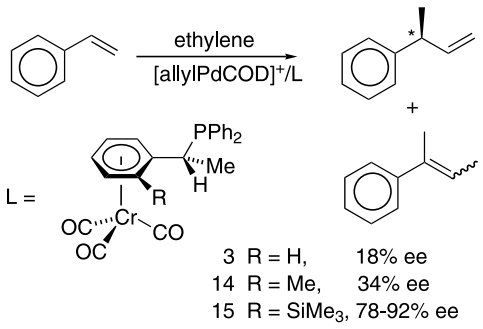
Scheme 17.

3.2. Isomerization

Isomerization of diethylgeranylamine for the production of optically pure (+)-citronellal in the presence of Rh/(*R*)-BINAP is an exceptional industrial process, leading to key intermediates for the fragrance and flavor industry. In the search for alternatives for this process, both Josiphos and Daniphos derivatives were evaluated [37]. Both classes of ligands gave very good results, the Daniphos ligands having higher enantioselectivities, but slower kinetics (Scheme 17).

3.3. Hydrovinylation

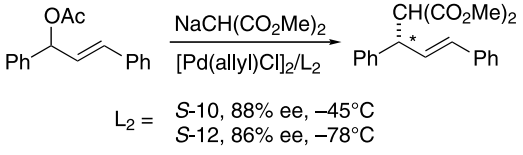
Asymmetric hydrovinylation has been pioneered by Bogdanovic [38] and Wilke [39] using nickel catalysts. Of special interest is the reaction between vinyl arenes



Scheme 18.

and ethylene, as enantioselective codimerization provides a convenient route to 2-arylpropionic acids. A very efficient system was found using a ligand derived from myrtenal, which at −70 °C gave enantioselectivities of >95% [39]. A catalytic system based on palladium was recently reported by Vogt et al. for the same reaction using the diastereomerically pure *tert*-butyl(methyl-*O*)phenylphosphinite possessing a stereogenic P-atom, which gave ee values up to 87% [40]. We then tested monophosphines with organometallic backbones. After initial success with monophosphines based on tri(carbonyl)iron complexes, we also investigated the monophosphines **3**, **14** and **15**. Even at room temperature, high activity and selectivity towards the codimers were observed with all ligands (Scheme 18).

Stability, activity and chemo- and enantioselectivity increased with increasing steric demand of the *ortho*-substituent R. Introduction of the trimethylsilyl group at this position (ligand **15**) therefore resulted in an excellent enantioselective system which belongs to the best Pd catalysts described so far for asymmetric hydrovinylation. Almost 70% conversion was observed within 15 min. The product was obtained in 78.5% ee and only a small amount of isomerization products was detected in the reaction mixture. However, at higher conversions, isomerization of the product to the internal achiral olefin took place. Therefore, after 0.5 h and at complete conversion, selectivity towards 3-phenylbut-1-ene has dropped to 48.5%; but even at these high conversions, chemoselectivity toward the codimers remained very good (98%). The consecutive isomerization reaction goes along with a kinetic resolution. Due to this, the ee of the product rises to 92% within 0.5 h. Another feature is the remarkable stability of the catalytic system. No Pd(black) formation was observed after the reaction, which is quite unusual when using a monodentate phosphine ligand. The steric bulk of ligands **3**, **14** and **15** probably prevents the formation of binuclear palladium species. The increased stability and activity of the catalytic system going from **14** to **15** agrees with this explanation [20].



Scheme 19.

3.4. Allylic alkylation and sulfonation

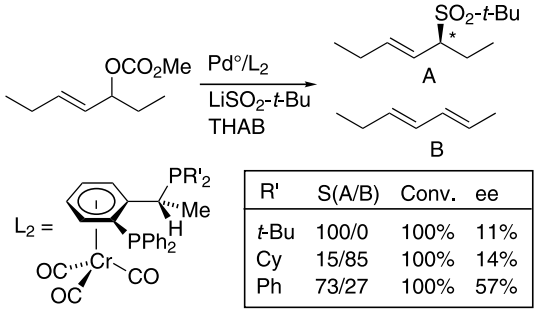
Complexes **10** and **12**, as their (*S*) isomers, had already been prepared by Uemura and coworkers [26] by another route. In the standard palladium-catalyzed allylic alkylation reaction of 1,3-diphenyl-1-acetoxypropene with sodium dimethyl malonate, these compounds gave ee values of up to 88% (Scheme 19).

