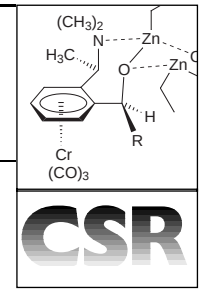
Planar chiral arene chromium(0) complexes: potential ligands for asymmetric catalysis



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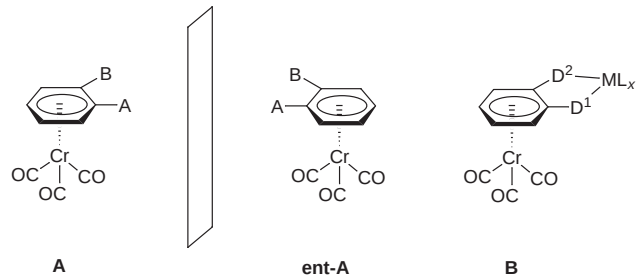
Planar chiral (η⁶-arene) tricarbonyl chromium(0) complexes are well-studied compounds in synthetic organic chemistry. However, the number of investigations concerned with their application in asymmetric catalysis is rather low. This review aims to summarise the main approaches toward the stereoselective synthesis of planar chiral derivatives of (η⁶-benzene) tricarbonyl chromium(0) and to present recent applications of such complexes as ligands in enantioselective catalytic processes.

1 Introduction

The first aimed synthesis of (η⁶-benzene) tricarbonyl chromium(0) from benzene and hexacarbonyl chromium(0) was achieved in 1958 by Natta.[1] The general structure of such compounds is a characteristic half-sandwich complex in which the six π-electrons of the arene are bound to the central chromium atom in a η⁶-fashion. The remaining three carbonyl ligands are coordinated in such a way that the molecule's overall structure is pseudo tetrahedral. Such arrangement has been compared to a 'three leg piano stool'.

For various reasons, these complexes have found general synthetic interest: their preparation is mostly easier than the synthesis of the related cyclopentadienyl transition metal complexes, the products are usually crystalline which makes them easy to purify, and as a consequence of the metal complexation of the arene several transformations become feasible which cannot be carried out on the metal-free arene ring.[2,3] Furthermore, both the chromophoric character of the complexes and the characteristic proton NMR shifts of the hydrogen atoms of the complexed arenes allow an unambiguous detection of such complexes and, among other things, have made them suitable markers in bioorganometallic chemistry.[4]

It was the fact that those derivatives which bear an unsymmetrically 1,2- or 1,3-disubstituted arene ligand are no longer superimposable with their mirror image that made them interesting for modern organometallic chemistry. Enantiomers like **A** and **ent-A** have been termed *planar chiral compounds*.[5,6]



The stereochemical descriptor for an element of planar chirality is usually determined following the rules introduced by Schlögl:[7] the arene ring is monitored from that side which is not

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Kilian Muñiz, born in 1970, studied chemistry at Universität Hannover (Germany) and at Imperial College, London (UK). In 1996, he completed his Diploma (Universität Hannover) with a research project on Fischer carbene complexes at Universidad de Oviedo (Spain) under the joint guidance of Professor J. Barluenga and Professor H. M. R. Hoffmann. Currently, he is working on his PhD in the group of Professor C. Bolm at RWTH Aachen (Germany). His research interests are in the area of transition metal chemistry, mainly in the synthesis of enantiomerically pure organometallic compounds and their application in asymmetric transformations.

Kilian Muñiz

coordinated to the chromium moiety. The priority of the substituents is then determined employing the Cahn–Ingold–Prelog (CIP) rules. If the shortest path from the substituent displaying highest priority to the following one is clockwise, the absolute configuration is denoted as *R*p, and the opposite case is referred to as *S*p. For example, if one imagines a priority order for the two substituents of complex **A** as A > B, the absolute planar chirality is *S*p. There exists also a different procedure for the stereochemical assignment consisting of an extension of the CIP system which results in opposite planar chiral descriptors.[6] Throughout this text, we shall employ the original rules by Schlögl.

Chromium complexes of planar chirality have extensively been applied as stoichiometric auxiliaries and/or suitable starting materials for asymmetric synthesis of biologically interesting substances.[3,8] An aspect that so far has not been exploited in detail is the use of those arene complexes that display two donor functionalities D^1 and D^2 and, when complexed to other transition metals, are thereby able to serve as bidentate ligands in organometallic complexes of the general type **B**.

In order to determine the *status quo* of such complexes in asymmetric catalysis, we will first describe general synthetic routes toward optically active 1,2-disubstituted (η^6-**a**rene) **c**hromium **t**ricarbonyl **c**omplexes (hereafter referred to as 'ACTCs') and then present an overview on their application in catalytic processes.

