DALTON PERSPECTIVE

The chemistry of chiral heterometallocenes

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Received 14th September 2001, Accepted 17th October 2001
First published as an Advance Article on the web 20th November 2001

Chiral heterometallocene derivatives, namely phospha- and azaferrocenes, have recently attracted considerable interest with regard to their stereochemical properties. This perspective summarises recent developments in this field. General synthetic approaches for the construction of various compounds are presented, as well as access to enantiomerically pure material. Reactions that make use of the metallocene-based chirality in subsequent transformations are discussed, including the use as ligands for the stereoselective assembly of metal complexes and applications in enantioselective catalysis.

Introduction

Since their discovery, metallocenes have been at the forefront of organometallic chemistry for almost 50 years. Among other areas of research, the stereochemical properties of metallocenes have been investigated in great detail. This is particularly true for ferrocene, where the early work on enantiomerically pure compounds dates back to the Sixties but systematic studies on synthetic and mechanistic aspects, as well as applications leading to a real breakthrough, have been performed only during the last 10–15 years. Meanwhile, a repertoire of powerful synthetic methods is available and ferrocene derivatives have found widespread applications as chiral ligands in asymmetric catalysis in both academia and industry.[1]

With respect to the preparation of polyolefins with controlled tacticity, chiral *ansa* derivatives of bent metallocenes of group IV metals have been the subject of tremendous attention. They have also found application in stereoselective organic synthesis.[2]

Quite early on in the history of metallocene chemistry, heterocyclic analogues of ferrocene were investigated as well, and derivatives like aza- and phosphaferrocenes, in which an anionic Cp ligand is replaced by an anionic heterocycle, are especially numerous. However, the stereochemical aspects of the chemistry of these heterometallocenes remained largely unexplored until recently, although the first report on a chiral non-racemic azaferrocene was published as early as 1969.

This article summarises the recent chemistry of chiral heterometallocenes with the focus largely on aza- and phosphaferrocenes, which have been introduced mainly as chiral ligands for catalysis and the construction of chiral transition metal complexes.

General considerations

The chirality of ferrocene derivatives usually arises from disubstitution of one Cp ring with two different substituents. Whereas a monosubstituted ferrocene can have C_s symmetry, the mirror plane is destroyed by a second, unique substituent. The two faces of the disubstituted cyclopentadienyl ring are enantiotopic and enantiomeric complexes arise from the coordination of the CpFe fragment to either of these two faces. The term "planar chirality" is frequently applied to describe this stereochemical situation. Unfortunately, several strategies for determining stereochemical descriptors to specify the configuration of a planar chiral metallocene derivative have been proposed and are still in use, causing a good deal of confusion in the literature.[3]

In a C_s symmetric monoheteroferrocene, introduction of one substituent onto the heterocycle is sufficient to render the molecule chiral, giving rise to enantiomers. Several approaches are conceivable in order to obtain a chiral heterometallocene in non-racemic form: (1) selective complexation of a CpM fragment to either of the two enantiotopic faces of the heterocycle, (2) selective introduction of the substituent to either of the two enantiotopic α- or β-positions, and (3) resolution of a racemic mixture. In contrast to ferrocene chemistry, where several sophisticated methods for enantio- or diastereoselective modification have been developed, non-racemic heterometallocenes are, to date, almost exclusively prepared by resolution strategies.

Phosphaferrocenes

Phosphaferrocenes are a well-known class of heterometallocenes. The compound 3,4-dimethylphosphaferrocene was first prepared in 1977 by Mathey and co-workers,[4] who conducted a thorough investigation of this and related compounds.[5] Electrophilic substitution reactions like acylation and formylation are possible and occur selectively on the phospholyl ring, although deprotonation using different bases could not be accomplished. Mathey also showed, that phosphaferrocenes may act as ligands for transition metals *via* P coordination. With the sp^2 P atom as part of the aromatic phospholyl system coordinated to the CpFe fragment, the phosphaferrocene constitutes a rather unique ligand system, which differs considerably from the widespread PR_3 ligands with sp^3 hybridized P atoms in both steric and electronic properties. An energetically low-lying lone pair and the high p_z character of the LUMO on phosphorus lead to moderate σ donor but good π acceptor properties.

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DOI: 10.1039/b108375a

Based on the pioneering work of Mathey, a phosphaferrocene nucleus appeared as an interesting building block for the construction of chiral bidentate chelate ligands by introduction of an appropriate donor substituent into the α-position of the phospholyl ring, which breaks the lateral symmetry of the heterometallocene and incorporates the chirality into the system. In contrast to the ferrocene-based ligands, where a metal is coordinated by the two donor substituents, the phosphaferrocene coordinates *via* the ring P atom. Thus, in the latter case, the metal atom is in the immediate vicinity of the chiral metallocene unit, which might be beneficial for the stereoselectivity of reactions taking place on the coordinated metal site as, for example, is the case in asymmetric catalysis.

