An Efficient Asymmetric Synthesis of 2-Substituted Ferrocenecarboxaldehydes

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Received January 15, 1997[⊗]

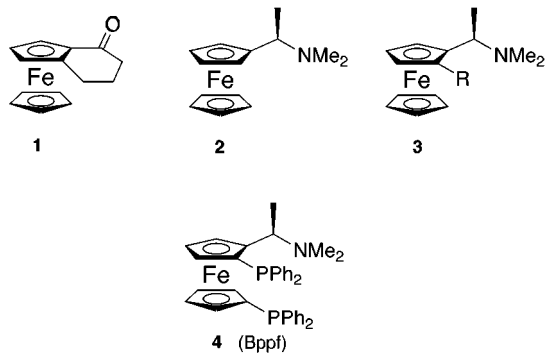
Ferrocenecarboxaldehyde is readily transformed into the acetal of (*S*)-1,2,4-butanetriol (1,3-dioxane structure) and further methylated to give acetal **15**. This can then be ortho-lithiated using *t*-BuLi with very high diastereoselectivity (98% de). Electrophilic quenching provided a large array of compounds of established stereochemistry. Controlled hydrolysis leads to many ortho-substituted ferrocenecarboxaldehydes (98% ee) which themselves are starting materials in the synthesis of various classes of enantiopure ferrocene derivatives with planar chirality of predictable absolute configuration.

Introduction

Since the discovery of ferrocene in 1951,[1,2] thousands of its derivatives have been prepared. The chemistry of ferrocene is very rich and diversified and is of interest in many areas such as material science, electrochemistry, asymmetric catalysis, etc.[3] The unique structure of ferrocene allows one to create chiral compounds, especially 1,2-disubstituted derivatives. The first optically active compound, **1** has been prepared by Thomson in 1959[4] (Scheme 1). Since then, ferrocenyl derivatives with planar chirality have been synthesized.[5−8] The synthesis of the enantiopure compounds has always involved a resolution stage. The most synthetically useful method has been the use of the ferrocenyl amine **2**, resolved using tartaric acid.[9] Ugi *et al.* discovered that ortho-lithiation of **2** by *n*-BuLi, followed by electrophilic quenching, gave a 96:4 ratio of the two possible diastereomers **3**.[10] The Ugi method has been widely applied to prepare ferrocenyl compounds with planar chirality, for example the chiral diphosphine **4** (Bppf) synthesized by Hayashi *et al.* in 1974 and used as a chiral ligand in asymmetric catalysis.[11]

The strategy of using an *ortho-directing group* is a key process for the creation of planar chirality from the attached chiral auxiliary. This is represented in a simplified way in Scheme 2. An ideal approach would be to create the final compound **8** with recovery of the chiral auxiliary Z*. This condition is not fulfilled in Ugi's method since the original asymmetric center in **2** is either retained in the product, such as **3**, or is destroyed (*e.g.* by hydrogenolysis or β-elimination of nitrogen). An alternative strategy for the creation of planar chirality in a ferrocene system is based on the enantioselective metalation of an achiral monosubstituted ferrocene such as **9**. If Z is an ortho-directing group, there is the possibility of chiral recognition in the deprotonation of one of the two enantiotopic hydrogens by a chiral base such as *s*-BuLi/sparteine. An early attempt by Nozaki *et al.* in 1969 was made in the case of Z = *i*-Pr.[12] The isopropyl groups acted as *meta*-orientating groups, but 1,3-disubstituted ferrocenes were isolated in very low enantiomeric excess. The first positive results in directed enantioselective ortho-metalation were obtained only very recently with Z = $P(O)Ph_2$, $C(O)N$*i*-Pr_2, or CH_2NR_2 by Simpkins *et al.*,[13] Snieckus *et al.*,[14] and Uemura *et al.*,[15] respectively.

Scheme 1



In this article, we wish to give the full account of our efforts to set up an efficient route to ferrocene derivatives with planar chirality.[16] This approach gives the first practical asymmetric synthesis of this class of compounds with a recoverable chiral auxiliary using the chiral ortho-directing strategy **5** → **8** depicted in Scheme 2, where Z* is a chiral acetal.[17,18] Since our initial publication in

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1997.

(1) Keally, T. J.; Pauson, P. J. *Nature* **1951**, *168*, 1039.
(2) Wilkinson, G.; Rosenblum, M.; Whiting, M. C.; Woodward, R. B. *J. Am. Chem. Soc.* **1952**, *74*, 2125.
(3) *Ferrocenes*; Hayashi, T., Togni, A., Eds.; VCH: Weinheim, 1995.
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(11) (a) Hayashi, T.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, *15*, 405. (b) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M. M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138.
(12) (a) Aratani, T.; Gonda, T.; Nozaki, H. *Tetrahedron Lett.* **1969**, *10*, 2265. (b) Aratani, T.; Gonda, T.; Nozaki, H. *Tetrahedron* **1970**, *26*, 5453.
(13) Price, D.; Simpkin, N. S. *Tetrahedron Lett.* **1995**, *36*, 6135.
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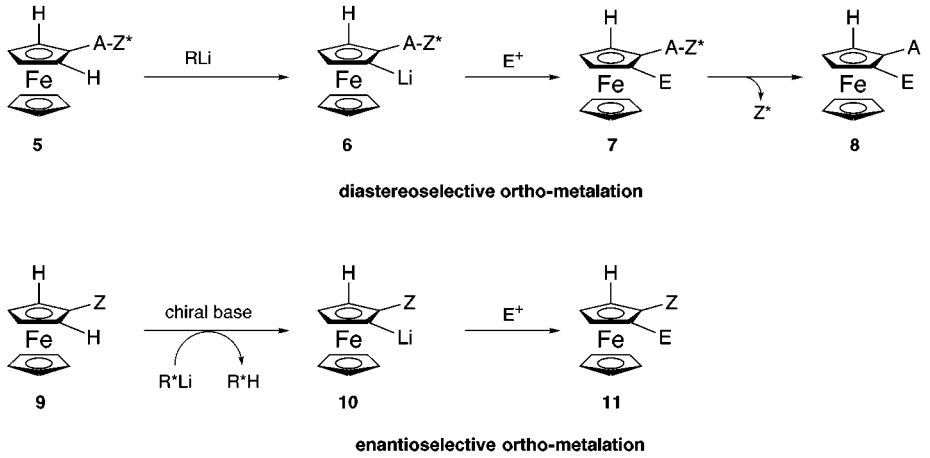
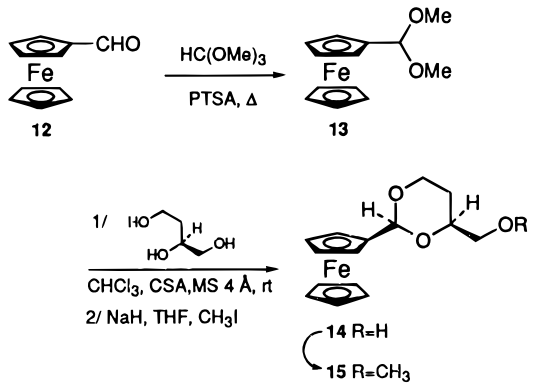
S0022-3263(97)00075-3 CCC: $14.00

Scheme 2



Scheme 3



1993, three other groups have described a similar strategy where the chiral ortho-directing group Z* on the monosubstituted ferrocene **5** is an oxazoline moiety.[19−21]

Results and Discussion

Preparation of Chiral Acetal 15. For the purpose of our investigation, we selected chiral acetal **15** as a suitable target (*vide supra*). A large scale preparation of acetal **15** has been developed. Thus, ferrocenecarboxaldehyde **12** was quantitatively converted to the known dimethyl acetal **13**[22] by heating in neat trimethyl orthoformate in the presence of an acid catalyst (Scheme 3). Transacetalization of the crude acetal **13** with (*S*)-(−)-1,2,4-butanetriol (commercially available or prepared by reduction of malic acid[23]) was then studied under various conditions in order to optimize the formation of the desired *cis*-1,3-dioxane derivative. It was found that the formation of the epimeric mixture of *cis*- and *trans*-dioxolanes (thermodynamic products) could be minimized if the transacetalisation was performed at room temperature in the presence of activated molecular sieves with camphorsulfonic acid as catalyst. Under these conditions, the ^{1}H NMR spectrum of the crude reaction mixture showed almost exclusive conversion (about 90%) into acetal **14**, along with a few percent of the dioxolanes and recovered aldehyde **12**. Pure acetal **14** could then be isolated by recrystallization in toluene and chromatographic separation of the mother liquors. This preparation has been routinely performed using 50 g of ferrocenecarboxaldehyde (0.23 mol scale) with an average yield of 80%. Only one epimer is detected in the ^{1}H NMR spectrum of acetal **14**, and the *cis*-1,3-dioxane structure was established by comparison with other 1,3-dioxanes obtained by similar reactions with other arylaldehydes.[24] Since both enantiomers of 1,2,4-butanetriol are commercially available, it is possible to have access to both the (*R*)- and (*S*)-acetals **14**.[25,26] Protection of the free hydroxyl group as its methyl ether was then performed using NaH and MeI in THF and gave the desired acetal **15** in a quantitative yield.

Ortho-Lithiation. Diastereoselective ortho-metalation involving chiral ferrocenylacetals was unknown when we started this work.[17,18] Initially, several simple chiral acetals were screened, such as **16** (Scheme 4). We observed unselective lithiation by *t*-BuLi (after quenching with chlorotrimethylsilane), with deprotonation occurring on the substituted cyclopentadienyl ring on *ortho* and *meta* positions as well as deprotonation on the unsubstituted cyclopentadienyl ring. Acetal **15** with a methoxymethyl side chain was then selected in the hope of

(17) The very first diastereoselective ortho-lithiation on a ferrocene using a removable chiral auxiliary was reported by Nozaki *et al.* in 1969 (see ref 12). A successful variation using *O*-methylprolinol as a chiral auxiliary was recently reported: Ganter, C.; Wagner, T. *Chem. Ber.* **1995**, *128*, 1157.

(18) A similar strategy has been applied by others in the cymanthrene and benchrothrene series, see (a) Kondo, Y.; Green, J. R.; Ho, J. *J. Org. Chem.* **1991**, *56*, 7199. (b) Loim, N. M.; Kondratenko, M. A.; Sokolov, V. I. *Dokl. Akad. Nauk. SSSR* **1991**, 320, 1123. (c) Aubé, J.; Heppert, J. A.; Milligan, M. L.; Smith, M. J., Zenk, P. *J. Org. Chem.* **1992**, *57*, 3563. (d) Loim, N. M.; Kondratenko, M. A.; Sokolov, V. I.; Turdybekov,K. M.; Struchnov, Y. T. *J. Organometal. Chem. USSR (Engl.)* **1992**, *5*, 575. (e) Kondo, Y.; Green, J. R.; Ho, J. *J. Org. Chem.* **1993**, *58*, 6182. (f) Loim, N. M.; Kondratenko, M. A.; Sokolov, V. I. *Russ. Chem. Bull.* **1993**, *42*, 166. (g) Loim, N. M.; Kondratenko, M. A.; Sokolov, V. I. *J. Org. Chem.* **1994**, *59*, 7485. (h) Alexakis, A.; Kanger, T.; Mangeney, P.; Rose-Munch, F.; Perrotey, A.; Rose, E. *Tetrahedron: Asymmetry* **1995**, *6*, 47. (i) Uemura, M.; Daimon, A.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1943.

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(21) Nishibayashi, Y.; Uemura, S. *Synlett* **1995**, 79.

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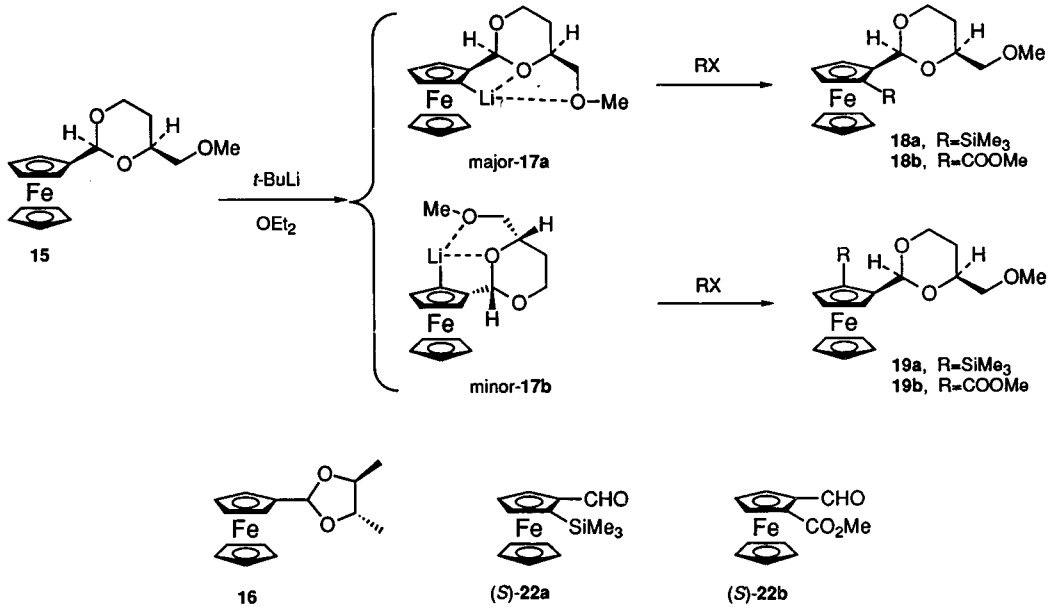
(23) (a) Herradón, B.; Cueto, S.; Morcuende, A.; Valverde, S. *Tetrahedron: Asymmetry* **1993**, *4*, 845. (b) Hanessian, S.; Ugolini, A.; Dube,D.; Glamyan, A. *Can. J. Chem.* **1984**, *62*, 2146.

(24) (a) Hungerbühler, E.; Seebach, D.; Wasmuth, D. *Helv. Chim. Acta* **1981**, *64*, 1467. (b) Pawlak, J.; Nakanishi, K.; Iwashira, T.; Borowski, E. *J. Org. Chem.* **1987**, *52*, 2896.

(25) However, the price of the (*R*)-(+)-1,2,4-butanetriol limits the possibility of a large scale preparation. This limitation could be outcomed by using biocatalytic resolution of the (±)-**14**.[26]

(26) We found that the *O*-acetate of **14** (90% ee at 50% conversion) could be obtained by resolution of the racemic hydroxyacetal by *Pseudomonas fluorescens* lipases and vinyl acetate in dry THF by analogy with Herradón, B.; Valverde, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1479.

