Synthesis of Chiral Ferrocenyl-Substituted β-Amino Cyclopentadienes and Their Complexation to Transition Metals

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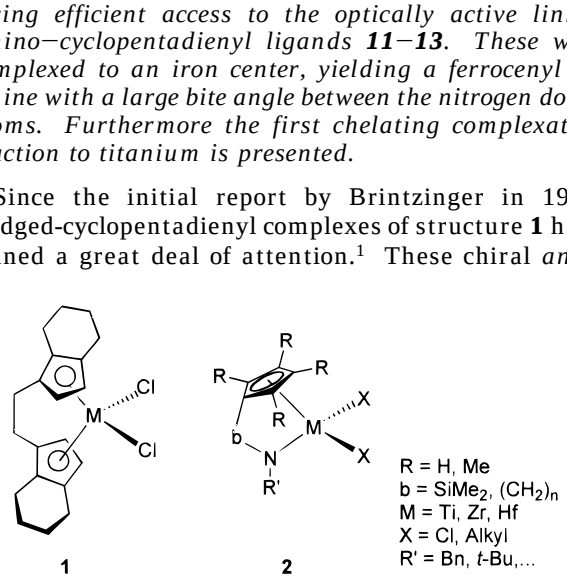
Summary: CBS reduction of the (chloroacyl)ferrocenes ***3*** *provides the chloro alcohols* ***5*** *with ≥98% ee, which upon treatment with cyclopentadienides yield the chiral β- or γ-hydroxy cyclopentadienes* ***6*** *and* ***7****. The hydroxyl function of* ***6*** *and* ***7*** *can be substituted with full retention of configuration by a range of N- or S-nucleophiles, giving efficient access to the optically active linked amino−cyclopentadienyl ligands* ***11*****−****13****. These were complexed to an iron center, yielding a ferrocenyl diamine with a large bite angle between the nitrogen donor atoms. Furthermore the first chelating complexation reaction to titanium is presented.*

Since the initial report by Brintzinger in 1979, bridged-cyclopentadienyl complexes of structure **1** have gained a great deal of attention.[1] These chiral *ansa*-metallocenes have found many applications as catalysts in the stereoregular polymerization of α-olefins as well as in asymmetric hydrogenation and carbomagnesation reactions of double bonds.[2] For all these reactions it is necessary to have diastereomerically and enantiomerically pure complexes available. This is not an easily solved problem, since the complexation of the second cyclopentadienyl moiety of a bis(cyclopentadienyl) ligand with only one of its diastereotopic faces to the central metal is difficult to control.[3] Even if this problem can be adequately addressed, giving the diastereomerically pure *rac*-metallocene, a cumbersome resolution procedure is still needed to access the enantiomerically pure complex.[4] To circumvent these difficulties, several authors developed stereospecific syntheses for *ansa*-metallocenes starting with an elaborated optically active ligand system, which makes a diastereo- and enantioselective complexation possible.[5] However, simpler solutions are still being sought.



1 **2**

The replacement of one cyclopentadienyl ligand in *ansa*-metallocenes by an amido ligand, as depicted in the structures **2**, on the one hand removes the stereochemical problems in the complexation process and on the other hand creates an electronically more unsaturated and sterically more accessible metal center.[6] Recently, such linked amido−cyclopentadienyl complexes have shown their potential as novel catalysts for copolymerizations with ethene.[7] Chiral derivatives have been prepared by utilizing planar chirality on the cyclopentadienyl ring[8] or by introducing the chiral subtituent R′ on the nitrogen atom.[9] Herein we describe the efficient and flexible synthesis of optically active