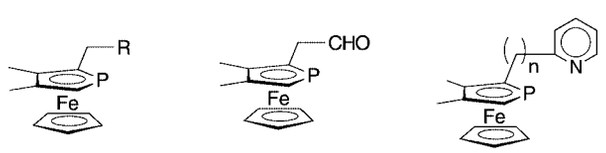
The steric properties of the molecule may be tuned by introducing substituents on the Cp ring, and the donor substituent on the phospholyl ring can be widely modified with regard to its steric bulk, the nature of the donor function and the length of the backbone.

Construction of bidentate phosphaferrocene ligands

It was found in our laboratory that the formyl derivative **1** is a starting material well suited for the preparation of a variety of different chelate ligands, as the formyl group is of high synthetic potential and may be easily transformed into more valuable groups. The aldehyde **1** is obtained from 3,4-dimethylphosphaferrocene through a Vilsmeyer reaction[6] as a racemic mixture of the enantiomers, which can easily be resolved (see next section).

(R)-**1** (S)-**1**

Starting from the aldehyde, a number of different P,P and P,N ligands were synthesised by straightforward transformations. For example, aminomethyl- and aminoethyl-substituted-ligands **2** and **3** were prepared by reductive amination (**2**) or nitroaldol condensation with subsequent reduction and methylation at nitrogen (**3**).†[7] The amino group in ligand **2** can be replaced by a PCy_2 group to give ligand **4**, and other P,P ligands like **5** were prepared by the substitution of mesylates with lithium phosphides.[8] The spectrum of available ligands was enlarged with the aldehyde **6**, obtained from **1** by extension with a CH_2 unit *via* a Wittig reaction. Addition of lithiated pyridine or α-picoline to the aldehyde **1** gave the P,N ligands **7** and **8**, respectively, after removal of the OH group.[9]

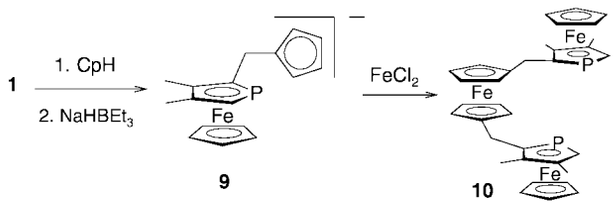


2, R = NMe_2
3, R = CH_2NMe_2
4, R = PCy_2
5, R = CH_2PPh_2

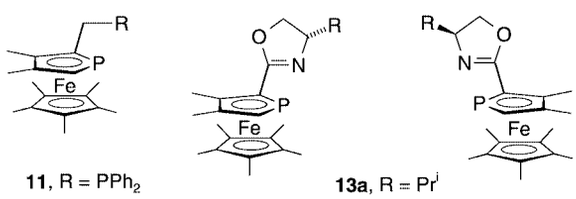
6

7, n = 1
8, n = 2

Incorporation of an anionic cyclopentadienyl group into the phosphaferrocene substituent introduces the possibility of η^5 : η^1 coordination. Anion **9** was prepared in a straightforward manner from aldehyde **1** by condensation with CpH and hydride addition to the resulting fulvene. The ferrocene derivative **10**, formed from the anion **9** and $FeCl_2$, is capable of acting as a bidentate P,P ligand.[10]



Fu and Qiao reported the synthesis of the Cp* derivative **11**, which was obtained from the appropriate aldehyde in a similar manner to that outlined above.[11] Starting from the trifluoroacetyl phosphaferrocene **12**, Fu *et al.* also synthesised the diastereomeric oxazolines **13**, which can coordinate to a metal atom as P,N chelate ligands.[12]



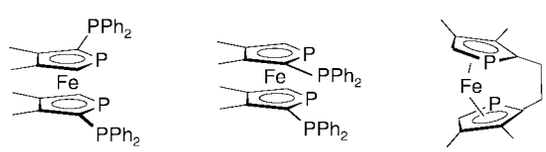
11, R = PPh_2
12, R = $COCF_3$

(R)

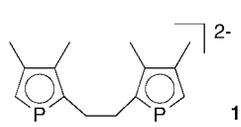
13a, R = Pr^i
13b, R = Bu^t

(S)

The bis(diphenylphosphino) substituted 1,1′-diphosphaferrocene **14** was prepared by Mathey as a 15 : 85 mixture of *rac* and *meso* diastereomers, which were separated by chromatography. When treated with (norbornadiene)$Mo(CO)_4$, the $Mo(CO)_4$ complexes were formed, in which coordination occurs *via* the two PPh_2 moieties and the phospholyl P atoms remain uncoordinated. An X-ray diffraction study allowed the assignment of the *rac* and *meso* isomers.[13] No attempts to separate the enantiomers which form the *rac* diastereomer of ligand **14** were reported. Mathey *et al.* recently reported the synthesis of the 1,1′-diphosphaferrocenophane **15**, which was formed by treatment of the dihpospholyl dianion **16** with $FeCl_2$. This complexation proceeded diastereoselectively, giving only the C_2 symmetric *rac* diastereomer, the enantiomers of which were not separated.[14]



rac **14** meso rac-**15**



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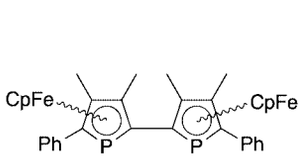
Mathey *et al.* also prepared the two complexes **17** and **18**, which feature singly and doubly connected metallocene units. Whereas two diastereomers were observed for the bis(phosphaferrocene) **17**, the bis(fulvalene)diiron analogue **18** was obtained as a single isomer. The stereochemical identity of neither compound has been determined.[15]