Scheme 4



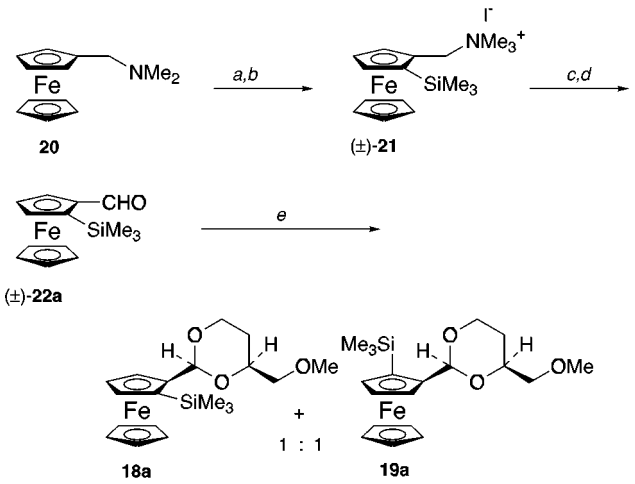
increasing the ortho-directing efficiency by lithium chelation.

Deprotonation of **15** by *t*-BuLi in diethyl ether was initially studied by the product distribution obtained after quenching with chlorotrimethylsilane, and we quickly discovered that there was exclusive ortho-deprotonation, giving a mixture of diastereomers **18a** and **19a**. The best conditions are the following: *t*-BuLi in hexane (1.1 equiv) is added at −78 °C to a 0.2−0.4 M solution of **15** in diethyl ether. The resulting suspension is then stirred at room temperature for 1 hour before addition of the electrophile. This addition was usually performed at −20 °C. The diastereoselectivity of the process was easily evaluated by analysis of the ^{1}H NMR spectrum of the crude product. In the case of the trimethylsilyl derivative **18a**, the diastereoisomeric ratio could be accurately measured using the signal (singlet) for the proton on the acetal carbon. A nonambiguous assignment for the above two signals of **18a**−**19a** was performed by preparing a 1:1 mixture of the two diastereomers. Thus, racemic aldehyde **22a** was synthesized in a four-step procedure from [(*N*,*N*-dimethylamino)methyl]ferrocene **20** (Scheme 5) and subjected to the standard acetalization−alkylation sequence. The two diastereoisomers gave clearly separated acetal group signals ($\delta = 5.47$ for **18a** and $\delta = 5.40$ for **19a**, $\Delta\delta = 10.5$ Hz) while only one diastereomer was detected in the ^{1}H NMR spectrum of the crude reaction mixture deriving from **15** (ortho-lithiation and electrophilic quenching with chlorotrimethylsilane).

When *t*-BuLi is added at −78 °C, there is an instantaneous change of color and formation of a bright yellow precipitate. During warming to room temperature, a bright orange precipitate appears which usually disappears during electrophilic quenching. We believe the first precipitate represents *t*-BuLi complexation by the substrate, with ortho-lithiation occurring at higher temperature with formation of the new precipitate. Thus, the very high diastereoselectivity (≥96% de, *vide supra*) was obtained by addition of the base at −78 °C and quenching at any temperature. If the metalation was performed at 0 °C, the de was between 80−90%.

The stereochemistry of the reaction was first established by correlation with compounds already described in the literature. Trapping of the *o*-lithio complex by

Scheme 5[a]

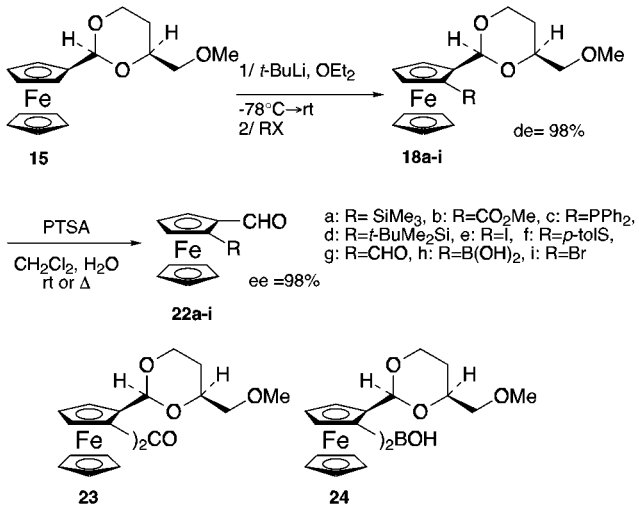


[a] Key: (a) (i) *n*-BuLi, OEt_2, rt. (ii) TMSCl (65%); (b) CH_3I, acetone, rt (97%); (c) $NaOH_{aq}$, 80 °C (83%); (d) MnO_2, $CHCl_3$ rt (87%); (e) (i) $HC(OMe)_3$, PTSA, 80 °C; (ii) (*S*)-(−)-1,2,4-butanetriol, $CHCl_3$, PTSA, (iii) NaH, CH_3I, THF (>90%).

chlorotrimethylsilane gave the TMS derivative **18a** in 85% yield. Hydrolytic treatment converted it into α-trimethylsilyl ferrocene carboxaldehyde **22a** ($[\alpha]_D = -202$, EtOH) in excellent yield. This ferrocene derivative has already been prepared with (*R*) configuration by Gokel *et al.*[27] ($[\alpha]_D = +194$, EtOH). Comparing the two rotations shows that **22a** has the (*S*) configuration and is optically pure with respect to the literature data. We also found that the two enantiomers of the racemic aldehyde **22a** could be separated by analytical HPLC using a chiral stationary phase (Chiralcel OD-H). Thus an enantioselectivity of 98% could be measured accurately and in a reproducible fashion on many batches of the silyl aldehyde **22a**. A second stereochemical correlation was possible after quenching the lithio derivative by methyl chloroformate. The resulting methyl ester **18b** was also obtained diastereomerically pure and hydrolyzed into aldehyde **22b** ($[\alpha]_D = +765$, EtOH). This

(27) Gokel, K.; Hoffmann, P.; Kleinmann, H.; Klusacek, H. *Tetrahedron Lett.* **1970**, *11*, 1771.

Scheme 6



compound has already been described by Schlögl *et al.*[28] ($[\alpha]_D = -760$, EtOH) with (*R*) configuration. This correlation is in full agreement with the conclusion obtained from the TMS derivative **18a**. A further stereochemical confirmation was given by a single crystal X-ray structure of acetal **18c** (R = PPh_2, see Supporting Information). Knowing the absolute configuration of the asymmetric (*S*) carbon of the chiral auxiliary, we deduced the (*S*) configuration for the planar chirality and hence the stereochemistry of the deprotonation. Furthermore, this structure also confirmed the *cis*-1,3-structure for the dioxane moiety. This study shows that deprotonation of acetal **15** by *t*-BuLi in diethyl ether gives almost exclusively the product organolithium **17a**. Presumably, there is a specific chelation of lithium by the methoxy group and one of the acetal oxygens in **17a**, while the alternate situation **17b** is disfavored. Molecular models show that **17b** could be disfavored by the endo orientation of the acetal oxygen which is not involved in the chelation, while in **17a** the oxygen is oriented exo by respect to iron. However, the picture in Scheme 4 is very approximate, since it involves neither solvent coordination nor aggregation of the lithium species. The reaction is under kinetic control and may also be discussed by considering the two competing transition states leading to **17a** and **17b** (for a similar discussion in the metalation of a ferrocenyloxazoline, see ref 20b). It is unlikely that chelate formation in **17a** and **17b** will involve boat or twist conformations. A chair conformation with 1,3-diaxial substituents gives rise to severe interactions between the ferrocene ring and methoxymethyl group. In this conformation, a coordination of lithium on the three oxygens is impossible in the organolithium precursor of the major product **18**, while it is very difficult to achieve for the organolithium leading to the minor product **19**. The diequatorial conformation (with chelates such as **17a** and **17b**) seems the most reasonable and is also indirectly supported by crystal structure of an acetal derivative (**18c**, *vide infra*).

Asymmetric Synthesis of Various α-Substituted Ferrocenecarboxaldehydes. Selected results for the diastereoselective ortho-lithiation−electrophilic quenching of the acetal **15** (Scheme 6) are collected in Table I. Optimized conditions involved addition of 1.1 equiv of *tert*-butyllithium to an ethereal solution of the acetal **15**

(28) Rapic, V.; Schlögl, K.; Steinitz, B. *Monatsh. Chem.* **1977**, *108*, 767.

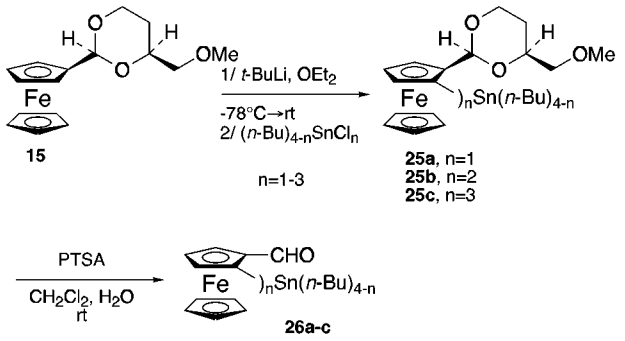
Table 1. Diastereoselective Syntheses of Ortho-Substituted Ferrocenyl Acetals 18a−i *via* Deprotonation and Electrophilic Quenching (Scheme 6)

entry	electrophile	R	product (%yield)
1	Me_3SiCl	Me_3Si	**18a** (85)
2	MeOCOCl	CO_2Me	**18b** (43)
			23 (37)
3	Ph_2PCl	Ph_2P	**18c** (90)
4	*t*-$BuMe_2SiOTf$	*t*-$BuMe_2Si$	**18d** (88)
5	$I(CH_2)_2I$	I	**18e** (90)
6	$(p\text{-TolS})_2$	*p*-TolS	**18f** (91)
7	$HCONMe_2$	CHO	**18g**(93)
8	$B(OMe)_3$ or $B(Oi\text{-Pr})_3$	$B(OH)_2$	**18h** (35) + **24** (25)
			18h (90)
9	*p*-xylylene dibromide	Br	**18i** (90)

Table 2. Reaction of Lithioferrocene 17a with Organostannyl Electrophiles (Scheme 7)

entry	electrophile	*n*	product (%yield)
1	*n*-Bu_3SnCl	1	**25a** (85)
2	*n*-Bu_2SnCl_2	2	**25b** (78)
3	*n*-$BuSnCl_3$	3	**25c** (80)

Scheme 7

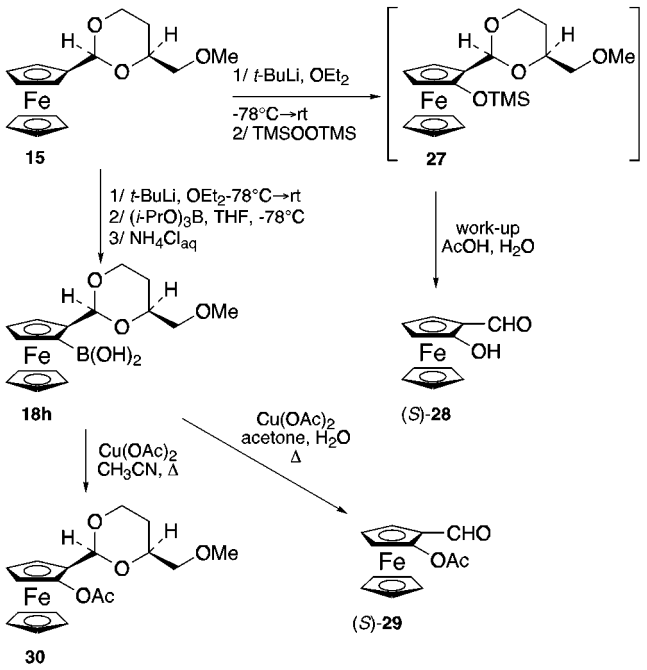


at low temperature and warming the reaction mixture to room temperature. The bright orange suspension of ortho-lithiated complex **17a** was then cooled before electrophilic quenching. In most cases, substituted acetals were isolated in high yields after flash chromatography on silica gel or by crystallization. A standard experiment was usually performed on a 1−2 mmol scale, but scale-up of the reaction could be realized without any decrease in the yield of the desired complex.[29] When methyl chloroformate was used as an electrophile, a modest yield (43%) was obtained for the ester **18b** since the bis-ferrocenyl ketone **23** was also formed in a 37% yield. An analogous result was obtained with trimethyl borate, and a mixture of boronic acid **18h** and borinic acid **24** was isolated along with the recovered starting material. However, with triisopropyl borate as the electrophile, polysubstitution could be avoided, and the boronic acid **18h** was formed in excellent yield. The possibility of controlling the extent of polysubstitution during reaction with chlorostannanes as electrophiles is also shown in Table II (Scheme 7). Good yields of ferrocenylstannanes **25a−c** were obtained after reaction of the lithio derivative with the appropriate chlorostannane electrophile.

Removal of the chiral auxiliary was performed under smooth conditions (Schemes 6, 7) to afford, after simple workup, the enantiopure ortho-substituted aldehydes **22a−i** and **26a−c** with excellent yields (>90% in most cases). Purification was usually made easy by elimina-

(29) For instance, preparations of aldehydes **22c** and **22e** were routinely performed on 50−100 mmol scale with good yields. Details are given in the experimental part.

Scheme 8



tion (in the aqueous phase) of the auxiliary (*S*)-methoxymethyl butanediol during the workup. Purification of the resulting aldehyde was then unnecessary in some cases. The (*S*)-methoxymethyl butanediol could be recovered from the aqueous phase and recycled by acetalization with ferrocenecarboxaldehyde **12** (see Experimental Section). Thus, a wide range of enantiopure α-substituted ferrocenyl aldehydes could be readily prepared by an appropriate choice of electrophile. Most of the aldehydes were isolated as highly colored solids or oils and showed good stability toward air oxidation.