Ligands **10**, **12** and **13** were also successfully employed in the palladium-catalyzed substitution reaction of allylic acetates with sulfur nucleophiles. Thus, reaction of racemic 3-acetoxyhept-4-ene with lithium *tert*-butylsulfinate in the presence of 1.5 mol% of Pd_2dba_3 and 4.5 mol% of the ligands gave complete conversion in all cases, but with marked differences in the product selectivities (Scheme 20) [27].

The highest ee with 57% was obtained with **12**, but here again there should be considerable scope for improvement by variation of the steric and electronic properties of the two ligand functions. The higher ee values obtained by Uemura in the allylic alkylation with these ligands are probably due to the use of the 1,3-diphenyl-3-acetoxypropene, a precursor that is known to give good enantioselectivities in this reaction.

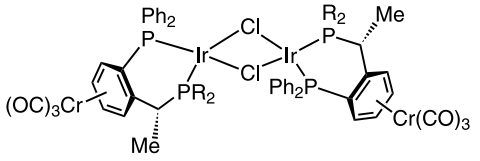
3.5. Hydroamination and hydrosilylation

Another reaction we investigated was hydroamination, a reaction recently pioneered by Togni and coworkers [38]. Ferrocene ligands such as Josiphos had been shown to give good enantioselectivities in this reaction. In a comparative study between the analogous Daniphos ligands **10** and **13** and their Josiphos analogues, the ligands were converted into the iridium complexes shown in Fig. 12. These were obtained as an inseparable mixture of *cis*/*trans* isomers. The reactions were performed as described in Ref. [38] without

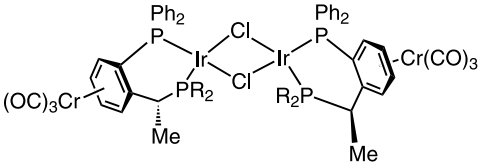


R'	S(A/B)	Conv.	ee
t-Bu	100/0	100%	11%
Cy	15/85	100%	14%
Ph	73/27	100%	57%

Scheme 20.

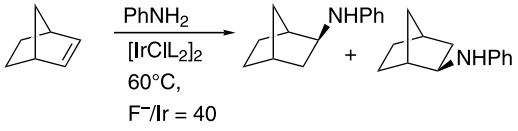


trans-**16** (R = Cy) **17** (R = t-Bu)



cis-**16** (R = Cy) **17** (R = t-Bu)

Fig. 12. *cis*- and *trans*-isomers of **16** and **17**.

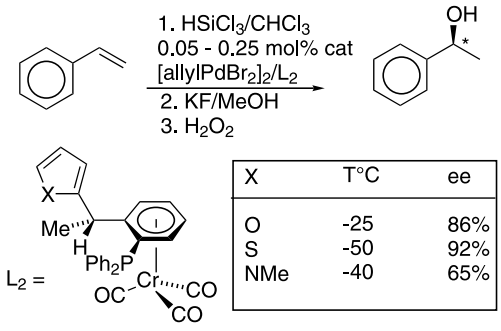


$[IrClL_2]_2$	yield, (TOF, h^{-1})	ee
16	26.8 (2.5)	13.3 %
17	1.1 (0.1)	64.0 %
18	trace	51.1 %
19	trace	70.3 %

Scheme 21.

solvent and with a catalyst concentration of 0.1 mol% of Ir. The same reactions under identical conditions were performed with the iridium complexes of Daniphos (PPh_2/PCy_2) **16** and its PPh_2/*t*-butyl analogue **17** and the corresponding ferrocene complexes **18** and **19**. A common reaction time of 96 h was adopted [27].

Only the Josiphos catalyst showed reasonable turnover but with considerable loss of enantioselectivity compared to the previous study carried out with a higher catalyst loading and lower temperatures [38]. Good ee values were obtained with the *t*-butyl derivative (64% ee). Unfortunately, with the Daniphos ligands only small amounts of the hydroamination product could be isolated. Nevertheless, these ligands showed a higher enantiomeric excess compared to the analogous ferrocene ligands (Scheme 21), the *tert*-butyl derivative **17** again being better than the cyclohexyl compound **16**. A reason for the low activity may be the thermal instability of the chromium catalysts, but possibly also competing side reactions such as hydroarylation of aniline with norbornene, as an as yet unidentified product was also detected. The hydroamination reaction appears to be extremely sensitive to small variations in the reaction parameters such as temperature and concentration of the added "naked" anion.