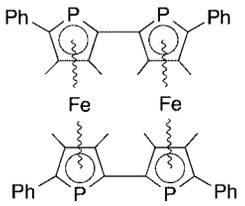
Enantiomerically pure phosphaferrocenes

As the aldehyde **1** was obtained from 3,4-dimethylphosphaferrocene as a racemic mixture, a separation of the enantiomers

† For the sake of brevity, only one enantiomer is shown in these and all subsequent drawings. Throughout the paper the depiction of only one enantiomer refers to the presence of the racemic mixture, unless otherwise indicated.



17



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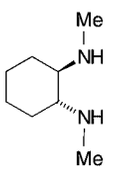
was devised in our laboratory by transforming the racemic aldehyde into the diastereomeric aminals by treatment with the enantiomerically pure diaminocyclohexane derivative **19**. The diastereomers **20a**,**b** are easily separated by column chromatography on silica on a preparative scale. Subsequent hydrolysis in the two-phase system hydrochloric acid–dichloromethane liberates the enantiomerically pure aldehydes, while the amine auxiliary can be recovered from the aqueous phase.[16]



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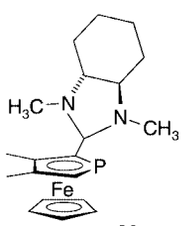
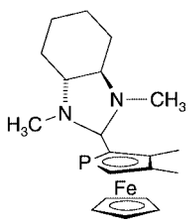


20a

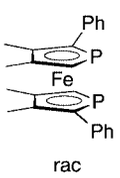


20b

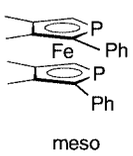
Although resolution of racemic mixtures is considered old-fashioned, the protocol described here has several advantages. As the resolution is carried out on the basic building block, many different enantiomerically pure derivatives can be obtained, as described in the preceding section, once the aldehydes have been resolved. The procedure is easy to handle, giving a virtually quantitative yield of both enantiomers in gram quantities. The enantiomeric purity of the aldehydes was assessed by HPLC and found to be >99% ee and the absolute configuration of one enantiomer was determined by an X-ray structure analysis.

In view of their potential use in asymmetric catalysis, Fu *et al.* have resolved individual enantiomeric phosphaferrocene-based ligands *via* preparative HPLC in small quantities. In addition, they reported the synthesis and separation of the diastereomeric oxazoline-bearing phosphaferrocenes **13** (*vide supra*). Although the starting material **12** was racemic, the use of enantiomerically pure aminoalcohols for oxazoline formation allowed easy separation of the diastereomers of **13** by column chromatography.

Reaction of 2-phenyl-3,4-phospholide with $FeCl_2$ gave the 1,1′-diphosphaferrocenes **21** as a 0.95 : 1 mixture of *rac* and *meso* isomers, which could be separated by HPLC. The enantiomers of the *rac* complex were further separated by HPLC on a chiral stationary phase and the absolute configuration of one enantiomer was assigned by X-ray diffraction.[17]

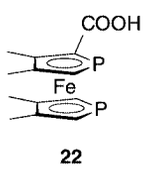


rac



21

meso

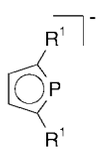


22

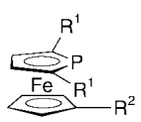
The enantiomers of 1,1′-diphosphaferrocene carboxylic acid **22** were recently separated by fractional crystallisation of their diastereomeric salts with (+)-brucine, and the absolute configuration of (+)-**22** was established by X-ray diffraction.[18]

Two approaches were reported to chiral phosphaferrocenes, which are chiral not because of unsymmetrical substitution of the phospholyl ring—as is the case for all the examples described above—but rather because of 2,5-disubstitution with chiral (−)-menthyl groups or due to a chirally modified cyclopentadienyl ligand, respectively.

The syntheses of the two compounds **24** and **28** may serve to illustrate the two main preparative routes to phosphaferrocenes: in the ionic approach, complex **24** was obtained by treatment of $[CpFe(mesitylene)]^+$ with the phospholyl anion **23**, which is available in three steps from (−)-menthylacetylene in good yield.[19] Because of the C_2 symmetry of the free phospholyl anion **23**, its two faces are homotopic, leading to only one stereoisomer in a π complexation reaction. However, as the C_2 symmetry is not maintained in the phosphaferrocene **24**, the two *β* hydrogen atoms are diastereotopic in the latter complex, giving rise to individual NMR resonances. In a similar manner, the derivative **26**, with an additional diphenylphosphinomethyl substituent on the Cp ring, was prepared by the reaction of phospholyl anion **23** with the cationic iron precursor **25**.[20] Complex **26**, which is again obtained as a single enantiomer, can be successfully employed as chiral P,P chelate ligand in enantioselective catalysis.