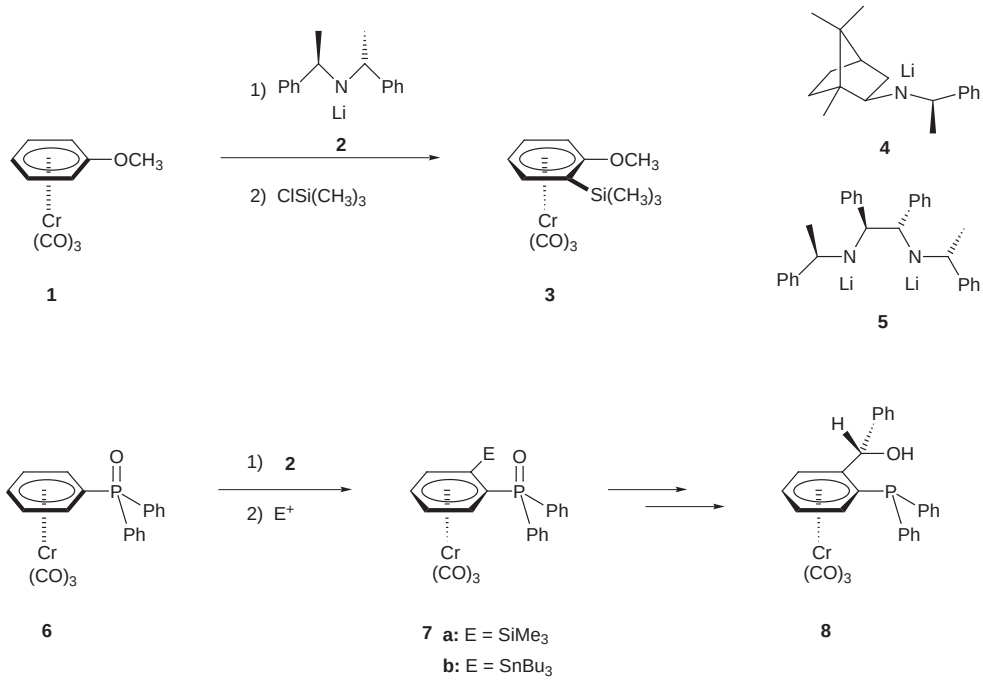
2 General synthetic routes

The use of chiral compounds as stoichiometric or substoichiometric auxiliaries requires extensive knowledge of efficient routes for their preparation. Generally, two different approaches toward optically active ACTCs can be distinguished which consist of the use of either external or internal chiral auxiliaries leading to enantiomeric or diastereomeric products, respectively. In this review the synthesis of the former will be discussed first. Attention will only be paid to those reactions that give direct access to such complexes in a stereoselective manner, thus excluding all kinds of enzymatic or chemical resolutions.

An elegant example of an external chiral auxiliary approach is based on the use of C_2-symmetric lithium amide bases such as **2** (Scheme 1).[9] It is assumed that prior to the lithiation a precoordination of the lithium amide to the methoxy substituent enables a highly selective differentiation between the two enantiotopic hydrogen atoms *ortho* to the methoxy group of complex **1**. This method is restricted in the sense that only certain donor functionalities are tolerated as substituents in the starting material, but anisole complexes like **1** give the corresponding 2-functionalised products **3** with very high enantioselectivities.

ACTC **3** can be further functionalised by a second lithiation at the remaining *ortho*-position followed by reaction with electrophiles like aldehydes giving rise to potential bidentate compounds. It should also be pointed out that **3** has emerged as a suitable starting material for the synthesis of natural products like (+)-ptilocaulin.[10] A related study was reported for the *N*,*N*-diisopropylcarbamate of tricarbonyl (η^6-phenol) chromium(0). In this case, chiral lithium base **4** proved slightly superior to **2** and various *ortho*-substituted products with enantioselectivities in the range of 64–73% ee were obtained.[11] When DMF was used as electrophile, a single recrystallisation of the resulting product led to a significant increase of the enantiomeric excess (95%).

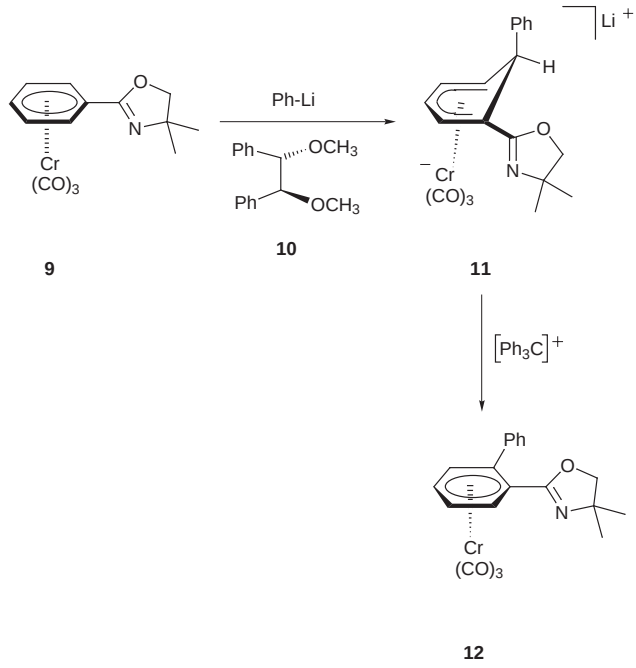
The fact that such functionalisation is not necessarily restricted to aromatic positions was shown for the chromium complex of isobenzofuran. When chiral base **5** was employed, deprotonation of this prochiral substrate was found to be highly selective, giving, after quenching with appropriate electrophiles, the (*R*,*R*p)-configuration products in up to 99% ee.[9] Here, chiral base **2** was less effective, leading to a product with 73% ee only. An interesting further extension has been described for ACTC **6**. Stereoselective deprotonation employing **2** as chiral base allowed the synthesis of the planar chiral derivatives **7a**,**b** in high yields and with enantiomeric excesses of up to 73%. For the present case, it is noteworthy that product **7a** has an *S*p configuration which is opposite to the *R*p configuration obtained for the functionalisation of **1**. Further modification of **7b** enabled the synthesis of complexes like **8** which by recrystallisation was obtained in nearly enantiomerically pure form (95% ee).[12] Due to its hydroxy functionality and phosphino group, **8** can be expected to be an interesting ligand precursor in future asymmetric processes.



1 **2** **3** **4** **5** **6** **7** **a:** E = $SiMe_3$ **b:** E = $SnBu_3$ **8**

Scheme 1

Another enantioselective synthesis of planar chiral complexes is a singular sequence which is based on a tandem reaction of nucleophilic addition and hydride abstraction.[13] This approach is limited to those arene chromium complexes which bear strong acceptor substituents like imines, hydrazones or oxazolines. By virtue of its relatively low electron density the aromatic ring is accessible for regioselective nucleophilic addition at the *ortho*-position. The mechanism is believed to be initiated by precoordination of the lithium species to the external chiral ligand **10**. A subsequent nucleophilic addition of this chirally modified lithium reagent to the arene occurs with an efficient stereodifferentiation between the two enantiotopic *ortho*-carbons of **9** to give the intermediary η^5-cyclohexadienyl complex **11**. This complex can either react further with electrophiles to yield chiral cyclohexadienes or, as is of interest in the present case, can be oxidised by hydride abstraction to yield the planar chiral arene complex **12** (Scheme 2). Following



