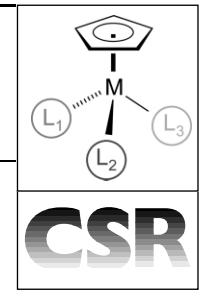
# Chiral organometallic half-sandwich complexes with defined metal configuration

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**Chiral organometallic half-sandwich complexes with stereogenic metal atoms are close relatives of chiral organic compounds with stereogenic carbon atoms. Similarities and differences between these two classes of compounds are outlined. Some representative metal complexes are discussed in an introductory section followed by a more detailed treatment of the available strategies to control the metal configuration by means of chiral auxiliaries. Special sections are devoted to the discussion of the configurational stability of chiral-at-metal complexes and their applications in stoichiometric and catalytic stereoselective reactions.**

## 1 Introduction

Coordination chemistry has been strongly related with stereochemical issues from its very beginning. In outlining the modern theory of coordination compounds at the beginning of the 20th century, Alfred Werner relied on stereochemical arguments to a large extent. The deduction of the octahedron as the most common coordination polyhedron was based, *inter alia*, on the number of stereoisomers which exist for complexes of general composition $[Ma_4b_2]$ and $[Ma_3b_3]$, for example. Furthermore, Werner postulated the existence of chiral metal complexes, provided a suitable set of achiral ligands is chosen. In 1911, he succeeded in isolating the first enantiomerically pure metal complex, which was obtained by resolution of a racemic mixture after repeated recrystallisations. This discovery was one of the milestones that paved the way for a general acceptance of Werners theory of coordination compounds, which is basically still in use today.[1]

The synthesis of chiral metal complexes and the elucidation of their stereochemical properties has been a challenging topic since the days of Alfred Werner. After more fundamental research had been carried out initially, the fact that chiral metal complexes play a crucial role in enantioselective catalysis brought a tremendous boost of interest within the last 30 years that culminated in the 2001 Nobel prize awarded jointly to Knowles, Noyori and Sharpless for their outstanding contributions in this field. It is interesting to note, however, that despite their importance in catalysis, the selective preparation of enantiomerically pure complexes with stereogenic metal atoms seems less well developed than the field of asymmetric organic synthesis. Possible reasons for this will be discussed in the next section.

Besides classical coordination compounds the stereochemical properties of chiral organometallic complexes were also studied soon after this field of chemistry began to develop in the fifties. For example, the chemistry of chiral ferrocene derivatives received thorough investigation. Again, after it became evident that chiral ferrocenes are suitable ligands for enantioselective catalysis, a new intense research effort started making use of much older fundamental work.

This article is mainly focused on chiral organometallic half-sandwich complexes which are reminiscent of organic compounds in that they comprise a metal atom surrounded by four different ligands in a tetrahedral arrangement, one of them being a cyclic π-ligand like cyclopentadienyl (Cp) or an arene. Chiral-at-metal complexes of this type were studied starting from the late sixties and a renewed interest is evident from the most recent literature. Special attention is given to the methods that allow the control of the metal configuration in such complexes.

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## 2 Chiral metal complexes—general considerations

In organic chemistry the basic building block for chiral compounds is the 'asymmetric carbon atom', *i.e.* a C atom bearing four different substituents. However, the situation is somewhat more complex in the case of transition metal complexes, because the metal atoms can adopt different coordination numbers and coordination polyhedra, the octahedron and tetrahedron being the most common ones. Increasing the coordination number leads to an increased number of isomers which are possible for a certain composition. Obviously, this makes the selective synthesis of one particular isomer a formidable task and strategies have been developed to solve this problem by decreasing the number of possible isomers.[1,2]

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The situation may be further complicated by the fact, that a complex may exist in two coordination polyhedra at the same time and an equilibrium between those might be encountered (trigonal bipyramidal and square pyramidal, for example, in the case of coordination number 5). Even if there is a strong preference for one coordination polyhedron, *e.g.* the octahedron for CN = 6, and a complex exhibits a high thermodynamic stability, it still may be kinetically labile. As a consequence, the stereochemical integrity of a complex might be lost by dissociation of a ligand and configurational rearrangement of the coordinatively unsaturated fragment before re-coordination of the ligand. This is in marked contrast to the situation of the tetrahedral $sp^3$-C atom, which is sufficiently inert to substitution in most cases, thereby endowing stereogenic carbon centres with a high configurational stability.

An interesting difference exists between tetrahedral compounds on one side and structures with other coordination numbers and polyhedra on the other side, regarding their basic stereochemical properties. For a tetrahedral complex Mabcd with achiral ligands a, b, c and d the permutation of 2 ligands yields inevitably the enantiomeric structure with an inverted configuration at the metal centre. Thus, in this special case the permutation of 2 ligands has the same effect as creating the mirror image of the given object. However, there are two properties involved which must not be confused. One property relates to the fact whether or not stereoisomeric structures result on a ligand permutation, while the second property refers to the local symmetry at a specific position in a molecule. Therefore, in the case of a tetrahedral complex Mabcd the metal atom M is termed stereogenic (permutation leads to a stereoisomer) and chirotopic (local $C_1$ symmetry), while in $Ma_2bc$ M qualifies as non stereogenic and achirotopic (local $C_s$ symmetry). It turns out that the tetrahedron is rather the exception than the rule, because the strict relation of the two properties as outlined above does not apply to most other coordination numbers and polyhedra. For example, in the case of a square planar complex Mabcd, the permutation of two ligands results surely in the formation of a distinct stereoisomer, hence M is a stereogenic centre. On the other hand, both isomers are mirror symmetric (pointgroup $C_s$), thus M is achirotopic and the two isomers are achiral diastereomers instead of enantiomers as in the case of the tetrahedron. The concept of stereogenicity and chirotopicity was introduced by Mislow and Siegel and has proven very helpful in analysing stereochemical problems.[3]

## 3 Some illustrative examples

A wealth of results on chiral organometallic half-sandwich compounds was contributed by Brunner starting with pioneering work in the late sixties and the first synthesis of an enantiomerically pure half-sandwich complex was reported in 1969.[4] The racemic mixture of cationic complex **1a,b** was treated with enantiopure menthoxide giving the diastereomeric acyl complexes **2a,b** which could be separated by fractional crystallisation. [Fig. 1] After cleaving off the menthoxide by treatment with gaseous HCl, the pure enantiomers of **1** were obtained, the enantiomeric nature was evident from mirror symmetric CD spectra. The configurational stability was high, no change in optical purity was observed for solutions in $CH_2Cl_2$ over a period of several days. Complex **1** features a metal atom with four different ligands attached to it in a tetrahedral fashion. However, it might be considered equally well as a derivative of an octahedron, in which three facial coordination sites are occupied by the Cp ligand. Thus, by confining the coordination sites a ligand can take up, a simplification of the isomer problem can be achieved.

