Synthesis and Applications of Chiral Cyclopentadienylmetal Complexes

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Contents

Ronald L. Halterman was born in 1957 in Riverside, CA, and was raised in San Bernardino, CA. He received his B.S. degree (summa cum laude, Phi Beta Kappa) in chemistry in 1980 from the University of California in Riverside where he did undergraduate research with M. Mark Midland and spent his junior year at Georg August Universität in Göttingen, Germany. After completing his doctoral work in 1985 under K. Peter C. Vollhardt at the University of California, Berkeley, he moved as an NIH Postdoctoral Fellow to the Massachusetts Institute of Technology where he worked in William R. Roush's laboratory. He began his academic career in 1987 at Boston University, and in 1991, he moved to the University of Oklahoma in Norman as an Associate Professor of Chemistry. In addition to chiral C_2-symmetrical cyclopentadienylmetal chemistry, his research interests include chiral D_4-symmetrical metalloporphyrin chemistry and stereoelectronic control of reactions of sterically unbiased substrates.

I. Introduction

Organometallic complexes containing chiral ligands are becoming increasingly important in synthetic methodology as catalytic or stoichiometric mediators of enantioselective reactions. The list of successfully applied chiral ligands is expanding well beyond the traditional entries of chiral phosphines, amines, imines, and alcohols to now include chiral cyclopentadienyl ligands. The application of η^5-cyclopentadienyl ligands as a support for introducing chirality is particularly attractive due to the wide variety of potentially synthetically useful organometallic complexes containing this ligand, the impressive bond strengths with which this ligand is attached to transition metals (up to 118 kcal/mol),[1] and the large array of possible structural modifications of the ligand which are synthetically approachable. Historically, the initial interest in chiral cyclopentadienylmetal complexes was mainly focused on the synthesis, resolution, and physical properties of these novel compounds. Subsequently, they had their first applications as stereochemical markers in studies concerned with the elucidation of mechanistic features of organometallic reactions. The most recent phase is concerned with the development of chiral cyclopentadienylmetal complexes for applications in asymmetric reactions of synthetic interest.

The chirality in cyclopentadienylmetal complexes can have several different origins. An organometallic complex may be chiral due to coordination of chiral or prochiral ligands to a nonstereogenic metal (ligand-derived chirality). Examples of cyclopentadienylmetal complexes of this type are compounds **1**[3] and **2**[4] in Figure 1. Alternatively, the chirality may arise from an asymmetric arrangement of achiral ligands around a nonstereogenic[2] metal (metal-centered chirality) or to a combination of these two factors, e.g. compounds **3**[5] and **4**,[6] which in analogy to typical carbon-centered chirality possess four different groups arranged in a pseudotetrahedreal manner about the metal in these examples. The scope of this review will be limited to those complexes which contain a chiral or prochiral cyclopentadienyl ligand and will include cyclopentadienes with fused aromatic rings (indenes) and will emphasize work found in the open, nonpatent literature.

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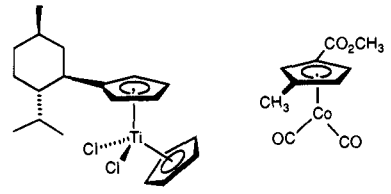
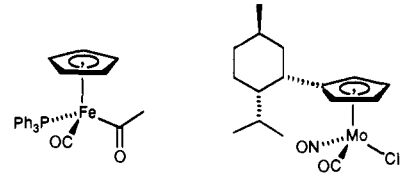


1[3] 2[4]

Cyclopentadienyl-Derived Chirality



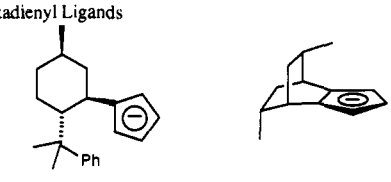
3[5] 4[6]

Metal-Centered Chirality

Combined Metal-Centered and Cyclopentadienyl-Derived Chirality

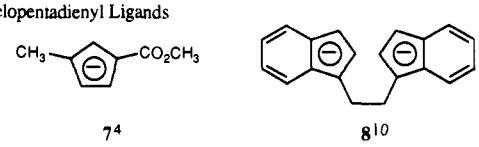
Figure 1. Examples of different types of chiral cyclopentadienylmetal complexes.

Homotopic Cyclopentadienyl Ligands



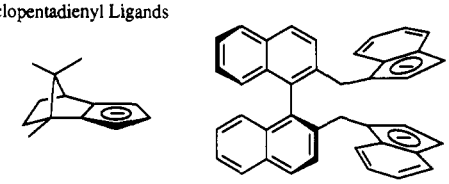
5[8] 6[9]

Enantiotopic Cyclopentadienyl Ligands



7[4] 8[10]

Diastereotopic Cyclopentadienyl Ligands



9[8] 10[11]

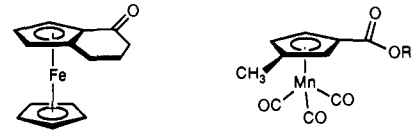
Figure 2. Examples of the three different types of chiral cyclopentadienyl ligands.

Although many of the chiral complexes covered in this review are resolved, chiral but racemic complexes are also included. The large class of metal-centered chiral complexes containing achiral cyclopentadienyl ligands is not covered here but has been reviewed elsewhere.[7]

It is useful to recognize three types of cyclopentadienyl ligand-derived chirality in cyclopentadienylmetal complexes, which depend on how the two faces of the ligand are related to one another. Homotopic faces of cyclopentadienyl ligands are equivalent either due to the presence of a C_2 axis of symmetry between the two faces or due to free rotation between a single substituent and the cyclopentadienyl moiety and produce a single stereoisomer when metalated. Enantiotopic faces of cyclopentadienyl ligands are related by a mirror plane and give enantiomeric compounds upon metalation with an achiral metal fragment. Diastereotopic faces of cyclopentadienyl ligands are not related by symmetry and can give a mixture of diastereomers when metalated. Examples of each type of ligand are given in Figure 2.

II. Early Examples of Chiral Cyclopentadienylmetal Complexes

The earliest reports of chiral cyclopentadienyl complexes were of 1,2-disubstituted ferrocene derivatives obtained by acylation of achiral ferrocenes[12] rather than through the metalation of a chiral or prochiral cyclopentadienyl ligand. The first reported resolution of a chiral cyclopentadienylmetal complex was the ferrocenyl complex **11** via a menthylhydrazone.[13] The first example of a chiral non-ferrocene species was the half-sandwich complex **12**, also obtained by the Friedel–Crafts acylation of the achiral organometallic complex, methylcyclopentadienylmanganese tricarbonyl.[14] Both the ferrocene and manganese complexes have cyclopentadienyl-derived chirality and contain prochiral, enantiotopic cyclopentadienyl ligands. Several derivatives of the manganese complex **12** were reported, one of them an ephedrine salt through which resolved **12** was obtained after fractional crystallization.[15] The synthesis of these compounds and related examples of chiral metallocene complexes has been reviewed.[16]

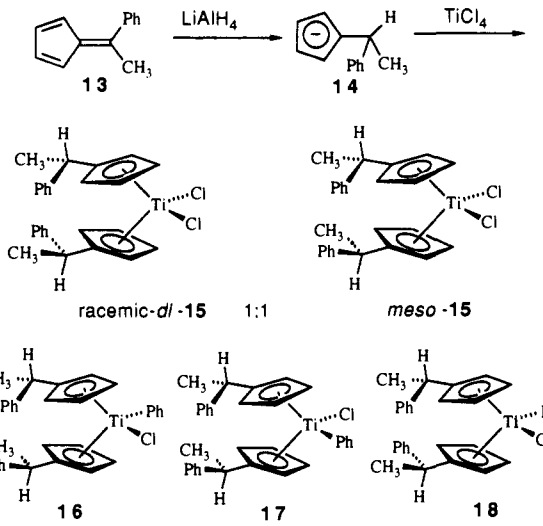


11[13] 12[15]

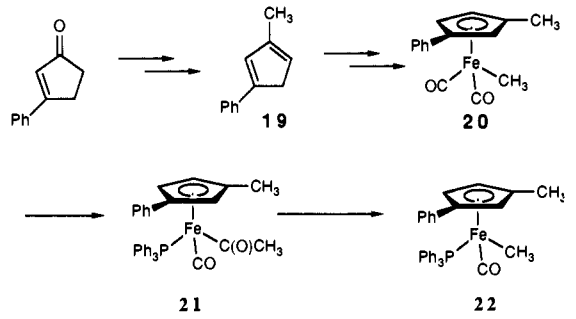
Tirouflet and collaborators reported the first synthesis and metalation of a chiral but racemic cyclopentadienyl ligand.[17] Reduction of 6-methyl-6-phenylfulvene (**13**) with $LiAlH_4$ produced the chiral, racemic cyclopentadienyl anion **14** (of the homotopic cyclopentadienyl ligand type), which upon treatment with $TiCl_4$ gave a 1:1 mixture of meso and racemic diastereomers of titanocene dichloride **15** (Scheme 1). Substitution of a chloride in *meso*-**15** with a phenyl group created two diastereomers, **16** and **17**. The titanium center in these compounds is pseudoasymmetric, or more descriptively, stereogenic but achirotopic.[2] A similar substitution in *dl*-**15** gave the two enantiomers of **18**. The titanium atom in these complexes is chirotopic and nonstereogenic.[2] Titanocene complexes of this type were extensively used in mechanistic studies on the stereochemistry of ligand substitution.

An early example of the use of chiral cyclopentadienylmetal complexes in mechanistic studies was the proof of stereospecificity of the photochemical decarbonylation of acyliron complexes (Scheme 2).[18] For this study, the prochiral ligand 1-methyl-3-phenylcyclopentadiene (**19**) was prepared from 3-phenyl-2-cyclopentenone and methylmagnesium bromide. Metalation of the enantiotopic faces of this ligand led to the formation of racemic dicarbonyl **20** which was converted into a separable mixture of diastereomeric acyliron compounds **21** upon addition of triphenylphosphine. Since a single diastereomer of acyliron **21** decarbonylated specifically to a single diastereomer of alkyliron **22**, it was concluded that photochemical decarbonylation was stereospecific. Whether this reaction was proceeding by stereospecific retention or inversion

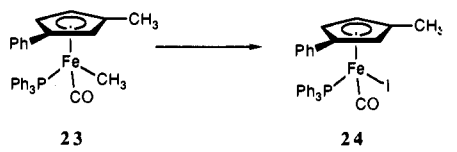
Scheme 1[17]



Scheme 2[18]



Scheme 3[21]



could not be determined by this study, but was later determined to go by retention of configuration.[19]

The mechanism of the electrophilic substitution in cyclopentadienyliron complexes was also investigated using a chiral cyclopentadienyl ligand as a stereochemical marker.[20] For example, the stereochemistry of the conversion of methyliron **23** to iodoiron **24** was shown to take place with complete retention of configuration at iron (Scheme 3).[21]

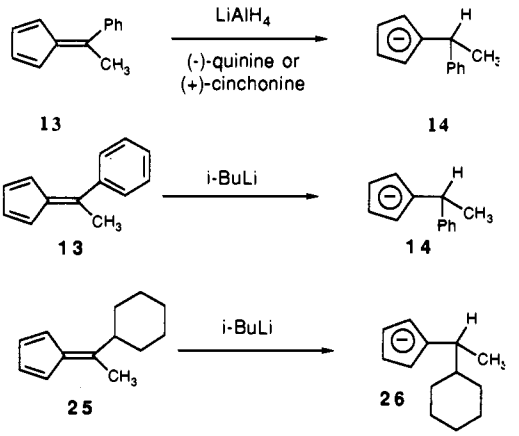
Following this period of mechanistic applications of chiral cyclopentadienylmetal complexes, attention turned to preparing enantiomerically enriched cyclopentadienyl ligands with the intent of applying organometallic complexes containing these chiral auxiliaries in asymmetric reactions. The following three sections will cover in turn, the synthesis of chiral or prochiral ligands, the formation of chiral organometallic complexes and finally their application in asymmetric reactions.

III. Synthesis of Chiral Cyclopentadienes

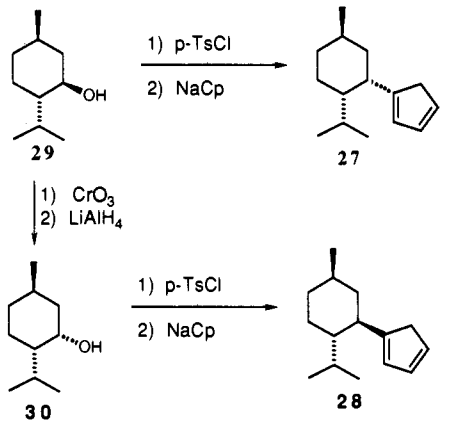
A. Monosubstituted Cyclopentadienes

The initial report of a synthetically prepared enantiomerically enriched monosubstituted cyclopentadiene was in 1976 by Leblanc and Moise who asymmetrically reduced fulvene **13** with $LiAlH_4$ in the presence of (−)-quinine or (+)-cinchonine to produce (1-phenylethyl)cyclopentadienyl anion (**14**) in low enantiomeric purity (Scheme 4).[22] Metalation of this enantiomerically enriched ligand yielded metallocenes which exhibited optical activity.[17b,22,23]

Scheme 4[22,24]



Scheme 5[3]

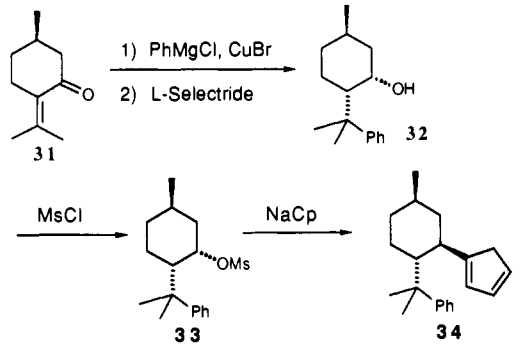


Erker has recently reported a novel reduction of 6-methyl-6-phenylfulvene (**13**) by a β-hydride addition from isobutyllithium to produce **14** (Scheme 4).[24] The reduction of 6-cyclohexyl-6-methylfulvene (**25**) to the chiral cyclopentadienyl ligand **26** was also successful using isobutyllithium. Attempted asymmetric reductions of fulvenes **13** or **25** by delivery of a β-hydride from chiral organolithium reagents failed to give enantiomerically enriched products.

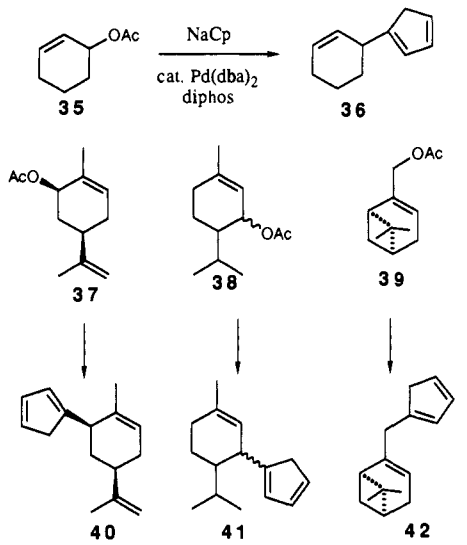
The first example of natural product-derived monosubstituted cyclopentadienes appeared in a paper in 1978 by Kagan and collaborators[3] in which they described the preparation of (−)-menthylcyclopentadiene (MCp, **27**) and (+)-neomenthylcyclopentadiene (NMCp, **28**) from inexpensive, enantiomerically pure (−)-menthol. Their synthesis of these ligands is shown in Scheme 5. The neomenthyl-substituted ligand **27** was prepared directly by the cyclopentadienylsodium displacement of the *p*-toluenesulfonate ester of (−)-menthol (**29**). By initially epimerizing (−)-menthol (**29**) by an oxidation–reduction sequence to (+)-neomenthol **30**, the menthyl substituted ligand **28** could be analogously prepared.

A more substituted terpene-derived cyclopentadiene was efficiently prepared from menthone **31** by Hal-

Scheme 6[8]



Scheme 7[25]

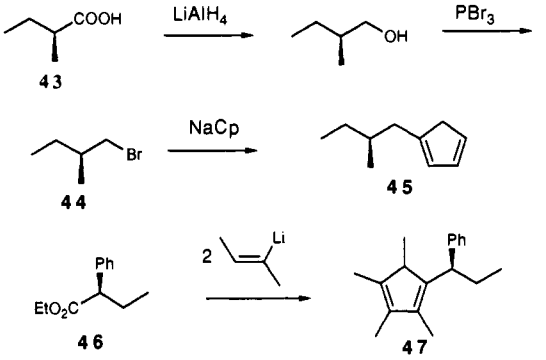


terman and Vollhardt[8] (Scheme 6). Conjugate addition of phenylmagnesium chloride followed by a stereoselective reduction yielded the phenyl-substituted neomenthol **32**. Conversion of this alcohol to the methanesulfonate ester **33**, followed by displacement with cyclopentadienylsodium gave the monosubstituted (phenylmenthyl)cyclopentadiene (PhMCp) ligand **34**.

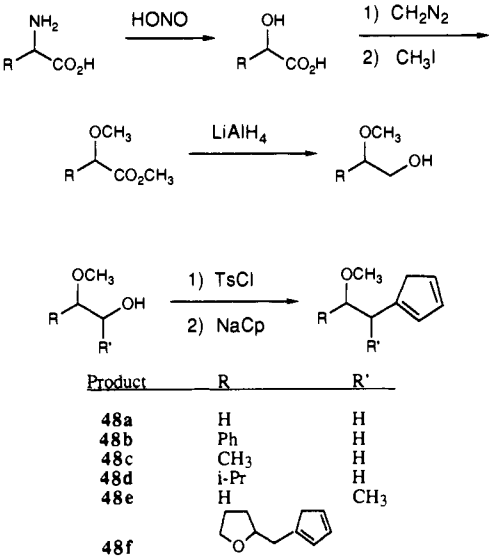
The preparation of several allylic substituted cyclopentadienes has been accomplished by adding cyclopentadienyl anion to allylic acetates in the presence of catalytic amounts of palladium as shown in Scheme 7.[25] The use of either racemic cyclohexenyl acetate (**35**) or carvenyl acetate (**37**) resulted in the formation of racemic chiral cyclopentadienes **36** and **40**. Starting from a mixture of cis and trans isomers of piperitenyl acetate (**38**) led to an inseparable mixture of cis and trans isomers of chiral cyclopentadiene **41**. Myrtenyl acetate (**39**) was converted to enantiomerically enriched monosubstituted cyclopentadiene **42**.