X	T°C	ee
O	-25	86%
S	-50	92%
NMe	-40	65%

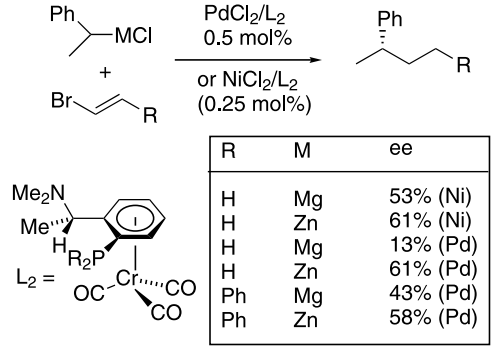
Scheme 22.

The catalytic hydrosilylation of alkenes with trichlorosilane provides a powerful method for the in situ conversion of olefins to alcohols, complementing hydroboration protocols. Pd-catalyzed reactions due to their lower catalyst loading are generally preferred over Rh-catalyzed hydroboration [39]. Pd-catalyzed hydrosilylation with ferrocene ligands was first pioneered by Hayashi et al. [40] and Pioda and Togni [41]. Corresponding reactions with arenechromium ligands were recently reported by Weber and Jones [42]. They introduced heterocycles into the side chain of arenechromium complexes by performing an electrophilic aromatic substitution with the chromium-stabilized benzylic cations (Scheme 22).

Hydrosilylation was conducted using a variety of substituted styrene substrates, followed by in situ addition of fluoride and immediate oxidation, which gave good yields of the corresponding (*S*)-alcohols with moderate to high enantioselectivity. The highest ee value of 92% was obtained at $-50\,^{\circ}$ with the thiophene derivative and $[allylPdBr]_2$ as the metal precursor (Scheme 22).

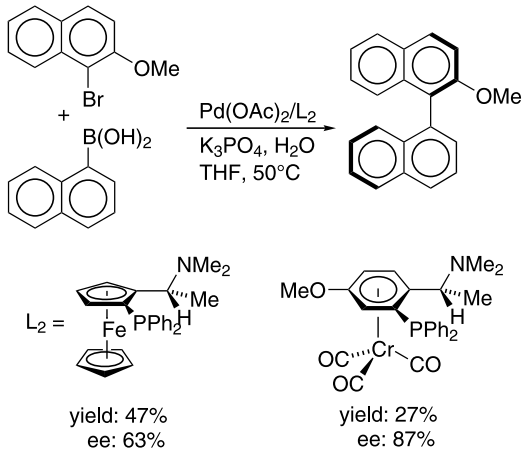
3.6. Cross-coupling and Suzuki coupling reactions

The first example of the application of bidentate arenechromium complexes in catalysis was published by Uemura, who in 1992 reported on the first synthesis of such complexes and their application in the asymmetric cross-coupling reaction [43]. The (*S*)-PPh_2/NMe_2 ligand



R	M	ee
H	Mg	53% (Ni)
H	Zn	61% (Ni)
H	Mg	13% (Pd)
H	Zn	61% (Pd)
Ph	Mg	43% (Pd)
Ph	Zn	58% (Pd)

Scheme 23.



Scheme 24.

and some of its derivatives were applied to the reaction of zinc and magnesium benzyl chlorides with allylic bromides and gave up to 61% ee (Scheme 23).

As the final example for the application of bidentate organometallic ligands in homogeneous catalysis, we wish to report preliminary results on the enantioselective Suzuki coupling [44].

There are as yet few examples for enantioselective Suzuki couplings [45–47]. Cammidge and Crépy [46] used planar-chiral ferrocene derivatives with PPh_2/NMe_2 ligand functions which gave up to 86% ee. We have performed experiments using both ferrocene as well as arenechromium bidentate ligands and the result is shown in Scheme 24.

The yield for the chromium complex was lower, but the enantioselectivity was higher than that for the corresponding ferrocene catalyst. We need to do further experiments with other derivatives to optimize the reaction conditions.

4. Conclusions

We have shown that starting from optically active phenylethylamine and its derivatives a large library of mono- and bidentate ligands based on arenechromium-tricarbonyl complexes can be prepared by a combinatorial synthetic approach. These complexes are similar to the well-known family of "Josiphos" ligands, but differ both in steric as well as electronic properties. The chromium complexes closely match the corresponding ferrocene derivatives in enantioselectivity in a number of catalytic applications. At the current state it is impossible to argue the respective merits of the two systems, the ferrocene ligands, due to their industrial applications, being clearly more established and mature. It is interesting to note that for most catalytic systems a different ligand gives the highest ee values. Structural data confirm that the "Daniphos" ligands are readily adaptable to most metal environments.