The Re complex $CpRe(PPh_3)(NO)CH_3$ (**3**) was thoroughly investigated by Gladysz. The compound is easily available in

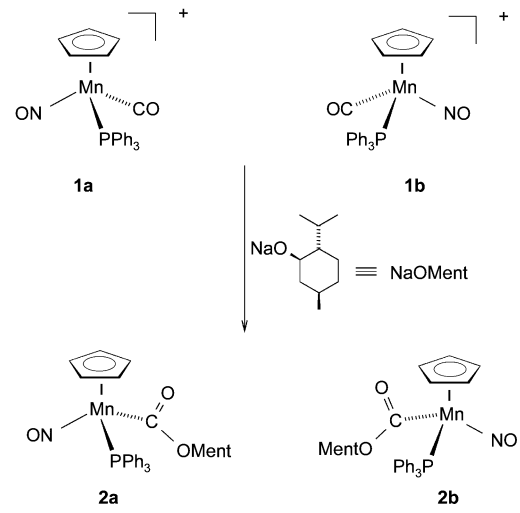



**Fig. 1**

enantiopure form *via* resolution of the racemate. On protonation of **3** at –80 °C in dichloromethane, $CH_4$ is released and the cationic species **4** is formed as a solvate with one weakly coordinated molecule of $CH_2Cl_2$. [Fig. 2] Formation of the

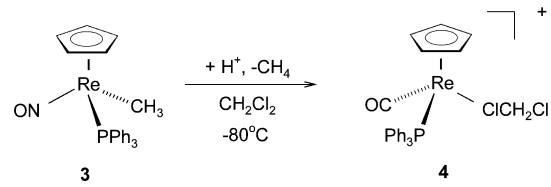



**Fig. 2**

solvate **4** as well as the replacement of the $CH_2Cl_2$ by an unsaturated substrate like a carbonyl compound or an olefin proceeds with retention of configuration at the Re centre at low temperature. Solvate **4** is configurationally stable in solution up to −20 °C, where decomposition starts to occur. The stereochemical implications of the interaction of the chiral-at-metal Lewis acid **4** with unsaturated substrates were studied in detail.[5]

The topologically related iron complexes **5** were also prepared by resolution of a racemic mixture. They are configurationally stable and have found application in the stoichiometric asymmetric synthesis of organic compounds.[6] [Fig. 3] For example, the propionyl derivative **6** can be

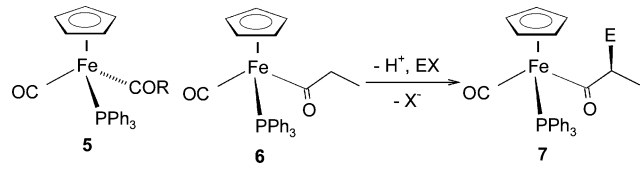



**Fig. 3**

deprotonated and treated with an electrophile, leading to complex **7** with a stereogenic centre in α position to the carbonyl group. The high enantioselectivity of this reaction sequence (ee > 98%) is due to the bulky $PPh_3$ ligand, one phenyl group of which protects one of the two diastereotopic faces of the intermediate enolate from electrophilic attack. Thus, the defined configuration at the metal centre in combination with the bulky $PPh_3$ ligand plays a crucial role in efficiently controlling the stereochemical course of the reaction. Moreover, steric arguments are usually sought to explain the course of stereodifferentiating reactions in general. While these argu-

ments seem convincing because of their imaginary plausibility, there might be other factors at work as well which are less obvious. For example, the chiral molybdenum complex **8** can be attacked at the diastereotopic terminal carbons of the allyl ligand by nucleophiles such as deuteride, alcoholate or enamines, leading to chiral olefin complexes **9**. [Fig. 4] In

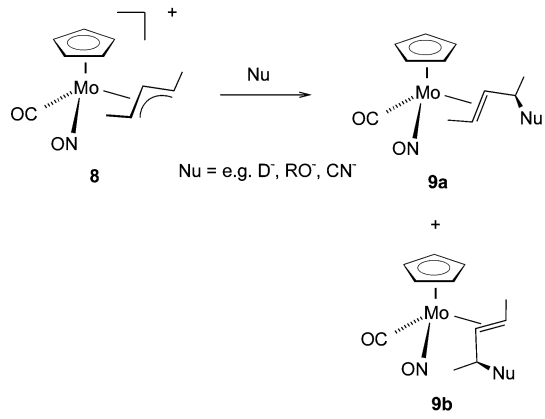



**Fig. 4**

contrast to the iron complexes **5**, which feature CO and $PPh_3$ ligands, complex **8** might be considered as almost mirror symmetric from a steric point of view, because of the very similar size of the CO and NO ligands and one would not expect the attack at the allyl termini to be selective. However, Faller demonstrated that the attack does indeed occur with a high selectivity and this was explained by the electronic asymmetry of the complex. While being sterically almost indistinguishable, the CO and NO ligands exert quite distinct electronic trans effects leading to different degrees of reactivity at the two allylic termini.[7]

## 4 The question of configurational stability

When dealing with chiral-at-metal complexes, the configurational stability of these compounds is a crucial issue that deserves some further consideration. A complex may be configurationally stable over weeks under forcing conditions, while others tend to racemise or epimerise within a few second even at low temperatures. A useful division can be made by relating the rate of configurational change to the timescale of preparation and isolation. Then, in one case, complexes may be termed configurationally stable, if it is possible to isolate and manipulate them faster than epimerisation occurs, while configurationally labile are those complexes that can not be obtained in a stereochemically defined manner due to their fast epimerisation.