Two additional examples of the synthesis of chiral monosubstituted cyclopentadienes from naturally occurring enantiomerically enriched compounds are shown in Scheme 8. The conversion of the chiral carboxylic acid **43** into the cyclopentadiene **45** via the bromo alkylating agent **44**[26] parallels Kagan's earlier alkylation of menthyl tosylates with cyclopentadiene.[3] On the basis of Bercaw's synthesis of pentaalkylcyclopentadienes from the addition of 2 equiv of 2-butenyllithium to an ester,[27] the first chiral pentaalkylcyclopentadiene **47** was prepared by utilizing the naturally derived, enantiomerically enriched ethyl 2-phenylbutanoate (**46**) in an analogous condensation.[28]

Scheme 8[26,28]



Scheme 9[29]



Product	R	R'
48a	H	H
48b	Ph	H
48c	CH_3	H
48d	i-Pr	H
48e	H	CH_3
48f		

Recently several new chiral monosubstituted cyclopentadienes which are suited for chelation have been prepared by Qian by the functionalization of cyclopentadiene with enantiomerically pure tosylates derived from natural products.[29] These ligands, **48a–f**, each containing an ethereal oxygen in the chiral substituent, were prepared from mandelic acid, tetrahydrofur-2-ylmethanol, 1-methyl-2-methoxyethanol, 2-methoxypropanoic acid, lactic acid, and valine as shown in Scheme 9. No indication of the enantiomeric purity of these ligands was mentioned.

A large number of chiral but apparently racemic monosubstituted cyclopentadienes have also been reported by Qian.[30] The details of the syntheses are unavailable here, but have been published in China.[31] These and related[32] new substituted cyclopentadienes are shown in Figure 3.

B. Annulated Cyclopentadienes

In order to provide cyclopentadienes with better-defined asymmetry, several groups have prepared annulated cyclopentadienes with rigidly held, sterically different groups in the vicinity of a coordinated metal. Unlike the chiral monosubstituted cyclopentadienyl ligands where both faces of the ligand are rendered equivalent due to free rotation about the single σ-bond, the faces in annulated cyclopentadienyl ligands can be either homotopic, enantiotopic, or diastereotopic depending of the nature of the substitution. The case where the two ligand faces are diastereotopic is often

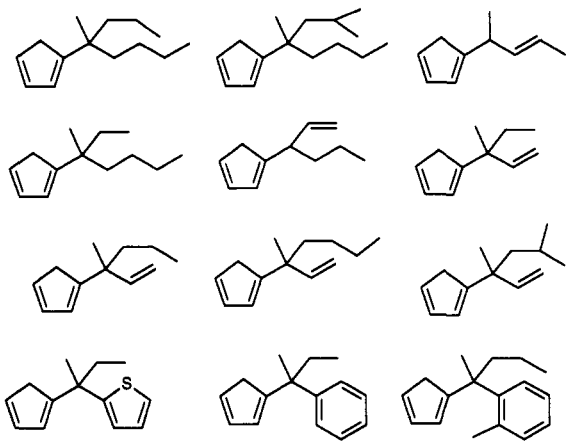


Figure 3. Recently reported chiral but racemic monosubstituted cyclopentadienes.[30,31,32]

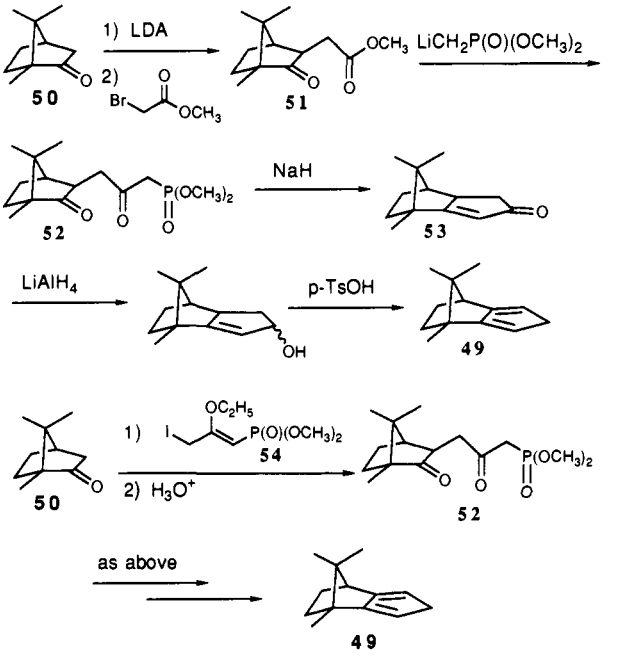
problematic since diastereomeric mixtures may ensue upon nonselective metalation. This class of C_1-symmetrical ligands, however, is quite common due to their facile preparation from naturally occurring, enantiomerically enriched compounds and can in many cases be diastereoselectively metalated. Although the metalation of C_2-symmetrical annulated cyclopentadienes can inherently give only one stereoisomer due to the homotopicity of the two ligand faces, the synthesis of this class of ligands is generally more challenging, usually relying on an asymmetric synthesis from achiral precursors. The two strategies for the introduction of the cyclopentadienyl moiety in all of these cases are either by a cyclopentaannulation sequence or by direct introduction of a cyclopentadiene to an appropriately functionalized substrate. The formation of metal complexes from chiral cyclopentadienes will be discussed in section IV.A.

1. C_1-Symmetrical Ligands

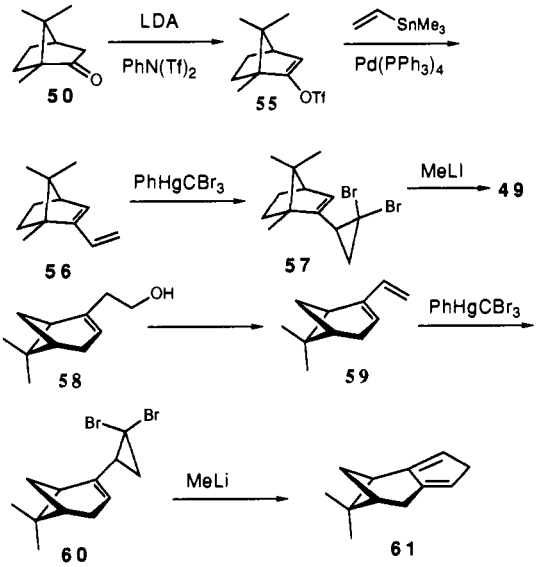
The first application of an annulated chiral cyclopentadiene for the formation of enantiomerically enriched cyclopentadienylmetal complexes used the camphor-derived ligand **49**, originally synthesized in small scale in low yield by a bis-Wittig olefination reaction of camphorquinone.[33] Since efforts to improve the yield of this reaction were unsuccessful,[8] the preparatively useful synthesis shown in Scheme 10 was developed by Halterman and Vollhardt and initially reported in 1986.[34] A synthetic strategy involving a cyclopentannulation was chosen involving the addition of a suitable three carbon fragment to camphor followed by ring closure to form the five-membered ring. Thus, alkylation of (+)-camphor (**50**) with methyl bromoacetate yielded the keto ester **51** which was reacted with the anion of dimethyl methylphosphonate to give the phosphonate **52**. Deprotonation of **52** initiated a Horner–Emmons ring closure, affording cyclopentenone **53** which was converted by a reduction–dehydration sequence to the chiral cyclopentadiene (CamCp) **49** as shown in Scheme 10. More recently, Paquette has reported a variation of this synthesis in which camphor is alkylated directly by the three-carbon phosphonate **54**.[35] After hydrolysis, the directly resulting phosphonate **52** was carried forward to cyclopentadiene **49** as above.

Shortly after the appearance of the initial camphor-derived cyclopentadiene synthesis, Paquette published

Scheme 10[8,34,35]



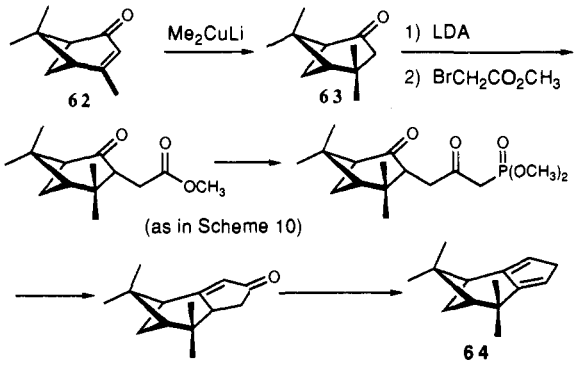
Scheme 11[36]



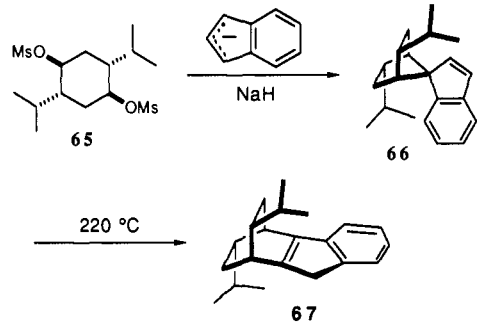
an alternative preparation of the camphor-derived ligand **49** and a synthesis of the nopol-derived chiral annulated cyclopentadiene **61** elegantly based on a Skattebøl rearrangement.[36] Thus, coupling the vinyl triflate derivative **55** of camphor with a vinyltin reagent provided the substituted butadiene **56**. Selective cyclopropanation of the less substituted double bond in diene **56** gave vinyl cyclopropane **57** which could be directly converted to cyclopentadiene **49** via the Skattebøl rearrangement shown in Scheme 11. In a related syntheses nopol (**58**) was converted via base-promoted elimination to the nopadiene **59**. Cyclopropanation of the less substituted double bond in diene **59** followed by the methyllithium-induced Skattebøl rearrangement of cyclopropane **60** directly gave the desired nopol-derived cyclopentadiene **61**, which due to its incorporation of the pinene skeleton has been abbreviated (PinCp).

Paquette has also synthesized a chiral annulated cyclopentadiene starting from verbenone (**62**) (Scheme

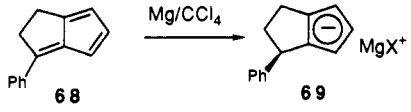
Scheme 12[37]



Scheme 13[38]



Scheme 14[39]



12).[37] After conjugate addition of a methyl group to enantiomerically enriched verbenone, the resulting ketone **63** is converted to the desired chiral annulated cyclopentadiene **64** following the cyclopentannulation procedures shown above in Scheme 8.[8,34,35]

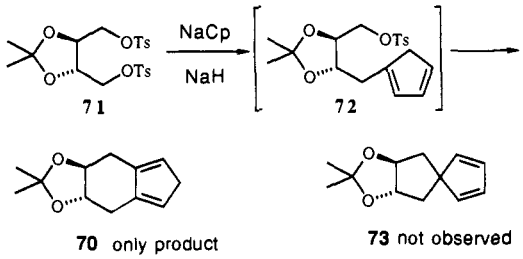
The synthesis of the first chiral annulated indene is shown in Scheme 13.[38] The reaction of the bis(methanesulfonate) ester **65** with indenyl anion in the presence of excess sodium hydride initially formed spiroannulated indene **66** which could be converted to the desired fused annulated indene **67** upon thermolysis. The synthesis of the C_2-symmetrical bis(methanesulfonate) ester **65** was developed for the preparation of C_2-symmetrical annulated cyclopentadienes and is discussed below.

Brintzinger has reported the chiral C_1-symmetrical cyclopentadienyl ligand, 4*H*-4-phenyl-5,6-dihydropentalenide (**69**), which was unexpectedly produced in the attempted coupling of 3-phenyl-1,2-dihydropentalene (**68**) with Mg/CCl_4 (Scheme 14).[39]

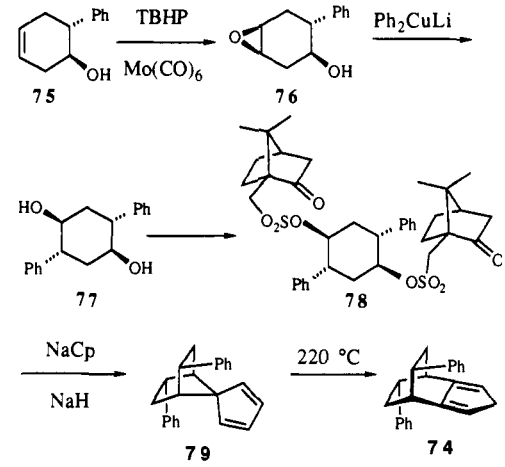
2. C_2-Symmetrical Annulated Cyclopentadienes

In order to avoid the demonstrated problem of forming a mixture of diastereomers when C_1-symmetrical annulated cyclopentadienes are metalated (vide infra), recent syntheses of chiral annulated cyclopentadienes have focused on the preparation of ligands in which the two faces of the cyclopentadienyl moieties are related by C_2 symmetry. Metalation of either homotopic face in these ligands must result in the formation of the same stereoisomer, thus providing a cleaner and potentially higher yielding formation of chiral cyclopentadienylmetal complexes.

Scheme 15[34,8]



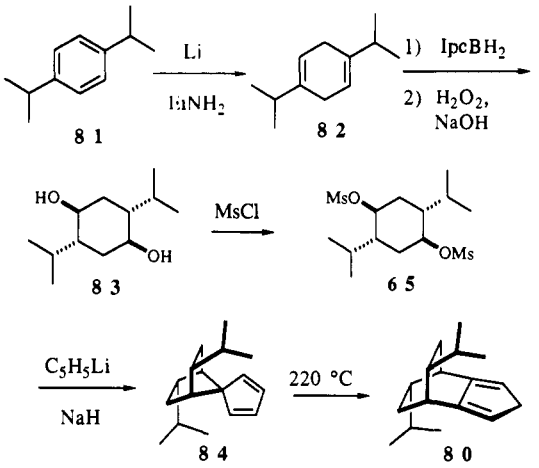
Scheme 16[40]



The first published preparation of a C_2-symmetrical annulated cyclopentadienyl ligand was the tartrate-derived ligand **70** reported by Halterman and Vollhardt in 1986[34] and was also the first example of a synthesis using the strategy of bisalkylating cyclopentadiene. Alkylation of cyclopentadienylsodium by the tartrate-derived, commercially available bis(*p*-toluenesulfonate) ester **71** presumably gave cyclopentadiene **72** which was deprotonated in situ by excess sodium hydride, leading to displacement of the second leaving group to yield directly the desired annulated cyclopentadiene **70** (Scheme 15). This transformation was of further interest in that the spiroannulated cyclopentadiene **73** was not observed, perhaps because of the unfavorable trans-fused bicyclo[3.3.0]octane framework in **73**.[8,34]

The development of tartrate-derived C_2-symmetrical cyclopentadiene **70** illustrated a problem in relying on natural products to provide the chirality in ligands—it is quite easy to prepare, but the location and nature of the asymmetry in this ligand apparently make it unremarkable for applications as a stereoselective organometallic reagent. In order to overcome the deficiencies in relying on the chiral pool for starting materials, a class of designed C_2-symmetrical annulated cyclopentadienes synthesized from achiral starting materials has been successfully developed and applied. In the first example of this class of compounds, a bicyclo[2.2.2]octane framework fused to the cyclopentadiene was used to rigidly hold sterically different groups near a coordinated metal. The first report of these designed ligands was the substituted bicyclooctane-fused cyclopentadiene (DiPh-BCOCp) **74** published in 1987.[40] A key in this synthesis of BCOCp **74** was the introduction of leaving groups appropriately placed trans to the adjacent phenyl substituents (Scheme 16). The needed 1,4-cyclohexanediol **77** was efficiently prepared by using

Scheme 17[9,41]

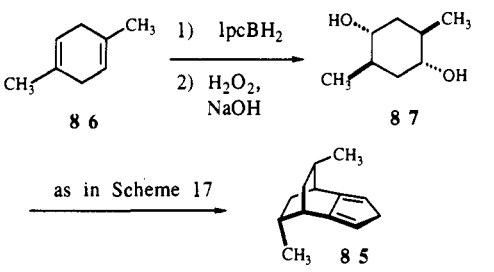


the hydroxyl group in readily available cyclohexenol **75** to direct an epoxidation to form epoxide **76** which could then be regioselectively opened with an organocuprate reagent to form the proper diol **77**. The conversion to enantiomerically enriched cyclopentadiene **74** relied on a chromatographic separation of diastereomeric sulfonate esters **78**, potentially limiting the scale in which this ligand could be prepared in enantiomerically enriched form. Once the resolution was effected, the bisalkylation of cyclopentadiene initially produced the spiroannulated cyclopentadiene **79** rather than the desired fused cyclopentadiene **74**. Conversion of the spiroannulated diene **79** to the desired product was accomplished through a series of thermal-induced sigmatropic rearrangements.

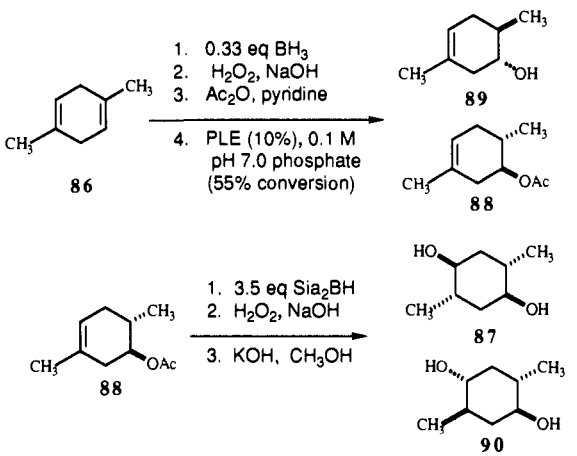
Asymmetric catalytic hydrogenations using a titanocene dichloride complex derived from DiPhBCOCp (**74**) were quite stereoselective, boding well for other stereoselective reactions using complexes of this type (section V.A). The requirement for a resolution of diastereomeric sulfonate esters in the synthesis of cyclopentadiene **74**, however, limits its large-scale synthesis and applications and led to the development of alternate syntheses of this type of ligand.

Recently, Halterman and Chen have published a more efficient synthesis of this class of bicyclo[2.2.2]octane-fused cyclopentadienyl ligands containing methyl and isopropyl substituents relying on an asymmetric hydroboration–oxidation reaction to provide enantiomerically enriched compounds.[9,41] Their asymmetric synthesis of the diisopropyl-substituted BCOCp ligand **80** (Scheme 17) started with the conversion of 1,4-diisopropylbenzene (**81**) into cyclohexadiene **82** by a modified Birch reduction. Exposure of cyclohexadiene **82** to excess enantiomerically pure monoisopinocamphenylborane (from (+)-(1*R*)-α-pinene) followed by oxidation with basic hydrogen peroxide gave an initial mixture of C_2- and C_i-symmetric diols in a ratio of 6:1 from which the C_2-symmetric diol **83** was isolated and found to have after a simple recrystallization an enantiomeric purity of greater than 95%. Bisalkylation of cyclopentadiene with the bis(methanesulfonate) ester **65** in the presence of sodium hydride provided the spiroannulated cyclopentadiene **84** in multigram quantities. Thermolysis of spirodiene **84** at 220 °C in a sealed tube of toluene effected a [1,5]-sigmatropic alkyl shift followed by successive hydrogen shifts resulting in the formation of the thermodynamically stable fused cyclopentadiene **80**. The enantiomeric integrity of this desired chiral ligand was confirmed by using a complex chiral shift reagent.