We next turned to the preparation of 2-hydroxy-1-formylferrocene **28** (Scheme 8) which can be considered as a chiral analog of salicylaldehyde. Substituted salicylaldehydes are readily transformed into chiral or achiral salen ligands, and recent reports in the literature have proved the efficiency of some of those chiral ligands in asymmetric catalysis.[30] During the course of this work, the preparation of (−)-**28** in a four-step synthesis from the corresponding 2-hydroxy-1-carboxyferrocene (after resolution of the racemic mixture) was reported by Ito *et al.*[31] As an alternative route, we studied the reaction of the *o*-lithio derivative **17a** with various oxidants. While reaction with *t*-BuOOLi[32] gave mostly recovered starting material **15** after hydrolytic workup, the use of TMSOOTMS[33] as an oxidant (Scheme 8) led cleanly to the desired hydroxy aldehyde **28** without isolation of the silylated intermediate **27**. (−)-2-Hydroxy-1-formylferrocene **28** has been fully characterized, although it proved to be fairly unstable toward air oxidation, and should be stored after purification under inert atmosphere. This reaction also allowed us to assign the (*S*) configuration of the compound (−)-**28** prepared by Ito *et al.* and hence the (*S*) configuration of the (−)-2-hydroxy-1-carboxyferrocene, which was the precursor in this synthesis. In view of the instability of the hydroxy aldehyde **28** and the hazard in manipulating the trimethylsilyl peroxide on a larger scale, an alternative route to an *O*-protected 2-hydroxy-1-formylferrocene was also investigated. Thus reaction of the boronic acid **18h** with an excess of cupric acetate in boiling acetone/water[34] yielded (*S*)-2-acetoxy-1-formyl ferrocene **29** in a 25% yield. In this reaction, the chiral auxiliary was simultaneously removed. In contrast with the hydroxy aldehyde **28**, the *O*-protected aldehyde **29** proved stable, and no particular precaution was required for its purification or handling. This oxidative process occurred without loss of the chiral auxiliary when the reaction was performed in anhydrous acetonitrile and gave **30** in 33% yield. In both cases, the major byproduct of the reaction was ferrocenecarboxaldehyde **12** or dioxane **15** which probably result from the reaction of a chiral *o*-ferrocenyl radical intermediate with the solvent. However, in no case did we isolate a biferrocene as a byproduct. The stable chiral acyloxyferrocene complexes **29** and **30** might be interesting precursors of various chiral alkoxyferrocenes by applying reactions already reported for acetoxy ferrocene[35] and 1,1′-diacetoxyferrocene.[36]

Inspired by the very rich chemistry of *o*-aminobenzaldehyde and *o*-aminophenyl ketones for the preparation of various heterocyclic compounds,[37] we decided to synthesize the unknown chiral 2-amino-1-formyl ferrocene **33a** starting from acetal **15**. Although aminoferrocenes are known,[38] most of the standard preparative methods could not be applied to the present case. Among reagents acting as an electrophilic source of nitrogen,[39] *O*-benzyl hydroxylamine has been used with lithioferrocene to yield aminoferrocene, albeit with a low yield.[40] A high-yielding preparation of alkyl and arylamines through electrophilic amination of higher order cuprates with the commercially available *N*,*O*-bis(trimethylsilyl)hydroxylamine was recently reported by Ricci *et al.*[41] We focussed on this method for the synthesis of the aminoferrocene derivative **33a** (Scheme 9). The mixed higher order cyanocuprates **31a,b** were prepared by reaction of 1 equiv of the *o*-lithioferrocene **17a** in diethyl ether with a THF solution of lithium 2-thienylcyanocuprate or lihium (*tert*-butylethynyl)cyanocuprate at −78 °C, followed by warming the bright orange suspension to −50 °C. One equivalent of *N*,*O*-bis(trimethylsilyl)hydroxylamine was then added at this temperature followed by slow warming of the reaction mixture to room temperature. Hydrolytic workup and chromatographic purification yielded the desired stable *o*-aminoferrocenyl acetal **32a** in 39−56% yield. We

(30) (a) Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.* **1994**, *59*, 1939. (b) Hansen, K. B; Leighton, J. L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 10924. (c) Nishikori, H.; Katsuki, T. *Tetrahedron Letters* **1996**, *37*, 9245.

(31) Sawamura, M.; Sasaki, H.; Nakata, T.; Ito, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2725.

(32) Julia, M.; Pfeuty Saint-Jalmes, V.; Verpeaux, J. N. *Synlett* **1993**, 233.

(33) Taddei, M.; Ricci, A. *Synthesis* **1986**, 633.

(34) Nesmejanov, A. N.; Sasonowa, W. A.; Drosd, V. N. *Chem. Ber.* **1960**, *93*, 2717.

(35) Akabori, S.; Sato, M.; Ebine, S. *Synthesis* **1981**, 278.

(36) Akabori, S.; Habata, Y.; Sakamoto, Y.; Sato, M.; Ebine, S. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 537.

(37) (a) Caluwe, P. *Tetrahedron* **1980**, *36*, 2359. (b) Cheng, C.-C.; Yan, S.-J. *Org. React.* **1982**, *28*, 37.

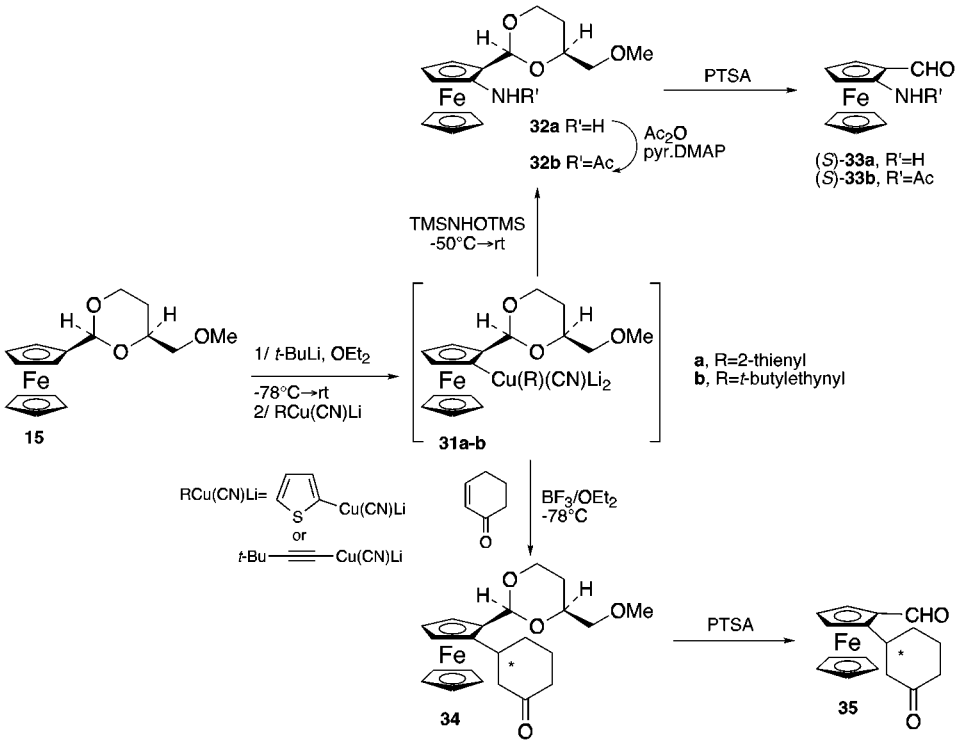
(38) Some chiral amino ferrocenes have been obtained starting from the corresponding carboxylic acid through a Curtius rearrangement, see for instance (a) Lehner, H.; Schlögl, K. *Monat. Chem.* **1970**, *101*, 895. (b) Rapic, V.; Schlögl, K.; Steinitz, B. *Monat. Chem.* **1977**, *108*, 767. Aminoferrocene has been prepared by reaction of copper phthalimide on ferroceneboronic acid followed by deprotection of the phthalide derivative, see: Montserrat, N.; Parkins, A. W.; Tomkins, A. R. *J. Chem. Res. (S)* **1995**, 336. For a preparation involving the reaction of the sodium salt of an amide on bromoferrocene in the presence of a copper(I) salt, see: Herberhold, M.; Ellinger, M.; Kremnitz *J. Organomet. Chem.* **1983**, *241*, 227.

(39) Review on electrophilic amination of carbanions: Erdik, E.; Ay, M. *Chem. Rev.* **1989**, *89*, 1947.

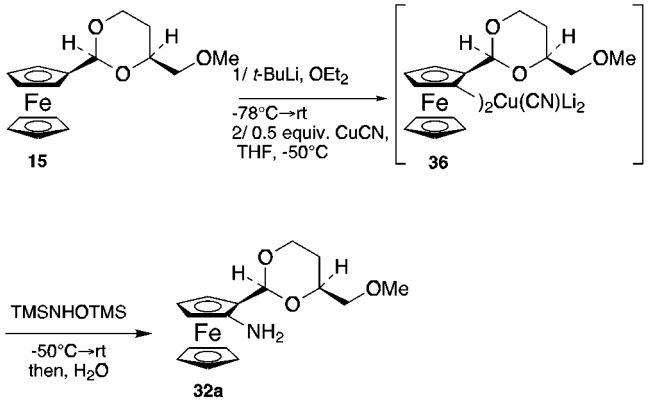
(40) Knox, R. G.; Pauson, P. L.; Willison, D. *Organometallics* **1990**, *9*, 301.

(41) Casarini, A.; Dembrech, P.; Lazzari, D.; Marini, E.; Reginato, G.; Ricci, A.; Seconi, G. *J. Org. Chem.* **1993**, *58*, 5620.

Scheme 9



Scheme 10



checked that the formation of an organocuprate was necessary by directly reacting the electrophilic nitrogen source with the lithio derivative **17a**. After hydrolytic workup, the starting acetal **15** was recovered quantitatively and no trace of the amino derivative **32a** could be detected. This reaction was easily performed on a small scale (typically 2 mmol of acetal **15**), but the chemical yield significantly dropped when the reaction was scaled up. With 50 mmol of the organocuprate **15b**, the aminoacetal **32a** was isolated in only 18% yield, and the unreacted acetal **15** was quantitatively recovered after chromatographic separation. A simpler procedure was then used for the synthesis of **32a** by preparing the bis-ferrocenylcyanocuprate **36** (Scheme 10). Under those conditions, the amino derivative **32a** was isolated in 36% yield and could be easily separated from the starting ferrocenylacetal **15** by flash chromatography, the latter being quantitatively recovered and recycled. The desired 2-amino-1-formylferrocene (*S*)-**33a** was isolated as a stable red solid after hydrolysis of the acetal **32a**. However, this compound was prone to polymerization under acidic conditions, and isolated yields remained modest (around 25%). On the other hand, protection of the amino group by acetylation followed by elimination of the chiral auxiliary gave (*S*)-2-acetamido-1-formylferrocene **33b** which proved stable under acidic conditions.

It should be noted at this point that the new ferrocenylcyanocuprates **31a,b** prepared above displayed unusual reactivity toward electrophiles as compared with the previous results in the literature. Ferrocenylcopper reagents have usually been described as polymeric structures with low solubility in organic solvents. In contrast, the use of the higher order cuprate methodology[42] allowed us to perform the first example of a 1,4-addition of a ferrocenylcopper reagent. Thus, reaction of the ferrocenylcyanocuprates **31a,b** with cyclohexenone at −78 °C and in the presence of boron trifluoride, yielded the 1,4 adduct **34** in yields of up to 70%. Under the same conditions, the reaction of the lithio derivative **17a** yielded only the 1,2 adduct. The acetal derivative **34** and the corresponding keto aldehyde **35** were single diastereoisomers though the stereochemistry of the new stereogenic center has not yet been determined. This preliminary result is promising for the development of a new method for the stereocontrolled formation of ferrocene−carbon bonds by the use of ferrocene derived higher order cuprates.[43]

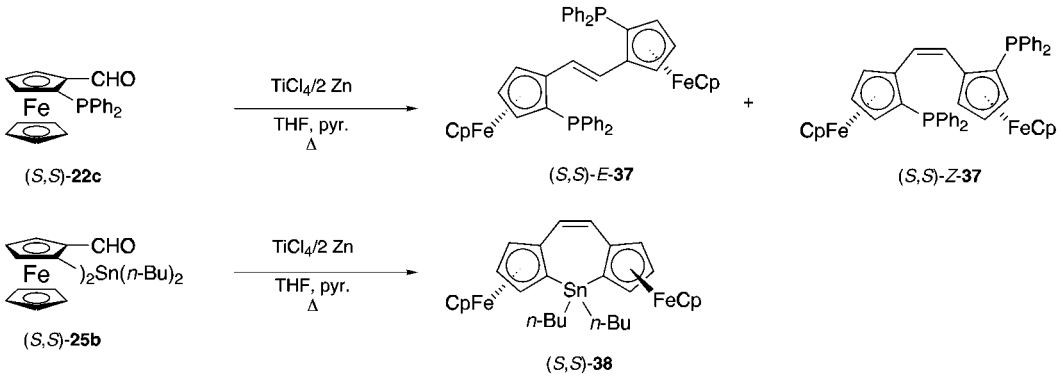
Applications to Asymmetric Catalysis. Having established a general method for the preparation of enantiopure ferrocenyl aldehydes, we then explored the possibility of synthesizing some new chiral ligands for asymmetric catalysis.[44] We were particularly interested in coupling two molecules of the phosphino aldehyde **22c** to prepare new chiral ferrocenyl diphosphines. A McMurry coupling of aldehyde **22c** was successful using an

(42) Lipshutz, B. H. In *Organometallics in Synthesis*; Schlosser, M., Ed.; John Wiley & Son Ltd.: New York, 1994.

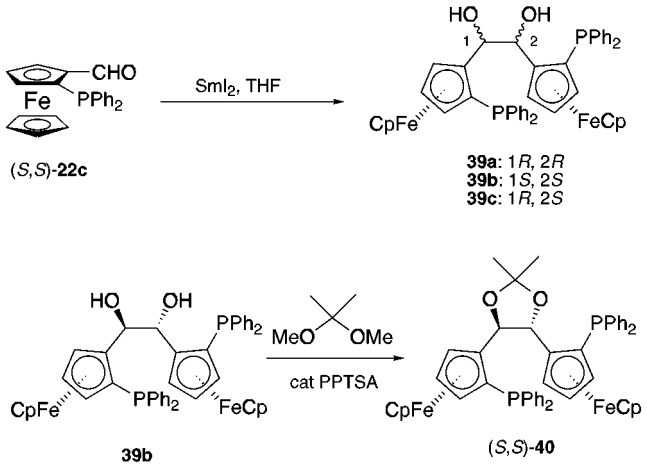
(43) The formation of lithium bis-ferrocenylcyanocuprate has recently been described by our group for the preparation of biferrocene: Kagan, H. B.; Diter, P.; Gref, A.; Guillaneux, D.; Masson-Szymczak, A.; Rebière, F.; Riant, O.; Samuel, O.; Taudien, S. *Pure Appl. Chem.* **1996**, *68*, 29. See also: Spescha, M.; Duffy, N. W.; Robinson, B. H., Simpson, J. *Organometallics* **1994**, *13*, 4895.