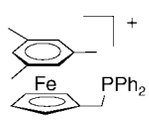


23



24, R^2 = H

26, R^2 = CH_2PPh_2



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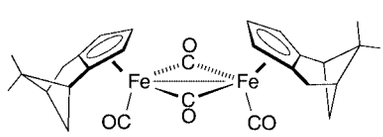
R^1 = (–)-menthyl

The second important synthetic route involves a thermal reaction between a phosphole and $[C_5R_5Fe(CO)_2]_2$ in a high boiling solvent. According to this scheme, treatment of the pinene-fused Cp iron complex **27** with 1-*tert*-butyl-3,4-dimethylphosphole in xylene gave phosphaferrocene **28**, leading to diastereotopic *α* positions on the phospholyl ring. Therefore, in the subsequent Vilsmeyer reaction, the diastereomeric formyl derivatives were not formed as an equimolar mixture but in a ratio of *ca.* 2 : 1.[21]



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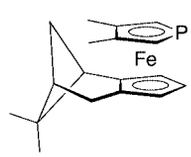
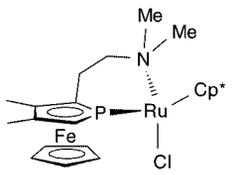


28

Making use of metallocene chirality

(a) Chiral metal complexes. The new chiral bidentate ligands were examined regarding their coordination properties, and a number of different metal complexes were prepared and characterised. In a typical example, treatment of the P,N ligand **3** with 0.25 equivalents of $[Cp^*RuCl]_4$ in thf gave in a smooth reaction the complex [Cp*RuCl(**3**)] (**29**) quantitatively, with the bidentate ligand forming a six-membered chelate ring with the metal atom. In the course of the complexation reaction, the Ru atom becomes a stereogenic centre, and it was found that only one diastereomer is formed within the detection limit of NMR spectroscopy.[7]

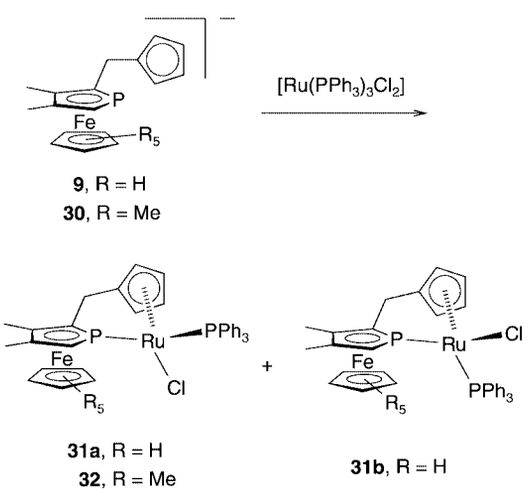
Thus, the phosphaferrocene-based chirality of the ligand exerts complete control over the metal configuration in the complex. In view of the exploitation of the ligand chirality, this is an encouraging result, especially because the formation



29

of CpRu complexes with other chiral P,P ligands gave low diastereoselectivities and the compounds were obtained almost as 1 : 1 mixtures of diastereomers.[22] For complex **29**, the observed relative configuration, as determined by X-ray diffraction, corresponds to the more stable isomer in which the sterically demanding Cp*- and CpFe groups avoid interference. For the hypothetical second diastereomer, which is obtained by formally interchanging the Cl and Cp* ligands on ruthenium, model inspection reveals a severe unfavourable steric interaction between the two bulky groups. In solution, complex **29** shows hemilabile coordination of the NMe_2 group to the ruthenium: at room temperature, the diastereotopic methyl protons give one broad signal, indicating a fast dangling of the NMe_2 donor on the NMR timescale. On cooling the NMR sample, the broad NMe_2 signal splits into two sharp resonances and an activation barrier of $\Delta G^{\#} = 53.6 \pm 1$ kJ mol^{-1} for the dynamic process was calculated from the NMR data.

In contrast to the bidentate P,X ligands, the phosphaferrocenyl-substituted Cp anion **9** opens up the possibility for $\eta^5 : \eta^1$ coordination, thus enabling the formation of chiral half-sandwich complexes with an intramolecularly tethered P donor. This class of complexes has attracted considerable attention during the last few years and ruthenium compounds of the type $[(Cp–L)Ru(PR_3)X]$ with stereogenic Ru atoms were investigated in particular.[23] In order to control the metal configuration in a diastereoselective complexation reaction, several chiral Cp–L ligands were designed, which resulted in de values of 18–83% in the subsequent complexation reactions. When the anion **9** was treated with $[(PPh_3)_3RuCl_2]$ in toluene at 90 °C overnight, the diastereomeric half-sandwich complexes **31a**,**b** were formed in a ratio of 95 : 5. This ratio was established for the crude product by ^{31}P NMR spectroscopy and reflects therefore the selectivity of the complexation reaction itself, unaffected by workup manipulations. This high selectivity can be further increased by replacement of the Cp ligand with the more sterically demanding Cp* ligand in the phosphaferrocene.