A major advantage of the chromium complexes is their easy availability in optically active form without any need for resolution. This also applies to other functional derivatives. In contrast to the cyclopentadienyl ring, arenes have an almost unlimited potential for controlled substitutional variation, accessible through standard reaction protocols.

We are currently extending our studies to other transition metal-catalyzed reactions such as hydrogen transfer, Diels-Alder reactions as well as hydroboration.

Acknowledgements

I wish to thank my coworkers Daniela Vasen ("Daniphos"), Elisabetta Alberico, Jutta Knuppertz, Wolfgang Braun and Daniel Totev who have prepared the complexes described in this review. I am grateful to Dr. Ulli Englert and AKS for performing the X-ray structure analyses. I also want to thank all other Ph.D. students and colleagues in academia and industry who have made valuable contributions to the catalytic applications in various collaborations referenced in the text. This work was generously funded by the Deutsche Forschungsgemeinschaft within the Collaborative Research Center (SFB) 380 "Asymmetric Syntheses with Chemical and Biological Means" and the Graduate Training Program 440 "Methods of Asymmetric Synthesis" as well as by the Fonds der Chemischen Industrie. I am particularly grateful to BASF for supplying us with samples of chiral amines.

References

[1] M.J. Burk, Handbook of Chiral Ligands, Marcel Dekker, New York, 1999, p. 339.
[2] M.J. Burk, Acc. Chem. Res. 33 (2000) 363.
[3] H.U. Blaser, Adv. Synth. Catal. 344 (2002) 17.
[4] H.U. Blaser, W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, Top. Catal. 19 (2002) 3.
[5] M. Wrighton, J. Am. Chem. Soc. 117 (1995) 3617.
[6] C.C. Brasse, U. Englert, A. Salzer, H. Waffenschmidt, P. Wasserscheid, Organometallics 19 (2000) 3818.
[7] O. Delacroix, J.A. Gladysz, Chem. Commun. (2003) 665.
[8] C. Bolm, K. Muñiz, Chem. Soc. Rev. 28 (1999) 51.
[9] S.E. Gibson, H. Ibrahim, Chem. Commun. (2002) 2465.
[10] (a) F. Balkenhohl, K. Ditrich, B. Hauer, W. Ladner, J. Prakt. Chem. 339 (1997) 339;
(b) F. Balkenhohl, B. Hauer, W. Ladner, U. Pressler, BASF AG, DE 4332938 (1993) [Chem. Abstr. 122 (1995) 289035].;
(c) K. Ditrich, F. Balkenhohl, W. Ladner, BASF AG, DE 19534208 (1995) [Chem. Abstr. 126 (1997) 277259].;
(d) W. Ladner, K. Ditrich, Chim. Oggi. 17 (1999) 51;
(e) G. Hieber, K. Ditrich, Chim. Oggi. 19 (2001) 16.