If enantiomeric complexes are formed in a reaction, thermodynamics dictate that an equilibrium mixture will always feature both enantiomers in a 1 : 1 ratio. Diastereomers, on the other hand, may differ in thermodynamic stability and the equilibrium ratio is therefore usually different from a 1 : 1 value. The ratio of diastereomeric complexes formed in a reaction gives thus a measure of the asymmetric induction by which a chiral auxiliary ligand can control the metal configuration. However, two limiting cases have to be considered in this context. If, under a given set of experimental conditions, the formation of diastereomers occurs irreversibly, *i.e.* with no equilibration between the isomeric products, the reaction is under kinetic control. In this case, the observed isomer ratio reflects the different rate of their formation and the value may be far off from the equilibrium value, which is dictated by thermodynamics. In the other extreme, the activation barrier for the interconversion of diastereomeric products is low enough, so that under the experimental conditions the equilibrium ratio is established, which is now under thermodynamic control. Care has to be taken when deciding, whether a reaction is under kinetic or thermodynamic control and misinterpretations have indeed been revealed in the literature[8] (*vide infra*).

In most cases the racemisation of a chiral-at-metal half-sandwich complex will occur *via* ligand dissociation to give a coordinatively unsaturated 16 electron intermediate which can have a pyramidal or planar ground state. The energy difference between these two structures and the barrier of their interconversion will thus determine the configurational stability of the starting complex and this problem has been addressed by theoretical calculations. It was shown that the simultaneous presence of good donors as well as good acceptor ligands leads to a preference of the pyramidal structure although the computed activation barriers were accessible at room temperature.[9] Furthermore, the spin state of the complex under consideration has also to be taken into account. For example, DFT calculations revealed that coordinatively unsaturated 16 electron fragments like [CpW(NO)(L)] may adopt singlet or triplet structures, which are separated by barriers of only 2–6 kcal $mol^{-1}$, depending on the nature of L. While the singlet state will adopt a pyramidal structure, a planar arrangement is predicted to be energetically preferable for the triplet species and this opens the possibility for a low-energy inversion pathway at the central metal atom *via* an intermediate spin-state change.[10]

Techniques used to determine experimentally the ratios of enantiomeric complexes and their evolution with time include polarimetry and CD spectroscopy, although these methods are not that straightforward as NMR spectroscopy is in the analysis of mixtures of diastereomeric complexes that differ in the configuration at the metal atom, where isomer ratios can be directly obtained from the integration of suitable signals in the $^1H$ or especially $^{31}P$ NMR spectra in the case of phosphine complexes.

It is interesting to compare the tremendous differences in the rates of racemisation observed for closely related species. For example, the cationic carbonyl complex **1** shows no sign of racemisation in dichloromethane solution at ambient temperature over a period of several weeks, whereas the neutral benzoyl species **10a** (X = H)—accessible *via* attack of PhLi to **1**—racemises quickly with a half-life of 49.5 min at 20 °C.[8]

Brunner has studied the influence of steric and electronic effects on the rate of racemisation in detail. It was shown that the CpMn derivatives **10a,b** racemise *via* dissociation of the $PAr_3$ ligand and varying the para substituents X and Y on the aryl groups in **10** allowed to modify the electronic structure while leaving the steric situation more or less unaffected (X, Y = $NMe_2$, OMe, F, $CF_3$ and others) . [Fig. 5] Racemisation is

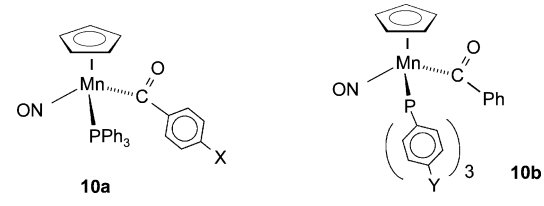



**Fig. 5**

slowed down in the case of electron releasing groups Y on the triaryl phosphine and/or electron withdrawing groups X in the para position of the benzoyl substituent. However, steric factors were shown to be operative as well, because derivatives CpMnCOPh(NO)L with L being good acceptors or donors like CO, $P(OEt_3)_3$ and $P(n\text{-}Bu)_3$ all turned out to be configurationally stable. This observation was explained by the smaller size of the latter ligands leading to a better steric fit around the central metal atom, whereas the presence of the bulkier ligand

$PPh_3$ leads to a steric overcrowding in complex **10**, which makes the dissociation of this ligand a much more facile process—a prerequisite for the subsequent racemisation of the coordinatively unsaturated intermediate.[11]

## 5 Controlling the metal configuration in chiral half-sandwich complexes

The chiral half-sandwich complexes **1**, **3** and **5** presented above were synthesized as racemic mixtures, which were subsequently resolved to yield optically active samples. In fact, when a stereogenic metal atom is the only element of chirality in a complex, there is currently no method available to achieve an enantioselective synthesis. However, one can think of methods to control the configuration of the metal atom during the synthesis by using chiral reagents that give rise to the formation of diastereomeric chiral-at-metal complexes and several approaches have been followed.

### 5.1 Substitution by chiral monodentate ligands

One simple approach to control the metal configuration is to introduce a chiral monodentate ligand. For example, if one of the two enantiotopic CO ligands in complex **11** is replaced by an achiral phosphine ligand like $PPh_3$ the enantiomeric products of course form in a ratio of 1 : 1. [Fig. 6] When chiral phosphine

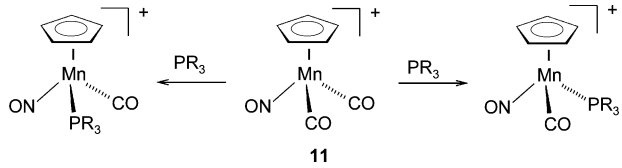



**Fig. 6**

derivatives are employed, diastereomeric complexes result, which may form in a ratio other than 1 : 1. However, the control of metal configuration exerted by chiral monodentate ligands is generally fairly low and mixtures of isomeric complexes are usually obtained. Even so, this may be useful, as due to their diastereomeric nature, these isomers are often separable by chromatography or crystallization. This strategy was first carried out to obtain both diastereomers of the (arene)Ru complex **12**.[12] [Fig. 7] Similarly, the displacement of one