Thus, with anion **30** under similar reaction conditions, only one diastereomeric half-sandwich complex, **32**, was observed in the crude product which was isolated in high yield after chromatographic workup.[24] In order to rationalise the high selectivity, it is helpful to look at the molecular structure of complex **32**, which was determined by X-ray diffraction. (Fig. 1) Two sterically demanding groups—the PPh_3 ligand and

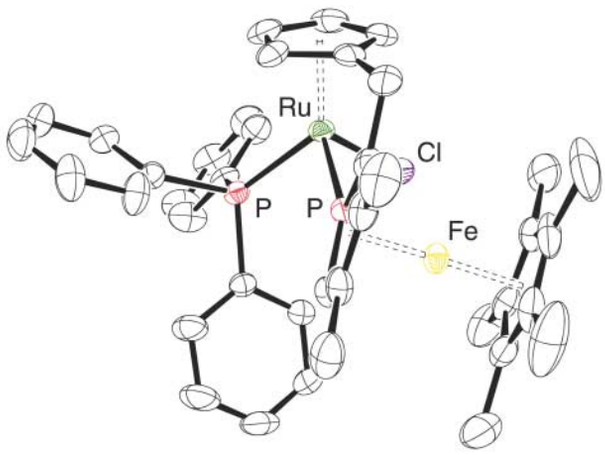
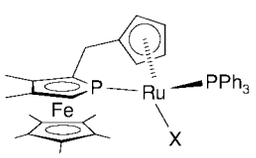


Fig. 1

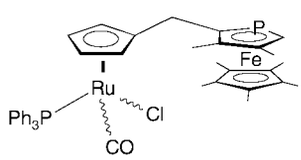
the Cp*Fe moiety—have to be accommodated at the ruthenium atom. Minimal steric interference results for the observed relative configuration, the two bulky groups pointing into different segments of space, as is evident from the view depicted in Fig. 1. In contrast, for the other diastereomer with opposite configuration at Ru—obtained by exchanging the positions of Cl and PPh_3—steric overcrowding results from the two bulky groups occupying overlapping segments of space.

Besides the selective synthesis of complex **32**, the configurational stability of the Ru atom in subsequent reactions is another interesting issue and such studies were carried out.[24] In polar solvents, the chloride is easily replaced by another ligand. Thus, halogen exchange with NaI in acetone–thf gives the iodide complex **33** in quantitative yield as a single diastereomer. An X-ray structure determination revealed that this substitution reaction proceeded with retention of configuration at Ru.[25]

When the chloride complex **32** was treated with NaOMe in MeOH, the quantitative substitution of chloride by hydride was observed and complex **34** was obtained as a single diastereomer. Thus, this reaction again proceeds in a stereochemically controlled way.



33, X = I
34, X = H
35$^+$, X = H_2



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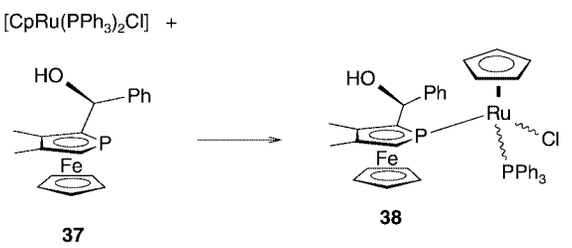
When the chloride is removed from complex **32** by treatment with Ag or Tl salts in acetone or CH_2Cl_2, the vacant coordination site can be occupied by a ligand which is not capable of bringing about the substitution reaction itself. In this manner, the cationic dihydrogen complex **35** was prepared by bubbling H_2 through a solution of $[(\mathbf{30})Ru(PPh_3)]^+$ in dichloromethane. The dihydrogen complex is again obtained as a single diastereomer. Although no crystal structure determination was carried out for this compound, we believe that the reaction proceeds with retention of configuration at Ru once more. A T_1 value of 15 ms at 298 K for the coordinated H_2 ligand characterised complex **35** as a dihydrogen complex and not as a dihydride. Deprotonation of cationic **35** with triethylamine

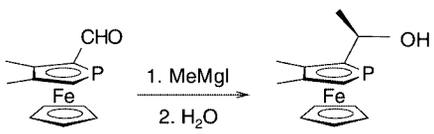
leads to the same diastereomeric hydride complex, **34**, as described in the preceding paragraph, as is evident from their identical NMR spectra.