9 **10** **11** **12**

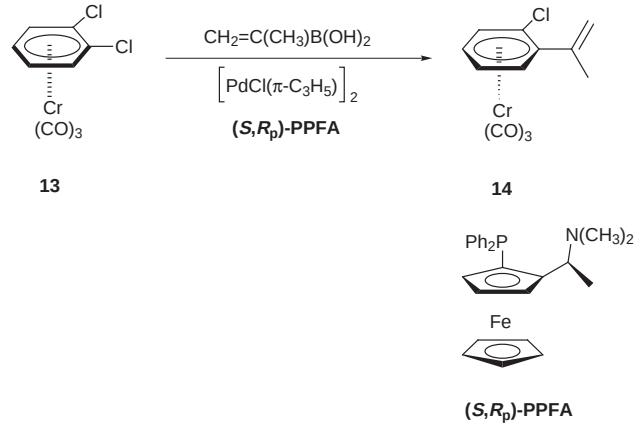
Scheme 2

this sequence, enantioselectivities of up to 98% ee were obtained for phenyllithium as nucleophile. It should also be mentioned that a diastereoselective version of this sequence is known where a chiral (*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP)-hydrazone was employed as internal auxiliary.[13]

The use of external chiral auxiliaries can be extended further to the application of asymmetric catalysis with chiral ligands. In doing so, planar chiral compounds can be obtained from prochiral precursors like the dichlorobenzene complex **13** (Scheme 3).

Under catalytic conditions using 10 mol% of palladium and 12 mol% of ferrocene (*S*,R_p)-**PPFA**, planar chiral complex **14** is formed in acceptable yield with a moderate enantioselectivity of 44% ee. The same catalytic system was also reported to be suitable for the cross-coupling reaction of **13** with arylboronic acids, although enantioselectivities again remained below 70% ee.[14] On the other hand, a structurally related prochiral ACTC bearing 1,3-dichloro-2-methylbenzene as the arene ligand, gave a coupling product with only 8% ee under these conditions.

Among the other approaches of employing internal chiral auxiliaries which have received much attention, the diastereoselective complexation of chirally modified arenes is one of the most effective ones. An appropriate chromium tricarbonyl precursor is directed by an asymmetric donor group in the side chain of the arene.[8,15] Such groups should effect a precoordination to the chromium moiety and thus enable a substantive differentiation of the two diastereotopic faces of the arene ring. This principle has widely been used in the synthesis of planar chiral arene complexes bearing benzylic alkoxy functionalities.[8]

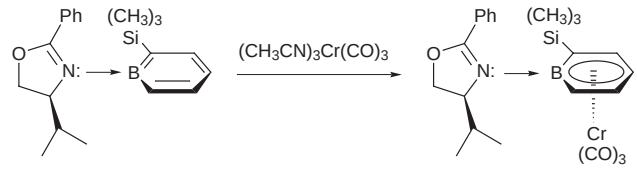


13 **14** **(*S*,R_p)-PPFA**

Scheme 3

Since most of these complexations are carried out under relatively harsh thermal conditions in order to allow the substitution of three carbonyls by the arene ring, equilibration can take place resulting in the formation of diastereomeric mixtures. As a consequence of the demand for milder reaction conditions, tricarbonyl(η^6-naphthalene)chromium(0) ('Kündig's reagent') has emerged as a suitable chromium tricarbonyl precursor:[3,8] this complex is known to be relatively labile because of a possible ring slippage *via* $\eta^6 \rightarrow \eta^4$ coordination. This process creates a free coordination site at the resulting unsaturated 16 e-chromium centre and allows a selective coordination of the incoming arene upon further displacement of the naphthalene.

An interesting complementary approach was recently reported for an optically active Lewis acid complex (Scheme 4):



15 **16**

Scheme 4

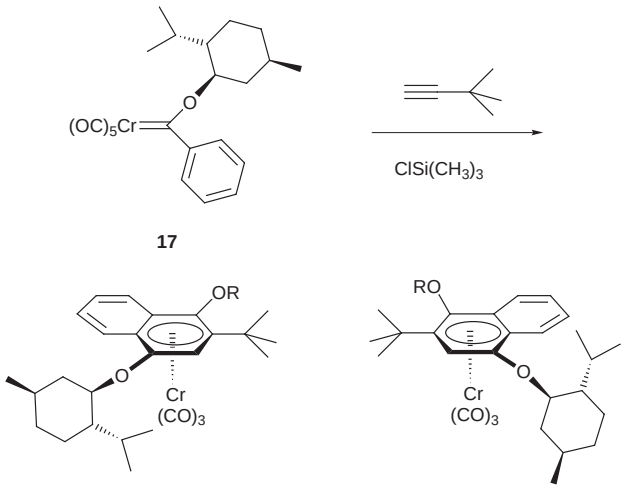
2-trimethylsilylborabenzene was coordinated to an enantiomerically pure 2-phenyloxazoline derived from (*S*)-leucinol affording the atropisomeric Lewis acid–base adduct **15**. Complexation of the borabenzene's π-system onto the chromium tricarbonyl fragment proved to be completely chemoselective and resulted in the formation of the planar chiral Lewis acid complex **16** as a single diastereoisomer.[16] To date, this example represents the only enantiopure planar chiral (η^6-arene) chromium tricarbonyl complex derived from a heteroarene.

An alternative route that does not rely on the complexation of an existing pre-manufactured arene ring onto the chromium tricarbonyl moiety is based on a benzannulation reaction of Fischer carbene complexes. In this procedure, which is also known as the 'Dötz reaction', an α,β-unsaturated carbene, an alkyne, and one molecule of carbon monoxide undergo a formal [3 + 2 + 1]-reaction within the coordination sphere of the metal to yield the arene ligand.

In the synthesis of planar chiral compounds, this approach is unique in the sense that only Fischer carbene complexes of pentacarbonylchromium(0) yield those products in which the metal is attached to the resulting arene group.

Diastereoselective Dötz reactions have been described for three possible routes: a first report in 1994 introduced a sequence based on achiral chromium carbene complexes.[17] Here, the stereochemical course of the reaction was governed by sterically demanding α-chiral propargylic (prop-2-ynylic) ethers and led to high diastereoselectivities of up to 92% de.