Scheme 18[41]



Scheme 19[9]

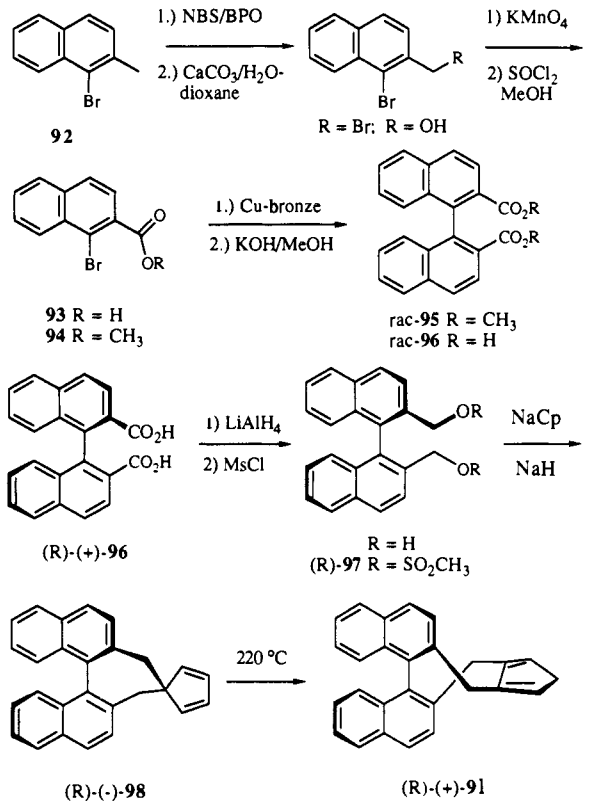


The enantiomerically enriched dimethyl-substituted bicyclooctane-fused cyclopentadiene **85** has also been asymmetrically prepared according to the above synthesis from readily available 1,4-dimethyl-1,4-cyclohexadiene (**86**) (Scheme 18).[41,9] The key asymmetric hydroboration produced a 3.6:1 mixture of C_2- and C_i-symmetrical diols. The C_2-symmetrical isomer **87** was separated by silica gel chromatography and exhibited an enantiomeric purity of >95%. The synthesis of cyclopentadiene **85** was completed as above by conversion of diol **87** to a bis(methanesulfonate) ester, followed by a bisalkylation of cyclopentadiene, and thermolysis.

In an attempt to improve on the stoichiometric replication of pinene's chirality, an alternative route to the enantiomerically pure C_2-symmetrical dimethylcyclohexanediol **87** relying on the catalytic enzymatic kinetic resolution of racemic dimethylcyclohexenyl acetate **8** using pig liver esterase was examined.[9] The racemic alcohol **89** was available by the monohydroboration/oxidation of 1,4-dimethyl-1,4-cyclohexadiene (**86**) (Scheme 19). The kinetic resolution of racemic acetate **88** is facile and fairly selective, producing a 44% yield of recovered acetate **88** with an enantiomeric purity of 88% at 55% conversion. The hydroboration of either the acetate **88** or the alcohol **89** with a variety of boranes produced a disappointingly poor yield of desired C_2-symmetric diol **87** along with the undesired C_i-symmetrical diol **90**, rendering this route less efficient overall than the asymmetric hydroboration route.

The synthesis of binaphthyldimethylenecyclopentadiene (BpDMCp) **91** has been reported by Colletti and Halterman.[42] Cyclopentadiene **91** is a ligand whose model indicates potentially advantageous placement of sterically large (C3 of the naphthyl) and small

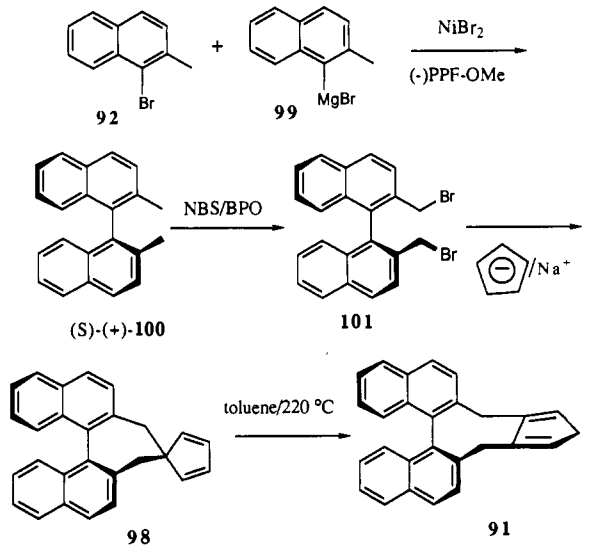
Scheme 20[42]



(equatorial hydrogen of the methylene) groups on either side of the cyclopentadiene. The synthetic strategy for the preparation of **91** was based on the established bisalkylation of cyclopentadiene in this case by an appropriate binaphthyl moiety. An initial synthesis of this ligand utilized the known 1,1′-binaphthyl-2,2′-dicarboxylic acid (**96**). By using a modification of an earlier procedure they were able to synthesize multigram amounts of racemic diacid **96** from 1-bromo-2-methylnaphthalene (**92**) as shown in Scheme 20. The copper-mediated Ullmann coupling of bromonaphthyl ester **94** followed by saponification of the resulting diester **95** provided racemic binaphthyl diacid **96**. Brucine resolution of the diacid **96** afforded either enantiomer of diacid **96** in good yield. The resolved 1,1′-binaphthyl-2,2′-dicarboxylic acid (**96**) was converted by reduction with lithium aluminum hydride followed by esterification with methanesulfonyl chloride into the dimesylate bisalkylating reagent **97**. Displacement of the methanesulfonate groups in intermediate (*R*)-**97** by cyclopentadiene/sodium hydride formed the spiroannulated diene (*R*)-(−)-**98**. The desired C_2-symmetrical, fused cyclopentadiene (*R*)-(+)-**91** was produced by the thermolysis of spirodiene (*R*)-(−)-**98** in toluene. The enantiomeric integrity of **91** was established by examining its ^1H NMR spectrum while titrating with a chiral lanthanide–silver shift reagent. The absence of racemization in the thermolytic formation of cyclopentadiene **91** was not unexpected since related 2,2′-dimethyl-1,1′-binaphthyl has a calculated barrier to racemization of 35 kcal/mol[43] which can be used as a lower limit to racemization since **91** is a much more rigid molecule locked into an eight-membered ring.

A more efficient, large-scale preparation of the BpDMCp ligand **91** was also developed based on the highly enantioselective nickel-catalyzed coupling of 1-bromo-2-methylnaphthalene **92** with its derived Grignard reagent **99** in the presence of the chiral phosphine PPF-OMe[44] to produce 2,2′-dimethyl-1,1′-binaphthyl (**100**) (Scheme 21).[42] Racemic **100** can also be obtained by a nickel-catalyzed coupling of bromide **92** and Grignard **99** in the presence of PPh_3. Dibromide (*S*)-(−)-**101** was prepared from dimethyl compound **100** and it proved to be a suitable alkylating reagent, forming spirodiene (*S*)-(+)-**98** upon treatment with freshly cracked cyclopentadiene/sodium hydride. The spirodiene **98** so produced was identical in all respects to that produced starting from the brucine-resolved diacid **96**. Thermolysis of the spirodiene as before gave (*S*)-(−)-**91**, which was confirmed to be enantiomerically pure by using the previous method of chiral shift spectroscopy. This four-step synthesis described produced (*S*)-(−)-**91** in about 30% overall yield from commercially available 1-bromo-2-methylnaphthalene (**92**). The chiral phosphine needed for the asymmetric catalytic coupling reaction is available as either enantiomer, enabling a facile, large-scale synthesis of both enantiomers of the chiral cyclopentadiene ligand (*S*)-**91** or (*R*)-**91**.

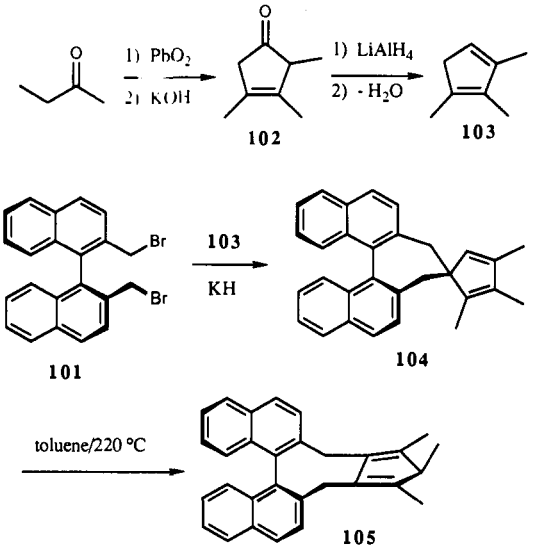
Scheme 21[42]



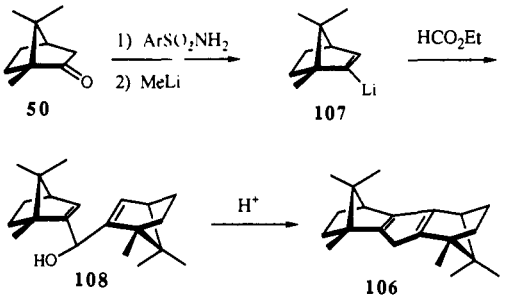
The first example of an annulated chiral pentaalkylcyclopentadiene has also been prepared from 2,2′-bis(bromomethyl)-1,1′-binaphthyl (**101**) by the bisalkylation of an appropriately substituted cyclopentadiene (Scheme 22).[45] Thus, the readily prepared trimethylcyclopentenone (**102**) which could be reduced and dehydrated to form 1,2,3-trimethylcyclopentadiene (**103**). Addition of the anion of **103** to dibromide **101** in the presence of excess potassium hydride gave spiroannulated cyclopentadiene **104** which could be thermolyzed to the desired pentaalkylcyclopentadiene **105** as a mixture of double bond isomers. Although this diene does not possess C_2 symmetry, once the anion is made, the two faces of the ligand become homotopic.

Using a synthesis similar to a preparation of pentamethylcyclopentadiene, Erker has prepared the C_2-symmetrical tetrasubstituted cyclopentadiene **106**, "dibornacyclopentadiene" containing two annulated chiral auxiliaries derived from camphor as shown in Scheme 23.[46] Camphor (**50**) was selectively converted into vinyl anion **107** which added twice to methyl formate, yielding the bis(allylic) alcohol **108** which could be closed in

Scheme 22[45]



Scheme 23[46]



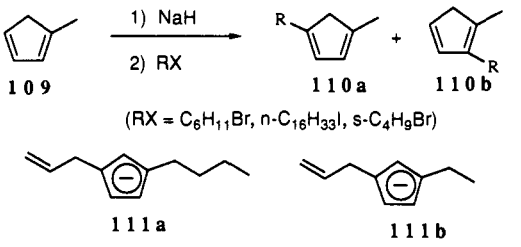
good overall yield to the desired tetrasubstituted chiral cyclopentadiene **106** by a Nazarov-type cyclization.

C. Polysubstituted Cyclopentadienes with Enantiotopic Faces

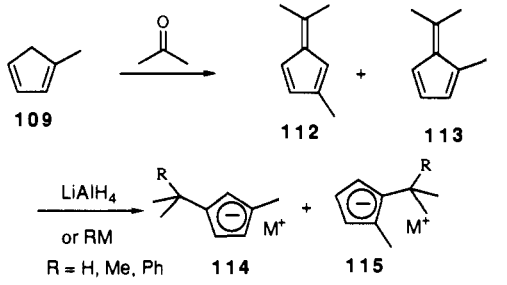
A large number of chiral cyclopentadienylmetal complexes contain substituted cyclopentadienyl moieties whose two faces are enantiotopic. Compounds of this type were among the earliest prepared chiral cyclopentadienylmetals, and they are still being actively studied, especially in linked cyclopentadienes (see section III.D). Chiral complexes containing this class of ligand can be prepared either from metalation of a prochiral, enantiotopic cyclopentadienyl ligand or by substitution of an achiral cyclopentadienylmetal complex. This section will cover only the preparation of prochiral substituted cyclopentadienes and includes dialkyl-, alkyl-, and acyl-, and alkyl- and silyl-substituted cyclopentadienes. Introduction of asymmetry in achiral cyclopentadienylmetal complexes is covered in section IV.D.

A series of disubstituted cyclopentadienes have been made by alkylating methylcyclopentadienylsodium with various primary or secondary alkyl halides (Scheme 24).[47] In each case an approximately equal mixture of 1,2- and 1,3-disubstituted cyclopentadienes **110a** and **110b** ensued. In each of these and related cases in later schemes, a mixture of double bond isomers of the substituted cyclopentadiene is formed, but only one isomer of each is normally represented. Related 1-allyl-3-butylcyclopentadienyl ligands **111a** and **111b** have also been reported.[30]

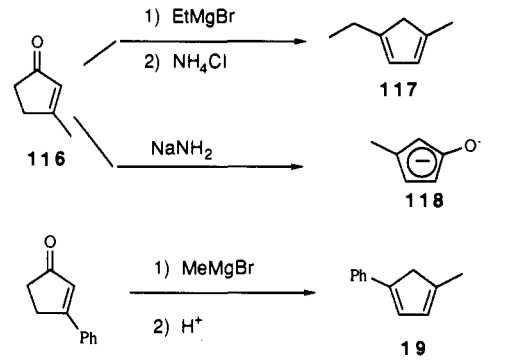
Scheme 24[47,30]



Scheme 25[48]



Scheme 26[49,50,18]

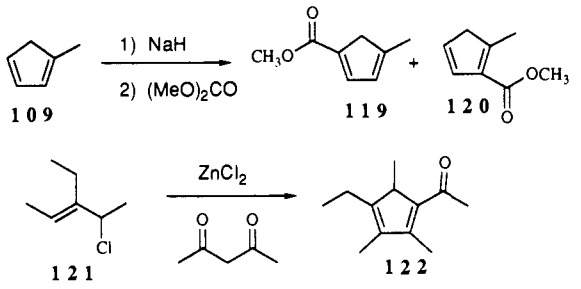


Treatment of methylcyclopentadiene **109** with acetone resulted in the formation of an 80:20 mixture of 1,3- and 1,2-isomers of methyl(isopropylidene)cyclopentadienes **112** and **113** (Scheme 25).[48] These isomers can be separated by gas chromatography. Addition of hydride, phenylmetal or methylmetal reagents to the substituted fulvenes **112** and **113** produced a series of 1,2- and 1,3-disubstituted cyclopentadienyl anions **114** and **115** which could be directly metalated (vide infra).

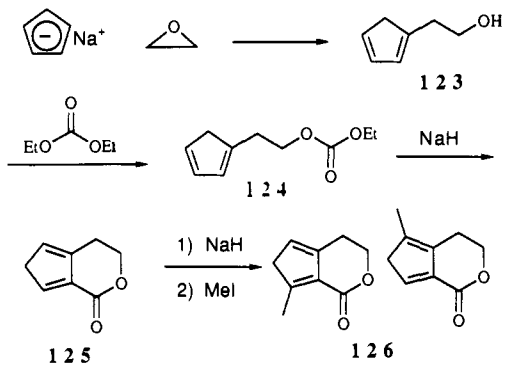
Ethylmagnesium bromide addition to 3-methylcyclopentenone (**116**) followed by acid-promoted elimination of water produced 1-ethyl-2-methylcyclopentadiene (**117**) as a single regioisomer (Scheme 26).[49] This method can also be applied in the formation of related 1,3-disubstituted cyclopentadienes containing a bridge between the rings (see section III.D). Treatment of 3-methylcyclopentenone with sodium amide leads to the 1,3-disubstituted cyclopentadienyl ligand **118**.[50] Addition of methylmagnesium bromide to 3-phenylcyclopent-2-enone followed by acid-promoted dehydration gave the 1,3-disubstituted cyclopentadiene **19**.[18]

Prochiral disubstituted cyclopentadienes containing a carbonyl group are well known. Addition of methylcyclopentadienyl anion to a number of carbonylating reagents will form mixtures of 1,2- and 1,3-disubstituted cyclopentadienes containing a methyl and an ester, ketone, aldehyde, or amide group. For example, treatment of methylcyclopentadienylsodium with dimethyl carbonate gives an approximately equal mixture

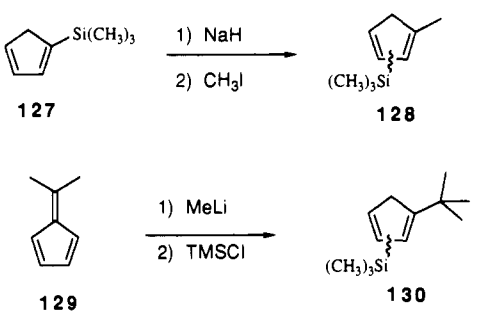
Scheme 27[4,51,52]



Scheme 28[53]



Scheme 29[54,56]



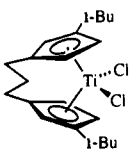
of 1-carbomethoxy-2-(or 3-)-methylcyclopentadienes (**119** and **120**, Scheme 27).[4,51] Another route into carbonyl-substituted prochiral cyclopentadienes employs a [3 + 2] cycloaddition strategy to provide highly alkylated acetylcyclopentadienes as shown in Scheme 27. Allylation of 2,4-pentanedione with allyl chloride **121** under conditions which favor the formation of carbocations ultimately led to formation of cyclopentadiene **122** which can be used as a prochiral, enantiotopic pentasubstituted cyclopentadienyl ligand.[52]

A series of lactone-annulated prochiral cyclopentadienes has been prepared from cyclopentadiene as shown in Scheme 28.[53] Addition of cyclopentadienylsodium to ethylene oxide produced cyclopentadienylethanol (**123**) which could be converted to a carbonate ester **124**. Deprotonation of the cyclopentadiene in **124** resulted in the formation of the prochiral, enantiotopic cyclopentadiene **125**. Methylation of **125** produced two isomers of the trisubstituted cyclopentadiene **126**.