The PPh_3 ligand in **32** can be replaced with PCy_3 by treatment with the phosphine in toluene, and the product was obtained as a single diastereomer. More interesting are the reactions in which the phosphaferrocene donor is replaced by another ligand. For example, heating complex **32** in toluene under an atmosphere of CO leads to the quantitative formation of the carbonyl complex **36**, which was obtained as a 1 : 1 mixture of diastereomers, indicating complete epimerisation at Ru. Thus, the presence of the chiral phosphaferrocenyl moiety in the molecule is not, on its own, sufficient to enable the preferential formation of one diastereomeric complex. Only in a chelating coordination mode, in which the chiral phosphaferrocene donor is attached to the metal in a conformationally rigid manner, the ligand is able to exert its stereodifferentiating effect in a powerful way. This finding is further corroborated by the outcome of the following substitution reaction: when one PPh_3 ligand in $CpRu(PPh_3)_2Cl$ is replaced by the chiral monodentate phosphaferrocene derivative **37**, the product **38** is obtained in quantitative yield but as a 1 : 1 mixture of diastereomers. Here, although the chiral donor is attached to the Ru atom, the substitution is completely unselective.



37 **38**

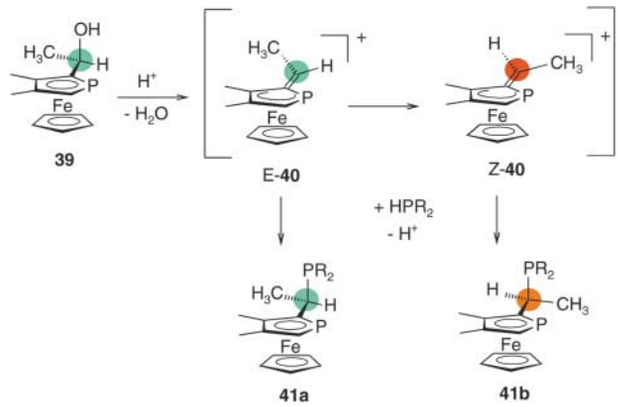
(b) Diastereoselective ligand functionalisation. The planar chirality of the substituted phosphaferrocenes not only allows the stereoselective formation of metal complexes, as described in the preceding section, but can also be exploited in the diastereoselective derivatisation of the phosphaferrocene moiety itself. Addition of MeMgI to the aldehyde **1** proceeds stereoselectively and leads only to one diastereomeric alcohol, **39**, when the reaction is carried out at −25 °C.[26] Interestingly, the $LiAlH_4$ reduction of the acetyl derivative is completely unselective and leads to a 1 : 1 mixture of diastereomers.[27]



1 **39**

The alcohol **39** could be used as a starting material for the preparation of P,P chelate ligands by protonation and release of a water molecule and subsequent treatment with a secondary phosphine. However, in contrast to analogous ferrocene compounds, for which the reaction proceeds with retention of configuration at the stereogenic centre,[28] in the phosphaferrocene case, the stereochemical course of the reaction may be controlled by the reaction conditions, leading to products formed either under retention or inversion of configuration at the stereogenic carbon atom. Detailed investigations lead to the mechanistic proposal outlined below.[26]

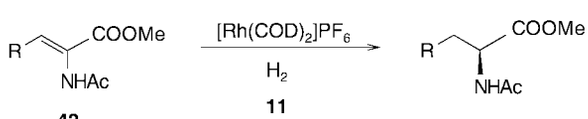
In analogy to the related ferrocene chemistry, it is assumed that loss of a water molecule from the protonated alcohol occurs selectively *trans* to the sterically demanding CpFe fragment. Thus, starting from the diastereomerically pure alcohol **39**, the fulvene-like cationic intermediate *E*-**40** is derived with



39 E-**40** Z-**40** **41a** **41b**

an *E* arrangement of the P atom and the Me group with respect to the exocyclic C–C bond. If a secondary phosphine is present in the reaction mixture, fast nucleophilic attack occurs, which leads to the substitution product **41a** under retention of configuration. In the absence of a nucleophilic reagent, a comparatively slow isomerisation takes place, converting the cationic species *E*-**40** to the thermodynamically more stable cation *Z*-**40**, which, upon *exo* attack by a nucleophile, gives rise to the formation of the substitution product **41b** with inverted configuration at the stereogenic centre when compared to the starting material **39**. The *Z* configuration of the more stable cation was elucidated by NOE measurements, and the structure of a subsequently obtained substitution product was determined by X-ray diffraction. In the reaction sequence described here, the planar chirality of the heterometallocene remains unchanged, the CpFe fragment making the release of the leaving group as well as the attack of the incoming nucleophile, occur selectively in the upper hemisphere of the molecule, which is not sterically blocked. The appreciable activation barrier for the *E*–*Z* isomerisation permits the formation of substitution products of either configuration by a judicious choice of reaction conditions.