[11] A. Salzer, M. Käser, in: W.A. Herrmann (Ed.), Synthetic Methods of Organometallic and Inorganic Chemistry, vol. 8, Georg Thieme, Stuttgart, 1997, p. 56.
[12] S.G. Davies, J. Blagg, C.L. Goodfellow, K.H. Sutton, J. Chem. Soc. Perkin Trans. I 35 (1987) 1805.
[13] J.A. Heppert, J. Aubé, M.E. Thomas-Miller, M.L. Milligan, F. Takusagawa, Organometallics 9 (1990) 727.
[14] E. Alberico, Dissertation RWTH (2003).
[15] E.P. Kündig, J.P. Leresche, L. Saudan, G. Bernardinelli, Tetrahedron 52 (1996) 7363.
[16] M. Uemura, T. Kobayashi, K. Isobe, T. Minami, Y. Hayashi, J. Org. Chem. 51 (1986) 2859.
[17] B. Calmuschi, U. Englert, D. Totev, A. Salzer, Unpublished results.
[18] U. Englert, A. Salzer, D. Vasen, Tetrahedron: Asymmetry 9 (1998) 1867.
[19] J.H. Cooley, E.J. Evain, Synthesis (1989) 1.
[20] U. Englert, R. Haerter, D. Vasen, A. Salzer, E.B. Eggeling, D. Vogt, Organometallics 18 (1999) 4390.
[21] (a) A. Pfletschinger, T.K. Dargel, J.W. Bats, H.G. Schmalz, Chem. Eur. J. 5 (1999) 537;
(b) C.A. Merlic, M.M. Miller, Organometallics 20 (2001) 373.
[22] S. Top, G. Jaouen, M. McGlinchey, Chem. Commun. (1980) 1110.
[23] S.G. Davies, T.J. Donahue, Synlett (1993) 323.
[24] J.D. Holmes, D.A.K. Jones, R. Pettit, J. Organomet. Chem. 4 (1965) 324.
[25] P.W.N. Christian, S.E. Gibsin, R. Gil, P.C.V. Jones, C.F. Marcos, F. Prechtl, A.T. Wierzchleyski, Recl. Trav. Chim. Pays-Bas 114 (1995) 195.
[26] Y. Hayashi, H. Sakai, M. Kaneta, M.J. Uemura, J. Organomet. Chem. 503 (1995) 143.
[27] D. Vasen, A. Salzer, F. Gerhards, H.J. Gais, N.H. Bieler, A. Togni, Organometallics 19 (2000) 539.
[28] J. Haberland, W. Hummel, A. Liese, O. Stelzer, T. Nickel, W. Braun, A. Salzer, in preparation.
[29] E. Alberico, U. Englert, A. Salzer, submitted.
[30] A. Togni, A. Breutel, M.C. Soares, N. Zanetti, T. Gerfin, V. Gramlich, F. Spindler, G. Rihs, Inorg. Chim. Acta 222 (1994) 213.
[31] Because of the rather long systematic names for these ligands, we refer in our laboratories to the PPh_2/PCy_2 ligand as "Daniphos", in analogy to "Josiphos".
[32] (a) K.E. Koenig, in: J.D. Morrison (Ed.), Asymmetric Syntheses, vol. 5, Academic Press, Orlando, 1985, p. 71;
(b) M.J. Burk, J. Am. Chem. Soc. 113 (1991) 8518.
[33] A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, J. Am. Chem. Soc. 116 (1994) 4062.
[34] Ciba Geigy AG, EP 0612 758 A1.
[35] W. Braun, H.-J. Drexler, D. Heller, A. Salzer, A. Spannenberg, J. Chem. Soc. Dalton Trans. (2003) 1606.
[36] (a) W. Braun, Dissertation, RWTH Aachen (2003);
(b) Merck-Eprova AG, PCT Int. Appl. (2001), WO 01/04120 A1 [Chem. Abstr. 134 (2001) 115967].
[37] C. Chapuis, M. Barthe, J.-Y. de Saint Laumer, Helv. Chim. Acta 84 (2001) 230.
[38] (a) R. Dorta, P. Egli, F. Zürcher, A. Togni, J. Am. Chem. Soc. 119 (1997) 10857;
(b) N.H. Bieler, R. Dorta, A. Togni, M. Eyer, EP 0909762 A2, 1999.
[39] (a) H. Brunner, H. Nishiyama, K. Ito, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, VCH, Weinheim, 1993, p. 303ff;
(b) Y. Uozumi, K. Kitayama, T. Hayashi, K. Yanagi, E. Fukuyo, Bull. Chem. Soc. Jpn. 68 (1995) 713.
[40] T. Hayashi, K. Tamao, Y. Katsuro, I. Nakae, M. Kumada, Tetrahedron Lett. 21 (1980) 1871.
[41] G. Pioda, A. Togni, Tetrahedron: Asymmetry 9 (1998) 3903.
[42] I. Weber, G.B. Jones, Tetrahedron Lett. 42 (2001) 6983.
[43] M. Uemura, R. Miyake, H. Nishimura, Y. Matsumoto, T. Hayashi, Tetrahedron: Asymmetry 3 (1992) 213.
[44] A. Grosse-Boewing, Diploma Thesis, RWTH Aachen, 2002.
[45] S.L. Buchwald, J. Yin, J. Am. Chem. Soc. 122 (2000) 12051.
[46] N. Cammidge, K.V.L. Crépy, Chem. Commun. (2000) 1723.
[47] A.S. Castanet, F. Colobert, P.-E. Brontin, M. Obringer, Tetrahedron: Asymmetry 13 (2002) 659.