(44) For the recent use of chiral ferrocenyl ligands in asymmetric catalysis, see refs 7, 8, and (a) Borman, S. *Chem. Eng. News* **1996**, 38. (b) Togni, A. *Chimia* **1996**, *50*, 86.

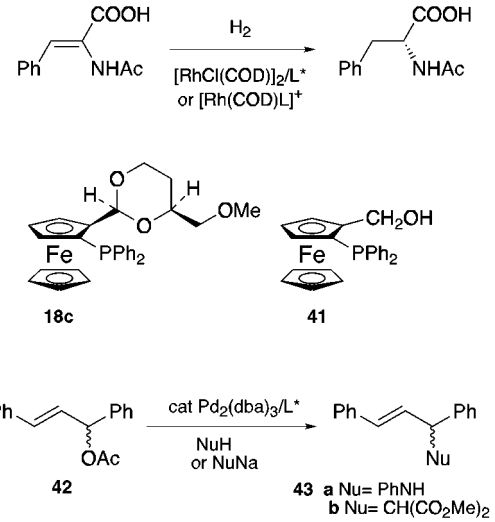
Scheme 11



Scheme 12



Scheme 13



excess of a low valent titanium reagent ("*in situ*" prepared) to yield a mixture (20:80) of *Z* and *E* diphosphines **37** in a 60% yield (Scheme 11). The *Z* and *E* isomers could be easily separated and characterized. In some experiments, only the *E* isomer was isolated but without any decrease of the final isolated yield. An intramolecular version of the McMurry coupling was also tested on bis-aldehyde **25b** to check the generality of this reaction for our substrates. In this latter case, chiral stannepine **38** was isolated in excellent yield (≥80%).

Another series of chiral diphosphines was also prepared by pinacol coupling of the phosphino aldehyde **22c** using samarium diiodide in THF (Scheme 12). A mixture of diols **39a**−**c** (40:30:30) was quantitatively formed, and three diastereoisomeric diphosphines **39a**−**c** could be isolated by chromatography. We were also able to prepare acetal derivative **40** of diol **39b**. The stereochemistry of the diastereoisomers has been assigned (see below). Hydroxyphosphine **41** was also prepared by sodium borohydride reduction of phosphino aldehyde **22c**.

The relative stereochemistry of diphosphine **39b** could be established by a single crystal X-ray determination (see Supporting Information), carried out on the diphosphine derived from the enantiomer of **22c**. Moreover, the absolute configuration deduced from this study is in agreement with our assignement by chemical correlation (*vide supra*). Compound **39a** has a C_2-symmetry while **39c** has a C_1-symmetry. Assignment of structures by ^{1}H and ^{13}C NMR could be easily made on this basis.

The catalytic efficiency of these new chiral bis-phosphines was checked for the asymmetric hydrogenation of *N*-acetyl dehydrophenylalanine using the rhodium complexes of some diphosphines as a catalyst (Scheme 13). The results are listed in Table 3. Interestingly, the

Table 3. Asymmetric Hydrogenation of *N*-Ac-Δ-Phe

entry[a,b]	ligand	%yield[c]	ee[d] (%)	conf [d]
1	(*E*)-**37**	93	60	*R*
2	**39 a**	100	89	*R*
3	**39 b**	40	85	*R*
4	**39 c**	100	85	*R*
5	**40**	100	45	*R*
6	**18c**	87	87	*R*
7	**41**	100	30	*R*

[a] 2 equiv of diphosphine or 4 equiv of monophosphine with respect to $[Rh(COD)Cl]_2$. 2% equiv of Rh with respect to substrate. [b] Entries 1 and 7: a cationic complex of rhodium was used (2% of rhodium with respect to substrate); solvent: methanol, pressure: 10 bars. [c] Isolated yield. [d] Ee and absolute configuration determined by polarimetry by comparison with the specific rotation of (*R*)-*N*-AcPhe ($[\alpha]_D = -45$ ($c = 1$, EtOH)).

E unsaturated diphosphine **37** gave a catalytically active rhodium complex (entry 1). Hydrogenation of (*Z*)-*N*-acetyl dehydrophenylalanine occurred under 10 atm of H_2, giving the product with 60% ee. Presumably, the C=C double bond of **37** is reduced *in situ* prior to hydrogenation of the substrate, as established for the double bond of norphos.[45] Diol diphosphines **39a**−**c** gave excellent rhodium catalysts for asymmetric hydrogenation (entries 2−4). The three isolated diastereomers led to (*R*)-*N*-acetylphenylalanine under atmosphere pressure of H_2. Dioxolane **40** is less enantioselective (entry 5). From comparison of the above data, it seems that the main contribution to the asymmetric induction is the planar chirality of the ligand. This is confirmed by the

(45) Kyba, P. E.; Davis, R. E.; Juri, P. N.; Shirley, K. R. *Inorg. Chem.* **1981**, *20*, 3616.

Table 4. Asymmetric Allylic Substitution on 42 Catalyzed by Chiral Palladium Complexes

entry	ligand[a]	nucleophile	yield[b] (%)	ee[c] (%)
1	**18c**[d]	$PhCH_2NH_2$		
2	**41**	$PhCH_2NH_2$	70	65
3	**18c**	$NaCH(CO_2Me)_2$	5	5 (*R*)
4	**41**	$NaCH(CO_2Me)_2$	63	25 (*S*)
5	**41**[d]	$NaCH(CO_2Me)_2$	10	14 (*R*)

[a] 1 equiv of ligand (unless otherwise stated) with respect to palladium (1% equiv of Pd with respect to **42**). [b] Isolated yield. [c] Measured by HPLC on a chiral Daicel OD-H column. [d] 2 equiv of ligand.

behavior of the monophosphine **18c**, giving *N*-acetylphenylalanine in 87% ee with *R* configuration (entry 6). Hydroxyphosphine **41** was also evaluated (entry 7) but proved to be a poor ligand for asymmetric hydrogenation (entry 7), as is often observed for hydroxymonophosphines.[46]

Hydrosilylation of acetophenone by diphenylsilane using a rhodium complex prepared *in situ* with **18c** as ligand gave racemic alcohol. Finally, allylic substitution was briefly investigated (transformation of **42** into **43**), catalyzed by a palladium complex. This complex was prepared *in situ* from $Pd_2(dba)_3$ and the chiral ligand, and the reactions were performed at room temperature. The results are listed in Table 4 and show that asymmetric substitutions could be obtained with moderate ee's (up to 65%).

Conclusion

A general method has been devised to prepare enantiomerically pure ortho-substituted ferrocene carboxaldehydes which are key compounds for the synthesis of many types of ferrocenes with planar chirality including mono and diphosphines. This method compares favorably with ortho-metalation of chiral oxazolines,[19−21] chiral sulfoxides,[47] phosphinoyl group,[13] C(O)N*i*-Pr_2,[14] and CH_2NR_2[15,17] where the ortho-directing group cannot conveniently be transformed into another functionality.[48,49] Our methodology is easily scaled-up and allows recovery of the chiral auxiliary and preparation of both enantiomers of a given target with predictable absolute configuration.[50]

Experimental Section

For general experimental details, see ref 16. Elemental analyses sometimes gave spurious results (especially for some ferrocenecarboxaldehydes), despite repeated purification and careful drying of the samples, possibly due to difficulty in sample combustion. In those cases, chemical purity was controlled by NMR spectroscopy, GC-MS and TLC. Ferrocenecarboxaldehyde was purchased from Aldrich or Fluka and (*S*)-(−)-1,2,4-butanetriol was purchased from Aldrich. *tert*-Butyllithium was purchased from Acros as 1.5 M solution in pentane and was regularly titrated using *N*-pivaloyltoluidine.[53] "Standard workup" refers to extraction of the reaction mixture with an organic solvent, washing of the extract with water and brine, drying over anhydrous magnesium sulfate, and removal of the solvents under reduced pressure on a rotary evaporator. Chiral analytical HPLC used a Chiralcel OD-H column. The absolute configuration of the planary chiral ferrocenes was given with the nomenclature of Schlögl.[6] Single crystal X-ray structures of **18c** and the enantiomer of **39b** were performed at the Laboratoire de chimie de coordination, CNRS, Toulouse. For details, see Supporting Information.

(2*S*,4*S*)-4-(Hydroxymethyl)-2-ferrocenyl-1,3-dioxane (14). To a solution of ferrocenecarboxaldehyde **12** (50 g, 233 mmol) in 300 mL of trimethyl orthoformate was added a catalytic amount of PTSA monohydrate (5% mol equiv, 2.2 g), and the dark solution was stirred at 80 °C overnight. Anhydrous K_2CO_3 was then added, and the stirring was maintained while the solution was allowed to cool. The suspension was diluted with ether and filtered on Celite, and the filter cake was washed with ether until the filtrate was colorless. After concentration under reduced pressure and drying on the vacuum pump overnight, crude acetal **13**[22] (60.9 g) was quantitatively isolated and directly used in the next step. (*S*)-(−)-1,2,4-Butanetriol (24.8 g, 233 mmol) was weighed in a 1 L flask and dried by mixing with toluene, removing the toluene by evaporation on a rotary evaporator (three times) and drying on a vacuum line overnight. The triol was then mixed with 300 mL of $CHCl_3$, 150 g of activated 4 Å molecular sieves, and a catalytic amount of camphorsulfonic acid (5% mol equiv, 2.7 g) in a 1 L flask fitted with a drying tube. The crude acetal was diluted with 100 mL of $CHCl_3$ and added to the flask. The reaction mixture was stirred overnight at rt and treated as before with K_2CO_3 before filtration on Celite, washing with dichloromethane, and concentration under reduced pressure. The crude crystalline reaction mixture was extracted with 250 mL of boiling toluene, and the hot solution was decanted from some remaining polymeric oil into a clean flask. The solution was allowed to cool and placed in a freezer (−20 °C) for 2−3 d. The yellow crystals formed were filtered, washed with a minimum volume of cold toluene, and dried, giving 49.1 g of yellow crystals (70% yield). The mother liquors were concentrated, and a second fraction of pure acetal was recovered after flash chromatography (FC) on silica gel (50:50 cyclohexane−EtOAc), the first fraction was aldehyde **12** followed by the desired dioxane. The last fraction was a mixture of the two isomeric dioxolanes. The average yield **14** is 80%. ^{1}H NMR δ 1.39 (1H, m), 1.83 (1H, m), 3.63 (3H, s), 3.90 (2H, m), 3.90 (2H, m), 4.12 (2H, m), 4.15 (5H, s), 4.21 (1H, m), 4.31 (2H, m), 5.40 (1H, s); MS (CI, NH_3) *m/e* 303 (M + 1, 100%), 302 (M, 84.5); Anal. Calcd for $C_{15}H_{18}FeO_3$: C, 59.60; H, 5.96. Found: C, 59.77; H, 6.01.

(2*S*,4*S*)-4-(Methoxymethyl)-2-ferrocenyl-1,3-dioxane (15). A dry Schlenk tube was charged with NaH (60% in mineral oil, 8 g, 198 mmol) under Ar. The hydride was washed three times with dry hexane under Ar and 60 mL dry THF were added. The suspension was cooled with an ice−water bath, and the dioxane **14** (40 g, 132 mmol) in 360 mL of dry THF was added dropwise via cannula (1−2 h) at this temperature (*caution*, hydrogen is evolved, and the reaction should be done in a well ventilated fume cupboard). Neat iodomethane was then injected (12.4 mL, 199 mmol), and the resulting suspension was slowly allowed to come to rt under magnetic stirring overnight. Excess NaH and CH_3I were destroyed at 0 °C by slow addition of methanol, and the reaction mixture was quenched with water. The solvents were evaporated under reduced pressure, and the residue was taken up in ether and washed with water and brine. After standard workup, the crude oil was filtered on silica gel (ether) to give a quantitative yield (41.5 g) of the desired acetal **15** as a brown oil which crystallized to an orange solid upon standing in a freezer: $[\alpha]_D = -32.5$ ($c = 1.14$, $CHCl_3$); ^{1}H NMR δ 1.47 (1H, m), 1.76 (1H, m), 3.40 (3H, s), 3.45 (2H, 2 dd AB), 3.88 (1H, m), 3.98 (1H, m), 4.05−4.35 (10H, m), 5.35 (1H, s); ^{13}C NMR

(46) Holz, J.; Börner, A.; Kless, A.; Borns, S.; Trinkhaus, S.; Selke, R.; Heller, D. *Tetrahedron: Asymmetry* **1995**, *6*, 1973.

(47) Rebiere, F.; Riant, O.; Ricard, L.; Kagan, H. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 568.

(48) Samakia *et al.*, however, succeded in transforming the oxazoline moiety (alkylation, reduction, and hydrolysis) into an aldehyde when a methyl group is present in the ortho position.[20a]

(49) Deprotection of a C_2-chiral 1,1′-bis(diphenylphosphino)-2,2′-bis(oxazolinyl)ferrocene to the corresponding *bis* methyl ester has been recently reported: Zhang, W.; Kida, T.; Nakarsuji, Y.; Ikeda, I. *Tetrahedron Lett.* **1996**, *37*, 7995.

(50) A recent application is the preparation of a chiral ferrocenyl diketonato ligand,[51] a useful ligand for asymmetric catalysis of the trimethylsilylcyanation of aldehydes. Orthosubstituted aldehydes such as **22** were also starting materials to prepare chiral ferrocenyl cations, which may be used as chiral Lewis acids.[52]

(51) Abiko, A.; Wang, G.-Q. *J. Org. Chem.* **1996**, *61*, 2264.

(52) (a) Taudien, S.; Riant, O.; Kagan, H. B. *Tetrahedron Lett.* **1995**, *36*, 3513. (b) Brunner, A.; Taudien, S.; Riant, O.; Kagan, H. B. *Chirality* **1997**, in press.

(53) Suffert, J. *J. Org. Chem.* **1989**, *54*, 509.