A more general approach is given for the use of those Fischer carbene complexes bearing chiral substituents like, for example, chiral pool derived alkoxy groups. For the reaction of the (−)-menthoxy carbene complex **17** with *tert*-butylacetylene, a 10:1 ratio of the two resulting diastereoisomers **18a** and **18b** was reported (Scheme 5).[18]



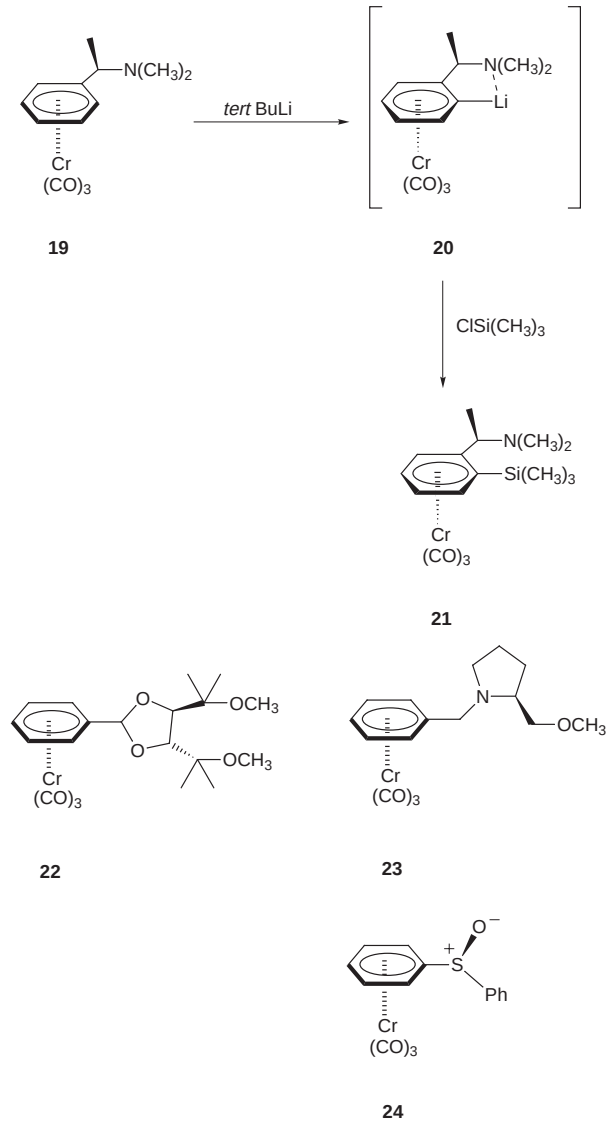
Scheme 5

It was suggested[19] that an *E*/*Z*-isomerisation due to rotation around the carbene carbon–oxygen bond would prevent the formation of an even more selective arrangement during the first two steps of the benzannulation. Indeed, complete diastereoselection was never observed.

In a complementary approach a series of chiral cyclohexenyl carbene complexes of chromium was submitted to a benzannulation.[19] Again, diastereoselectivities remained below 90% and although a detailed discussion based on kinetic studies and theoretical calculations was made, the exact stereochemical course of the Dötz reaction still remains to be further elucidated in order to allow the achievement of complete stereoselection.

Most approaches for the synthesis of planar chiral ACTCs still rely on diastereoselective transformations and use the directing power of internal chiral auxiliaries. Thus, enantiomerically pure substituents are capable of directing a base to selectively remove one of the two diastereotopic hydrogens in the *ortho*-position to create the element of planar chirality. This process is generally termed *directed ortho-metalation*[20] and it is closely related to the one discussed above for the use of chiral bases which were employed to differentiate the deprotonation of enantiotopic hydrogens. Most suitable *ortho*-directing groups consist of saturated oxygen or nitrogen functionalities like tertiary amines, ethers or acetals which all display free electron pairs. Hard Lewis acids of this type have been proved to be very efficient for precoordinating and selectively directing the incoming alkyllithium base. Thus, a diastereomerically pure lithiated intermediate is generated which upon quenching with electrophiles yields the 1,2-disubstituted arene chromium complexes displaying a plane of chirality.

Originally, this concept had been developed for the synthesis of optically pure ferrocene derivatives like PPFA, but was adapted successfully to the chemistry of ACTCs by the group of Davies and others: starting complex **19** is easily accessible from commercially available α-phenylethylamine by the Eschweiler–Clarke reaction followed by simple complexation with hexacarbonylchromium(0). This synthesis is even more convenient than the one for the corresponding *N*,*N*-dimethyl-α-ferrocenylethylamine which involves a resolution step. Selective deprotonation of ACTC **19** is then accomplished by means of *tert*-BuLi at low temperature resulting in the formation of lithiated intermediate **20**. The observed stereoselectivity has been explained by the assumption that during the deprotonation the most favourable conformation is obtained for a transition state of minimized steric interaction in which the benzylic methyl group points away from the bulky chromium tricarbonyl moiety below the aromatic plane (Scheme 6).



Scheme 6

Subsequent treatment of **20** with electrophiles like TMSCl yields planar chiral ACTC **21** as a single diastereoisomer.[21]

A related system was presented for the chromium complexes of *N*,*O*-dimethylephedrine and *N*,*O*-dimethylpseudoephedrine.[22] Again, complete diastereoselection was reported assuming the high stereoselectivity to derive from a favourable *N*,*O*-chelatisation of the metal in the lithiated intermediate.