Prochiral cyclopentadienes containing trimethylsilyl groups have also been prepared. Addition of methyl iodide to trimethylsilylcyclopentadienyl anion results in the formation of a mixture of disubstituted cyclopentadienes **128** (Scheme 29).[54] The orientation of the silyl group with respect to the methyl group is fluctional owing to the facile [1,5]-sigmatropic shift of the silyl group.[55] Addition of trimethylsilyl chloride to *tert*-butylcyclopentadienyllithium, prepared in situ by addition of methyllithium to 6,6-dimethylfulvene (**129**), has been reported to produce a mixture of *tert*-butyl(trimethylsilyl)cyclopentadienes (**130**).[56]

D. Bridged Bis(cyclopentadienes)

In order to restrict the normally free rotation[57] of the cyclopentadienyl rings in bis(cyclopentadienyl)metal complexes and to enable a more rational design of chiral complexes, the preparation of chiral ansa-metallocenes has become a very active field. *ansa*-Metallocenes now comprise an important class of chiral cyclopentadienylmetal complexes containing prochiral cyclopentadienyl ligands, in this case having the cyclopentadienyl moieties covalently linked together. The prefix ansa (Latin for bent handle, attached at both ends) was originally used to describe bridged aromatic compounds and was adopted by Brintzinger to describe the presence of an interannular bridge in metallocenes. Since Brintzinger's report in 1979 of the first C_2-symmetrical *ansa*-metallocene, trimethylenebis-[η^5-1-(3-*tert*-butylcyclopentadienyl)]titanium dichloride (**131**),[58] intensive work has gone into preparing different chiral *ansa*-metallocenes.



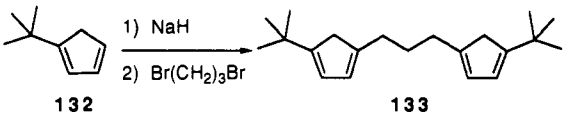
131

Brintzinger's synthesis of the 1,3-disubstituted *ansa*-bis(*tert*-butylcyclopentadiene) ligand **133** bridged by a 1,3-propanediyl moiety needed to form metallocene **131** was based on the regioselective 1,3-alkylation of the hindered *tert*-butylcyclopentadienyl anion with 1,3-dibromopropane (Scheme 30).[58] Although this route is successful for the 1,3-incorporation of relatively hindered substituents, it is not useful for alkyl substituents smaller than isopropyl due to the increasing formation of 1,2-disubstituted products.[59]

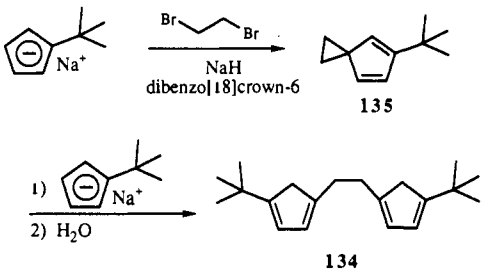
The preparation of the ethylene-bridged 1,3-disubstituted *ansa*-bis(*tert*-butylcyclopentadiene) ligand **134** has been prepared by addition of 1,2-dibromoethane to *tert*-butylcyclopentadienylsodium. The reaction initially formed spiro-cyclopropane **135** which further reacted at high temperature with more *tert*-butylcyclopentadienylsodium in the presence of a crown ether (Scheme 31).[60,61]

More general routes for the synthesis of bridged 1,3-disubstituted metallocenes have now appeared. In the first of these, Brintzinger synthesized tetramethylethylene-bridged bis(cyclopentadienes) by reductive coupling of 2-substituted 6,6-dimethylfulvenes **136** using Mg/CCl_4 (Scheme 32).[62] The starting 2-substituted 6,6-dimethylfulvenes **136** were obtained from either the pyrrolidine-induced condensation of acetone with substituted cyclopentadienes (R = *t*-Bu, *i*-Pr) or by using pyrrolidine, acetone, and a substituted cyclopentadienyllithium (R = α,α-dimethylbenzyl, 1-phenylcyclohexyl) or directly from acetone and (trimethylsilyl)-cyclopentadienyllithium. These substituted fulvenes **136** were reductively coupled with magnesium metal and CCl_4[63] to yield disubstituted di-Grignard com-

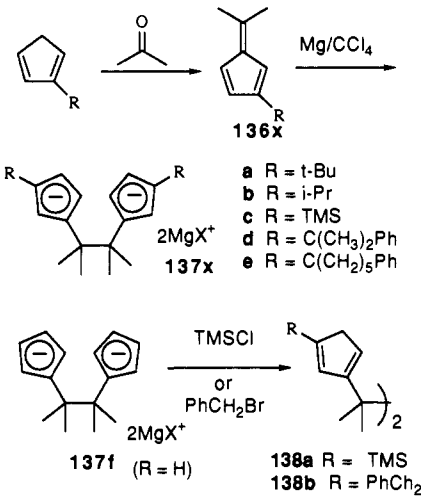
Scheme 30[58]



Scheme 31[60]



Scheme 32[62,63]

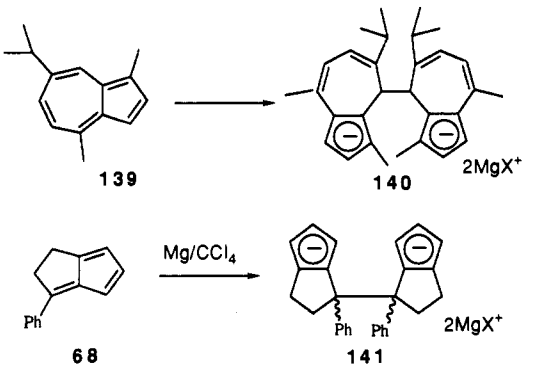


pounds **137** which could be precipitated from solution in fair yield. Treatment of the unsubstituted tetramethylethylene-bridged di-Grignard **137f**[61] (R = H) with either chlorotrimethylsilane or with benzyl bromide produced the substituted bridged bis(cyclopentadienes) **138c** and **138f** (R = TMS or $PhCH_2$) which could be converted to their lithium salts by treatment with *n*-butyllithium.

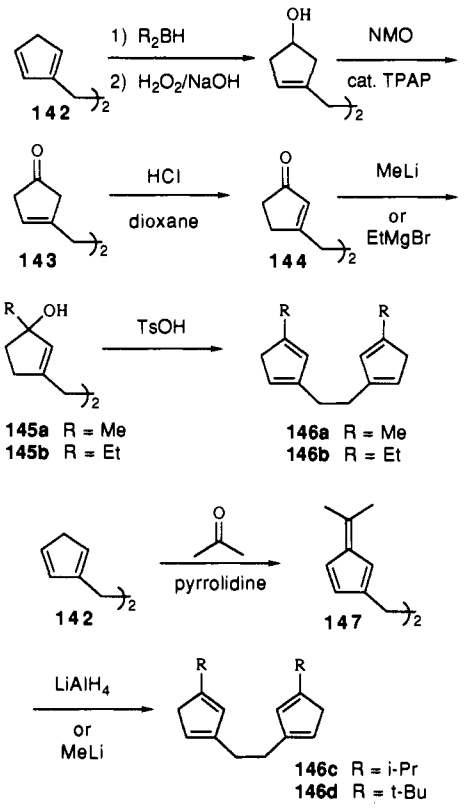
Brintzinger has also used a magnesium/carbon tetrachloride coupling method to link two molecules of guaiazulene **139** to form product **140** which is linked only at the least substituted position in the seven-membered ring and gave upon metalation (vide infra) only a single diastereomeric product[39] (Scheme 33). The phenyl-substituted dihydropentalene **68** could also be successfully coupled under similar conditions to give a mixture of meso and racemic isomers **141**.[64]

Recently, Collins has reported efficient routes to various substituted *ansa*-metallocenes cleverly based on selective functionalization of parent ethylene-bridged bis(cyclopentadiene) **142** which was obtained in high yield by the reaction of Cp_2Mg with 1,2-dibromoethane in a THF/HMPA solvent system. Selective oxidation of diene **142** by hydroboration/oxidation was highly regioselective, affording a single regioisomeric diol whose oxidation to the bridged bis-ketone **143** was best accomplished with *N*-methylmorpholine *N*-oxide using catalytic amounts of tetrapropylammonium perruthenate. Acid-catalyzed double bond migration

Scheme 33[64]



Scheme 34[65]

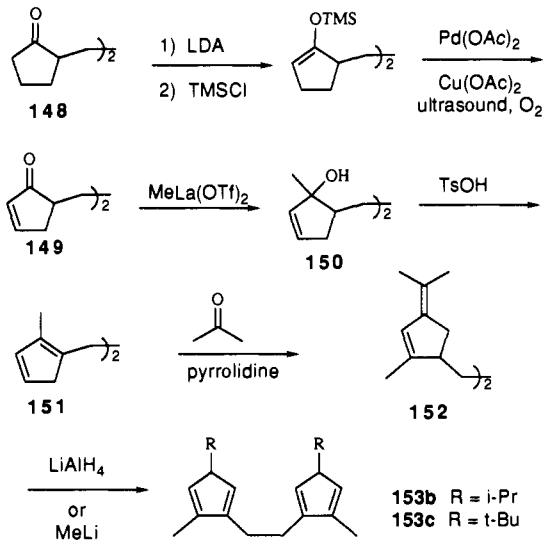


provided the key intermediate in this synthesis, the conjugated bridged cyclopentenone **144**. Addition of methyllithium, ethyllithium, or ethylmagnesium bromide to the enone **144**, followed by acid-promoted elimination of water from allylic alcohol **145** gave the 1,3-disubstituted ethylene-bridged bis(cyclopentadienes) **146a** and **146b** containing the methyl or ethyl substituents (Scheme 34).[65]

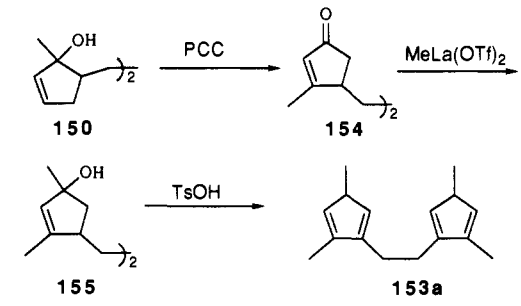
The parent ethylene-bridged bis(cyclopentadiene) **142** was also very efficiently converted into ethylene-bridged 1,3-disubstituted bis(cyclopentadienes) containing the isopropyl or *tert*-butyl substituents as shown in Scheme 34. Condensation of **142** with acetone gave the bridged bis(6,6-dimethylfulvene) **147** in greater than 95% regioisomeric purity which could be treated with either $LiAlH_4$ or MeLi to afford **146c** and **146d** (R = *i*-Pr or *t*-Bu).[65a] McLaughlin has prepared an analogous tetramethylethylene-bridged 1,3-disubstituted bis(cyclopentadiene).[65b]

Collins has also reported the preparation of 3,5-disubstituted, ethylene-bridged *ansa*-titanocene dichlorides. The synthesis of the ligands used in these

Scheme 35[65,66]



Scheme 36[66]

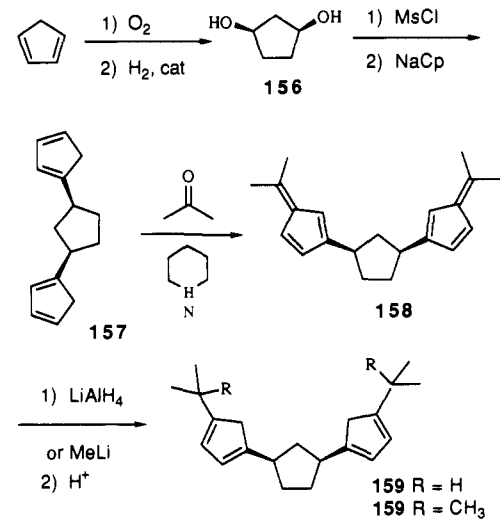


complexes started with a two-step conversion of the known ethylene-bridged diketone **148** to bis(cyclopentenone) **149** via a TMS enol ether (Scheme 35).[66] The 5-methyl substituent, common to each of the ligands in this family, was introduced with a non-acidic methyllanthanum reagent followed by acid-catalyzed elimination of water from allylic alcohol **150** affording bis(cyclopentadiene) **151**. Bis(fulvene) **152**, which was obtained from the condensation of acetone and **151**, gave upon treatment with either $LiAlH_4$ or MeLi quantitatively the 3-isopropyl-5-methyl- or 3-*tert*-butyl-5-methyl-substituted ethylene-bridged bis(cyclopentadienes) **153b** and **153c**, respectively.

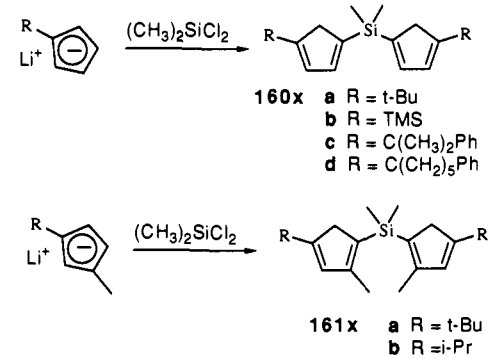
The ethylene-bridged bis(3,5-dimethylcyclopentadiene) ligand **153a** was synthesized from the allylic alcohol intermediate **150** (Scheme 36). Treatment of **150**, whose preparation was described above, with buffered pyridinium chlorochromate (PCC) effected a 1,3-transposed oxidation to yield bis-enone **154** which was converted to the desired ligand **153a** upon addition of a methyllanthanum reagent followed by elimination of water from allylic alcohol **155**.[66]

The synthesis of bis(cyclopentadienes) bridged by a cyclopentane-1,3-diyl moiety has been developed in an attempt to further restrict conformational mobility about the linking group.[67] Conversion of cyclopentadiene to *cis*-1,3-dihydroxycyclopentane (**156**) was carried out as shown in Scheme 37. After activation of the two hydroxyl groups as sulfonate esters, addition of cyclopentadienylsodium gave *cis*-1,3-bis(cyclopentadiene)cyclopentane (**157**) which was converted to bis(fulvene) **158** by condensation with acetone in the presence of pyrrolidine. Bis(fulvene) **158** was converted

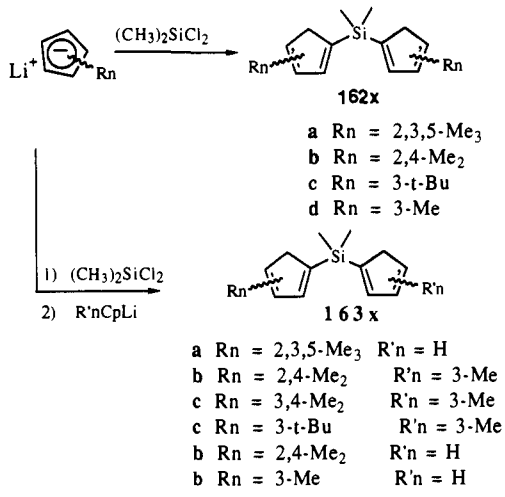
Scheme 37[67]



Scheme 38[68]



Scheme 39[69]



to either the isopropyl derivative **159a** or the *tert*-butyl derivative **159b** upon addition of either $LiAlH_4$ or MeLi. Since the two faces of each cyclopentadiene in these bridged cyclopentadienes are diastereotopic, metalation can give rise to multiple isomers in contrast to the simpler meso- and *dl*-isomers formed in the metalation of enantiotopic ligand faces in *ansa*-bis(cyclopentadienes) **146** and **153**.

Dimethylsilane has also been used to bridge substituted cyclopentadienes, forming prochiral bis(cyclopentadienes) as shown in Schemes 38 and 39.[68,69] The procedure used by Brintzinger for obtaining these silyl-bridged cyclopentadienes was simply addition of 2

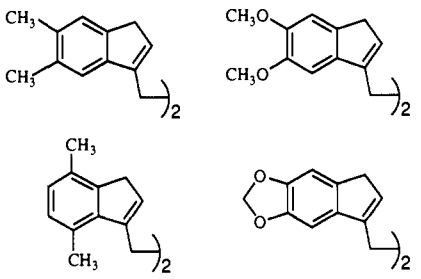


Figure 4. Substituted bis(indenes).[75]

equivalents of the appropriately substituted cyclopentadienyllithium reagent to dichlorodimethylsilane, resulting in silyl substitution at the least hindered position on the cyclopentadiene (Scheme 38). In the instances where the substituent on the cyclopentadiene was sufficiently large (i.e. products **160a–d**, from R = $C(CH_3)_3$, $Si(CH_3)_3$, $C(CH_3)_2Ph$, $C(CH_2)_5Ph$), the bis(3-R-cyclopentadienes) formed cleanly.[68] In the instances where two substituents were present on the cyclopentadiene, the silane added in the least hindered position next to the methyl group, forming dimethylsilyl-bridged bis(2-methyl-4-*tert*-butylcyclopentadiene) and bis(2-methyl-4-isopropylcyclopentadiene) ligands **161a** and **161b**.

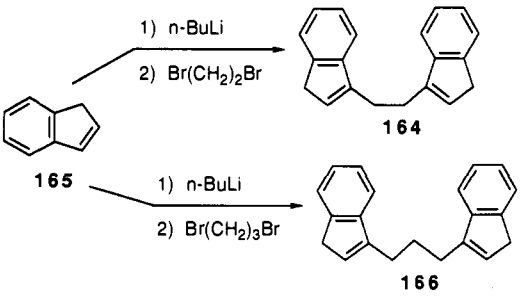
In a related procedure Yamazaki has prepared several other dimethylsilyl-bridged substituted bis(cyclopentadienes) by either double addition of a single cyclopentadienyl anion to dichlorodimethylsilane to produce symmetrical bis(cyclopentadienes) **162** or by sequential addition of different cyclopentadienes to yield unsymmetrical bis(cyclopentadienes) **163** (Scheme 39).[69] The positional isomers were not determined until after metalation of these ligands, allowing the possibility that other isomers of, for example, the bridged 3-methylcyclopentadiene were formed in the ligand synthesis, but not converted to isolable metallocene complexes.