δ 27.9, 59.3, 66.55, 66.57, 66.6, 67.7, 67.8, 68.7, 69.5, 75.5, 75.9, 85.9, 100.0; MS (EI) *m/e* 318 (M + 2, 5.5%), 317 (35.5), 316 (M, 100), 214 (34); Anal. Calcd for $C_{16}H_{20}FeO_3$: C, 60.75; H, 6.33. Found: C, 60.91; H, 6.25.

General Procedure for the Asymmetric Deprotonation of Acetal 15. A dry Schlenk tube was charged with the acetal **15** under Ar and dissolved in dry ether (5−10 mL of ether per 2 mmol of acetal). The solution was cooled to −78 °C, and *t*-BuLi (1.1 equiv as a 1.5 M solution) was injected dropwise, yielding after a few min a bright yellow precipitate. After 10 min stirring, the cooling bath was removed and the mixture was allowed to stir at rt for 1 h. Upon warming, the precipitate dissolved and and a bright orange precipitate of lithiated acetal gradually formed (in some cases, agglomeration of the precipitate was observed). The mixture was cooled again to −30 °C, and an electrophile was added neat or as a solution in ether or THF. The solution was further stirred at rt (1−15 h) before quenching and standard aqueous workup. The crude acetal was purified by FC on silica gel or crystallization.

Preparation of (±)-α-(Trimethylsilyl)ferrocenecarboxaldehyde (22a) from 20: Step 1. A dry Schlenk tube was charged with 6.08 g of [(*N*,*N*-dimethylamino)methyl]ferrocene (**20**) (25 mmol) in 25 mL of dry ether. The brown solution was cooled with an ice−water bath, and 17.2 mL of a 1.6 M solution of *n*-BuLi (27.5 mmol, 1.1 equiv) was injected dropwise. The cooling bath was removed, and the bright orange solution was stirred at rt for 4 h before cooling to −20 °C. TMSCl (3.81 mL, 30 mmol, 1.2 equiv) was injected, and the suspension was stirred at rt overnight before quenching with a 2 M NaOH solution. After standard workup, the brown oil was purified by FC on silica gel (50:50 cyclohexane−ether). A 5.1 g amount of a mobile brown oil was isolated (65% yield) and dissolved in 40 mL of acetone. A 5 mL volume of CH_3I (80 mmol) was added in one portion, and the solution was heated at 60 °C for 5 min and left at rt for 1 h. The brown solid mass was broken with a spatula and poured into 250 mL of ether with stirring. The yellow salt (±)-**21** was filtered, washed with ether, and dried *in vacuo* (7.57 g, 97% yield). **Step 2.** The iodomethylate **21** (4.1 g, 9 mmol) was suspended in a solution prepared with 1.5 g of NaOH and 40 mL of water, and the mixture was stirred at 80 °C for 4 h. After cooling, the orange oil was extracted with ether and treated as usual. The [α-(trimethylsilyl)ferrocenyl]methanol was isolated as an orange solid after FC on silica (75:25 cyclohexane−ether) (2.15 g, 83% yield). A 2.0 g amount of the racemic alcohol (7 mmol) was dissolved in 50 mL of $CHCl_3$, and 20 g of activated MnO_2 was added. After 45 min stirring, a TLC check (SiO_2, 50:50 cyclohexane−ether) showed no starting material and only one red-orange spot for the desired aldehyde. The mixture was filtered on Celite, and the Celite pad was washed with dichloromethane until the washing remained colorless. Removal of the solvents gave pure aldehyde (±)-**22a** (>95% by TLC and ^{1}H NMR) which was used in the next step without further purification (1.74 g, 87% yield). HPLC analysis on a chiral OD-H column (hexane/*i*-PrOH: 99/1, 0.5 mL/min, λ = 254 nm) gave two well separated peaks for the two enantiomers of the racemic aldehyde (12.7 min (*R*) and 14.5 min (*S*)).

Derivatization of Racemic 22a with (*S*)-1,2,4-Butanetriol. The procedure for the preparation of acetal **14** was done in the same condition using aldehyde (±)-**22a** (1.2 g, 4.15 mmol) and (*S*)-1,2,4-butanetriol (630 mg). The crude reaction mixture was filtered on a small pad of silica gel (73:30 cyclohexane−EtOAc) to give a brown oil which was directly used in the methylation step. The resulting crude oil was analyzed by ^{1}H NMR. Analysis shows the presence of a 1:1 mixture for **18a**−**19a** (δ(OCHO) = 5.47 for **18a** and 5.40 for **19a**) along with a small amount of the four corresponding isomeric dioxolanes (δ(OCHO) = 5.79; 5.80; 5.91 and 5.92).

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-[α-(trimethylsilyl)ferrocenyl]-1,3-dioxane (18a). Following the standard procedure, the quenching was realized with TMSCl (1.3 equiv). The acetal was isolated as a brown waxy solid following FC on silica (70:30 cyclohexane−ether) in a 85% yield: $[\alpha]_D$ = -40.0 (*c* = 0.71, $CHCl_3$); ^{1}H NMR δ 0.25 (9H, s), 1.48 (1H, m), 1.75 (1H, m), 3.33 (3H, s), 3.40 (2H, m), 3.80 (2H, m), 4.03 (1H, m), 4.12 (5H, s), 4.24 (2H, m), 4.57 (1H, m), 5.47 (1H, s); ^{13}C NMR δ 0.2, 28.2, 59.1, 66.7, 68.9, 69,6, 69.7, 74.6, 75.4, 75,6, 70.1, 100.7; MS (EI) *m/e* 390 (M + 2, 12.%), 389 (50.5), 388 (M, 100). Anal. Calcd for $C_{19}H_{28}FeO_3Si$: C, 58.76; H, 7.22. Found: C, 58.81; H, 7.29.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-carbomethoxyferrocenyl)-1,3-dioxane (18a) and (S_{Fc},$S_{Fc'}$)-Bis[α-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]-ferrocenyl] Ketone (23). Following the standard procedure, the quenching was realized with methyl chloroformate (5 equiv) at −20 °C. The acetal **18a** was isolated as a brown oil following FC on silica gel (50:50 cyclohexane−ether) in a 43% yield: $[\alpha]_D$ = 9.0 (*c* = 0.7, $CHCl_3$); ^{1}H NMR δ 1.57 (1H, m), 1.83 (1H, m), 3.31 (3H, s), 3.40 (2H, m), 3.80 (3H, s,), 4.04 (2H, m), 4.20 (5H, s), 4.32 (2H, m), 4.71 (2H, m), 6.0 (1H, s,); MS (EI) *m/e* 375 (M + 1, 11.5%), 374 (M, 49). Anal. Calcd for $C_{18}H_{22}FeO_5$: C, 57.75; H, 5.88. Found: C, 58.46; H, 6.18. A second elution with EtOAc as eluent and crystallization from ether yielded the ketone **23** as a byproduct (red crystals, 37% yield): $[\alpha]_D$ = +98 (*c* = 0.305, $CHCl_3$); ^{1}H NMR δ 1.50 (1H, m), 1.83 (1H, m), 3.23 (3H, s), 3.40 (2H, m), 4.15 (7H, m), 4.31 (2H, m), 4.53 (1H, m), 4.78 (1H, 1H, m), 6.33 (1H, s); MS (EI) *m/e* 661 (M + 3, 40.5%), 660 (100), 659 (58), 658 (M, 22). Anal. Calcd for $C_{33}H_{38}Fe_2O_7$: C, 60.18; H, 5.77. Found: C, 59.65; H, 5.67.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-[α-(diphenylphosphino)ferrocenyl]-1,3-dioxane (18c). Following the standard procedure, the quenching was realized with chlorodiphenylphosphine (1.2 equiv). Acetal **18c** was isolated as a brown solid following FC on silica gel (90:10 cyclohexane−ether) in a 90% yield: mp 88−89 °C; ^{31}P NMR δ −21.40 (1P, s); $[\alpha]_D$ = −187 (*c* = 0.95, $CHCl_3$); ^{1}H NMR δ 1.38 (1H, m), 1.69 (1H, m), 2.87 (2H, d), 3.02 (3H, s), 3.67 (2H, m), 3.87 (1H, m), 4.00 (5H, s), 4.21 (2H, m), 4.63 (1H, m), 5.60 (1H, d, J_{P-H} = 2.5 Hz), 7.10−7.50 (10H, m).; MS (EI) *m/e* 502 (M + 2, 9.9%), 501 (42.5), 500 (M, 100), 499 (48); Anal. Calcd for $C_{28}H_{29}FeO_3P$: C, 67.20; H, 5.80; P, 6.20. Found: C, 66.89; H, 7.92; P, 6.06. See Supporting Information for crystal X-ray structure of **18c**.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-[α-(*tert*-butyldimethylsilyl)ferrocenyl]-1,3-dioxane (18d). Following the standard procedure, the quenching was realized with *tert*-butyldimethylsilyl triflate (1.1 equiv). The acetal was isolated as a brown oil following FC on silica gel (80:20 cyclohexane−ether) in a 87% yield: $[\alpha]_D$ = −27 (*c* = 0.74, chloroform); ^{1}H NMR δ 0.25 and 0.34 (6H, 2s), 0.81 (9H, bs), 1.49 (1H, m, *J* = 1.3 Hz *J* = 13.1 Hz), 1.75 (1H, m, *J* = 5.2 Hz), 3.29 (3H, s), 3.35 (2H, m, *J* = 5.2 Hz *J* = 9.8 Hz), 3.85 (2H, m), 3.98 (1H, m), 4.09 (5H, s), 4.10−4.35 (3H, m), 4.61 (1H, m), 5.30 (1H, s). ^{13}C NMR δ −4.3, −4.0, 17.5, 26.8, 28.3, 59.1, 66.35, 66.9, 69.1, 69.7, 70.3, 75.3, 75.3, 75.8, 90.6, 100.6. MS (EI) *m/e* 432 (M + 2, 7%), 431 (24), 430 (M, 77.5), 271 (100); Anal. Calcd for $C_{22}H_{34}FeO_3Si$: C, 61.39; H, 7.91. Found: C, 61.38; H, 8.06.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-[α-(*p*-tolylthio)ferrocenyl]-1,3-dioxane (18f). Following the standard procedure, the quenching was realized with *p*-tolyl disulfide (1.2 equiv in ether). Acetal **18f** was isolated as yellow brown crystals following FC on silica gel (6:1 cyclohexane−ether) in a 91% yield: $[\alpha]_D$ = +51 (*c* = 0.6, $CHCl_3$). ^{1}H NMR δ 1.45 (1H, m), 1.75 (1H, m), 2.22 (3H, s), 3.17 (3H, s), 3.30 (2H, m), 3.70−4.40 (5H, m), 4.21 (5H, s), 4.57 (1H, m), 5.55 (1H, s), 7.0 (4H, dd). MS (EI) *m/e* (440, M + 2, 15.2%), 439 (50.5), 438 (M, 100). Anal. Calcd for $C_{23}H_{26}FeO_3S$: C, 63.02; H, 5.98. Found: C, 63.08; H, 5.99.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-formylferrocenyl)-1,3-dioxane (18g). Following the standard procedure, the quenching was realized with DMF (1.3 equiv, 24 h stirring at rt). The acetal was isolated as a dark red solid following FC on silica gel (50:50 cyclohexane−ether to remove starting material and then ether) in a 93% yield. $[\alpha]_D$ = −370 (*c* = 0.128, $CHCl_3$), ^{1}H NMR δ 1.50 (1H, m), 1.80 (1H, m), 3.36 (3H, m), 3.45 (2H, m), 4.26 (5H, s), 3.85−4.27 (3H, m), 4.52 (1H, m), 4.76 (2H, m), 5.67 (1H, s), 10.21 (1H, s). MS (EI) *m/e* 345 (M + 1, 23%), 344 (M, 22.5), 251 (31.9), 177 (100); IR (CsI) 1671 cm^{-1}. Anal. Calcd for $C_{17}H_{20}FeO_4$: C, 59.32; H, 5.86. Found: C, 59.55; H, 5.99.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-[α-boronoferrocenyl)-1,3-dioxane (18h) and (S_{Fc},$S_{Fc'}$)-Bis[α-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]ferrocenyl]borinic acid (24). Procedure A (with trimethylborate or triisopropyl borate in ether). Following the standard procedure, the metalation was

performed on 1.6 g of acetal **15** (5 mmol) in 25 mL of ether. After cooling the suspension to −78 °C, triisopropyl borate (1.73 mL, 7.5 mmol, 1.5 equiv) was injected, and the suspension was slowly allowed to warm to rt with strong stirring over 15 h. After quenching with water, the brown organic phase was separated, and the yellow aqueous phase was saturated with sodium chloride and extracted with EtOAc until the organic extracts remained colorless. The organic phase was dried over magnesium sulfate, and the solvents were removed under reduced pressure on a rotary evaporator without heating. The resulting brown oil was purified by flash chomatography (50:50 cyclohexane−ether to ether). A first fraction contained recovered starting material. A second fraction gave the acid **24** as a yellow powder (after crystallization from cold ether−pentane) (400 mg, 24% yield), and the last polar one, the boronic acid **18h** as a yellow foam (620 mg, 35% yield). **Procedure B** (with triisopropyl borate in ether−THF). Following the standard procedure, the metalation was performed on 1.6 g of acetal **15** (5 mmol) in 25 mL of ether. After cooling the suspension at −78 °C, triisopropyl borate (1.73 mL, 7.5 mmol, 1.5 equiv) was injected followed by 20 mL of dry THF. The resulting orange solution was stirred at −78 °C for 2 h (TLC on SiO_2 with ether shows the boronic acid as the sole product with traces of starting acetal and borinic acid). The reaction mixture was then quenched with water at this temperature and treated as in procedure A. The boronic acid **18h** was isolated with yield > 90%. Care should be taken in handling solution of the boronic acid **18h** during purification as partial hydrolysis of the acetal group was observed in some cases when solvents were removed on a rotary evaporator while heating the water bath. Data for **18h**: ^{1}H NMR δ 1.50 (1H, m), 1.90 (1H, m), 3.44 (3H, s), 3.53 (2H, d), 4.18 (5H, s), 3.85−4.50 (6H, m), 5.45 (1H, s), 6.03 (2H, bs). ^{13}C NMR δ 27.1, 59.3, 66.8, 69.5, 70.8, 72.5, 74.9, 75.5, 76.6, 101.4; MS (EI) *m/e* 342 (M − H_2O, 100%), 317 (78). Anal. Calcd for $C_{16}H_{21}FeBO_5$: C, 53.38; H, 5.88; B, 3.00. Found: C, 53.31; H, 5.88; B, 2.75.