Another example for an ACTC bearing an *ortho*-directing group is given with tartrate derived acetal **22** which undergoes *ortho*-functionalisation with up to 94% de.[23] Several similar systems are known that are formally all based on chiral pool derived acetals of the chromium complex of benzaldehyde.[24]

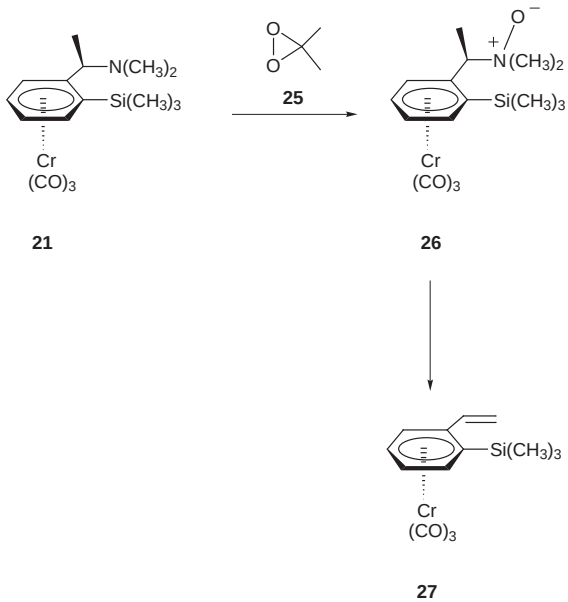
We have recently reported on the use of chromium complex **23** prepared from benzylated SMP.[25] Here, the reaction is

assumed to proceed *via* an intermediate lithium species in which the metal is coordinated to both the amine and the oxygen of the alkoxy group giving rise to a highly favoured chelate structure. Consequently, diastereoselectivities of up to 97% de have been achieved in reactions with a variety of electrophiles.

It was further demonstrated from the use of sulfoxide derived ACTC **24** that the stereogenic centre of the *ortho*-directing group need not necessarily be a chiral carbon atom. Again, diastereomeric excesses were excellent with up to 99% de. Interestingly, upon using 2.5 equivalents of base, both *ortho*-hydrogen atoms can be removed and subsequent treatment with an electrophile now furnishes the second diastereoisomer with opposite planar chirality. This can be explained by the assumption that the second lithiation on the remaining, originally less favoured *ortho*-position yields a non-chelated aryllithium which then undergoes a faster reaction with the electrophile. To date, these sequences represent the only examples for a directed *ortho*-metalation in which both diastereoisomers can be obtained selectively by simple control of the amounts of base added.[26]

Having generated the element of planar chirality *via* diastereoselective processes with the help of internal control, one can further manipulate the resulting diastereomeric products. For instance, removal of the original chiral *ortho*-directing group leaves an enantiomeric arene chromium complex with only planar chirality. This goal has been found to be of particular difficulty. Thus, in most cases, the removal of chiral diols from their respective acetals was not successful, particularly when compounds with *ortho*-substituents other than TMS or methyl had been prepared.[23,24]

An elegant procedure for the mild removal of a tertiary amino group was reported by Gibson, née Thomas.[27] In the presence of dimethyldioxirane (**25**), amine complexes like **21** are smoothly converted into their corresponding *N*-oxides at low temperature which, upon warming, undergo a Cope elimination (Scheme 7).



21 **26** **27**

Scheme 7

The resulting enantiopure *ortho*-substituted styrene complexes like **27** can then be transformed further.

For the present discussion in this review, however, it is usually more interesting to maintain the former *ortho*-directing group as a potential donor atom for coordination of transition metals. This approach has been pursued for those *ortho*-directing groups based on amines like **19** or **23**. We have recently shown that **23** is a suitable starting material for the synthesis of a series of potential ligands and ligand precursors bearing both the heteroatoms of the SMP moiety combined with phosphino or hydroxy groups created in the *ortho*-functionalisation step.[25]

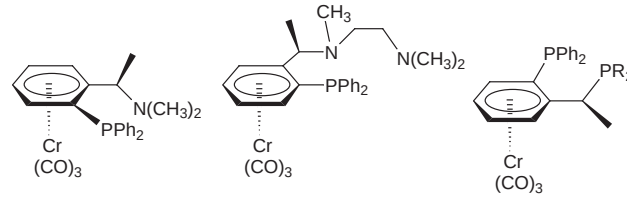
3 Catalyses

While the use of achiral ACTCs in catalytic hydrogenation and isomerisation reactions is well-studied,[28] planar chiral derivatives for asymmetric catalysis have so far received only scant attention. This is even more surprising taking into account their structural relationship to the great number of successfully employed ferrocene ligands.

It is evident that due to their structural properties ACTCs cannot serve as ligands in oxidation chemistry since under normal oxidative conditions decomposition of the complex will take place. However, they have been employed in the two other areas of asymmetric catalysis, C–C-bond formation and multiple bond reduction.

In the area of C–C-bond formation, two palladium catalysed processes involving planar chiral diastereomerically pure ACTCs are known: asymmetric cross couplings and nucleophilic substitutions.

For the purpose of an efficient coordination to palladium, four bidentate ACTCs have been synthesised: complex **28**



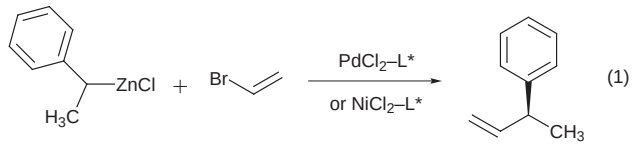
28 **29**

30 **a:** R = Ph
b: R = C_6H_{11}

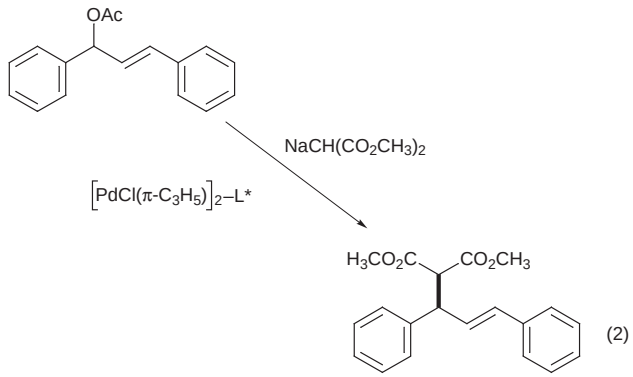
represents a derivative of **19** and was obtained *via* the above described *ortho*-functionalisation.[29] Diaminophosphine **29** was prepared in an analogous manner using (*R*)-*N*,*N*,*N'*-trimethyl-*N'*-(α-phenylethyl)ethylenediamine as starting material.[30] ACTCs **30a,b** were synthesised similarly starting from the chromium complexes of (*S*)-α-phenylethyl methoxymethyl ether followed by a two step sequence of diastereoselective *ortho*-phosphorylation and nucleophilic displacement at the benzylic position.[30]