E. Bridged Bis(indenes)

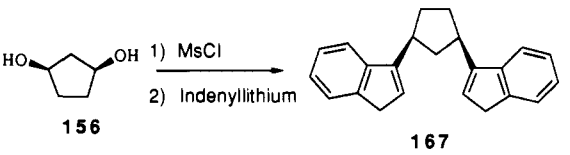
The most ubiquitous *ansa*-bis(cyclopentadiene) is clearly ethylene-1,2-bis(3-indene) (**164**), originally reported in 1967[70] and initially applied as a ligand in *ansa*-metallocenes by Brintzinger in 1982.[10] The synthesis of this bidentate ligand can be accomplished by deprotonating indene (**165**) with *n*-butyllithium followed by addition of 1,2-dibromoethane as shown in Scheme 40. A common side product in this reaction is a spiro-cyclopropane formed by intramolecular bisalkylation of indene rather than the desired intermolecular alkylation. Several modifications involving solvent and reaction conditions have led to improved yields.[71–73] After formation of *ansa*-metallocenes with bis(indene) **164**, the two double bonds in each six-membered ring can be hydrogenated, leading to the ethylene-1,2-bis(4,5,6,7-tetrahydro-3-indenyl) ligand.[10] In a related reaction, addition of indenyllithium to 1,3-dibromopropane leads to a 1,3-propanediyl-bridged bis(3-indene) **166** which can be converted to bridged metallocenes containing the tetrahydroindenyl ligand.[74] Collins has prepared several substituted ethylene-bridged bis(indenes) which are shown in Figure 4.[75]

The 1,3-dihydroxycyclopentane compound **156** described above for the bridging of cyclopentadienes has also been applied in the formation of *cis*-cyclopentane-1,3-diyl bis(3-indene) (**167**) (Scheme 41).[67] Displacement of the sulfonate esters derived from diol **156** by excess indenyllithium gave a good yield of bis(indene) **167**.

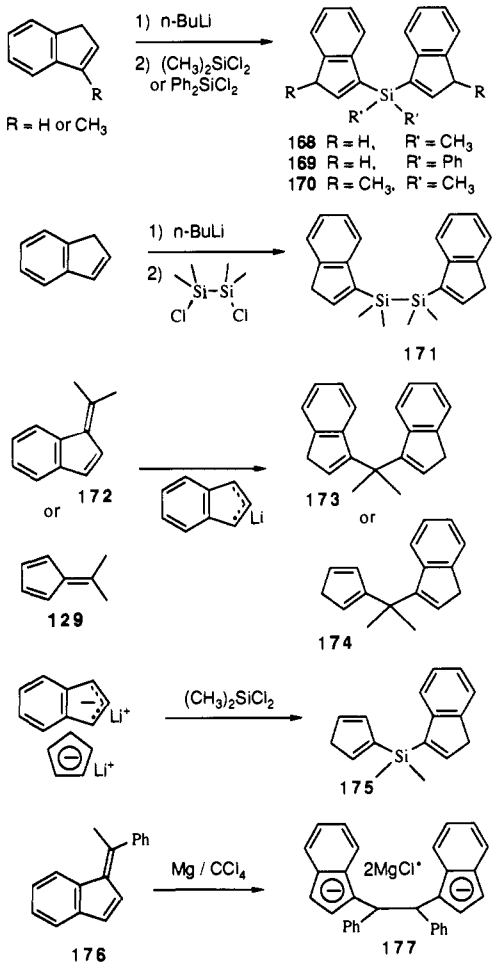
Scheme 40[68]



Scheme 41[67]

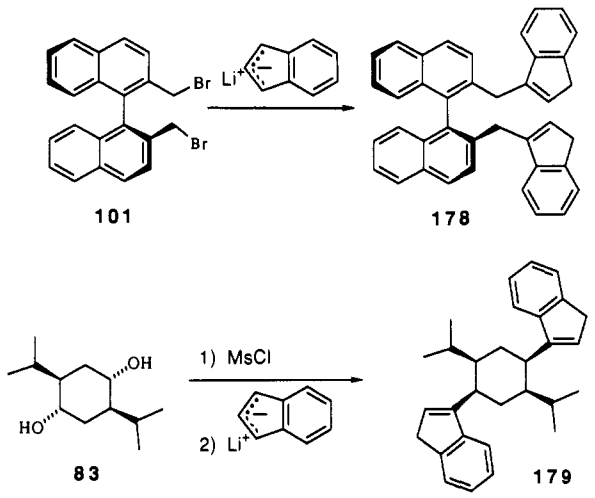


Scheme 42[76]



The preparation of dimethyl- and diphenylsilyl-bridged bis(3-indenes) **168–170** have been reported from the reaction of indenyllithium or 3-methylindenyllithium with dichlorodimethylsilane or dichlorodiphenylsilane as shown in Scheme 42.[76] Several related bridged indenes have also been reported.[76] Addition of indenyllithium to dichlorotetramethyldisilane afforded the disilane-bridged bis(3-indene) **171**. Using dichlorodimethylgermane gave a dimethylgermanyl analog of dim-

Scheme 43[11,38]



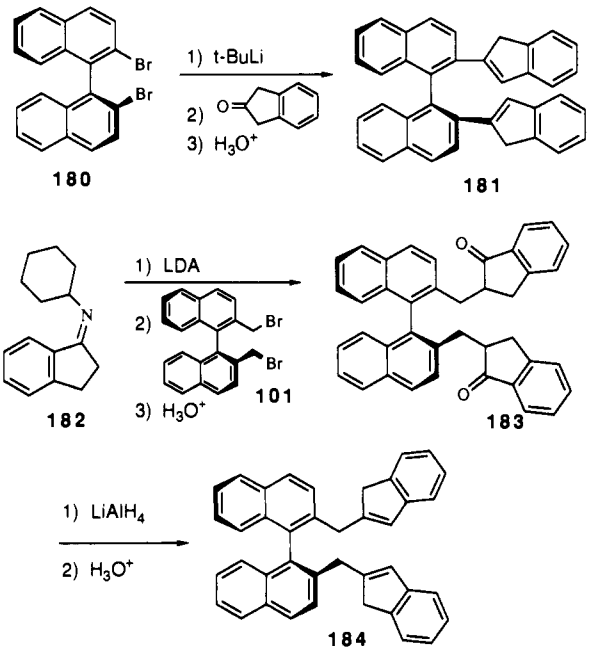
ethylsilyl-bridged bis(1-indene) **168**. The dimethylmethyl-bridged bis(3-indene) and cyclopentadienyl(3-indenyl)(dimethyl)methane ligands **173** and **174** were prepared by the reaction of indenyllithium with benzofulvene **172** or fulvene **129**. Concurrent addition of indenyllithium and cyclopentadienylsodium to dichlorodimethylsilane gave the cyclopentadienyl(1-indenyl)-(dimethyl)silane ligand **175**. Phenylbenzofulvene (**176**) could be coupled with magnesium and carbon tetrachloride to give 1,2-diphenylethanediyl-*ansa*-bis(3-indene) **177**.[76]

Metalation of Brintzinger's ethylene-bridged *ansa*-bis(3-indene) **164** can produce a mixture of meso and generally desired C_2-symmetrical racemic metallocene isomers due to the enantiomeric relationship between the two faces of each cyclopentadienyl moiety in the ligand. By incorporating a chiral bridging group, the two faces of the ligand are rendered diastereotopic, and metalation could in theory be selective for the direct formation of one enantiomerically pure complex. The first example of using a chiral group to form a bridge between two indenes has recently been reported in which 2 equiv of indenyllithium were added to enantiomerically enriched 2,2′-bis(bromomethyl)-1,1′-binaphthalene (**101**), forming the chiral bis(3-indenyl) ligand **178** (Scheme 43).[11] A related example uses the chiral cyclohexanediol **83** to bridge two indenyl groups in the bis(indene) ligand **179**.[38]

Conceptually, a method for ensuring the formation of a single isomer of *ansa*-bis(indenes) would be to use a chiral group to bridge the indenyl ligands at the symmetrical 2-position. Complexes of this type would stand the best chance for successful application if the chiral bridging group rigidly held the bis(2-indenyl) ligands in a chiral configuration. For example, the 1,1′-binaphthyl-bridged bis(2-indene) ligand **181** has been prepared by the addition of 2 equiv of 2-indanone to 2,2′-dilithio-1,1′-binaphthalene, which can be prepared from enantiomerically pure 1,1′-binaphthyl 2,2′-dibromide **180**, followed by acid-promoted elimination (Scheme 44).[77] Since the faces of the ligand are equivalent due to rotation about the bond between the naphthyl and indenyl moieties, metalation can give only one product.

The synthesis of a similar chiral *ansa*-bis(2-indene) **183** having 1,1′-binaphthyl-2,2′-dimethanediyl bridging two achiral 2-indenyl ligands is also shown in Scheme

Scheme 44[77,78]



44. In this synthesis 2,2′-bis(bromomethyl)-1,1′-binaphthyl (**101**), which is available in enantiomerically pure form, is reacted with deprotonated cyclohexylimine of 1-indanone **182** to yield after hydrolysis bis(1-indanone) **183** bridged at its 2-position. Reduction of the carbonyls to hydroxyl groups followed by acid-promoted elimination gave the 1,1′-binaphthyl-2,2′-dimethanediyl bridged bis(2-indenyl) ligand **184**.[78] Again, metalation of the two equivalent faces of these indenyl ligands can inherently produce only one chiral stereoisomer.

IV. Synthesis of Chiral Cyclopentadienylmetal Complexes

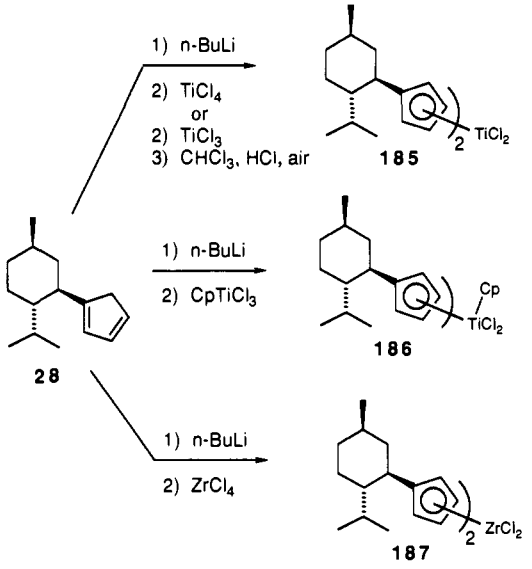
Chiral cyclopentadienylmetal complexes can be obtained in two general ways, metalation of chiral or prochiral cyclopentadienyl ligands or by converting achiral cyclopentadienylmetal complexes by appropriate functionalization into chiral derivatives. This section will cover in turn metalation of chiral or prochiral monocyclopentadienyl ligands, metalation of bridged bis(cyclopentadienyl) and bridged bis(indenyl) ligands, and conclude with derivatization of achiral cyclopentadienylmetal complexes. Within each section typical methods for forming complexes of a particular group (e.g. Ti, Zr, and Hf) using chiral monosubstituted, annulated, or prochiral, enantiotopic polysubstituted cyclopentadienes will be covered with a more complete tabular listing of complexes formed by these methods.

A. Metalation of Chiral or Prochiral Cyclopentadienes

1. Monosubstituted Chiral Cyclopentadienes

Since the two faces of monosubstituted cyclopentadienyl ligands are equivalent due to free rotation of the cyclopentadienyl moiety, metalation with an achiral metal fragment of 1 equiv of such ligands will produce only one stereoisomer (and its enantiomer if the starting cyclopentadienyl ligand was racemic). Metal complexation of 2 equiv of these chiral monosubstituted cy-

Scheme 45[3,8,26]

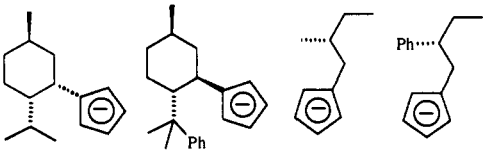


clopentadienyl ligands can produce only one enantiomerically pure C_2-symmetrical metallocene if the original ligand is enantiomerically pure, or a mixture of a meso-metallocene and racemic C_2-symmetrical metallocene if the chiral cyclopentadienyl ligand was racemic. Avoidance of the meso-diastereomer is a strong reason for synthesizing and using enantiomerically pure chiral cyclopentadienyl ligands.

The most intensively studied group of chiral cyclopentadienylmetal complexes is the bent metallocene dichlorides of the group 4 metals (Ti, Zr, Hf). Preparation of C_2-symmetrical bis(cyclopentadienyl)titanium dichlorides containing 2 equiv of a chiral, enantiomerically pure monosubstituted cyclopentadiene has been successfully accomplished by addition of the cyclopentadienyl anion (generally prepared by deprotonation of the chiral cyclopentadiene with *n*-butyllithium, less frequently by sodium hydride or potassium hydride) in an ethereal solvent to $TiCl_4$. The use of $TiCl_3$ followed by oxidation of the initially formed Ti(III) species in chloroform in the presence of air and HCl has become widely used and often gives improved yields of the titanocene dichlorides.[79] Addition of the chiral cyclopentadienyl anion to achiral cyclopentadienyltitanium trichloride enables access to titanocenes containing one chiral cyclopentadienyl ligand. Zirconium tetrachloride can be added to 2 equiv of the chiral cyclopentadienyl ligand to provide chiral zirconocene dichlorides. In Scheme 45, Kagan's preparations of bis(menthylcyclopentadienyl)titanium dichloride (**185**), cyclopentadienyl(menthylcyclopentadienyl)titanium dichloride (**186**), and bis(menthylcyclopentadienyl)zirconium dichloride (**187**) are shown.[3] Table 1 contains a listing of similar chiral metallocene halides containing one or two chiral and enantiomerically pure cyclopentadienyl ligands.[38,26] Analogous hafnocene dichlorides **198** and **200** containing chiral, enantiomerically pure cyclopentadienyl ligands **191** and **192** have also been prepared and converted to several derivatives including hafnium diodides, dibromides, dihydrides, dialkoxides, diacetates, dithiolates, and dimethyl complexes.[26]

An alternative route to forming chiral but racemic monosubstituted cyclopentadienyl anion involves reduction of unsymmetrical 6,6-disubstituted fulvenes.

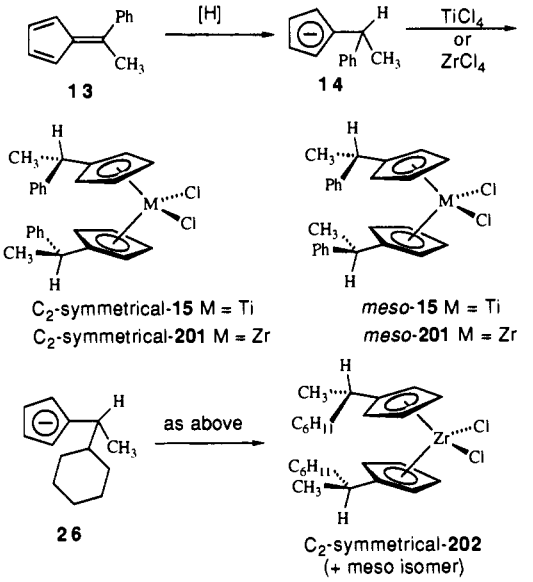
Table 1. Chiral Bis(Cyclopentadienyl)metal Dichlorides of the Type $(Cp^1)(Cp^2)MCl_2$



189 190 191 192

Cp^1	Cp^2	M	complex
189	189	Ti	193
189	189	Zr	194
189	Cp	Ti	195
190	190	Ti	196
191	191	Zr	197
191	191	Hf	198
192	192	Zr	199
192	192	Hf	200

Scheme 46[17,24]



The racemic cyclopentadienyllithium complexes so produced can be directly trapped with $TiCl_4$ or with $ZrCl_4$ to give a mixture of chiral, C_2-symmetrical and achiral, *meso*-bis(cyclopentadienyl)metal dichlorides. For example, in Scheme 46, the reduction of 6-methyl-6-phenylfulvene (**13**) can be accomplished with either $LiAlH_4$[17] or by β-hydride delivery from isobutyllithium[24] and the resulting cyclopentadienyl anion **14** trapped with either $TiCl_4$ or $ZrCl_4$, giving metallocenes **15** or **201** as mixtures of racemic and meso diastereomers. Through repeated recrystallizations the racemic, C_2-symmetrical diastereomers can usually be obtained. In a similar reaction, Erker reduced 6-cyclohexyl-6-methylfulvene (**25**) with isobutyllithium and trapped the resulting cyclopentadienyl anion **26** to form a mixture of racemic and meso isomers of zirconocene dichloride **202**.[24] The use of $LiAlH_4$ in the presence of chiral amines has enabled the production of C_2-symmetrical titanocene **15** in low enantiomeric purity by the asymmetric reduction of fulvene **13**.[22] Qian has reported several bis(cyclopentadienyl)titanium dichloride complexes of unspecified stereoisomeric identity.[29-31]

Several mono(cyclopentadienyl)metal complexes of the later transition metals containing a chiral cyclopentadienyl moiety have been reported and these complexes are shown in Figure 5. Treatment of the

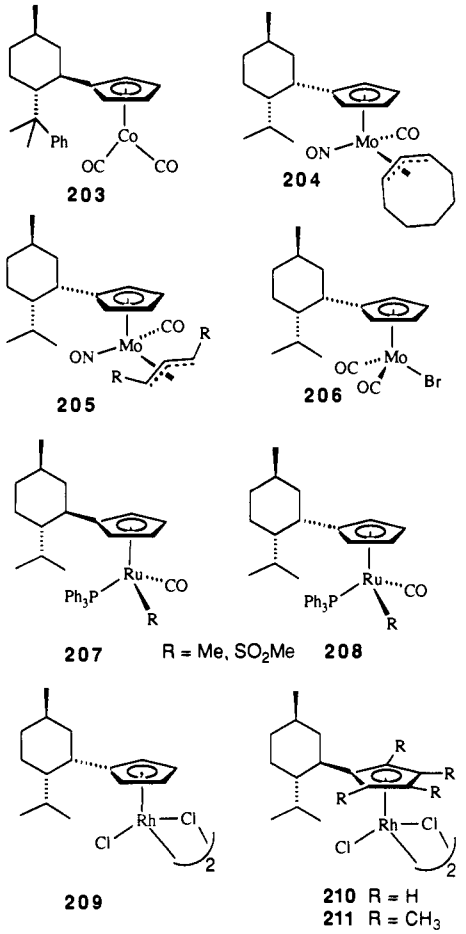


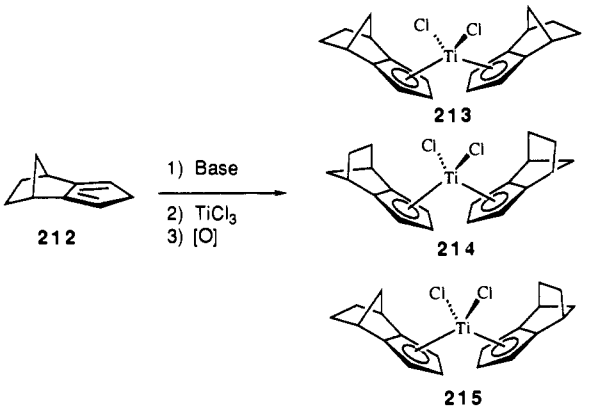
Figure 5. Chiral mono(cyclopentadienyl)metal complexes.[8,80-82]

phenylmenthyl-derived cyclopentadiene **34** with dicobalt octacarbonyl formed the chiral cyclopentadienylcobalt dicarbonyl **203**.[8] Faller has reported several cyclopentadienylmolybdenum complexes such as **204** and **205** containing the neomenthylcyclopentadienyl ligand.[80] The entry in these compounds, chiral cyclopentadienylmolybdenum dicarbonyl **206**, was produced by the addition of the chiral cyclopentadienyllithium to a molybdenum bromide. Several ruthenium complexes such as **207** and **208**, prepared from either the menthylcyclopentadiene (**27**) or the neomenthylcyclopentadiene (**28**), have been reported.[81] The presence of the chiral auxiliary on the cyclopentadiene in both the molybdenum and ruthenium complexes enabled resolution of diastereomers possessing a stereogenic metal center. A family of chiral cyclopentadienylrhodium complexes including **209–211** has been recently reported which contain menthyl- or neomenthyl-substituted cyclopentadienyl or tetramethylcyclopentadienyl ligands.[82]

2. Annulated Chiral Cyclopentadienylmetal Complexes

The annulated cyclopentadienes described in section II.B were comprised of either C_1-symmetrical or C_2-symmetrical ligands. The key difference between these two classes of ligands is that coordination of a single C_1-symmetrical cyclopentadienyl ligand to an achiral metal may produce two diastereomers (plus their enantiomers if the cyclopentadienyl ligand was racemic) due to the nonequivalence of the faces in the cyclopentadienyl ligand. In contrast, only one mono(cyclopentadienyl)metal complex (and its enantiomer if the starting ligand was racemic) is inherently possible when the metal is coordinated to either of the equivalent faces of the cyclopentadienyl ligand. The situation is even more complicated when bis(cyclopentadienyl)-metal complexes are formed from C_1-symmetrical annulated cyclopentadienes. In this case a mixture of three diastereomers may in principle form from an enantiomerically pure cyclopentadiene. On the other hand, metalation of 2 equiv of a racemic C_2-symmetrical annulated cyclopentadiene would still give a manageable mixture of meso- and *dl*-diastereomers.