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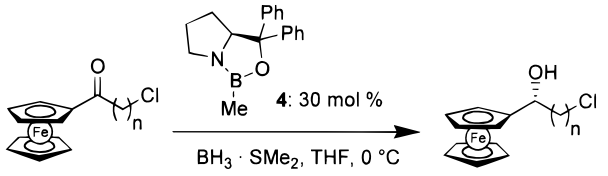
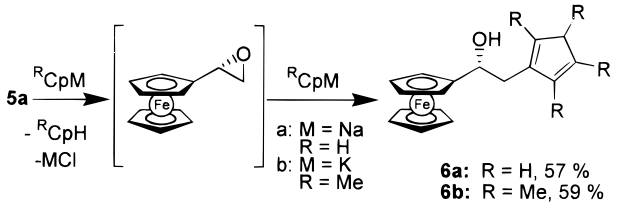
Scheme 1

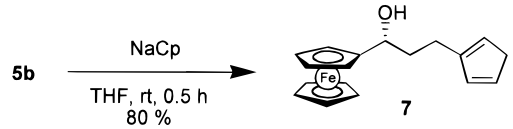


3a: n = 1
3b: n = 2

5a: n = 1, 94 %, 99 % *ee*
5b: n = 2, 91 %, 98 % *ee*

Scheme 2



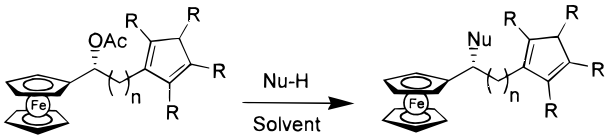


linked amino−cyclopentadienyl ligands with an asymmetric center in the bridge and our initial attempts to coordinate them to transition-metal centers.

The synthesis of the chiral ligands started with a CBS reduction of the chloro-functionalized ferrocenyl ketones **3**, which in turn are easily available by Friedel−Crafts acylation ($Cl(CH_2)_nCOCl$, $AlCl_3$, CH_2Cl_2) of ferrocene.[10] The resulting alcohols **5** were obtained in good yields with selectivities exceeding 98% ee using 30 mol % of the oxazaborolidine **4** as catalyst (Scheme 1).[11]

The alkyl chloride function in **5a** was substituted by an excess of cyclopentadienyl (NaCp, THF, room temperature, 2 days, 57%) and tetramethylcyclopentadienyl anions ($K^{Me}Cp$, THF, 65 °C, 4 h, 59%), respectively. The substitution is not a direct process but involves the initial formation of the corresponding epoxide by HCl elimination. The intermediate epoxide is then opened by the nucleophile, affording the β-hydroxy cyclopentadienes **6** (Scheme 2).[12] In a similar way, direct substitution of the chloride in **5b** could be easily effected (NaCp, THF, room temperature, 0.5 h, 80%), yielding the γ-hydroxy cyclopentadiene **7** with a three-carbon spacing between the potential coordination sites.

Table 1. Substitution of the Cyclopentadienyl-Substituted Ferrocenyl Acetates 9 and 10 by Nitrogen and Sulfur Nucleophiles



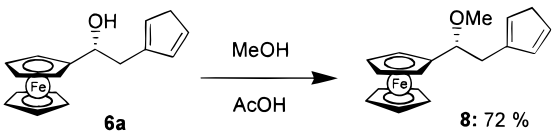
9a: n = 1, R = H
9b: n = 1, R = Me
10: n = 2, R = H

11: n = 1, R = H
12: n = 1, R = Me
13: n = 2, R = H

entry no.	**11−13**	*n*	R	Nu[a]	yield/%
1	**11a**	1	H	N(H)Bn	64
2	**11b**	1	H	N(H)-*t*-Bu	77
3	**11c**	1	H	SMe	32
4	**11d**	1	H	SAc	78
5	**12a**	1	Me	N(H)Bn	42
6	**12b**	1	Me	N(H)-*i*-Pr	45
7	**12c**	1	Me	N(H)-*t*-Bu	33
8	**13a**	2	H	N(H)Me	73
9	**13b**	2	H	N(H)Bn	66
10	**13c**	2	H	N(H)-*i*-Pr	64
11	**13d**	2	H	N(H)-*t*-Bu	49

[a] MeOH/water was used as solvent for the substitution with N-nucleophiles, while acetic acid was used for S-nucleophiles.