Using **28** as the ligand in palladium catalysed cross-coupling reactions between 1-phenylethyl zinc chloride and vinyl bromide [eqn. (1)] the coupling product was generated with an enantiomeric excess of up to 61%. Enantioselectivities were lower for the corresponding magnesium reagent and for the use of 2-phenylvinyl bromide. Alternatively, nickel(II) chloride could be used as the metal source and the complex was then generated *in situ*, albeit without achieving a change in enantioselectivity (61% ee) and by getting slightly lower chemical yields.[29]

Another well-studied reaction which relies on palladium catalysis, the Tsuji–Trost reaction, consists of an allylic alkylation *via* nucleophilic displacement. Here, complexes **29** and **30a** were employed as ligands and, again, the catalytically active species was formed *in situ*.[30] For the standard system, the reaction of 1,3-diphenylacetoxypropene with sodium dimethyl malonate, an enantiomeric excess of 94% in favour of the (*S*)-enantiomer was achieved with **29** [eqn. (2)]. Under the same conditions, catalysis relying on ligand **30a** led to a moderate ee of only 61%, and the reaction needed to be carried out at a much lower temperature (−78 °C) in order to obtain at least 86% ee. Due to the change in absolute configuration of ligand **29** compared to **30** the product now was of *R*-configuration.



(1)



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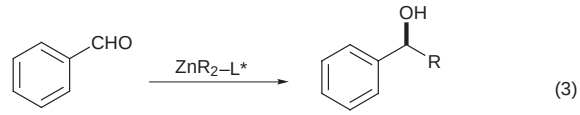

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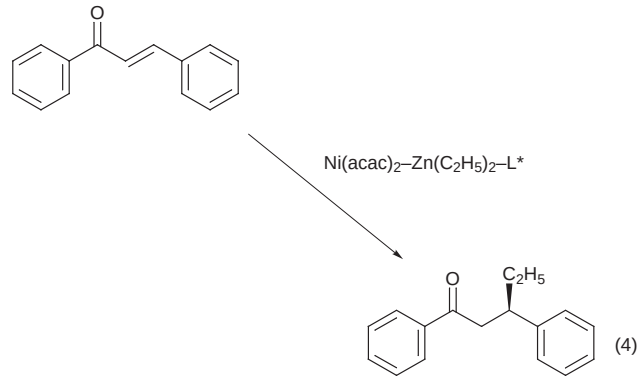
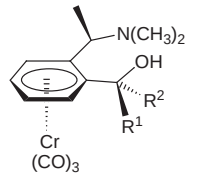
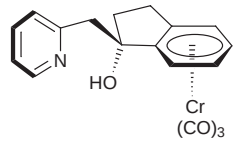


(4)

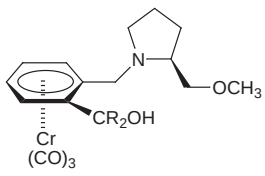
In a different reaction for the formation of C–C bonds, aldehydes can be converted into chiral secondary alcohols by means of dialkylzinc reagents in the presence of substoichiometric amounts of suitable ligands. For this type of catalysis three structurally related catalyst precursors have been described: a whole series of these compounds could again be obtained from ACTC **19** *via* an *ortho*-functionalisation using ketones or aldehydes as electrophiles to give **31a–c** and **31d**,**e**,





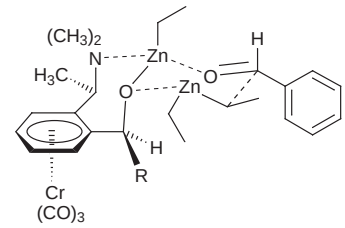
31 **a:** R^1, R^2 = H
b: R^1, R^2 = Et
c: R^1, R^2 = Ph
d: R^1 = Et, R^2 = H
e: R^1= Ph, R^2 = H

32



33 **a:** R = H
b: R = Ph

respectively.[31] For the latter case, the creation of the new stereocentre at the benzylic position was reported to be highly selective yielding diastereomerically pure compounds. In the diethylzinc addition to benzaldehyde [eqn. (3); R = Et), 5 mol% of ACTCs **31b** or **c** led to the formation of (*S*)-1-phenylpropanol with very high enantioselectivities. On the other hand, the hydroxymethyl compound **31a**, that lacks sterically demanding substituents in the benzylic position, led to only 15% ee. Introduction of additional stereocenters in the benzylic position was found to have no beneficial effect and the enantiomeric excesses of products from catalyses with ACTCs **31d** and **e** were identical or slightly lower. However, a change of absolute configuration at this stereogenic centre from (*S*) to (*R*) resulted in a dramatic decrease in enantioselectivity. Switching planar chirality by the use of a complex in which the chromium moiety was attached to the other face of the arene ring than in **31b** also decreased the enantiomeric excess of the catalysis product (29% ee). Thus, it has to be concluded that in order to achieve excellent enantioselectivities an efficient internal cooperation of all stereoelements of the ligand is essential. For the present system, ACTC **31b** evidently displays an optimum combination of planar and central chirality, and a transition state **C** was proposed containing seven- and six-membered chelate rings.



C

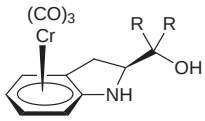
A different ligand type was presented with ACTC **32**.[32] This complex was derived from the enantiopure chromium complex of indan-1-one and its synthesis involved a nucleophilic addition of 2-(lithiomethyl)pyridine to the carbonyl function. In a similar manner, three other structurally related complexes were synthesised. Amongst the four different ligands, complex **32** performed best, yielding (*S*)-1-phenylpropanol with 70% ee from the reaction of benzaldehyde with diethylzinc [eqn. (3); R = Et]. It is noteworthy that a dramatic effect was observed when the uncomplexed ligands were employed. In the case of **32**, the arene ligand alone catalysed the formation of a product with only 10% ee.