Scheme 47[83]

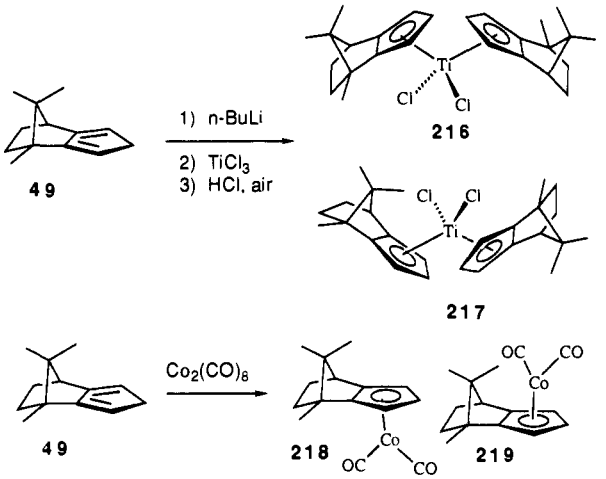


The possible mixtures of bis(cyclopentadienyl)metal complexes mentioned here are the theoretically possible ones; in practice a good degree of selectivity is seen in the metalation of C_1-symmetrical cyclopentadienyl ligands. One popular C_1-symmetrical annulated cyclopentadiene contains a norbornane ring fused to the cyclopentadiene. Paquette has extensively studied this system (both chiral and achiral variants) which could metalate either diastereotopic face of these ligands to form exo–exo complex **213**, exo–endo complex **214**, or endo–endo complex **215** (Scheme 47).[83] A related study on the facial preference for coordination of lithium to these cyclopentadienes has recently appeared.[84]

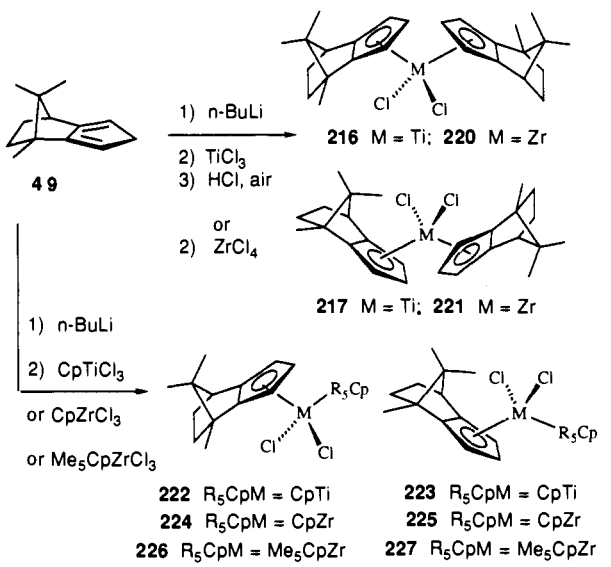
The first report of metalating C_1-symmetrical annulated cyclopentadienyl ligands was in 1986 by Halterman and Vollhardt in which the enantiomerically pure camphor-derived cyclopentadiene **49** was incorporated into titanocene dichloride and cobalt dicarbonyl complexes (Scheme 48).[34,8] Addition of $TiCl_3$ to the anion of **49** resulted in the formation of two titanocene dichloride complexes, the C_2-symmetrical isomer **216** and the C_1-symmetrical isomer **217** in a ratio of 95:5. The two cyclopentadienylcobalt dicarbonyl complexes **218** and **219** were formed in a 3:1 ratio upon addition of $Co_2(CO)_8$ to CamCp **49**. In each instance metalation of the endo-face of the tricyclic cyclopentadienyl ligand was favored, presumably due to avoidance of nonbonded interactions with the methyl group on the methano bridge.

Paquette has published extensive studies of π-facial preference in the complexation of C_1-symmetrical annulated enantiomerically pure cyclopentadienes derived from camphor, verbenone, and nopol. Metalation of the anion of camphor-derived cyclopentadiene **49** with $TiCl_3$ followed by oxidation gave a 9:1 mixture of titanocene dichlorides **216** and **217** while complexation with $CpTiCl_3$ led to a 7:1 mixture of metallocene dichlo-

Scheme 48[34,8]



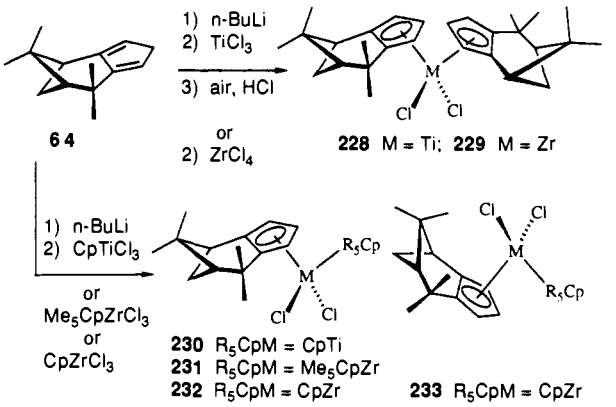
Scheme 49[35,36]



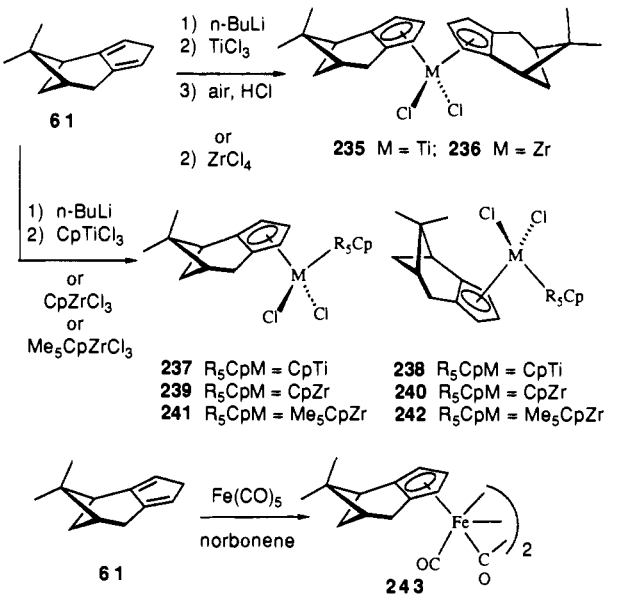
rides **222** and **223** (Scheme 49).[35,36] When analogous metalations were performed using $ZrCl_4$, $CpZrCl_3$, or $(Me_5Cp)ZrCl_3$ a 13:1 ratio of bis(camphorCp($ZrCl_2$ complexes **220** and **221**, a 2:1 mixture of Cp(camphorCp)$ZrCl_2$ complexes **224** and **225**, and a 1.4:1 mixture of (Me_5Cp)(camphorCp)$ZrCl_2$ **226** and **227** were obtained. In all cases, metalation preferentially occurred on the bottom, or endo face of this isodicyclopentadienyl derivative.

Metalation of the anion of enantiomerically enriched verbenone-derived C_1-symmetrical cyclopentadiene **64** with $TiCl_3$, $ZrCl_4$, $CpTiCl_3$, or $(Me_5Cp)ZrCl_3$ occurred exclusively on the bottom face of the cyclopentadienyl ligand to produce metallocene dichlorides **228–231**. Only in the case where cyclopentadiene **64** was metalated with $CpZrCl_3$ was a mixture of two isomers **232** and **233** obtained (Scheme 50).[37] Interestingly, the enantiomeric purity of the commercially available verbenone used in the ligand synthesis was only on the order of 57% ee. The presence of the minor enantiomer was not noticed until a small amount of the *meso*-titanocene dichloride **234** was isolated by crystallization and its structure determined by X-ray crystallography—a fact necessitating the existence of both antipodes of the ligand.[85] Since only a very small amount of this meso-isomer was obtained from the metalation with $TiCl_3$, a large degree of enantiomer recognition must be operating in the metalation.

Scheme 50[37,85]

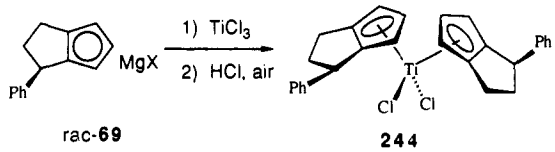


Scheme 51[86,36]

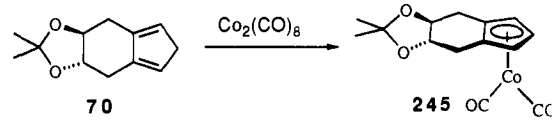


In his study of the metalation of nopol-derived cyclopentadiene **61** (pineneCp), Paquette was able in some cases to reverse the facial selectivity by varying the metalation conditions.[86] Metalation with either $TiCl_3$, $TiCl_4$, or $ZrCl_4$ gave exclusively metallocenes **235** and **236** by metalation of the bottom face of the ligand as oriented in Scheme 51. Metalation of the anion of ligand **61** with $CpTiCl_3$ at −78 °C followed by warming to 20 °C gave a 1:5 ratio of titanocenes **237** and **238** due to preferential reaction on the top face, while the same metalation at higher temperatures give a 3:1 ratio of **237** and **238** favoring metalation of the bottom face of **61**. When $CpZrCl_3$ was employed in these reactions, the low-temperature mixing followed by heating yielded exclusively bottom-metalated zirconocene dichloride **239**, while mixing at room temperature followed by heating produced a 1:3.5 mixture of metallocenes **239** and **240**, favoring metalation of the top face. Regardless of reaction conditions, metalation of nopol-derived cyclopentadiene **61** with $(Me_5Cp)ZrCl_3$ gave a 2:1 mixture of bottom- and top-metalated complexes **241** and **242**. Heating cyclopentadiene **61** with $Fe(CO)_5$ in the presence of norbornene as a hydrogen acceptor gave a good yield of cyclopentadienyliron dicarbonyl dimer **243** as the single isomer having the metal near the unmethylated methano bridge.[36]

Scheme 52[39]



Scheme 53[34,8]



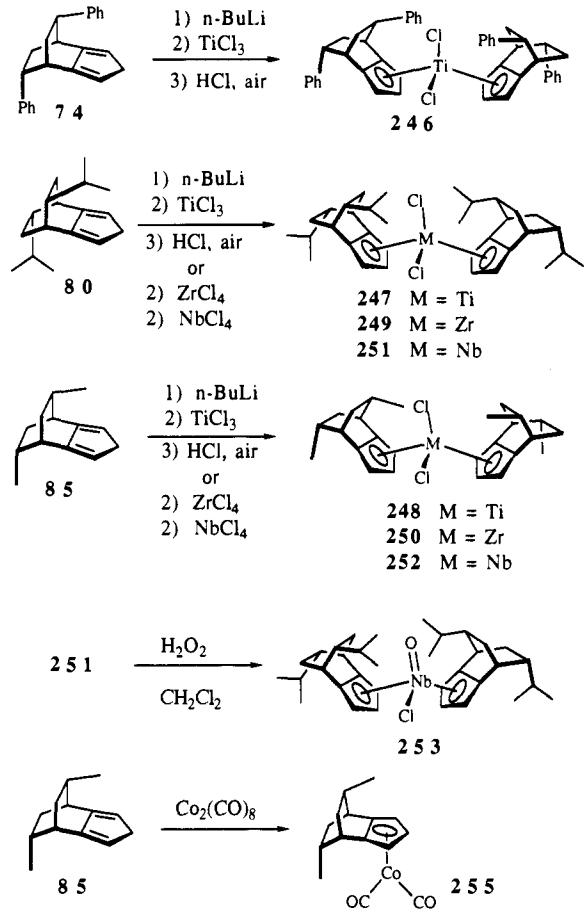
A final example of metalating C_1-symmetrical annulated cyclopentadienes is the formation of the C_2-symmetric titanocene dichloride **244** obtained by Brintzinger upon addition of $TiCl_3$ to the chiral cyclopentadienylmagnesium salt **69** (Scheme 52).[39] The racemic ligand **69** had been unexpectedly formed in an attempted magnesium-induced coupling reaction of phenyldihydropenatalene **68**. Although it is not surprising for the titanium to be trans to the sterically hindering phenyl group in metallocene **244**, it is surprising that only the one C_2-symmetrical isomer was isolated and none of the potentially formed meso-isomer. Given the low isolated yield (6%) of metallocene **244**, it is possible that other isomers formed, but were not isolated.

3. C_2-Symmetrical Annulated Cyclopentadienes

Metalation of the readily obtained, enantiomerically pure, tartrate-derived cyclopentadiene **70** with dicobalt octacarbonyl necessarily formed a single isomer of the cyclopentadienylcobalt dicarbonyl **245** and was the first example of metalating a C_2-symmetrical annulated cyclopentadienyl ligand (Scheme 53).[34,8] Attempted metalation of this ligand with more Lewis acidic metals failed, presumably due to the presence of an acid-sensitive ketal moiety.

The three C_2-symmetrical, enantiomerically pure, bicyclooctane-fused cyclopentadienes **74**, **80**, and **85** containing diphenyl, diisopropyl, and dimethyl substituents have been used to form titanocene dichlorides, niobocene dichlorides, oxoniobocene chlorides, and cyclopentadienylcobalt dicarbonyl complexes (Scheme 54). Metalation of **74**, **80**, and **85** with $TiCl_3$ followed by oxidation gave in each case C_2-symmetrical titanocene dichlorides **246**,[40] **247**, and **248**[9,41] as the sole isomeric products. The solid-state structures of titanocene complexes **246** and **248** derived form either the diphenyl-substituted or the dimethyl-substituted ligands **74** or **85** were determined by X-ray diffraction. The ligands **80** and **85** containing the diisopropyl substituents and the dimethyl substituents were successfully metalated with $ZrCl_4$ to form again only the single C_2-symmetrical zirconocene dichlorides **249** and **250**.[9] These zirconocene dichloride complexes could also be converted into zirconocene dimethyl complexes by addition of methyllithium. Metalation of these same ligands **80** and **85** with $NbCl_4$ gave initially the paramagnetic niobocene dichlorides **251** and **252** which were oxidized to give a single isomer of the oxoniobocene chlorides **253** and **254**.[9] Treatment of the dimethyl-substituted bicyclooctane-fused cyclopentadiene

Scheme 54[40,9,41,87]



85 with $Co_2(CO)_8$ led to a single isomer of the chiral cyclopentadienylcobalt dicarbonyl **255**.[87]

Binaphthyldimethylenecyclopentadiene (BpDMCp) **91** has been used to form titanocene and zirconocene dichlorides as well as cyclopentadienyl iron carbonyl complexes (Scheme 55).[42] Treatment of the anion of cyclopentadiene **91** with either $TiCl_3$ followed by oxidation or by $ZrCl_4$ gave the metallocene dichlorides **256** and **257** as single C_2-symmetrical isomers. Titanocene dichloride **256** was determined by X-ray diffraction to possess an axis of C_2 symmetry in the solid state. Metalation of the anion of **91** with $CpTiCl_3$ gave the titanocene dichloride **258** which contains only one chiral cyclopentadienyl ligand. The chiral zirconocene dichloride **257** could be converted into either the dimethyl or dibenzyl derivatives upon treatment with methyllithium or benzylpotassium.[45] The binaphthyl-derived cyclopentadiene **91** could also be metalated with iron carbonyl to give the cyclopentadienyliron dicarbonyl dimer **259** which could be converted upon treatment with iodine to the iodoiron complex **260** which could be further alkylated to the methyliron species **261**.[42]

Erker has formed a chiral monocyclopentadienylzirconium trichloride complex **262** by metalation of the C_2-symmetrical dinorbornacyclopentadiene **106** with $ZrCl_4$[46] (Scheme 56). Presumably due to the severe steric congestion imposed by this highly substituted ligand, only a single cyclopentadienyl ligand can attach to the zirconium.