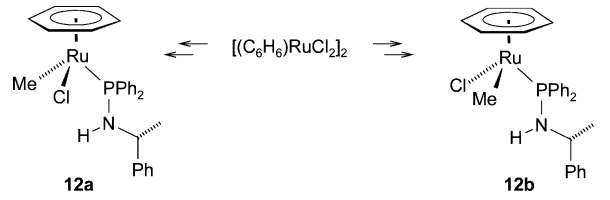



**Fig. 7**

carbonyl group in $CpMo(CO)_2NO$ by different chiral monodentate phosphine ligands $PR_3$ afforded the respective chiral-at-metal complexes $CpMo(CO)(NO)(PR_3)$ as mixtures of diastereomers with ratios ranging from 50 : 50 to 70 : 30, which could be separated by chromatography.[13]

If the cationic iron dicarbonyl complex **13** is treated with mentholate, nucleophilic attack of the anion to either of the two enantiotopic CO ligands occurs leading to neutral diastereomeric acyl complexes **14**, which can be separated by crystallisation. [Fig. 8] In this case, the desymmetrisation of the starting complex **13** is achieved by modification of a ligand instead of substitution.[14] A third alternative is illustrated by the reaction of

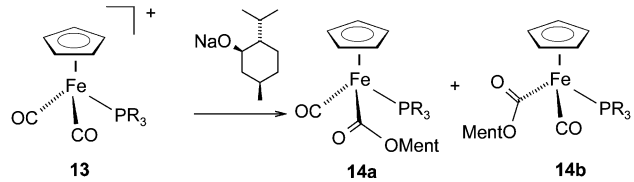



**Fig. 8**

the menthyl ether derivative **15** with $PPh_3$. In this case the chiral auxiliary is attached to the metal atom before ligand substitution of diastereotopic CO groups leads to the diastereomeric products **16a** and **16b** with stereogenic metal centres.[15] [Fig. 9]

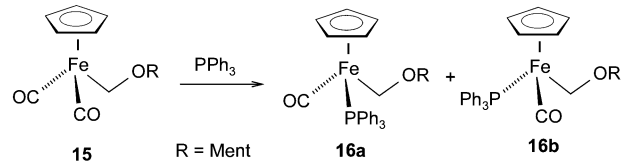



**Fig. 9**

### 5.2 Chiral Cp equivalents

Another method to influence the metal configuration is to replace the $C_5H_5$ ligand in a precursor complex by a chiral Cp equivalent and among others menthyl and neomenthyl substituents have been used for this purpose. For example, the reaction of $nmCpRu(CO)_2I$ (**17**, nm = neomenthyl) with $PPh_3$ afforded the diastereomeric complexes **18a** and **18b** in a ratio of *ca.* 60 : 40, which could be separated by chromatography.[16] [Fig. 10] The pure diastereomers were configurationally stable

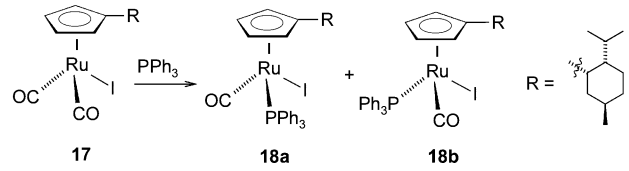
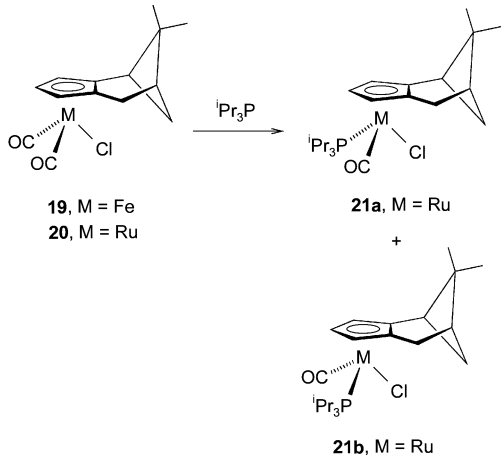



**Fig. 10**

in toluene solution at 80 °C for 24 h as shown by unchanged $^{31}P$ NMR spectra. Although being diastereomers, the CD spectra of **18a** and **18b** are virtually mirror symmetric, indicating that the chiroptical properties are mainly dominated by the metal configuration and not by the stereogenic carbon atoms of the neomenthyl substituent. This is a fairly general observation and holds also, for example, for the epimeric pairs of complexes **2** and **12**.

The reaction of $PCpM(CO)_2Cl$ [PCp = pinene-fused cyclopentadienyl; **19**, M = Fe; **20**, M = Ru] with phosphines $PR_3$ under various conditions was studied by Salzer.[17] Due to the chiral PCp ligand, the two diastereotopic carbonyl groups were differentiated in substitution reactions, leading to the preferential formation of one diastereomeric product. The selectivity increased with increasing steric bulk of the phosphine $PR_3$ and a diastereomeric ratio of 82 : 18 was achieved in the best case. It is illustrating to note the different results observed under photochemical and thermal conditions for the substitution of CO by $iPr_3P$ in the Ru complex **20**. [Fig. 11] In xylene under reflux the diastereomeric products **21** were obtained in a ratio of 3 : 1, while on irradiation a 1 : 2 ratio was observed. However, when this latter mixture was heated to 140 °C, the isomer ratio gradually turned to 3 : 1, the value observed in the thermal reaction, which therefore corresponds to the thermodynamic equilibrium value.