Finally, ACTCs **33a,b** were obtained from **23** as described above.[25] They were employed in the asymmetric addition of dimethyl or diethylzinc to benzaldehyde [eqn. (3); R = Me or Et], and ferrocenecarbaldehyde. Catalyst loading had to be 10 mol% in order to obtain acceptable conversion and enantioselectivities (ee_{max}: 86%). It was observed that complex **33b** performed much better than **33a**, which is in accord with the observation made for the series of ACTCs **31**.[31]

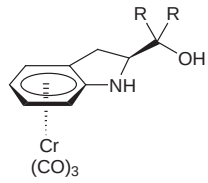
A related catalytic reaction is the nickel catalysed asymmetric conjugate addition of dialkylzincs to Michael acceptors such as chalcones [eqn. (4)]. For this purpose, ACTC **31e** performed best. Using 5 mol% of nickel salt and a high ligand loading of

50 mol%, the product was obtained in 90% chemical yield having an enantiomeric excess of 62%. However, these figures imply that this catalytic system is rather ineffective. Even when both the nickel salt and the ligand precursor were used in stoichiometric quantities, an ee of only 78% was obtained.[31]

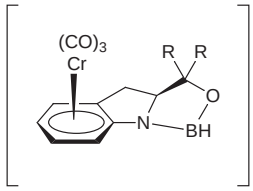
For asymmetric catalytic reductions, two different approaches are known. The first is based on borane mediated hydrogen transfer and has been extensively investigated. ACTCs **34a,b** and **35a,b** are readily prepared starting with a



34 a: R = H
b: R = Me

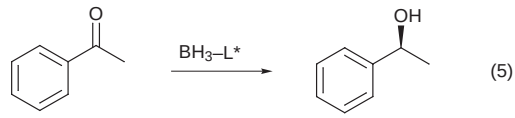


35 a: R = H
b: R = Me

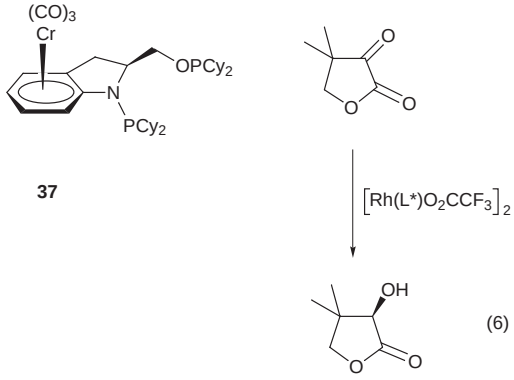


36 a: R = H
b: R = Me

complexation of (*S*)-indoline-2-carboxylic acid with the chromium tricarbonyl fragment followed by hydride reduction or alkyl addition to the resulting complex to give the final amino alcohols.[33] When treated with a solution of borane in THF a catalyst like **36** is proposed to be formed**.** With 10 mol% of BH_3–oxazaborolidine catalyst **36a**, an enantiomeric excess of 50% was obtained in the reduction of acetophenone [eqn. (5)].



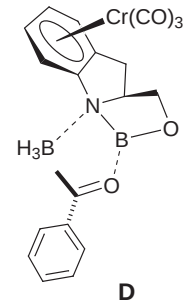
(5)



37

(6)

Use of a bulkier substrate like 9-acetylphenanthrene led to a rise in enantioselectivity (62% ee). However, acceptable enantiomeric excesses could only be obtained with stoichiometric amounts of **34**. For the reduction of acetophenone, it was further found that catalyst precursor **35a** with opposite (*S*p)-planar chirality but identical central chirality gave a significantly lower enantioselectivity (25% ee). Relating this drop in ee to the change from (*R*p)- to (*S*p)-configuration suggests an internal mismatched case of stereoelements for (*S*,*S*p)-**35a**. Interestingly, for the other two diastereomers **34b** and **35b**, which in their side chains bear two additional methyl groups, the reaction outcome was found to be the reverse. Here, a higher enantiomeric excess was obtained in catalyses with the diastereomer having (*S*p)-configuration (39% ee for ACTC **35b** compared to 20% ee for **34b**). All these results have been explained by an assumed transition state **D** which is depicted for ACTC **34a** representing the most efficient catalyst precursor



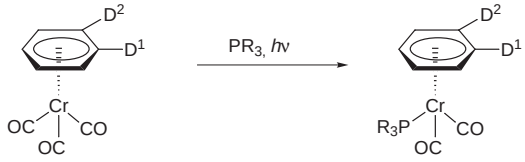
D

within this set. In **D**, the bulky tricarbonylchromium(0) moiety enables an appropriate distinction between the methyl and the phenyl group by minimising steric interactions with the carbonyl ligands after coordination of acetophenone and borane onto the oxazaborolidine catalyst. For ACTC **35a**, the chromium moiety is located on the opposite side of the arene leading to a lower selectivity in the coordination step. For the other pair of diastereomers, it was suggested that in the case of **34b** the additional two methyl groups would cause unfavourable interactions with the chromium moiety leading to a highly strained overall complex. Thus, **35b** which does not suffer from such interactions is a better catalyst precursor.

Another catalytic reaction, where ACTCs have been used, is the carbonyl reduction with molecular hydrogen catalysed by a complex derived from a ligand, bearing a phosphite and a phosphinite group, and rhodium salts. Ligand **37** was obtained by conversion of **34a** into the corresponding diphosphine derivative.[34] Interestingly, the analoguous complex bearing two diphenylphosphinite groups could not be synthesised since conversion stopped after generation of the aminophosphinite. ACTC **37** was employed as ligand for an *in situ* complexation to rhodium sources $[Rh(COD)Cl]_2$ and $[Rh(COD)OCOCF_3]_2$. The complex obtained from $[Rh(COD)OCOCF_3]_2$ was used as catalyst for the asymmetric hydrogenation of dihydro-4,4-dimethylfuran-2,3-dione [eqn. (6)] and a product with an enantiomeric excess of > 99% was obtained. Interestingly, the enantiomeric excesses for the two catalysts derived from either ACTC **37** or its uncomplexed arene were found to be equally high indicating that in this case the phosphite/phosphinite structure dominates the course of the catalysis. However, when the substrate was *N*-benzylbenzoylformamide catalysts derived from **37** and the respective Rh(I)-source performed better than the ones prepared from the uncomplexed arene. This indicates that either the additional stereoelement or the electronic change resulting from the complexation has a significant influence on the catalysis.