Data for **24**: ^{1}H NMR δ 1.55 (1H, m), 1.85 (1H, m), 3.39 (3H, s), 3.55 (2H, m), 4.14 (5H, s), 3.90−4.40 (3H, m), 4.32 (1H, m), 4.40 (1H, m), 4.64 (1H, m), 5.80 (1H, s), 8.37 (1H, s). ^{13}C NMR δ 28.2, 59.2, 66.9, 69.7, 70.7, 71.8, 75.5, 76.2, 76.3, 91.2, 101.1. MS (EI) *m/e* 658 (M, 8.33%), 121 (100). Anal. Calcd for $C_{32}H_{39}Fe_2BO_7$: C, 58.40; H, 5.98; B, 1.65. Found: C, 57.84; H, 5.93; B, 1.79.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-bromoferrocenyl)-1,3-dioxane (18i). Following the standard procedure, the lithio derivative was prepared from acetal **15** (1.08 g, 3 mmol) in 15 mL of ether. The supension of lithio complex was cooled with an ice−water bath, and a solution of α,α′-dibromo-*p*-xylene (870 mg, 3.3 mmol) in 20 mL of ether was quickly cannulated, giving almost immediately a colorless gellike precipitate in a yellow solution. After 30 min, the reaction mixture was quenched with water, filtered on Celite, and treated as usual. ^{1}H NMR analysis of the crude brown oil indicates a 95/5 mixture of **18i**/**15**. The pure acetal couldn't be separated from the starting acetal, neither by chromatography or crystallization and was directly used in the hydrolysis step: ^{1}H NMR δ 5.48 (1H, s).

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-iodoferrocenyl)-1,3-dioxane (18e). Following the standard procedure, the lithio derivative was prepared from acetal **15** (31.6 g, 0.1 mol) and 73.5 mL of a 1.5 M solution of *t*-BuLi (0.11 mol) in 300 mL of ether. The supension of lithio complex was cooled to −78 °C, and a solution of 1,2-diiodoethane (33.8 g, 120 mmol, 1.2 equiv) in 150 mL dry THF was slowly added dropwise via cannula. After the end of the addition, the dark solution was warmed to rt in about 30 min and quenched with water. After dilution with ether, the organic phase was washed with a 10% sodium thiosulfate solution and treated as usual. A 44 g amount of a dark brown oil was isolated (>95%) and used directly for the hydrolysis (^{1}H NMR indicates only the presence of the desired acetal **18e** contaminated with a small amount of starting material). An analytical sample was obtained by careful FC on silica gel (80:20 cyclohexane−ether): $[\alpha]_D = -35$ (c = 1.02, $CHCl_3$); ^{1}H NMR δ 1.50 (1H, m), 1.80 (1H, m), 3.35 (3H, s), 3.42 (2H, m), 4.01 (2H, m), 4.15 (5H, s), 4.18 (1H, m), 4.29 (1H, m,), 4.38 (1H, m), 4.42 (1H, m), 5.38 (1H, s,). ^{13}C NMR δ 26.8, 27.9, 41.4, 66.08, 66.9, 68.6, 68.8, 71.7, 74.7, 75.2, 76.1, 85.9, 100.8. MS (EI) *m/e* 444 (M + 2, 5.5%), 443 (30.5), 442 (M, 100). Anal. Calcd for $C_{16}H_{19}FeO_3I$: C, 43.43; H, 4.30. Found: C, 43.91; H, 4.19.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-(tributylstannyl)-ferrocenyl)-1,3-dioxane (25a). Following the standard procedure, the quenching was realized with tri-*n*-butylstannyl chloride (1.2 equiv). Acetal **25a** was isolated as a brown oil following FC on silica gel (90:10 cyclohexane−ether) in a 85% yield: $[\alpha]_D = -11.5$ (c = 0.985, $CHCl_3$); ^{1}H NMR δ 0.8−1.6 (28H, m), 1.76 (1H, m), 3.37 (1H, m), 3.44 (2H, m), 3.87 (1H, m), 3.95 (1H, m), 4.10 (5H, s), 4.20 (1H, m), 4.25 (1H, m), 4.49 (1H, m), 5.28 (1H, s,). ^{13}C NMR δ 10.6, 13.7, 27.5, 29.2, 28.3, 59.1, 66.5, 68.6, 69.0, 69.9, 74.7, 75.5, 75.7, 91.1, 100.8; MS (EI) *m/e* 607 (M + 2, 20.65%), 606 (28), 605 (M, 20.65), 333 (100). Anal. Calcd for $C_{28}H_{47}FeO_3Sn$: C, 55.54; H, 7.77. Found: C, 55.80; H, 7.53.

(S_{Fc},$S_{Fc'}$)-Bis[α-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]ferrocenyl]di-*n*-butylstannane (25b). Following the standard procedure, the lithio complex was prepared starting from acetal **15** (1.9 g, 6 mmol). The quenching was realized by addition of di-*n*-butyldichlorostannane (911 mg, 3 mmol) as a solution in ether at −78 °C, warming at rt, and stirring overnight. Bis-acetal **25b** was isolated as a viscous orange oil following FC on silica gel (70:30 to 50:50 cyclohexane−ether) in a 78% yield: ^{1}H NMR δ 0.95 (6H, t), 1.2−1.8 (16H, m), 3.36 (6H, s,), 3.38 (4H, m), 3.60−4.20 (8H, m), 4.28 (2H, m), 4.49 (2H, m), 5.11 (2H, s). Anal. Calcd for $C_{40}H_{56}Fe_2O_6Sn$: C, 55.65; H, 6.54. Found: C, 55.77; H, 6.37.

(S_{Fc},$S_{Fc'}$,$S_{Fc''}$)-*Tris*[α-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]ferrocenyl-*n*-butylstannane (25c). Following the standard procedure, the lithio complex was prepared starting from acetal **15** (5.56 g, 17.6 mmol). The quenching was realized by addition of *n*-butyltrichlorostannane (977 μL, 5.8 mmol, 0.3 equiv), warming to rt, and stirring overnight. Tris-acetal **25c** was isolated as an orange foam following FC on silica gel (70:30 to 50:50 cyclohexane−ether) in a 80% yield. ^{1}H NMR δ 0.9−2.0 (11H, m), 3.32 (9H, s,), 3.35 (6H, m), 3.40−4.40 (15H, m), 4.15 (15H, s), 4.54 (3H, m), 5.02 (3H, s); MS (EI, 70 eV) *m/e* 1122 (M + 1, 16%), 1121 (M, 16), 316 (59.8). Anal. Calcd for $C_{59}H_{66}Fe_3O_9Sn$: C, 55.70; H, 5.94. Found: C, 55.91; H, 6.01.

General Procedure for Acetal Hydrolysis. The purified acetal (0.5−1 mmol) was dissolved under Ar in 7 mL of dichloromethane, and 3 mL of water were added followed by 200 mg of PTSA monohydrate. The dark biphasic solution was stirred at rt for 1−15 h until no starting material remains by TLC (in some cases, it was necessary to heat the solution to reflux). The reaction mixture was extracted with ether, and the organic phase was washed several times with water, dried over $MgSO_4$, and concentrated. The crude aldehyde was purified by FC on silica gel. In large scale preparation, it was usually found that the crude aldehyde was sufficiently pure for further purposes and the purification step could be omitted. The typical yields of purified aldehyde were in the range of 90−99%.

(*S*)-α-(Trimethylsilyl)ferrocenecarboxaldehyde (22a). Following the standard procedure, the pure aldehyde was isolated as a waxy red-orange solid after FC on silica gel (70:30 cyclohexane−ether): $[\alpha]_D = -202$ (c = 0.245, EtOH) (lit.[27] $[\alpha]_D = +194$ (c = 0.28, EtOH), (*R*)-conf). ^{1}H NMR (C_6D_6) δ 0.35 (9H, s), 3.90 (5H, s), 4.20 (2H, m), 4.57 (1H, m), 9.93 (1H, s). ^{13}C NMR ($CDCl_3$) δ 04, 66.1, 69.6, 73.6, 74.7, 79.7, 194.3. Anal. Calcd for $C_{14}H_{18}FeOSi$: C, 58.75; H, 6.34. Found: C, 58.95; H, 6.42.

(*S*)-α-Carbomethoxyferrocenecarboxaldehyde (22b). Following the standard procedure, the pure aldehyde was isolated as an unstable dark red oil after FC on silica gel (75:25 cyclohexane−ether). The aldehyde could be conserved under Ar in the fridge at −20 °C: $[\alpha]_D = +765$ (c = 0.465, EtOH) (lit.[28] $[\alpha]_D = -760$ (EtOH), (*R*)-conf). ^{1}H NMR δ 3.86 (3H, s), 4.34 (5H, s), 4.78, (1H, t), 5.14 (2H, d), 10.65 (1H, s).

(*S*)-α-(Diphenylphosphino)ferrocenecarboxaldehyde (22c). Following the standard procedure, the pure aldehyde **22c** was isolated as a red solid after FC on silica gel (70:30 cyclohexane−ether): mp 149−150 °C. $[\alpha]_D = +107.5$ (c = 0.275, $CHCl_3$). ^{31}P NMR δ −23.20 (s). ^{1}H NMR δ 4.05 (1H,

s), 4.20 (5H, s), 4.68 (1H, m), 5.10 (1H, bs), 7.10−7.60 (10H, m), 10.20 (1H, d, J_{P-H} = 2.75 Hz). ^{13}C NMR δ 70.9, 71.5, 74.0, 76.5, 80.5 (J_{P-C} = 15Hz), 83.4 (J_{P-C} = 15 Hz), 128.3, 129.5, 132.1 (J_{P-C} = 18 Hz), 134.9 (J_{P-C} = 21 Hz), 136.3 (J_{P-C} < 10Hz), 193.3 (J_{P-C} = 10.5 Hz). MS (EI) *m/e* 399 (M + 1, 52.5%), 398 (M, 100). Anal. Calcd for $C_{23}H_{19}FeOP$: C, 69.35; H, 4.77. Found: C, 67.85; H, 4.82.

(*S*)-(α-*tert*-Butyldimethylsilyl)ferrocenecarboxaldehyde (22d). Following the standard procedure, the pure aldehyde was isolated as a waxy red-orange solid after FC on silica gel (80:20 cyclohexane−ether): $[\alpha]_D$ = +325 (*c* = 0.30, $CHCl_3$). ^{1}H NMR δ 0.30 (3H, s); 0.43 (3H, s); 1.56 (9H, s); 4.23 (5H, s); 4.60 (1H, m); 4.76 (1H, m), 5.05 (1H, m); 10.0 (1H, s). MS (EI, 70 eV) *m/e* 329 (M + 1, 2.50%), 328 (M, 6.7), 271 (100). Anal. Calcd for $C_{17}H_{24}FeOSi$: C, 62.19; H, 7.32. Found: C, 62.29; H, 7.43.

(*S*)-(α-*p*-Tolylthio)ferrocenecarboxaldehyde (22f). Following the standard procedure, the pure aldehyde was isolated as yellow-brown crystals after FC on silica gel (6:1 cyclohexane−ether): $[\alpha]_D$ = +840 (*c* = 0.036, $CHCl_3$). ^{1}H NMR δ 2.24 (3H, s), 4.33 (5H, s), 4.74 (2H, m), 5.02 (1H, m), 6.97 (4H, dd), 10.18 (1H, s). ^{13}C NMR δ 20.9, 69.3, 71.3, 73.2, 79.6, 79.8, 81.5, 127.1, 129.6, 135.4, 135.7, 193.9. MS (EI) *m/e* 338 (M + 2, 19.65%), 337 (55), 336 (M, 79), 180 (100). Anal. Calcd for $C_{18}H_{16}FeOS$: C, 64.30; H, 4.80; S, 9.54. Found: C, 64.13; H, 4.91; S, 9.13.

(*S*)-α-Boronoferrocenecarboxaldehyde (22h). Following the standard procedure, the pure aldehyde was isolated as a deep red solid. According to analysis, the boronic acid contains some amounts of boroxine: ^{1}H NMR δ 4.28 (5H, s), 4.83 (1H, m), 4.89 (1H, m), 5.08 (1H, m), 6.78 (2H, bs), 9.84 (1H, s). Anal. Calcd for $C_{11}H_{11}FeBO_3$: C, 51.24; H, 4.30. Calcd for $C_{33}H_{27}Fe_3B_3O_6$ (boroxine): C, 55.01 H, 3.75. Found: C, 53.01; H, 4.68.

(*S*)-α-Bromoferrocenecarboxaldehyde (22i). Following the standard procedure, the pure aldehyde was isolated as a brown solid after FC on silica (70:30 cyclohexane−ether). Due to its instability, the aldehyde must be stored in a freezer under inert atmosphere. ^{1}H NMR δ 4.31 (5H, s), 4.59 (1H, m), 4.79 (1H, s), 4.83 (1H, s), 10.14 (1H, s). ^{13}C NMR δ 66.4, 71.1, 72.0, 74.8, 79.9, 192.7.

(*S*)-α-Iodoferrocenecarboxaldehyde (22e). Following the standard procedure, the crude adduct **18e** (44 g, ≈0.1 mol *vide infra*) was dissolved in 300 mL of degassed dichloromethane and 150 mL of water under Ar, and PTSA monohydrate (27 g) was added with stirring. The solution was heated at 50 °C under Ar for 24 h. After standard workup, the dark brown oil was dissolved in ether and filtered on a small column of silica gel to remove polymeric impurities. The oil was extracted with boiling heptane, and the hot solution was filtered and allowed to cool. Upon cooling to rt, crystals started to appear, and the flask was placed in a freezer (−20 °C) overnight. The dark brown crystals were collected, washed with heptane, and dried. The recovery for the first crop of crystals was 23.6 g (69% yield from acetal **15**). The ^{1}H NMR analysis of the mother liquors indicated the presence of a mixture of aldehyde **22e** and acetal **18e**. The hydrolysis was repeated on this fraction, and another crop of crystals (10%) was isolated after workup and crystallization from heptane: $[\alpha]_D$ = +558 (*c* = 0.35, $CHCl_3$). ^{1}H NMR δ 4.27 (5H, s), 4.67 (1H, m), 4.81 (1H, m), 4.88 (1H, m), 10.02 (1H, s). ^{13}C NMR δ 67.6, 72.5, 73.7, 79.5, 194.4. MS (EI) *m/e* 341 (M + 1, 8.25%), 340 (M, 54.75), 212 (100). Anal. Calcd for $C_{11}H_9FeOI$: C, 38.82; H, 2.65; I, 37.35. Found: C, 39.85; H, 2.58; I, 37.09.