**19**, M = Fe
**20**, M = Ru

**21a**, M = Ru

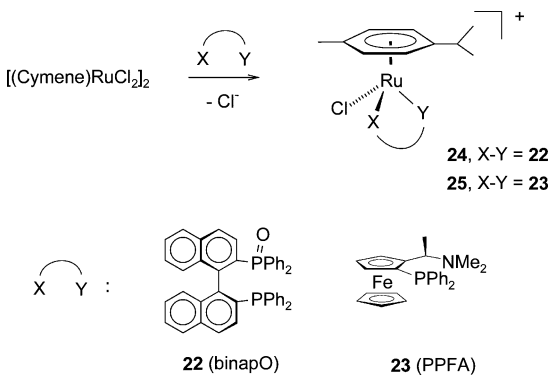
+

**21b**, M = Ru

**Fig. 11**

### 5.3 Substitution by chiral chelate ligands

In contrast to the poor performance of monodentate ligands, chiral chelate ligands have been widely used as powerful auxiliaries to control the metal configuration in diastereomeric half-sandwich complexes. For example, reaction of the arene ruthenium precursor $[(cymene)RuCl_2]_2$ with the chiral chelate ligands **22** and **23** afforded the respective cationic complexes **24**[18] and **25**[19] as single diastereomers. [Fig. 12]



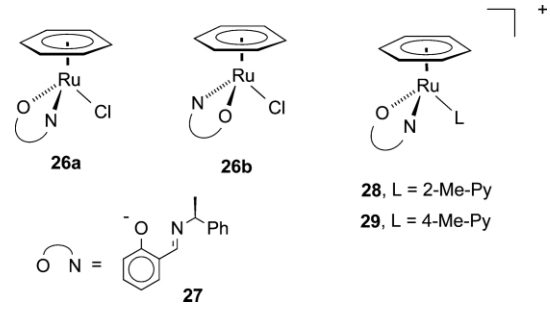

**24**, X-Y = **22**
**25**, X-Y = **23**

**22** (binapO)

**23** (PPFA)

**Fig. 12**

The related (benzene)Ru complexes **26a** and **26b** were obtained in a ratio of 86 : 14 from the reaction of $[(C_6H_6)RuCl_2]_2$ with the sodium salt of anion **27**.[20] One diastereomer of the salicylideniminato complexes **26** was characterized by X-ray diffraction analysis. Careful examination of the crystals under the microscope suggested that only one diastereomer was present in the solid state. However, the configurational stability in solution is very low, as solutions of **26** prepared and immediately analysed by NMR spectroscopy at −80 °C showed the same 86 : 14 ratio of diastereomers as observed for the crude material after synthesis at room temperature. Thus, the thermodynamic ratio is established rapidly even at this low temperature. The chloride ligand in **26** could be removed by treatment with $AgPF_6$ and, after addition of 2-Mepy or 4-Mepy, the corresponding pyridine adducts **28** and **29** were isolated in high yields as a 67 : 33 mixture of diastereomers in the case of **29** and a single isomer in the case of **28**, respectively. [Fig. 13] For the 4-Mepy compound **29**, the NMR analysis of an acetone solution of one crystal prepared and measured at −80 °C revealed the presence of only one diastereomer. In this case, the rate of epimerisation was slow enough to be followed by NMR analysis and a value of 82 min for the half-life was determined at −35 °C. Although the interconversion of diastereomers was slow at low temperature and could be studied by spectroscopy, complex **29** is not configurationally stable on the preparative time scale. Due to the configurational lability of complexes **26**




**26a**

**26b**

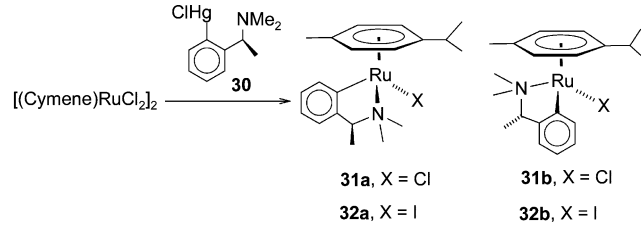
**28**, L = 2-Me-Py
**29**, L = 4-Me-Py

**27**

**Fig. 13**

and **29**, it is not possible to specify, whether the substitution of Cl for pyridine occurs with retention or inversion at Ru. For complex **28** with the more bulky ligand 2-Mepy, the difference of thermodynamic stabilities of the two diastereomers is much more pronounced and only one species is observed in solution by NMR spectroscopy. Due to the methyl group in the 2-position of the pyridine, there is an appreciable barrier of rotation about the Ru–N bond and two rotamers can be observed in a ratio of approximately 1 : 1 at −80 °C.[20]

The diastereomers **31a** and **31b**, obtained from the reaction of $[(cymene)RuCl_2]_2$ with the Hg salt of ortho-deprotonated phenethylamin (**30**), are another interesting example for the care that has to be taken when the configurational stability at a metal centre is under question. [Fig. 14] A ratio of 83 : 17 is observed



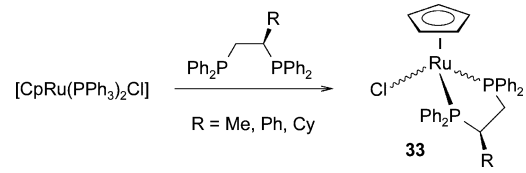

**31a**, X = Cl
**32a**, X = I

**31b**, X = Cl
**32b**, X = I

**Fig. 14**

by NMR spectroscopy over a temperature range from −20 to 50 °C, which remains unchanged over a period of days and this was taken as proof for the configurational stability at the Ru atom. However, it turned out that a solution of crystals, prepared and investigated at −80 °C, contained only the major diastereomer. At higher temperature the minor diastereomer formed and the equilibrium ratio of 83 : 17 was finally approached. The rate of epimerisation was studied at different temperatures and values of 98.1 kJ $mol^{-1}$ and 43.6 J $mol^{-1}$ K were calculated for the enthalpy and entropy of activation, respectively. Therefore, the stereogenic metal atom is configurationally labile under the conditions of preparation and the ratio of 83 : 17 reflects the thermodynamic equilibrium. The same is true for the iodo complexes **32**, which were obtained from **31** by halide metathesis as a 89 : 11 mixture of diastereomers. Again, as both complexes are labile, no information is available regarding the stereochemical course of the substitution reaction.[21]

The synthesis of diastereomeric CpRu complexes with chiral bidentate ligands has been investigated as well. Consiglio reported low diastereomer ratios for complexes of type **33**, prepared by the replacement of both $PPh_3$ ligands in $CpRu(PPh_3)_2Cl$ by several chiral P,P ligands.[22] [Fig. 15]




**33**

**Fig. 15**

Complexes **34**[23] and **35**[24] were obtained as single diastereomers by treatment of $[CpRu(MeCN)_3]^+$ or $[Cp^*RuCl]_4$ with the