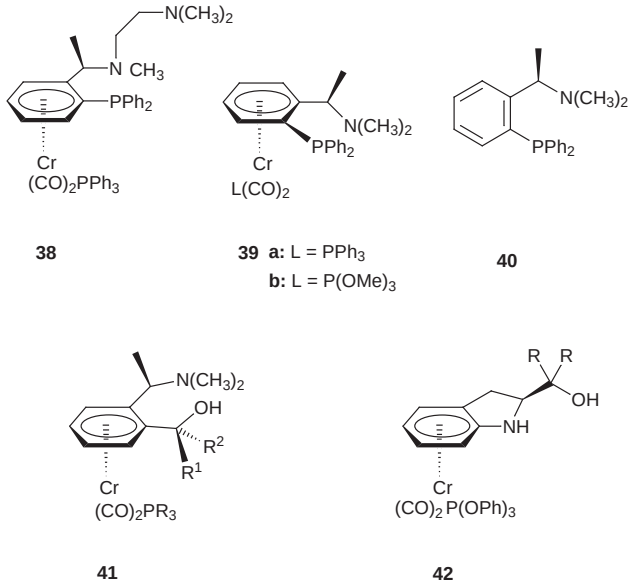
3.1 Further modifications of the catalyst structures

One of the most interesting features of chromium arene complexes relies on the possible electronic and steric tuning by substitution of one of the carbonyl ligands by a different donor molecule, as for example tertiary phosphines (**E**→**F**, Scheme 8). Such an exchange has been carried out on complexes **29**, **28**,



Scheme 8

31b–d, and **34** leading to the corresponding phosphine or phosphite complexes **38**, **39a,b**, **41**, and **42**, respectively. A



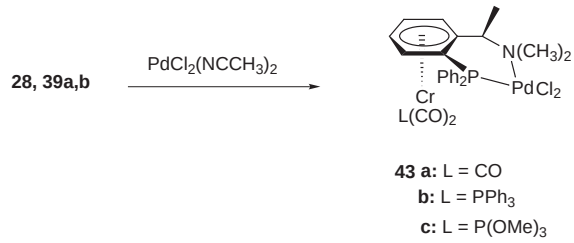
large influence on the electronic properties of the complex as a whole can be expected since phosphorus ligands are weaker π-acceptors than the carbonyl group.[35] As a general consequence the electron density of the arene ligand and thereby the basicity of the diphenylphosphino group should be increased. This assumption is in agreement with the results observed in the catalysed asymmetric Tsuji–Trost alkylation with **38** as ligand, which leads to a product with lower ee compared to the one obtained from a reaction with parent complex **29**. This suggests that by the diminished π-acceptor character of the coordinating phosphino group a less efficient chiral recognition of the enantiotopic carbon centres in the intermediate η^3-allyl complex results.

For the catalytic system derived from **28** the following observations were made: ACTC **28** itself is the best ligand for the asymmetric cross-coupling described above [eqn. (1)] giving the desired product with an enantiomeric excess of 61%. Catalysis with the corresponding uncomplexed arene **40** as ligand yields a product with only 40% ee indicating that either the electronic consequences resulting from the complexation of **40** to the $Cr(CO)_3$ fragment or the additional element of planar chirality have a decisive influence on the reaction outcome. Use of phosphine and phosphinite substituted complexes **39a** and **39b** also affords products with lower enantiomeric excess (37 and 17% ee, respectively).[29] Thus, electronic reasons cannot be solely responsible for the course of the catalysis, since substitution by the weaker π-acceptor PPh_3 leads to a lower decrease in selectivity. It is therefore reasonable to argue that the element of planar chirality has a decisive influence on the catalysis and that the observed differences in the enantiomeric excesses are due to steric interactions to a significant extent.

A positive influence of such a substitution was reported for the diethylzinc addition reactions.[31] Thus, complexes of the general structure **41** were found to be superior to their tricarbonyl parent complexes regardless whether the substitution of the carbonyl was accomplished by PPh_3 or $P(OPh)_3$. This indicates that the additional steric bulk of these ligands rather than the electronic tuning was the reason for this beneficial effect.

Another substitution of this kind was reported for the oxazaborolidine system.[33] Thus, ACTC **42** yielded a product with only 18% ee in the borane mediated reduction of acetophenone. This result was explained assuming disfavoured steric interactions resulting in a partly reverse coordination preference. However, electronic reasons have to be taken into account here also, because an increase of the electron density of the arene will undoubtedly affect the electronic nature of the amine and thereby decrease the Lewis acidity of the whole complex.

While so far a lot of data are available for ferrocene ligands, structural elucidation of the corresponding ACTCs has not been carried out extensively. Moreover, most catalysts and catalyst precursors have been formed *in situ* and no insight into their respective structures has been gained (for example, the catalysts in the alkylzinc and the borane chemistry, the rhodium based hydrogenation catalysts and most complexes involving palladium as the metal centre). The only exceptions are complexes **43a–c** which were obtained from simple complexation of



Scheme 9

palladium(II) chloride with ligands **28** and **39a,b**. Although they were characterised in the usual way, their solid state structures were not reported.[29]

It is even more surprising that there exist only two X-ray crystal structures for ACTCs that have been employed in asymmetric catalysis. Such structural determinations were carried out for **30a**[30] and **31e**.[31]

Finally, with the exception of the NMR data for **43a–c**[29] no investigations on solution structures of chiral catalysts derived from ACTCs have been reported in the literature either.

4 Conclusion

We have presented a brief overview on the most efficient routes for the preparation of optically pure ACTCs. It has been shown that although a variety of different synthetic strategies exists, there is still a need for more general approaches that allow the efficient preparation of a greater number of complexes. Such novel routes must also lead to the development of suitable syntheses of enantiopure ACTCs with sole planar chirality. So far, asymmetric catalyses with such ligands have not been reported.

In contrast, optically active ACTCs with both planar and central chirality have been extensively tested and their capability to serve as ligands for asymmetric transformations has widely been demonstrated. However, we believe that the full potential of such ligands has not been exploited in depth yet. We expect that ACTCs will play a much broader role in the near future. In order to achieve this goal, it will be necessary to study mechanistic details of the catalyses and to pay much more attention to the structural elucidation of respective transition metal complexes in which ACTCs act as (multidentate) ligands.

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