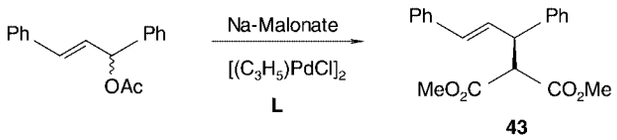
(c) Enantioselective catalysis. The new class of phosphaferrocene-based chiral ligands was employed in several enantioselective catalytic reactions. Initial experiments with bidentate ligands such as **2**–**5** were rather disappointing, as ee values of 15–20% were obtained in the Rh-catalyzed hydrogenation of dehydroamino acid derivatives **42** and the Pd-catalyzed allylic substitution of 1,3-diphenylallyl acetate with sodium malonate as the nucleophile.[29] However, a tremendous increase in selectivity for the hydrogenation was observed by Fu and Qiao for a more sterically demanding Cp* derivative. Thus, ligand **11** gave ee values as high as 96%, depending on the solvent and the exact nature of the unsaturated starting material **42**.[11]



42 **11** up to 96 % ee

With the trinuclear metallocene derivative **10**, 79% ee was obtained in the allylic substitution reaction involving 1,3-diphenylallylic acetate and sodium malonate.[24] A more detailed analysis of this reaction was carried out with the oxazoline ligand system **13**.[12] It was shown that the planar chirality of the phosphaferrocene, and not the central chirality of the oxazoline, is the dominant element of stereocontrol. Thus, with the same configuration at the oxazoline carbons, the valine-derived ligands (*S*)-**13a** and (*R*)-**13a**, differing only in the configuration of their planar chirality, give the substitution product **43** as the (*R*)-enantiomer with 68% ee and the (*S*)-enantiomer

with 79% ee, respectively. The same trend holds for the *tert*-leucine-derived ligands (*S*)-**13b** and (*R*)-**13b** with a bulky *tert*-butyl group at the oxazoline ring. Again, a reversal of the configuration in the allylic product is observed when the planar chirality of the ligand is changed. The observed ee values in this case are 73% (*R*) and 82% (*S*).



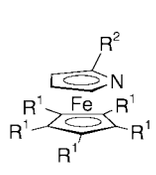
43

The complex [(**26**)$PdCl_2$] gave ee values up to 99% in the allylic substitution. In that case, the enantioselectivity varied with the Pd to ligand ratio. An excess of ligand leads to the formation of bis(monodentate) complexes, in which the phospholyl donors are not coordinated. With the chirality far away from the active metal center, these complexes were blamed for a drop in selectivity.[20]

The P,P ligand **11** was also successfully applied in the Rh catalyzed enantioselective isomerisation of allylic alcohols. Depending on the structure of the substrate, the solvent and the counterion, up to 86% ee was achieved, which is the best result so far obtained for this reaction. The structure of the complex [(cod)Rh(**11**)]PF_6 was established by X-ray diffraction.[30]

Azaferrocenes

Like phosphaferrocene, the nitrogen analogue azaferrocene has been known for a long time. The first report[31] of the compound dates back to 1964, and in 1969, the first paper concerning a chiral non-racemic derivative was published by Schlögl *et al.* Optically active 2-methylazaferrocene was obtained by fractional crystallisation with a chiral acid, although the enantiomeric purity was not assessed.[32] After this early report, the stereochemical properties of chiral azaferrocene derivatives remained unexplored for almost 30 years, while other aspects of the chemistry of azaferrocenes were studied in considerable detail.[33] In 1996, Fu and co-workers started to explore the application of chiral enantiopure azaferrocenes and related compounds in asymmetric catalysis. Derivatives of **44** and **45** were used in various enantioselective nucleophilic catalytic reactions, such as the addition of alcohols to ketenes, the rearrangement of O-acylated enolates and the acylation of secondary alcohols. Derivatives **45** are chirally modified analogues of DMAP and were applied with particular success. The Ru analogues of **45** were examined as well.[34]



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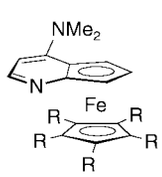
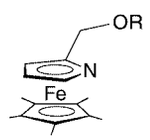


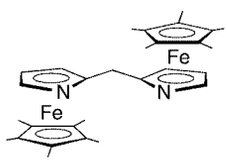
45

Enantiomerically pure azaferrocenes were obtained by separation *via* chiral HPLC. The silyl ether **46** served as a nucleophilic catalyst in the kinetic resolution of secondary alcohols by acylation with diketene or acetic anhydride,[35] and in the enantioselective addition of methanol to different arylalkylketenes.[36] The diphenyl carbinol **47** gave high ee values in the enantioselective addition of organozinc reagents to aldehydes.[37] Fu *et al.* also prepared the bisazaferrocene **48** in a one pot synthesis starting from di(2-pyrrolyl)methane. *rac* and *meso* diastereomers were separated by flash chromatography and the pure enantiomers of **48** were isolated by chiral HPLC. The bisazaferrocene **48** served as an efficient ligand in the Cu-catalyzed enantioselective cyclopropanation of olefins with diazoalkanes. In that context, the crystal structure of the cationic Cu(I) styrene complex with **48** was determined by X-ray diffraction.[38]