The cyclopentadienyl alcohols **6** and **7** may themselves act as ligands for transition metals.[13] However, they proved to be valuable starting materials for further elaboration because the hydroxyl group in a position α to the ferrocenyl moiety can be easily exchanged for other donor functionalities.[14] These derivatization reactions proceed under very mild solvolytic conditions and do not affect the sensitive diene part of the molecule. Thus, substitution by a methoxy group could be achieved by simply stirring **6a** in methanol with some acetic acid as catalyst, affording ligand **8** in 72% yield (eq 1).



(1)

For most purposes it is preferable to activate the hydroxyl function by conversion to the corresponding acetate (Ac_2O, pyridine, room temperature, 12 h, then removal of the volatiles) prior to substitution. The acetates **9** and **10**, which are obtained in quantitative yields, can then be treated with an appropriate nucleophile in the same flask. For example, the acetates **9** and **10** were subjected to reaction with several primary amines (Table 1; entries 1, 2, and 5−11), NaSMe (entry 3), and KSAc (entry 4). Further possible options include

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(12) Two distinguishable H-shift isomers were found for all compounds with an unsubstituted cyclopentadienyl moiety. Up to four isomers could be detected by NMR for the tetramethyl-substituted cyclopentadienes.

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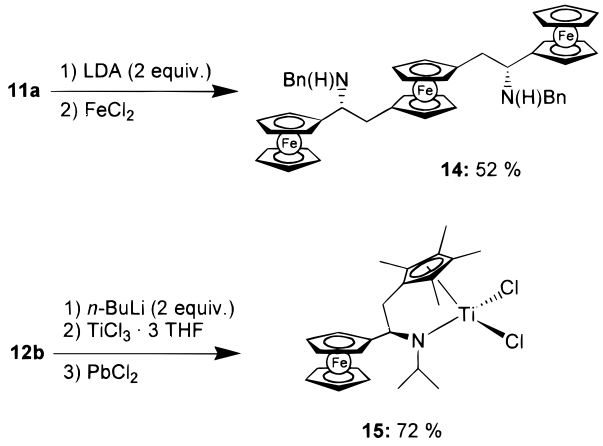
substitution with ammonia, secondary amines, phosphines (*e.g.* R_2PH), and even carbon nucleophiles.[15]

In conclusion, we have developed an efficient enantioselective route to chiral cyclopentadienes with a linked functionality in a β- or γ-position capable of acting as a second coordination site for a given central metal.[16] The synthetic approach is highly flexible because four parameters can be independently varied: (a) the length of the linking carbon chain, (b) the substitution pattern of the cyclopentadienyl moiety, (c) the nature of the donor atom in the bridge, and (d) the substituents on the donor atom.

With the new ligands **11**−**13** in hand, we investigated their suitability for complexation to transition metals. For a simple test doubly deprotonated **11a** (2 equiv of LDA, THF, −78 °C, 2 h) was allowed to react with iron(II) chloride (−78 to 0 °C, 1 h), yielding the triferrocene **14**, which has a diamine ligand with a large bite angle between the donor atoms (Scheme 3).[17]

The complexation of **12b** to a titanium center was achieved by following a well-established protocol.[18] Thus, the dianion (2 equiv of *n*-BuLi, THF, room temperature, 2 h) of the isopropylamino-substituted ligand **12b** was subsequently treated with $TiCl_3$·3THF and lead(II) chloride, providing the desired bridged complex **15** in 72% yield (Scheme 3).

Scheme 3



Studies with respect to the catalytic activity of **15** in polymerization and asymmetric hydrogenation reactions are currently underway.

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Supporting Information Available: Text giving experimental procedures, analytical data, and copies of the NMR spectra for the compounds **3** and **5**−**15** (12 pages). Ordering information is given on any current masthead page.

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