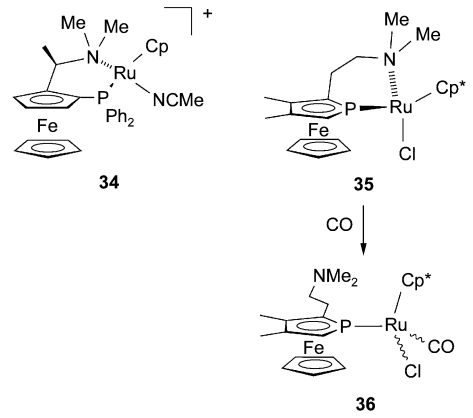



**Fig. 16**

respective organometallic P,N ligands. [Fig. 16] In solution, the $NMe_2$ group of complex **35** shows a hemilabile coordination mode and can easily be displaced by other ligands. For example, the reaction with CO proceeds cleanly to yield the mono carbonyl derivatives **36**. This substitution proceeds with complete epimerisation at Ru and a 1 : 1 mixture of diastereomers of **36** is formed. Thus, it is not sufficient to just have the chiral donor group attached to the metal atom to ensure a highly biased ratio of diastereomeric complexes. Only in the chelate coordination mode the rigidity of the assembly is high enough to enable an efficient stereodifferentiation at the metal centre.

Related half-sandwich complexes of the four-legged-piano-stool type have been prepared as well, starting from $[CpM(CO)_3Cl]$ (M = Mo, W). Treatment with the chiral bidentate N,N ligand **38** resulted in the displacement of chloride and one carbonyl group and the diastereomeric complexes **37a** and **37b** were formed, which could be separated by crystallisation. [Fig. 17] The ratio of diastereomers formed in the complexation reaction was not reported in the literature.[25]

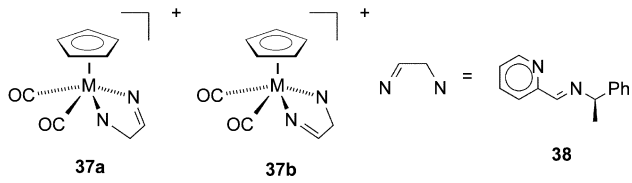



**Fig. 17**

### 5.4 Cp-ligands with tethered chiral donor groups

The approach of controlling a metal configuration by using a chiral donor group that is tethered to a π bonded cyclic ligand has been pursued recently by several groups with varying degrees of success and Ru half-sandwich complexes appear to have been studied particularly well. Cp anions with different chiral P donor functions were synthesized and treated with $[Ru(PPh_3)_3Cl_2]$ to yield the respective half-sandwich complexes **39**–**43**. [Figs. 18 and 19] Quite different chiral donor groups were employed ranging from tartaric acid derived systems (**39**) to chiral phosphaferrocene units (**43**). The observed diastereomer ratios ranged from 59 : 41 up to > 99 : < 1. In contrast to complexes **39**–**41**,[26–28] where the chirality resides in the backbone of the structure and has to be transmitted to the metal centre by P-bonded aryl groups, the P coordinated Ru atom is closely located to the chiral donor group in the case of the phosphaferrocene derivatives **42** and **43**, which leads to particularly high isomer ratios.[29] [Fig. 19] Whereas for the Cp based system **42** the two diastereomers **42a** and **42b** are formed in a 90 : 10 ratio, only one isomer is observed in the case

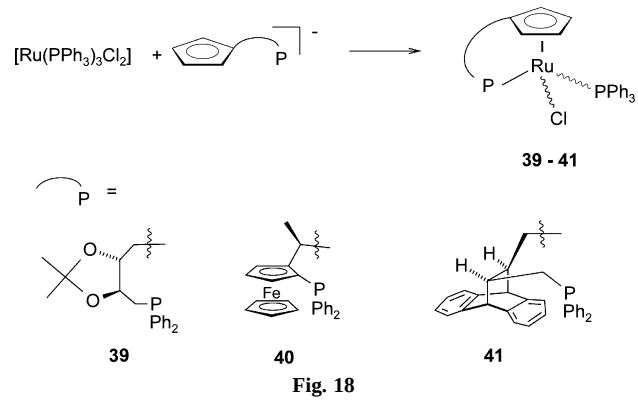



**Fig. 18**

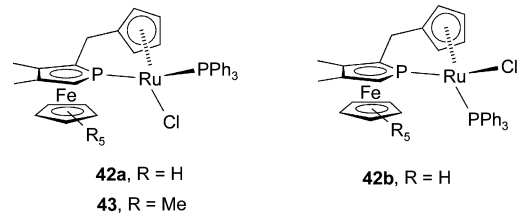



**Fig. 19**

of the sterically more demanding Cp* substituted derivative **43**. The complex syntheses are carried out in refluxing toluene and the diastereomer ratios were determined by $^{31}P$ NMR spectroscopy from the crude reaction mixtures, so that they are not affected by workup manipulations and truly reflect the degree of stereodifferentiation in the complexation reactions. The reactions are under thermodynamic control, as a 4 : 1-mixture of **42a**, **b**, obtained in another manner, equilibrates in hot toluene to approach the 90 : 10 value already observed in the original preparation. Substitution of the Cl ligand in **43** by a couple of ligands including I, $H_2$, MeCN proceeds with retention of configuration at the Ru centre, whereas breaking the chelate coordination by decomplexation of the phosphaferrocene donor results in loss of stereochemical integrity and chiral-at-Ru complexes are obtained as 1 : 1 mixtures of diastereomers.