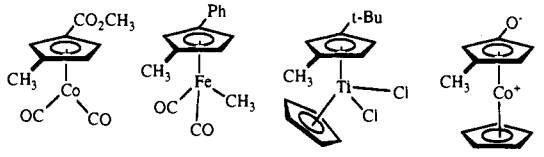
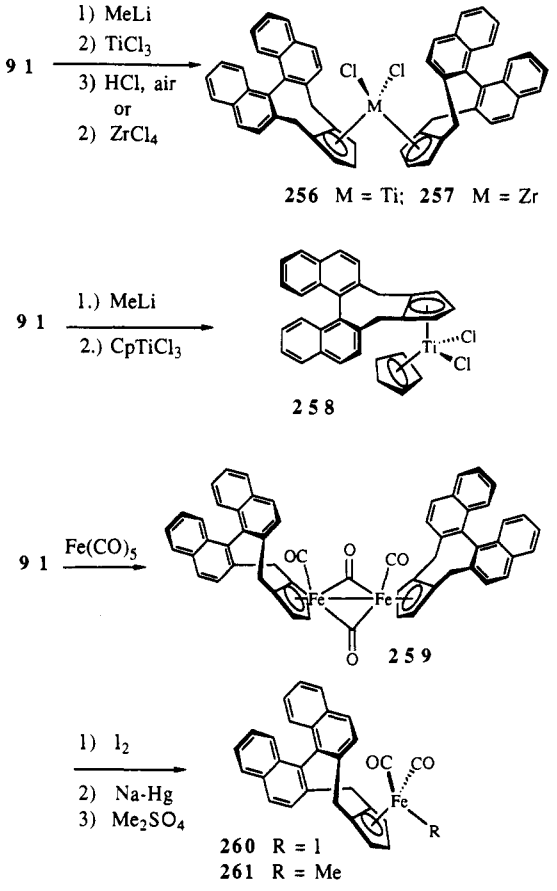
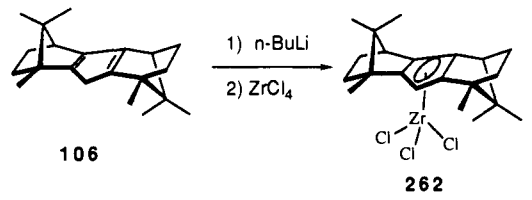


Figure 6. Chiral cyclopentadienylmetal complexes prepared from enantiotopic cyclopentadienyl ligands.[4,18,48,50]

Scheme 55[42]



Scheme 56[46]



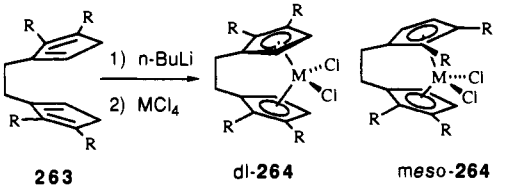
4. Metalation of Prochiral, Enantiotopic Cyclopentadienes

Although the earliest chiral cyclopentadienylmetal complexes consisted of a metal bound to a prochiral, enantiotopic cyclopentadiene, many of these complexes were formed by derivatization of achiral monosubstituted cyclopentadienylmetal complexes and will be discussed in section IV.D. Several examples of chiral cyclopentadienylmetal complexes formed by the metalation of prochiral, enantiotopic cyclopentadienyl ligands are shown in Figure 6.

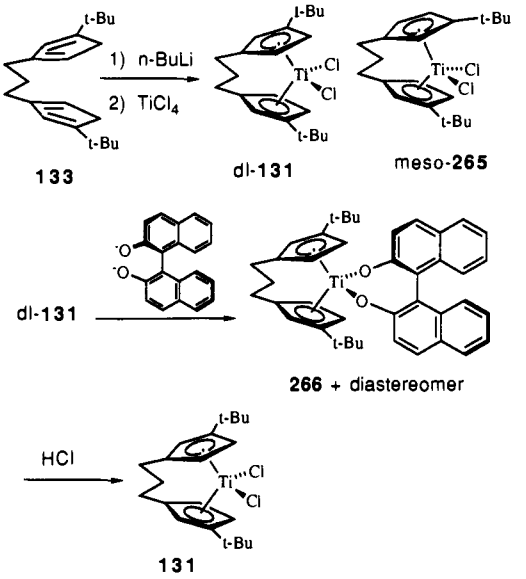
B. *ansa*-Metallocenes from Bis(cyclopentadienes)

Metalation of two cyclopentadienyl ligands covalently linked by a one-, two-, or three-atom chain produces *ansa*-metallocenes containing the important characteristic of restricted rotation of the normally freely rotating cyclopentadienyl ligand. Introducing additional substitution on these bridged cyclopentadienyl rings can produce chiral metallocene complexes. Due both to practical, synthetic considerations in the preparation of *ansa*-metallocenes and to interpretation of any stereochemistry induced in reactions using these complexes, the preparation of *ansa*-metallocenes containing two equivalent cyclopentadienyl rings related by C_2 symmetry has been desirable. As illustrated in Scheme 57, appropriate metalation of equivalently substituted bridged cyclopentadienes **263** can produce *ansa*-metallocenes **264** containing either the desired C_2-symmetrical relationship between the rings or an undesired C_S-symmetrical relationship. Two general classes of chiral *ansa*-metallocenes have been developed, those based on bridged bis(indenes) and those incorporating other alkyl substituents.

Scheme 57

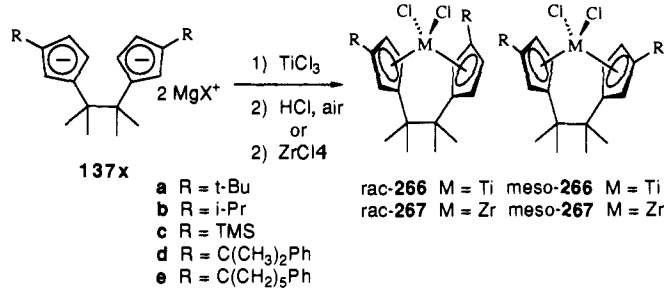


Scheme 58[58]

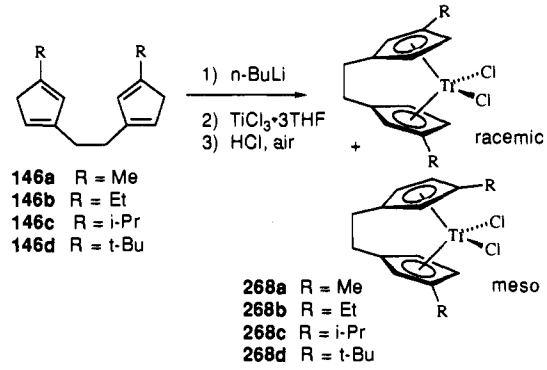


The first report of an *ansa*-metallocene was Brintzinger's 1979 publication of the trimethylene-bridged *ansa*-bis(3-*tert*-butylcyclopentadienyl)titanium dichloride **131** which was prepared by metalating the dianion of bridged cyclopentadiene **133** with $TiCl_3$ (Scheme 58).[58] Only the single C_2-symmetrical bridged titanocene dichloride **131** was isolated, presumably due to steric considerations preventing formation of the meso-isomer. The racemic C_2-symmetrical titanocene dichloride **131** could be resolved into its enantiomers by its addition to enantiomerically pure 1,1′-bi-2-naphthol. This reaction could produce two diastereomeric titanocene dialkoxide complexes, but only the single diastereomeric complex **266** was isolated by HPLC, presumably due to steric forces hindering the formation or isolation of the second diastereomer. The pure diastereomeric complex **266** could be treated with

Scheme 59[62,63]



Scheme 60[65]



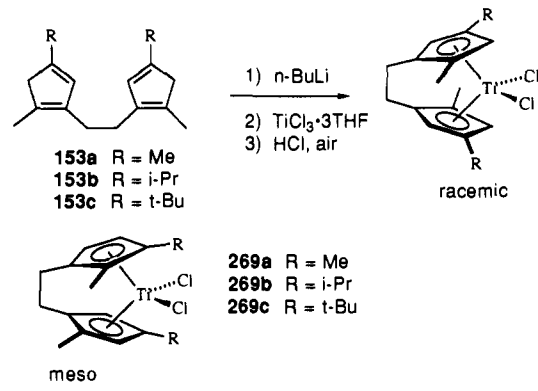
HCl to reform the now enantiomerically pure C_2-symmetric titanocene dichloride **131**.

The tetramethylethylene-bridged *ansa*-bis(3-R-cyclopentadienyl) complexes **137** and **138** (R = *t*-Bu, *i*-Pr, TMS, $C(CH_3)_2Ph$, $C(CH_2)_5Ph$, and CH_2Ph) could be treated with $TiCl_3$ followed by oxidation or by $ZrCl_4$ to give mixtures of racemic C_2-symmetrical and *meso*-metallocene dichlorides **266** and **267** (Scheme 59).[62,63] Fractional crystallization enabled separation of the meso- and *dl*-isomers in most cases. The identity of the meso- and *dl*-isomers were determined in some cases by converting the metallocene dichlorides to metallocene dimethyls which would have equivalent methyl groups in the C_2-symmetrical isomer, but nonequivalent methyl groups in the meso-isomer. The structures of some compounds were established by X-ray crystallography. Similar results were found by McLaughlin when he metalated the lithium salt of **137a** with titanium chlorides.[65b]

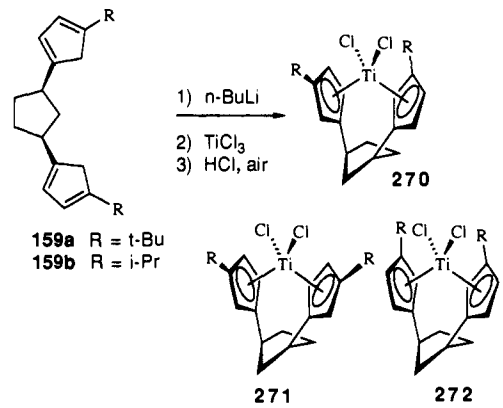
Each of the 1,3-disubstituted ethylene-bridged bis(cyclopentadienes) **146** (R = Me, Et, *i*-Pr, and *t*-Bu) whose preparation by Collins was discussed in section III.D was converted via the corresponding dianion to *ansa*-titanocene dichlorides **268** by metalation with $TiCl_3$–3THF followed by oxidation with HCl in the presence of air (Scheme 60).[63] In each case, a mixture of meso and racemic isomers of **268** was formed with the meso diastereomers being the major product in each case. Only the isopropyl- and *tert*-butyl-substituted titanocenes **268c** and **268d** could be purified into pure racemic isomers by fractional crystallization, and their structures were confirmed by X-ray diffraction.

The 3,5-disubstituted titanocene dichlorides **269** were prepared by Collins from the reaction of the dilithium salts of the ansa ligands **153** with $TiCl_3$–3THF followed by oxidation with HCl in air (Scheme 61).[66] In each of these cases, the formation of the racemic isomer was favored. In addition, photolysis of these titanocene dichlorides effected an equilibration give racemic/meso

Scheme 61[66]



Scheme 62[67]



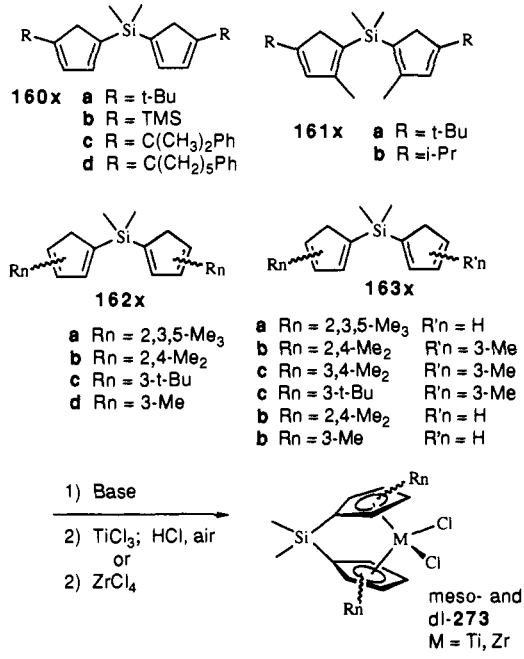
ratios of 2.6:1 for **269a**, 3.8:1 for **269b**, and >15:1 for **269c**. Each of these mixtures could be separated by either crystallization or silica gel chromatography. The X-ray structure of *rac*-**269c** has been determined.

Metalation of the *n*-butyllithium-generated anions of cyclopentane-1,3-diyl bridged *ansa*-bis(3-R-cyclopentadienes) **159a** and **159b** (R = *i*-Pr and *t*-Bu) was accomplished with $TiCl_3$–$(thf)_3$ followed by oxidation to give a mixture of two meso-symmetrical isomers **271** and **272** having the substituents on the cyclopentadienyl ring both located either over the methylene or over the ethylene portions of the bridging cyclopentane and C_1-symmetrical isomers **270** having a local C_2-symmetrical orientation of the substituted cyclopentadienyl rings near the metal (Scheme 62).[67] In both cases, the isomers could be separated by fractional crystallization and their identities established by NMR spectroscopy and X-ray structure determinations.

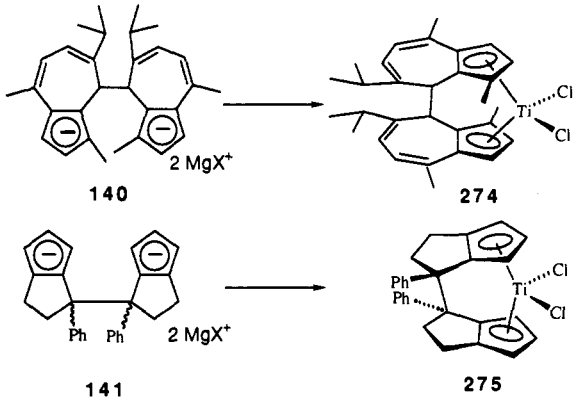
The substituted prochiral silyl-bridged *ansa*-bis(cyclopentadienes) **160–163** were deprotonated and metalated with either $TiCl_3$ or $ZrCl_4$ to give mixtures of meso and racemic C_2-symmetrical *ansa*-metallocene dichlorides **273** (Scheme 63).[68,69] In some cases the isomers were separable and their identities were established by either X-ray crystallography or by NMR spectroscopy.

Brintzinger has reported the metalation of the rather interesting bis(cyclopentadienyl) ligands **140** and **141** which were prepared from the coupling of guaiazulene and phenylepentalene (Scheme 64). Addition of $TiCl_3$ to the anions of ligands **140** and **141** followed by oxidation produced in the first case only the racemic C_2-symmetrical isomer of **274** and in the second case a 2:1 mixture of racemic C_2-symmetrical and meso-

Scheme 63[68,69]



Scheme 64[62]

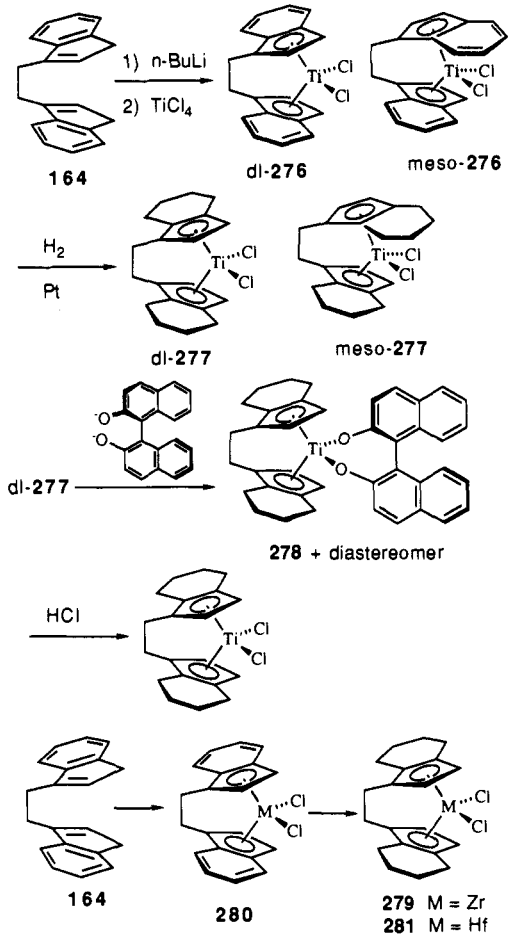


isomers of metallocene **275**.[64] The origin for the selectivity in the formation of the C_2-symmetrical isomer of **274** was not established as arising from selective coupling in the ligand preparation or selective complex formation of the C_2-symmetrical ligand.

C. *ansa*-Metallocenes from Bis(indenes)

Metalation of achiral *ansa*-bis(indenes) can lead to mixtures of meso and racemic C_2-symmetrical bis(indenyl)metal complexes since the two faces of each indenyl ligand are enantiotopic. Since Brintzinger's first report in **1982** of the metalation of ethylene-bridged *ansa*-bis(1-indene) **164**[10] with $TiCl_4$ to form *ansa*-titanocene dichloride **276** as a mixture of meso and racemic C_2-symmetrical isomers (Scheme 65), the preparation and application of this chiral bis(indenyl)metal complex and its derivatives have dominated the field of chiral metallocenes. Catalytic hydrogenation of the mixture of *ansa*-bis(indenyl)titanium dichloride **276** selectively reduces the diene affording in good yield the *ansa*-bis(tetrahydroindenyl)titanium dichloride **277**. The racemic C_2-symmetrical isomer *dl*-**277** was readily separable from the *meso*-**277** isomer by fractional crystallization. The racemic isomer could then be derivatized into diastereomeric alkoxides **278** upon treatment with enantiomerically pure 1,1'-bi-2-naphthol and this diastereomeric mixture could be separated by column chromatography. Treatment of diastereomerically pure alkoxide **278** with HCl regenerated now enantiomerically pure C_2-symmetrical titanocene dichloride **277**. Brintzinger has also reported the preparation of the ethylene-bridged bis(indenyl)zirconium dichlorides *dl*-**280** and its tetrahydroindenyl derivative **279**.[88] Both the ethylene-bridged *ansa*-bis(tetrahydroindenyl)titanium and -zirconium dichlorides **277** and **279** could be resolved with *O*-acetyl-R-mandelic acid.[89] Improved conditions for the metalation have been reported.[71-73] The ethylene-bridged *ansa*-bis(tetrahydroindenyl)-hafnium dichloride **281** has also been analogously prepared.[72,73]

Scheme 65[10,88,72,73]



Treatment of either the ethylene-bridged *ansa*-bis-(tetrahydro-1-indenyl)zirconium or -hafnium dichlorides **279** or **281** with methyllithium resulted in replacement of the chlorine atoms with methyl groups, forming dimethylzirconium and dimethylhafnium complexes **282** and **283**.[73,90] Addition of benzylpotassium to zirconium dichloride **279** resulted in formation of dibenzylzirconium complex **284**.[91] Exposure of either the zirconium or hafnium dichlorides **279** or **281** to hydride reagents gave in each case zirconium or hafnium dihydrides **285** and **286** which exist in dimeric forms. These organometallic complexes are of particular interest for the formation of cationic group 4 metallocenes (Scheme 66).