Recovery of the Chiral Auxiliary after Hydrolysis. The first aqueous washing from the above experiment was collected and neutralized with solid $NaHCO_3$. The water was removed by rotary evaporation, and the residue was taken up in EtOH. The solid sodium *p*-toluenesulfonate was filtered on Celite and washed with EtOH. The filtrate was concentrated, and the extraction and filtration were repeated twice with dichloromethane. After evaporation of the solvents, an oil still contaminated with some sodium *p*-toluenesulfonate was isolated. A fraction of this oil was distilled under reduced pressure to give a pure sample (4 g) of (*S*)-1-(methoxymethyl)-1,3-propanediol as a clear colorless oil. ^{1}H NMR δ 1.66 (2H, m), 2.61 (1H, m), 2.87 (1H, bs), 3.32 (2H, m), 3.37 (3H, s), 3.81 (2H, m), 4.0 (1H, m). The recovered diol could be recycled by reaction with 1 equiv of ferrocene carboxaldehyde **12** and a catalytic amount of PTSA in benzene using a Dean−Stark trap.

(*S*)-α-(Tributylstannyl)ferrocenecarboxaldehyde (26a). Following the standard procedure, the pure aldehyde was isolated as a red oil after FC on silica gel (90:10 cyclohexane−ether). $[\alpha]_D$ = −475 (*c* = 0.316, EtOH). ^{1}H NMR δ 0.90 (9H, t), 1.05 (6H, q), 1.36 (6H, t), 4.20 (5H, s), 4.48 (1H, m), 4.73 (1H, m), 4.92 (1H, m), 9.91 (1H, s); ^{13}C NMR δ 10.8, 13.7, 27.4, 27.0, 29.2, 65.9, 73.2, 75.4, 69.3, 80.0, 194.8; MS (EI) *m/e* 504 (M + 2, 0.58%), 503 (0.51), 502 (M, 0.53), 447 (100); Anal. Calcd for $C_{23}H_{36}FeOSn$: C, 54.98; H, 7.17. Found: C, 56.24; H, 7.67.

(S_{Fc},$S_{Fc'}$)-Bis(α-formylferrocenyl)dibutylstannane (26b). Following the standard procedure, the purified aldehyde **26b** was isolated as a red-orange oil which slowly crystallizes upon standing after FC on silica gel (70:30 cyclohexane−ether. ^{1}H NMR δ 0.80−1.90 (18H, m), 4.22 (10H, s), 4.80 (2H, m), 4.73 (2H, m), 4.94 (2H, m), 9.99 (2H, s).

(S_{Fc},$S_{Fc'}$,$S_{Fc''}$)-*Tris*(α-formylferrocenyl)-*n*-butylstannane (26c). Following the standard procedure, the pure aldehyde **26c** was isolated as an orange powder after FC on silica gel (60:40 cyclohexane−ether). ^{1}H NMR δ 0.97 (3H, t), 0.9−2.0 (6H, m), 4.20 (15H, s), 4.39 (3H, m,), 4.75 (3H, m), 5.0 (3H, m), 10.08 (3H, s). ^{13}C NMR δ 14.0, 17.0, 27.0, 29.0, 70.0, 72.5, 74.3, 75.6, 81.0, 83.7, 194.2. MS (EI, 70 eV) *m/e* 814 (M, 9.10%), 758 (M-*n*-C_4H_9, 83). Anal. Calcd for $C_{37}H_{36}Fe_3O_3Sn$: C, 54.53; H, 4.46. Found: C, 54.25; H, 4.57.

(*S*)-α-Hydroxyferrocenecarboxaldehyde (28). *Due to extensive air oxidation of the hydroxyaldehyde **28**, all the manipulations, including workup and purification, should be done under inert atmosphere using standard Schlenk tube manipulations.* Organolithium derivative **17a** was prepared from 790 mg of acetal **15** (2.5 mmol) following the general procedure. Then was introduced dropwise 490 mg (2.75 mmol, 1.1 equiv) of bis(trimethylsilyl) peroxide[33] by a Teflon microsyringe at −78 °C. *Caution!* By using metal needles for the addition of the peroxide we have observed an explosion, and we advise taking safety precautions as much as possible! The amber suspension was warmed to rt by stirring for an additional 24 h, and the resulting dark brown solution was cooled and treated with 20 mL of degassed water for 10 min. The layers were separated, and the aqueous layer was extracted twice with ether to remove some starting material and byproducts. The basic aqueous layer was treated with diluted acetic acid to pH 5 and extracted twice with ether, and the organic layer was dried over magnesium sulfate, filtered, and concentrated. The resulting red oil (550 mg, 95%) decomposed very quickly by giving a dark brown residue and should be purified before by FC on silica gel (1:1 cyclohexane−ether) under Ar. Evaporation of the deep red fraction afforded 150 mg of a dark red solid **28** (26% due to considerable decomposition): $[\alpha]_D$ = −1280 (*c* = 0.03, $CHCl_3$); −1690 (*c* = 0.14, $CHCl_3$); (lit.[31] $[\alpha]_D$ = −2155 (*c* = 0.52, $CHCl_3$ unknown configuration). For this highly colored substance we were unable to perform with our cell (*l* = 1 dm) the measurement at higher concentration as in ref 31. ^{1}H NMR δ 4.16 (s, 1H); 4.24 (s, 6H); 4.67 (s, 1H), 6.90 (s, 1H); 10.07 (s, 1H). MS (EI, 70 eV) *m/e* 230 (M, 100%); 164 (65).

(*S*)-α-Acetoxyferrocenecarboxaldehyde (29). To a degassed solution of boronic acid **18h** (630 mg, 1.75 mg) in acetone (20 mL) and water (15 mL) was added 1.75 g of $Cu(OAc)_2$ (8.75 mmol, 5 equiv), and the mixture was heated at 60 °C under Ar until TLC check (SiO_2, 70:30 cyclohexane−ether) showed complete consumption of starting material (3 h). The reaction mixture was filtered on Celite and extracted with ether. The organic phase was washed with a dilute solution of ammonia and treated as usual. FC on silica gel (70:30 cyclohexane−ether) delivers first an orange band of ferrocenecarboxaldehyde **12** followed by a second orange band. Evaporation of the second fraction yielded the desired aldehyde **29** as an brown solid (120 mg, 25%). ^{1}H NMR δ 2.24 (3H, s), 4.32 (5H, s), 4.42 (1H, m), 4.61 (1H, m), 4.85 (1H, m, C_5H_3), 10.05 (1H, s). ^{13}C NMR δ 21.0, 63.9, 65.9, 67.4, 70.1, 70.9, 116.6, 169.1, 191.5.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-acetoxyferrocenyl)-1,3-dioxane (30). Following the standard procedure (proce-

dure B, *vide supra*), the boronic acid **18h** was prepared from acetal **15** (1.6 g, 5 mmol). The crude boronic acid was dissolved in 20 mL of degassed CH_3CN with 2.4 g of $Cu(OAc)_2$ (12 mmol), and the bright green solution was heated at 60 °C for 2 h. After cooling, the reaction mixture was diluted with ether, and the turquoise blue precipitate was filtered on Celite and washed with ether. The filtrate was concentrated *in vacuo*, and the procedure was repeated once. The residue was purified by FC on silica gel (70:30 to 50:50 cyclohexane−ether) to give first acetal **15** (800 mg, 50% recovery). A second yellow band delivers the desired acetoxy acetal **30** as an orange oil (620 mg, 33% yield from **15**). ^{1}H NMR δ 1.45 (1H, m), 1.75 (1H, m), 2.15 (3H, s), 3.36 (3H, s), 3.40 (2H, m), 3.80−4.30 (4H, m), 4.21 (5H, s), 4.16 (1H, m), 4.38 (1H, m), 5.45 (1H, s). ^{13}C NMR δ 21.0, 28.1, 56.3, 61.7, 62.30, 66.7, 70.2, 75.5, 76.0, 77.2, 98.7, 113.6, 169.4.

General Procedure for the Preparation of Cuprates and Reaction with Electrophiles. Synthesis of (R_{Fc})-3-[α-[(2*S*,4*S*)-4-(Methoxymethyl)-1,3-dioxan-2-yl]ferrocenyl]cyclohexanone (34). Procedure A (with *tert*-butylacetylene). To a cooled (−78 °C) solution of *tert*-butylacetylene (370 μL, 3 mmol) in 4 mL of dry THF under Ar were added 2.4 mL of a 1.5 M solution of *n*-BuLi (3.6 mmol) dropwise by syringe. After 30 min, the temperature was raised to −50 °C, a suspension of CuCN (269 mg, 3 mmol) in 12 mL of dry THF was added via cannula, and stirring was maintained at this temperature for 30 min. The cyanocuprate solution was then added to a cooled (−50 °C) suspension of lithio complex **17a** (prepared from acetal **15** (630 mg, 2 mmol) in 5 mL of dry ether) via cannula. The bright orange solution was stirred at this temperature for 1 h before cooling to −78 °C. Cyclohexenone (230 μL, 2.4 mmol) and BF_3 etherate (370 μL, 2.4 mmol) were successively injected, and the reaction mixture was stirred at −78 °C for 1 h and slowly allowed to warm to rt overnight. The reaction mixture was quenched with an aqueous ammonia solution and worked-up. Purification by FC on silica gel (3:1 cyclohexane−ether) yielded the 1,4-addition adduct **34** as a golden-yellow viscous oil in a 69% yield.

Procedure B (with lithium thienylcyanocuprate). Lithioferrocene **17a** was prepared as as above from acetal **15** (630 mg, 2 mmol). After cooling the suspension to −50 °C, 8 mL of a 0.25 M solution of lithium 2-thienylcyanocuprate in THF (Aldrich, 2 mmol) was injected dropwise via syringe, and the bright orange solution was stirred at this temperature for 1 h. The same procedure as in procedure A was then followed. The yield of acetal **34** after chromatographic purification was 26%: $[\alpha]_D = -50$ ($c = 0.2$, $CHCl_3$). ^{1}H NMR δ 1.50−3.00 (11H, m), 3.33 (3H, s), 3.43 (2H, m), 4.10 (5H, s), 3.80−4.40 (6H, m), 5.41 (1H, s). ^{13}C NMR δ 27.9, 34.1, 37.4, 41.4, 47.5, 59.1, 65.9, 66.7, 67.1, 69.2, 75.5, 75.9, 82.8, 90.9, 100.2, 212.2. MS (EI) *m*/*e* 414 (M + 2, 28.6%), 413 (98), 412 (M, 100). IR (CsI) 1721 cm^{-1}. Anal. Calcd for $C_{22}H_{28}FeO_4$: C, 64.09; H, 6.85. Found: C, 65.04; H, 6.88.

(R_{Fc})-3-(α-Formylferrocenyl)cyclohexanone (35). Acetal **34** was converted to the corresponding aldehyde using the standard procedure for hydrolysis. Aldehyde **35** was isolated as yellow-brown crystals following FC on silica gel (ether): $[\alpha]_D = -190$ ($c = 0.098$, $CHCl_3$). ^{1}H NMR δ 1.50−2.90 (9H,m), 4.22 (5H, s), 4.45 (1H, bs), 4.48 (1H, m), 4.71 (1H, m), 10.00 (1H, s). ^{13}C NMR δ 24.4, 34.7, 36.9, 41.4, 69.3, 70.1, 71.2, 71.7, 94.9, 193.4, 211.4. MS (EI) *m*/*e* 311 (M + 1, 34%), 310 (M, 100); IR (CsI) 1457 cm^{-1}. Anal. Calcd for $C_{17}H_{18}FeO_2$: C, 65.83; H, 5.85. Found: C, 65.47; H, 6.03.

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-aminoferrocenyl)-1,3-dioxane (32a). Procedure A. Following the general procedure, the mixed cyanocuprate **31a** was prepared starting from 3.71 g of acetal **15** (11.75 mmol) and 48 mL of a 0.25 M lithium 2-thienylcyanocuprate solution (11.75 mmol). After cuprate formation at −50 °C, 1.5 g of *N*,*O*-bis(trimethylsilyl-)hydroxylamine (14.1 mmol, 1.2 equiv) was added dropwise via syringe at this temperature, and the reaction mixture was stirred at −50 °C for 1 h and slowly warmed to rt overnight. After standard workup, the brown oil was purified by FC on silica gel (ether). A first nonpolar brown band yielded unreacted starting acetal **15**, and a second polar orange band yielded the aminoacetal **32a** as an orange oil which crystallizes upon standing in a freezer (2.2 g, 56% yield).

Procedure B. By following the procedure used for the preparation of the mixed cuprate **31b**, the reaction was performed starting from 1.26 g of acetal **15** (4 mmol). Following the same procedure for the electrophilic quenching, the aminoacetal **34a** was isolated in a 39% yield (520 mg). However, we found that scaling-up the reaction significantly decreased the yield of aminoacetal. Thus, the reaction was performed in the same conditions starting from 15.8 g of acetal **15** (50 mmol). After chromatographic separation, unreacted starting acetal **15** (12.6 g, 40 mmol) was recovered (97% recovery), and 3 g of aminoacetal **32a** (9 mmol, 18% yield) was isolated.

Procedure C. Following the standard procedure, the lithio derivative was prepared from acetal **15** (3.16 g, 10 mmol) in 50 mL of ether. The suspension was cooled to −78 °C, and a precooled suspension of 450 mg CuCN (5 mmol) in 30 mL of dry THF was added via cannula. The mixture was stirred at −50 °C for 1 h before addition of the electrophile (890 mg, 5 mmol). The reaction was allowed to proceed at this temperature for 2 h before quenching with aqueous ammonia solution. Workup and purification as above yielded 600 mg of aminoacetal **32a** (36% yield) and 1.92 g of recovered acetal **15** (6 mmol): $[\alpha]_D = -77$ ($c = 0.068$, $CHCl_3$). MS (EI) *m*/*e* 333 (M + 2, 23.2%), 332 (91.1), 331 (M, 71.4).