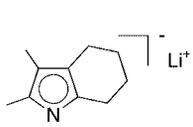
46, R = $SiEt_3$

47, R = CH_2CPh_2OH



48

Reaction of the tetrahydroindolyl anion **49** with [$(PPh_3)_3RuCl_2$] gave the bisazaruthenocene derivatives *rac*-**50** and *meso*-**50** as a 1 : 1 mixture, which can be separated by fractional crystallisation. The X-ray structure was determined for the *rac* diastereomer, but no attempts to separate the enantiomers were reported.[39]



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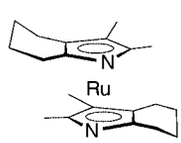
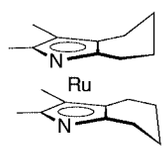
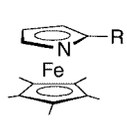


rac-**50**



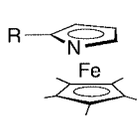
meso-**50**

An approach to enantiomerically pure 2-azaferrocenyl anions was recently devised. The protocol involves the metallation of pentamethylazaferrocene yielding a racemic mixture of the *α*-lithio derivatives **51a**,**b**, which, by treatment with enantiomerically pure sulfinate **52**, were transformed to the diastereomeric sulfoxides **53a**,**b**. These were separated by chromatography and characterised by X-ray diffraction. From the sulfoxides, the respective enantiomerically pure lithio compounds were obtained by cleaving the Cp(C)–S bond with *tert*-butyllithium. The anions are of sufficient configurational stability at −78 °C to allow the formation of substitution products by treatment with electrophiles in a highly enantioselective fashion. Thus, the iodide and the hydroxymethyl compound were obtained with ee >98%.[40]

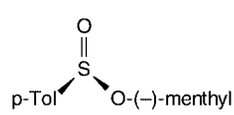


51a

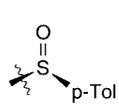
R = Li



51b



52

53a R = 

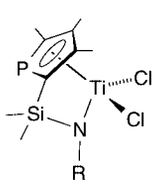
53b

Chiral η^5-phospholyl derivatives of group IV metals

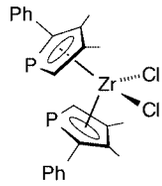
A few reports which describe unsymmetrically substituted phospholyl anions attached in an η^5-fashion to group IV metals exist. Thus, the titanium complexes **54** were prepared as racemates in view of their potential application as catalyst precursors for olefin polymerisation.[41] However, no special

attention was given to the stereochemical properties of the complexes.

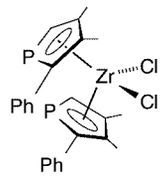
The reaction of the 2-phenyl-3,4-dimethylphospholyl anion with $ZrCl_4$, leading to the metallocene dichloride derivative **55**, was independently investigated by two groups.[42,43] Whereas the crude product of the reaction contained the *rac* and *meso* isomers in a *ca.* 65 : 35 ratio, recrystallisation afforded the pure *rac* diastereomer, which turned out to be configurationally labile in solution. Thus, slow isomerisation ($\tau_{1/2}$ = 12 h at room temperature in benzene) that re-established the original isomer ratio of *ca.* 65 : 35 was detected by ^{31}P NMR spectroscopy which is therefore believed to be thermodynamically controlled. Ring slippage of the phospholyl ligand from η^5 to η^1-P is considered a possible pathway to account for the stereochemical non-rigidity. The fact that coordinating solvents accelerate the isomerisation is in accord with this proposal, as they may lead to the stabilisation of coordinatively unsaturated intermediates. With the Hf analogue, the equilibration occurs much more rapidly ($\tau_{1/2}$ = 10 min). When activated with MAO, the diphosphazirconocene **55** is an active catalyst for ethylene polymerisation. Of course, the chirality of the catalyst has no impact in this reaction and olefin polymerisations making use of achiral phosphazirconocenes were described earlier.[44] Complex **55** may also act as a bidentate P,P chelate ligand and the $Mo(CO)_4$,[43] as well as the cationic (Binap)Rh[42] [Binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] complexes, were prepared, the structures of which have been determined by X-ray diffraction. When enantiomerically pure [{(*R*)-Binap}Rh(cod)]-OTf was used as a starting material for the preparation of the latter complex, dynamic resolution of the zirconocene ligand **55** was accomplished in that the *rac–meso* mixture of the free ligand was converted into one enantiomer in the complex.



54, R = Me, Bu^t



rac-**55**



meso-**55**

Conclusion

Systematic investigation of chiral heterometallocenes with regard to their stereochemical properties has evolved only within the past five years. During this short period, these compounds have proved to have an interesting chemistry and a number of applications have been recognised. Given the continuing interest in the topic, further aspects will certainly be revealed by future work. In particular, the application of the compounds in the field of enantioselective catalysis may lead to remarkable developments.

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