While in the above examples a donor substituted Cp anion was treated with a Ru precursor, Takahashi developed a different pathway to tethered CpRu complexes. [Fig. 20] The

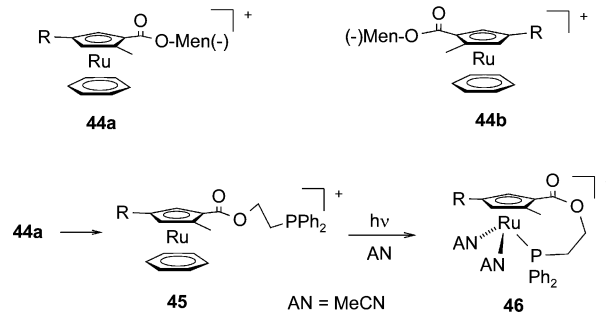



**Fig. 20**

enantiomeric complexes, that arise from complexation of an (arene)Ru fragment to the enantiotopic faces of a trisubstituted Cp ring, serve as starting material. The enantiomers can be resolved by crystallisation of their diastereomeric menthyl ester derivatives **44a** and **44b**, and subsequent transesterification reactions were employed to introduce a suitable donor function to the Cp ring. Phosphinoethyl derivative **45** is depicted as an example. Simultaneous displacement of the benzene ligand and coordination of the $PPh_2$ group is achieved by photolysis of complexes **45**, leading to the bis(acetonitrile) species **46**, which

reacts with different phosphines $PR_3$ to give chiral-at-metal complexes **47**.[30] [Fig. 21] The differentiation between the

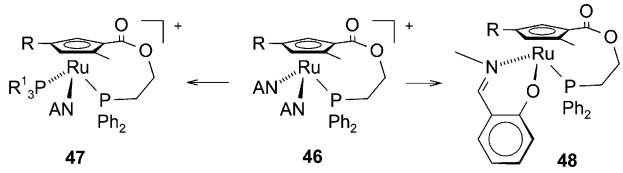


**Fig. 21**

diastereotopic acetonitrile ligands in **46** is good to excellent (de: 40– > 99%), depending on the substituent R on the Cp ring and the nature of the incoming phosphine. The best diastereoselectivities are found for the sterically demanding derivative with R = $^t$Bu and bulky phosphines like $PPh_3$ and $PBu_3$, where only one diastereomeric product can be observed by NMR spectroscopy.[31] Similarly, reaction of the bis(solvate) species **46** with sodium salicylideniminate resulted in the displacement of both MeCN ligands, leading to the corresponding chelate complexes **48**, with de values up to > 99%. These reactions were shown to be under thermodynamic control, as NMR samples of pure diastereomers converted to an equilibrium value at room temperature. The rate of these epimerisations as well as the equilibrium compositions were significantly solvent dependent, with the fastest transformations taking place in polar solvents like THF or acetonitrile.[32] In contrast to the good diastereoselectivities described for the above examples, the substitution of an acetonitrile ligand in complexes **49** by $PPh_3$ is much less stereoselective, giving the respective products **50** with de values ranging from 2 to 34%.[31] [Fig. 22] Thus, the

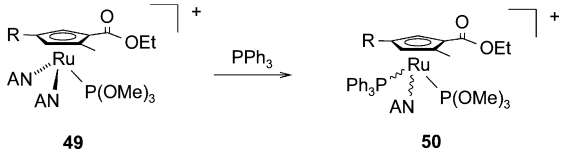


**Fig. 22**

intramolecular coordination of a tethered donor prevents rotation of the Cp ring and allows the planar chirality to be exploited in an efficient discrimination of the diastereotopic acetonitrile ligands in a substitution reaction.

A tethered P-ligand system, which combines the planar chirality of a π-coordinated indenyl ligand with the stereogenic centres of a neomenthyl substituent, was successfully used to prepare Rh half-sandwich complexes with controlled metal configuration. Thus, oxidative addition of MeI to complex **51** gave the diastereomeric acyl complexes **52** in a ratio of 98 : 2.[33] [Fig. 23]

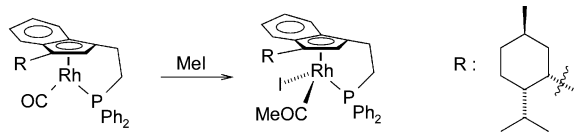


**Fig. 23**

A related approach was followed by Ward in the case of planar chiral (arene)Ru complexes with π-bound arene ligands, bearing a $PPh_2$ and a pyrazolyl donor function. The planar chiral $\eta^6$-arene complexes **53a,b** were obtained as a racemic mixture and could be separated by HPLC on a chiral stationary phase. [Fig. 24] Formation of the chiral-at-Ru complexes **54** by subsequent intramolecular coordination of the pyrazolyl donor function proceeds stereospecific, so that the configuration of the

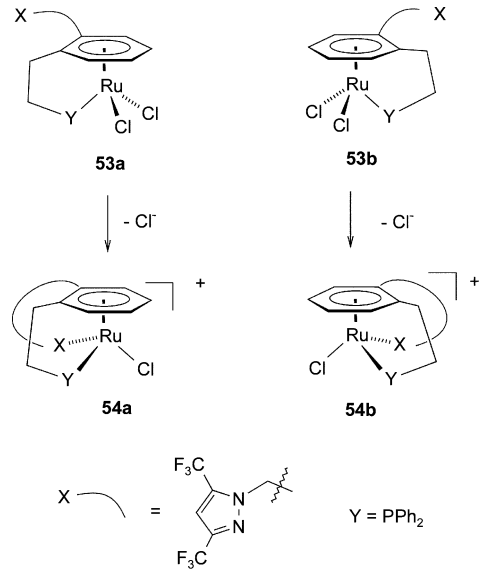


**Fig. 24**

planar chirality determines the metal configuration at Ru, because the donor functions X and Y cannot exchange their coordination sites for obvious steric reasons. Thus, by obstructing the possible epimerisation pathway, the protocol designed by Ward allows to place a metal atom in a defined chiral environment, even if the analogous complex with monodentate ligands would be configurationally labile.[34]

## 6 Applications

It was already pointed out, that the chiral acyl iron complexes of type **5** were successfully employed as chiral auxiliaries in quite a number of organic reactions including alkylations, aldol type reactions and Michael additions. The same is true for the chiral cationic molybdenum allyl complexes **8**, which were used to generate chiral olefins *via* nucleophilic attack (*vide supra*). While these two examples feature half-sandwich complexes in stoichiometric reactions, some applications in catalytic reactions are currently emerging.