(2*S*,4*S*,S_{Fc})-4-(Methoxymethyl)-2-(α-acetamidoferrocenyl)-1,3-dioxane (32b). To a solution of aminoacetal **32a** (95 mg, 0.287 mmol) in 2 mL of anhydrous pyridine under Ar was added 150 μL of Ac_2O (1.6 mmol) and a few crystals of DMAP. The orange solution was stirred at rt for 4 h until disappearance of the starting amine by TLC (SiO_2, ether). After dilution with toluene, solvents were removed by rotary evaporation, and the residue was purified by FC on silica gel (ether). Acetamide **32b** was isolated as a yellow-brown viscous oil in a 84% yield (80 mg). $[\alpha]_D = -1310$ ($c = 0.02$, $CHCl_3$). ^{1}H NMR δ 1.60 (1H, m), 1.90 (1H, m), 2.02 (3H, s), 3.44 (3H, s), 3.55 (2H, m), 4.06 (5H, s), 3.80−4.30 (6H, m), 5.22 (1H, bs), 5.62 (1H, s). MS (EI) *m*/*e* 374 (M + 1, 44.2%), 373 (M, 96.4).

(*S*)-α-Aminoferrocenecarboxaldehyde (33a). Following the standard procedure, hydrolysis of the acetal **32a** was run in about 30 min to avoid decomposition of the amino aldehyde in acidic medium. After complete disappearance of the starting material by TLC (SiO_2, ether), the reaction mixture was made alkaline by addition of 2 M NaOH solution followed by usual workup. The amino aldehyde was recovered quantitatively and was sufficiently pure for further purpose. An analytical sample was obtained by recrystallization in ether. The amino aldehyde proved to be very stable but quickly decomposed under acidic conditions. Extensive polymerization was also observed on attempts of chromatography on silica gel. $[\alpha]_D = -753$ ($c = 0.032$, $CHCl_3$). ^{1}H NMR δ 3.80 (2H, bs), 4.14 (5H, s), 4.18 (1H, m), 4.31 (1H, m), 4.40 (1H, m), 9.97 (1H, s). MS (EI) *m*/*e* 230 (M + 1, 14.4%), 229 (M, 86), 163 (100). IR (KBr) 1460 cm^{-1}.

(*S*)-α-(*N*-Acetylamino)ferrocenecarboxaldehyde (33b). Acetal **32b** was converted to the corresponding aldehyde using the standard procedure for hydrolysis. Aldehyde **33b** was isolated as a red oil following FC on silica gel (ether). $[\alpha]_D = -2665$ ($c = 0.068$, $CHCl_3$). ^{1}H NMR δ 2.10 (3H, s), 4.22 (5H, s), 4.40 (2H, bs), 5.78 (1H, bs), 8.66 (1H, bs), 10.03 (1H, s). MS (EI) *m*/*e* 272 (M + 1, 21%), 271 (M, 100). IR (Nujol, CsI) 1466 cm^{-1}. Anal. Calcd for $C_{13}H_{13}FeNO_2$: C, 57.60; H, 4.84; N, 5.17. Found: C, 57.79; H, 5.01; N, 4.97.

(S_{Fc},$S_{Fc'}$)-1,2-Bis[α-(Diphenylphosphino)ferrocenyl]-ethene (*Z*)-37 and (*E*)-37. These compounds were obtained from (*S*)-**22c** with the following procedure. To a suspension of $TiCl_4$−THF complex (1:2) (5.32 g, 16 mmol) in 30 mL of THF under Ar was added Zn powder (2.1 g, 32 mmol) by portions, and the resulting suspension was heated at reflux temperature for 1 h. The green color changed to dark violet and then to black. A solution of aldehyde **22c** (1.3 g, 3.25 mmol) and pyridine (0.5 mL) in 20 mL of THF was added under Ar at rt. The reaction mixture was then stirred overnight under reflux. After cooling, the reaction mixture was quenched with a 5% Na_2CO_3 solution, filtered on Celite, and washed with dichloromethane until the filtrate became colorless. After FC on silica gel (3:1 cyclohexane−ethyl acetate), 700 mg (60%) of product was isolated as a mixture of *E*/*Z* isomers (80:20 from

^{1}H NMR analysis). A further chromatography followed by recrystallization in ether afforded pure *E* and *Z* isomers as red colored solids: ***trans*-37:** mp 202 °C. $[\alpha]_D$ = 1040 (*c* = 0.6, $CHCl_3$). ^{31}P NMR δ −21.47 (s). ^{1}H NMR δ 3.67 (1H), 4.06 (5H, s_5), 4.3 (1H, m), 4.75 (1H, m), 6.77 (1H, s), 7.1−7.6 (10H, m). ^{13}C NMR δ 67.3, 70, 70.3 (5C), 72.0, 75.1, 89.4 (d, J_{P-C} = 15 Hz), 124.0 (d, J_{P-C} = 12 Hz, C=), 128.00, 128.05, 128.2, 129.1, 132.1 (J_{P-C} = 18 Hz), 135.2 (J_{P-C} = 21 Hz), 137.2 (J_{P-C} = 8Hz), 139.7 (J_{P-C} = 8Hz). Anal. Calcd for $C_{46}H_{38}Fe_2P_2$: C, 72.27; H, 5.01. Found: C, 71.96; H, 5.45. ***cis*-37:** mp > 250 °C. $[\alpha]_D$ = 250 (*c* = 0.6, $CHCl_3$). ^{31}P NMR δ −21.4 (s). ^{1}H NMR δ 3.65 (1H, m), 3.81(5H, s), 4.29 (1H, m), 4.61 (1H, m), 7.15−7.6 (10H, m). ^{13}C NMR δ 67.2, 69.1, 69.8, 70.3 (5C), 71.65, 89.3, 123.6 (d, J_{P-C} = 12Hz), 127.9, 128, 128.1, 128.15, 128.2, 129.1, 132.3 (J_{P-C} = 18.5Hz), 135 (d, J_{P-C} = 20Hz), 137.2, 139.8.

(S_{Fc},$S_{Fc'}$)-*Bis*-2:3,6:7-Ferroceno-di-*n*-butylstannepine (38). A two-necked Schlenk fitted with a septum and a reflux condenser was charged with $TiCl_4$−THF complex (1:2) (1.67 g, 5 mmol) under Ar, and the complex was slurried in 20 mL of dry THF. The suspension was cooled with an ice−water bath, zinc powder (653 mg, 10 mmol) was added by portions under Ar, the cooling bath was removed, and the black solution was refluxed for 1 h. The bis-aldehyde **25b** (330 mg, 0.5 mmol) in 15 mL of THF and 0.2 mL of dry pyridine was slowly injected via a cannula in to the refluxing solution of titanium reagent; reflux was maintained for 3 h (TLC on silica plate with *n*-hexane as eluent indicates no starting material and the formation of a single new spot). The reaction mixture was cooled and carefully quenched with saturated $NaHCO_3$ solution, and the mixture was filtered on Celite and washed with dichloromethane. After standard workup, the crude product was purified by FC on silica gel (95:5 cyclohexane−ether). The stannepine **38** was isolated as a dark orange oil (273 mg) in a 87% yield. ^{1}H NMR δ 0.90−1.80 (18H, m), 3.94 (10H, s), 4.10 (2H, m), 4.46 (2H, bs), 6.18 (2H, s). ^{13}C NMR δ 11.9, 13.8, 27.4 , 29.1 , 68.6, 68.9, 70.9, 71.3, 72.8, 74.6, 88.5, 127.0.

(S_{Fc},1*R*,2*S*,$S_{Fc'}$), (S_{Fc},1*R*,2*R*,$S_{Fc'}$) and (S_{Fc},1*S*,2*S*,$S_{Fc'}$)-1,2-Bis[α-(diphenylphosphino)ferrocenyl]ethane-1,2-diols (39a−c). These compounds were obtained from (*S*)-**22c** using the following procedure: To a solution of **22c** (2 g, 5 mmol) in 20 mL of dry THF under Ar was added dropwise via a cannula a solution of 100 mL of SmI_2 0.1 M in THF. After 30 min, the reaction was over. TLC (cyclohexane−ethyl acetate 5:1) showed three spots without the starting aldehyde. After quenching and standard workup, 1.6 g of crude product was obtained and purified on silica gel to give three compounds in the 40:30:30 proportions. The same reaction at −25 °C afforded these three diols in the 65:25:10 proportions. Diol (1*R*,2*S*)-**39c**: This compound was eluted first. Mp 190 °C. $[\alpha]_D$ = −195 (*c* = 0.7, $CHCl_3$). ^{31}P NMR δ −25.35 (s); −21.8 (s). ^{1}H NMR δ 3.75 (5H, s), 3.8 (1H, m), 3.85 (5H, s), 3.9 (1H, m), 3.95 (1H, m), 4,15 (2H, m), 4.7 (1H), 7.1−7.6 (20H, m). ^{13}C NMR δ 68.8 (d, *J* = 4 Hz), 69.0, 69.3 (5C), 69.5, 69.6 (5C), 70.3, 71.1, 71.1, 71.8, 72.1 (d), 73.5 (d, *J* = 10 Hz), 76, 127.6−130.2 (14C), 132.4 (d, *J* = 17 Hz, 2C), 133.4 (d, *J* = 19 Hz, 2C), 134.4 (d, *J* = 21 Hz, 2C), 135.2 (d, *J* = 21 Hz, 2C), 136 (d, *J* < 10Hz, 2C), 139.8 (d, *J* < 10Hz, 2C). HRMS calcd for $C_{46}H_{40}Fe_2O_2P_2$, *M* = 798.1204; obsd, *M* = 798.1213. Diol (1*R*,2*R*)-**39a**: Its R_f is closed to the R_f of diol **39c**: mp 210 °C. $[\alpha]_D$ = −320 (*c* = 1, $CHCl_3$). ^{31}P NMR δ −22.75 (s). ^{1}H NMR δ 4 (2H, m), 4.05 (10H, m), 4.23 (4H, m), 7−7.6 (20H, m). ^{13}C NMR δ 69.8 (10C), 70.4 (2C), 71.1 (d, *J* = 4.5 Hz, 2C), 71.3 (d, *J* = 4 Hz, 2C), 73 (d, *J* = 7 Hz, 2C), 94.4 (d, *J* = 20 Hz, 2C), 128−128.3 (12C), 129.1 (2C), 132.7 (d, *J* = 19 Hz, 4C), 134.9 (d, *J* = 21 Hz, 4C), 137 (*J* < 10, 2C), 139.1 (2C). HRMS calcd for $C_{46}H_{40}Fe_2O_2P_2$, *M* = 798.1204; obsd, *M* = 798.1197. Diol (1*S*,2*S*)-**39b**: It is the more polar of the three diols. Mp 95 °C. $[\alpha]_D$ = −310 (*c* = 1, $CHCl_3$). ^{31}P NMR δ −25.4 (s). ^{1}H NMR δ 3.7 (2H, m), 3.8 (10H, m), 4.25 (2H, m), 4.4 (2H, m), 4.55 (2H, m), 7.1−7.6 (20H, m). ^{13}C NMR δ 68.1 (2C), 69.2 (2C), 69.6 (10C), 71.7 (2C), 71.9 (2C), 93.8 (2C), 128 (m, 12C), 129 (2C), 133.1 (d, *J* = 20 Hz, 2C), 133.3 (d, *J* = 20 Hz, 2C), 134.9 (d, *J* = 20 Hz, 2C), 135.05 (d, *J* = 20 Hz, 2C), 137.5 (2C), 140 (2C). HRMS calcd for $C_{46}H_{40}Fe_2O_2P_2$ *M* = 798.1204; obsd, *M* = 798.1222. See Supporting Information for X-ray crystal structure of the enantiomer of **39b**.

(S_{Fc},1*S*,2*S*,$S_{Fc'}$)-1,2-(Isopropylidenedioxy)-1,2-bis[α-(diphenylphosphino)ferrocenyl]ethane (40). A 200 mg amount of diol **39b** in 10 mL of dimethoxypropane was heated at 60 °C overnight with 10 mg of pyridinium tosylate. The resulting suspension was diluted with ether, filtered on Celite, evaporated, and purified FC on silica gel (85:15 cyclohexane−EtOAc). A further recrystallization in hexane afforded 100 mg of dioxolane **40** as a yellow solid. $[\alpha]_D$ = −235 (*c* = 1, $CHCl_3$). ^{31}P NMR δ −23.7 (s). ^{1}H NMR δ 1.55 (6H, s), 3.55 (2H, m), 3.70 (2H, m), 3.95 (10H, s), 4.10 (2H, m), 4.60 (2H, m), 6.9−7.5 (20H, m). MS (DIC/NH_3) *m/e* 858 (M + 2 + NH^{4+} 4.11%), 857 (M + 1 + NH_4^+, 6.85%), 840 (M + 2, 45.66%), 839 (M + 1, 26%), 838 (M 7.76%), 187 (100%).

(*S*)-α-(Diphenylphosphino)ferrocenemethanol (41). To a solution of aldehyde **22c** (900 mg, 2.2 mmol) in 5 mL of EtOH under Ar was added 40 mg (1 mmol) of $NaBH_4$. The mixture was stirred 2 h at 40 °C. The standard workup afforded a quantitative amount of **41** as a yellow solid. Mp 102−103 °C. $[\alpha]_D$ = −250 (*c* = 1, $CHCl_3$). ^{31}P NMR δ −22.8 (s). ^{1}H NMR δ 3.75 (1H, m), 4.1 (5H, s), 4.28 (1H, m), 4.4 (1H, m), 4.5 (2H, s,), 7.1−7.6 (10H, m). MS (EI) *m/e* 400 (M, 82%), 183 (100%).

Asymmetric Catalysis. Standard procedures were used for the asymmetric hydrogenations[54] (see Table 3 for the experimental conditions) and allylic substitutions[55] (Table 4). The cationic rhodium complexes (Table 3, entries 1 and 7) were prepared according to the general reported methods.[56]

Crystallographic Data. The authors have deposited atomic coordinates for structures **18c** and enantiomer of **39b** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Acknowledgment. We are grateful to CNRS, Institut Universitaire de France and Université Paris-Sud for financial support. Two of us (S.T. and O.R.) thank DFG and MRES respectively for a fellowship. We also thank Dr. J. C. Daran for the X-ray structure determinations.

Supporting Information Available: Supplementary data supporting the X-ray crystallographic stucture of **18c** and enantiomer of **39b**: ORTEP representation, atomic coordinates, bond lengths, and bond angles (19 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO970075U

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