Cationic chiral-at-metal complexes with one labile ligand have found applications as chiral Lewis-acids for a couple of organic reactions. It is assumed, that activation and stereocontrol is achieved by coordination of one of the reactants to the metal, thereby placing it in a proper orientation for the subsequent stereoselective reaction. For example, the Cp complexes **55**, bearing chiral P,P-chelate ligands, were successfully used as Lewis-acids in enantioselective Diels–Alder-reactions and 1,3-dipolar cycloadditions. [Fig. 25] Note that the

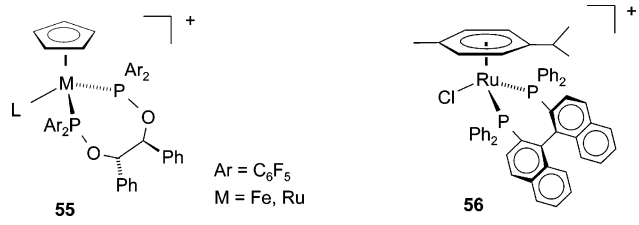


**Fig. 25**

metal atom in these compounds is chirotopic but non stereogenic, as due to the $C_2$ symmetry of the free ligand only one diastereomeric complex can form.[35]

It is interesting to compare the different performance of the related cationic (cymene)RuCl complexes **24** and **56**, bearing the ligands binap and its monoxide binapO in enantioselective

Diels–Alder reactions. [Figs. 12 and 25] While with the $C_2$ symmetric binap ligand the enantioselectivity did not exceed a value of 50% ee, values as high as 99% ee were obtained with the unsymmetrical bisphosphine monoxide **22**. With the two ligands being of comparable steric properties, the different performance was rationalized on the basis of an electronic asymmetry arising from the P,O *versus* P,P coordination mode.[18]

Noyori has developed (arene)Ru half-sandwich complexes of type **57** with N,N- or N,O-chelate ligands for the enantioselective transfer hydrogenation of ketones to secondary alcohols and some of the involved complex species could be isolated and characterized.[36] [Fig. 26] When chiral-at-metal complexes act

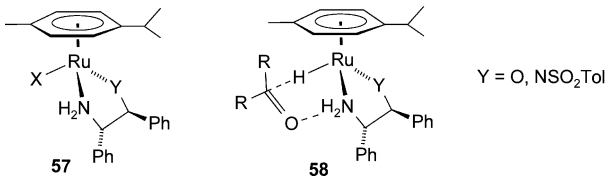



**Fig. 26**

as Lewis-acid catalysts as described in the preceding paragraph, a substrate molecule coordinates to the stereogenic metal centre in the course of the catalytic cycle. In contrast, in the case of the Ru catalysed transfer hydrogenation, the carbonyl substrate does not directly bind to the metal atom in any stage of the reaction. Instead, the ketone just approaches the coordination sphere of the metal, and two hydrogen atoms are subsequently transferred from Ru and N, respectively, to the CO double bond (**58**).

A series of Cp*Ru half-sandwich complexes with a number of chiral N,N chelate ligands was shown to be active in the enantioselective hydrogenation of ketones in $^{i}$PrOH with up to 95% ee and complexes such as **59** were suggested as intermediates in the catalytic cycle. [Fig. 27] However, no

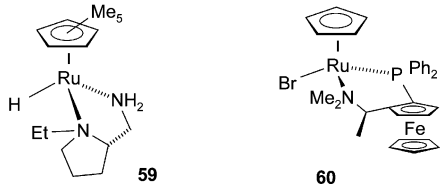



**Fig. 27**

transfer hydrogenation occurs with this system and the use of $H_2$ is required. It was proposed, that the alcohol assists in the cleavage of a metal bound $H_2$ molecule *via* hydrogen bonding.[37] On the other hand, Kirchner reported a high catalytic activity of the (cymene)Ru complex **25** and the related Cp derivative **60** in the transfer hydrogenation of ketones in $^{i}$PrOH, which did not require the use of molecular hydrogen.[19] Notably, although the chiral-at-metal complexes **25** and **60** formed with high diastereomeric ratios, only racemic alcohols were obtained in the catalytic reduction of prochiral ketones. This was attributed to a hemilabile coordination of the P,N ligand, leading to monodentate κ-P-bonded species of high stereochemical flexibility.

CpRu half-sandwich complexes have also found application as catalysts in allylic substitution reactions. For example, CpRu(COD)Cl was used as a precursor for the reaction of cyclic allyl carbonates with N-nucleophiles.[38] Similarly, the solvent complex $[Cp^*Ru(MeCN)_3]^+$ with three labile acetonitrile ligands acted as catalyst in the substitution of unsymmetrical allyl substrates with high regioselectivity, and retention of configuration was observed in the case of chiral allylic substrates.[39] In the two examples mentioned above, achiral complexes were used as catalysts and therefore the stereochemical course of the reaction could be controlled only by the use of a chiral substrate. In contrast, the chiral bis(acetonitrile) complex **46** with a tethered P-donor accomplished the substitution of 1,3-diphenyl allyl carbonate with N and C nucleophiles with moderate to high enantioselectivities.[40]

An interesting C–C bond forming reaction was developed by Trost. [Fig. 28] In this reconstitutive addition, a terminal

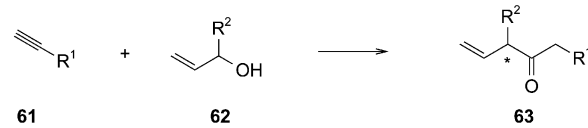



**Fig. 28**

acetylene **61** is coupled with a secondary allylic alcohol **62** in the coordination sphere of a half-sandwich Ru complex and the overall sequence involves the formation of a vinylidene species, which converts to an ($\eta^3$-allyl)Ru acyl complex after attack of the allylic alcohol. The configuration of the stereogenic centre in the organic product **63**, which is finally released from the Ru atom, could be controlled by using chiral Ru half-sandwich complexes like **41** and related species and ee values up to 50% ee were obtained for a product of type **63**.[28]

## 7 Conclusion and outlook

Organometallic chiral-at-metal half-sandwich complexes continue to be interesting subjects of current research. This article summarized the developments in this field from the early examples to most recent aspects. A number of strategies was presented that allow, at least partially, the control of the metal configuration by making use of a chiral auxiliary leading to the formation of diastereomeric complexes. The configurational stability of complexes with stereogenic metal atoms differs tremendously and examples were shown both for highly labile systems that epimerise rapidly, and robust complexes which retain their stereochemical integrity under harsh conditions over a period of time, long enough to allow for their isolation. Some applications of chiral half-sandwich complexes were presented, including both, stoichiometric as well as catalytic reactions. The increasing number of papers in the most recent literature that deal especially with catalytic applications can be taken as a promising sign for interesting future developments in this field.

## 8 Acknowledgements

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