Several other achiral *ansa*-bis(indenyl)metal complexes have been analogously formed. In all cases where

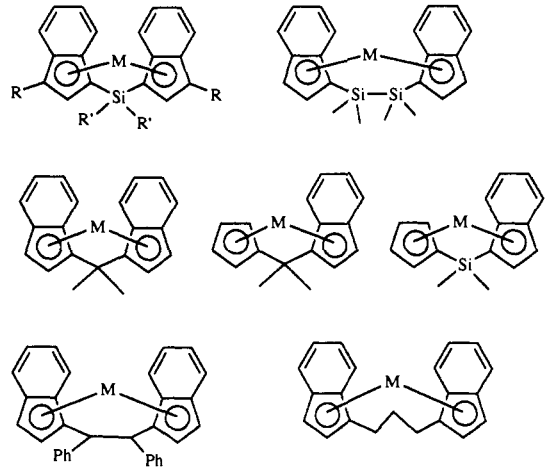
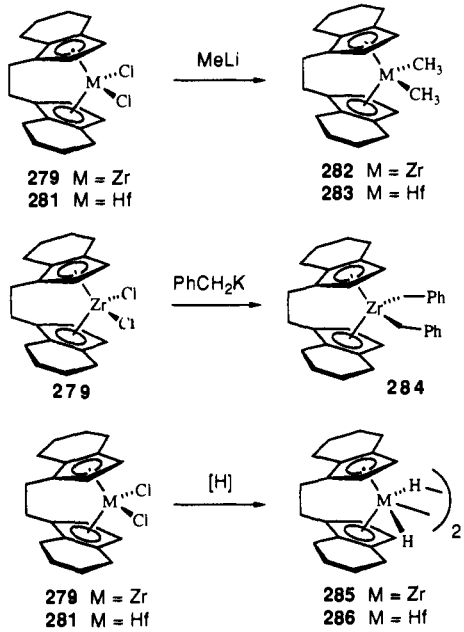


Figure 7. *ansa*-Metallocenes with M = $TiCl_2$ or $ZrCl_2$.[74,76]

Scheme 66[73,90,91]

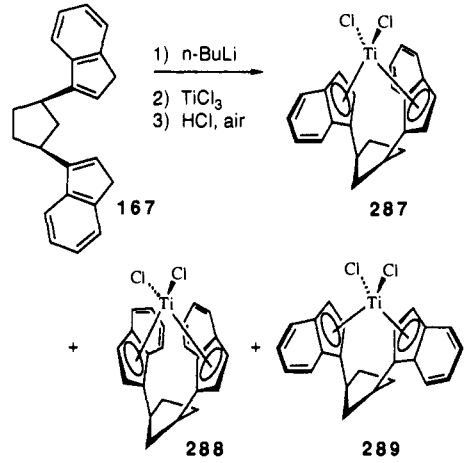


symmetrical bis(indenes) are metalated, a mixture of meso and racemic C_2-symmetrical metallocenes are formed. In the instances where the two bridged ligands are not equivalent, a racemic mixture of C_1-symmetrical metallocenes was produced (Figure 7).[74,76]

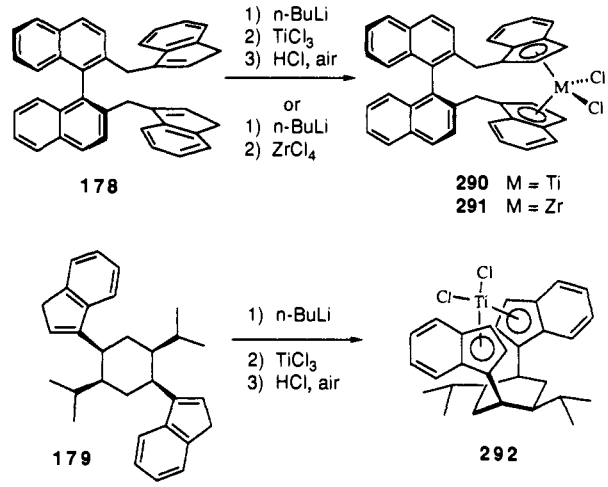
Metalation of the dianion of cyclopentane-1,3-diyl-bridged *ansa*-bis(1-indene) **167** with $TiCl_3$ produced a separable mixture of *ansa*-metallocene consisting of two C_s-symmetrical isomers **288** and **289** and one C_1-symmetrical isomer **287** (Scheme 67). The C_1-symmetrical isomer contains C_2-symmetry local to the metal when the unsymmetrical bridging group is disregarded.

When the *ansa*-bis(1-indenes) **178** and **179** bridged by the chiral 1,1′-binaphthyl-2,2′-dimethylene[11] or the 2,5-diisopropylcyclohexane-1,4-diyl[38] groups are metalated, a mixture of two C_2-symmetrical and one C_1-symmetrical metallocenes can in principle be formed since the two faces of each indenyl ligand are now diastereotopic rather than enantiotopic. Given energetic differences in the formation of these diastereomeric complexes, preferential formation of a single isomer is possible. When *ansa*-bis(1-indene) **178** was deprotonated and metalated with either $TiCl_3$ or $ZrCl_4$, only a single isomer of each C_2-symmetrical metallocene **290**

Scheme 67[67]



Scheme 68[11,38]

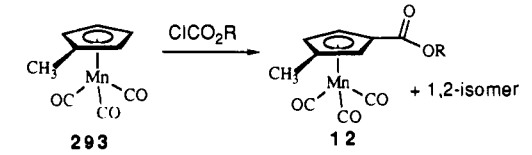


and **291** was formed and isolated (Scheme 68).[11] When the chiral *ansa*-bis(indenyl) ligand **179** was metalated with $TiCl_3$ a single C_2-symmetrical isomer of titanocene dichloride **292** was formed.[38] Some degree of evidently polymeric material was also formed in these metalations, which along with the modest isolated yields of the metallocene dichlorides indicated that the initial metalation of the first indenyl ligand was not highly stereoselective. For example in the metalation of the binaphthyl-bridged ligand **178**, of the two initially formed diastereomeric mono(indenyl)metal complexes, one had a suitable configuration which allowed intramolecular metalation of the second indenyl ligand to form the isolated products **290** and **291** containing either titanium or zirconium, the second intermediate diastereomer could not readily metalate intramolecularly and instead formed unisolable oligomeric material.

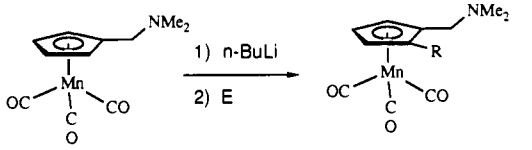
D. Derivatization of Achiral Cyclopentadienylmetals

Two general routes have been used for the conversion of achiral cyclopentadienylmetal complexes into chiral complexes which contain either chiral or prochiral cyclopentadienyl ligands. The first route developed was the introduction of a second substituent on the cyclopentadienyl ligand. The first chiral cyclopentadienyl metal complex was in fact made in this manner by the Friedel–Crafts acylation of ferrocene to form the racemic chiral ferrocene complex **11**.[12] Another early

Scheme 69[92]



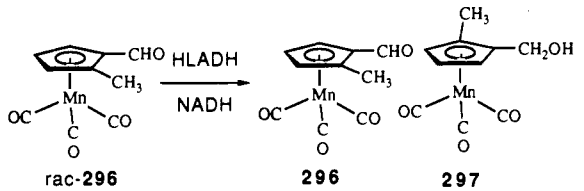
293 12



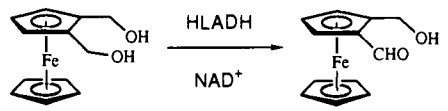
294

295a R = D, E = D_2O
295b R = CHO, E = DMF
295c R = PPh_2, E = $ClPPh_2$

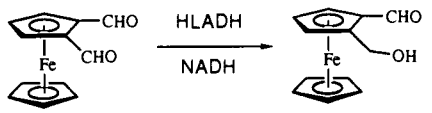
Scheme 70[93,40]



rac-296 296 297



298 299



300 299

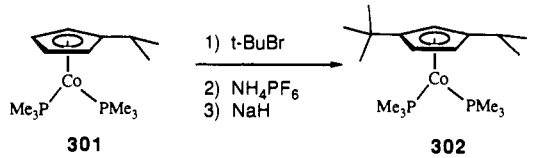
example was the Friedel–Crafts acylation of (methylcyclopentadienyl)manganese tricarbonyl **293** to form racemic disubstituted manganese complex **12** (Scheme 69).[14] A related method involves the deprotonation of cyclopentadienylmetal complex **294** followed by electrophilic substitution of the cyclopentadienyl moiety to give chiral disubstituted cyclopentadienylmetal complexes **295**.[92]

The racemic manganese complex **296** can be kinetically resolved into a pure enantiomer by an enzyme-mediated asymmetric reduction which preferentially reduces one enantiomer of **296** into the enantiomerically enriched alcohol **297** (Scheme 70).[93] In a related method the achiral dimethanol substituted ferrocene **298** was asymmetrically oxidized using enzymatic methods to give the chiral, enantiomerically enriched ferrocene **299**.[94] The enantiomer of ferrocene **299** was also asymmetrically prepared by enzyme-mediated asymmetric reduction of achiral dialdehyde **300**.[94]

Werner has converted achiral cyclopentadienylcobalt complexes into chiral ones by direct alkylation of the cyclopentadienyl ring followed by deprotonation.[95] In this way he has converted cyclopentadienylcobalt **301** into racemic mixtures of chiral complexes **302** (Scheme 71).

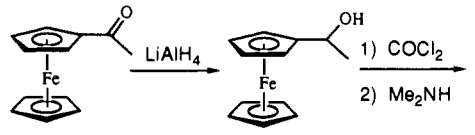
The second general route to convert achiral cyclopentadienylmetal complexes into chiral ones is to convert an achiral substituent on the cyclopentadienyl ligand into a chiral group. An example of this method is the reduction of achiral acetylferrocene **303** into the

Scheme 71[95]

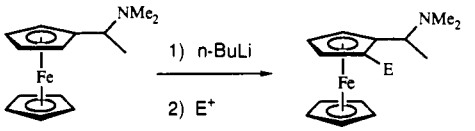


301 302

Scheme 72[96–99]

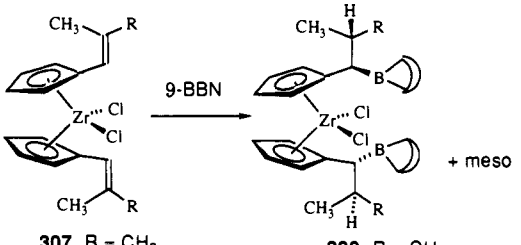


303 304



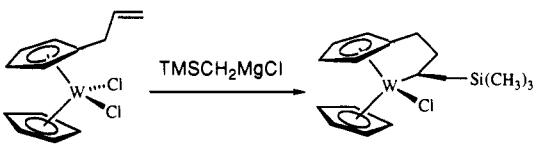
305 306

Scheme 73[100,101]



307 R = CH_3
308 R = Ph

309 R = CH_3
310 R = Ph



311 312

chiral (1-hydroxyethyl)ferrocene complex **304** (Scheme 72).[96] Racemic ferrocene **304** is the starting point for the synthesis of a class of chiral ferrocenylphosphines which are widely used as chiral ligands for asymmetric reactions.[97] Access to this and other classes of chiral ferrocenyl complexes is available through the conversion of ferrocene **304** into the amino-substituted ferrocene **305** which can be resolved.[98] Directed deprotonation and alkylation of amino-substituted ferrocene **305** has enabled the preparation of chiral ferrocenyl complexes **306**,[99] including chiral phosphines.[97] These chiral ferrocenyl complexes have been very successfully used in asymmetric reactions, but since their chemistry does not directly involve the transition metal, using the ferrocenyl moiety only as a scaffolding for their chiral ligands, these reactions fall outside of this review and are not covered here.

Erker has reported the conversion of the achiral zirconocene dichlorides **307** and **308** into metallocenes **309** and **310** by hydroboration with 9-BBN.[100] In each case the achiral alkene appended to the cyclopentadienyl ligands was converted into a chiral substituent. No stereoselectivity was observed; in each case a 1:1 mixture of meso- and *dl*-isomers of **309** and **310** were obtained (Scheme 73). In a related example, achiral allyl-

substituted tungstenocene dichloride **311** was converted to the chiral complex **312** upon addition of (trimethylsilyl)methyl anion.[101]

V. Applications of Chiral Cyclopentadienylmetal Complexes

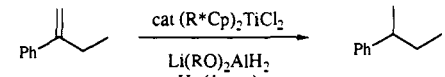
In the past few years, an increasing number of asymmetric reactions involving chiral cyclopentadienylmetal complexes have already appeared, but a number of potentially asymmetric reactions having precedence in known reactions involving achiral cyclopentadienylmetal complexes remain to be explored in this promising area of asymmetric induction. Reactions mediated by chiral cyclopentadienylmetal complexes are divided into three main areas: (1) catalytic enantioselective reactions including hydrogenations, ketone reductions, aldol reactions, epoxidations, and alkene isomerizations; (2) stoichiometric diastereoselective reactions including conversion of a coordinated nonstereogenic metal stereoselectively into a stereogenic center, cobalt-mediated cyclizations, and zirconocene-mediated aminations; and (3) catalytic polymerization of alkenes into stereoregular polymers. It is in the catalytic asymmetric applications that the largest potential for the application of chiral cyclopentadienylmetal complexes lies. These catalytic reactions combine the often unique reactivity of transition metal complexes with an ability to multiplicatively propagate their asymmetry with associated savings in material, costs, and time needed in synthetic applications.

A. Catalytic Enantioselective Reactions

1. Hydrogenation

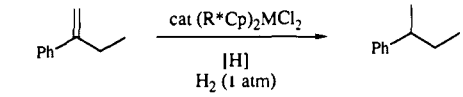
The enantioselective hydrogenation of simple, unfunctionalized alkenes was the first application of chiral cyclopentadienylmetal complexes in catalytic reactions and remains the most widely studied enantioselective transformation. Achiral bis(cyclopentadienyl)titanium dichloride was known to form upon its reduction an active catalyst for the hydrogenation of alkenes.[102] The scope of alkenes which can successfully serve as substrates in this reaction is limited to relatively unfunctionalized ones, excluding the important amine and carboxylic acid containing alkenes. The first example of catalytic enantioselective hydrogenation of alkenes using bis(cyclopentadienyl)titanium dichloride complexes was Kagan's use of chiral, enantiomerically pure menthyl- or neomenthyl-substituted cyclopentadienyl ligands in the hydrogenation of 2-phenyl-1-butene.[103] In this reduction, the bis(cyclopentadienyl)-titanium dichloride catalyst precursor was reduced with various aluminum hydrides and the substrate 2-phenyl-1-butene hydrogenated under 1 atm of hydrogen between −5 and 35 °C. Several different combinations of cyclopentadienyl ligands were applied, including titanium dichloride complexes containing bis(neomenthylcyclopentadienyl) **193**, bis(menthylcyclopentadienyl) **184**, or one menthyl- or neomenthylcyclopentadienyl ligand with one cyclopentadienyl ligand **186** or **195**. The optimal reaction used bis(menthylcyclopentadienyl)titanium complex **185** which gave 75 turnovers in the reduction, producing (*S*)-2-phenylbutane in a modest 28% ee (Table 2).

Table 2. Kagan's Asymmetric Hydrogenation of 2-Phenyl-1-butene[103]



$(R^*Cp)_2TiCl_2$	T (°C)	% ee
$(MCp)_2TiCl_2$ **185**	5	28
$(MCp)_2TiCl_2$ **185**	20	15
$(NMCp)_2TiCl_2$ **193**	20	7
(MCp)CpTiCl$_2$ **186**	5	23
(MCp)CpTiCl$_2$ **186**	20	8
(NMCp)CpTiCl$_2$ **195**	5	15
(NMCp)CpTiCl$_2$ **195**	20	10

Table 3. Asymmetric Hydrogenation of 2-Phenyl-1-butene[8,26,36,40]



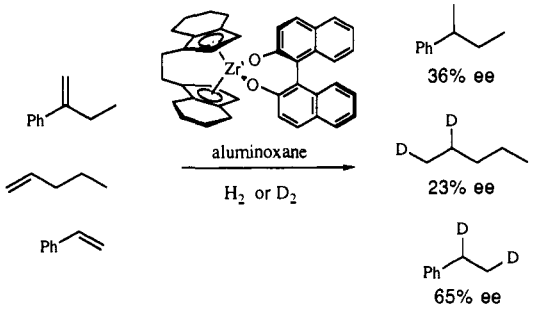
$(R^*Cp)_2TiCl_2$	T (°C)	% ee
$(PhMenCp)_2TiCl_2$ **196**	23	33
$(2\text{-Me-1-butylCp})_2ZrCl_2$ **197**	23	<2
$(2\text{-Ph-1-butylCp})_2ZrCl_2$ **199**	23	<2
$(2\text{-Me-1-butylCp})_2HfCl_2$ **198**	23	<2
$(2\text{-Ph-1-butylCp})_2HfCl_2$ **200**	23	<2
$(CamCp)_2TiCl_2$ **216**	−20	34
$(PinCp)_2TiCl_2$ **235**	−20	7
$(DiPh\text{-}BCOCp)_2TiCl_2$ **246**	25	68
$(DiPh\text{-}BCOCp)_2TiCl_2$ **246**	−75	95

Several other metallocene dichloride precatalysts containing monosubstituted chiral cyclopentadienyl ligands have been applied in the asymmetric hydrogenation of 2-phenyl-1-butene with enantioselectivities no higher than that obtained with catalysts employing the menthylcyclopentadienyl ligand. These precatalysts include titanocene dichloride **296** containing the (phenylmenthyl)cyclopentadienyl ligand[8] and the bis(cyclopentadienyl)zirconium dichlorides and -hafnium dichlorides **197–200** containing ligands having a chiral auxiliary separated from the cyclopentadienyl moiety by a methylene group (Table 3).[26] Although the catalytic activity of these latter complexes was quite high, the virtual lack of asymmetric induction is understandable in terms of conformational mobility and remoteness of the stereocenter in the ligands. These metallocene dichloride precatalysts were all activated by initial treatment with alkyllithium reagents.

The application of titanocene dichloride catalysts containing annulated chiral cyclopentadienyl ligands fared only marginally better than the catalysts containing the simple menthylcyclopentadienyl ligand in inducing asymmetry in the hydrogenation of 2-phenyl-1-butene (Table 3). The titanocene dichloride **235** containing a nopol-derived chiral annulated cyclopentadienyl ligand gave significantly lower enantioselectivity while metallocene dichloride **216** containing a camphor-derived ligand gave slightly higher enantioselectivity in this hydrogenation. Of all the chiral cyclopentadienylmetal complexes synthesized from enantiomerically pure natural products, the use of the camphor-derived ligand did give the highest enantioselectivity in the hydrogenation of 2-phenyl-1-butene.

The most selective chiral metallocene catalyst for the hydrogenation of 2-phenyl-1-butene published to

Scheme 74[104]



date is titanocene dichloride **246** containing an unnaturally derived C_2-symmetrical biscyclooctane-fused cyclopentadienyl ligand.[40] After initial activation of the titanocene dichloride with *n*-BuLi at 0 °C, hydrogenation at −78 °C gave 95% enantiomeric excess with 25 turnovers. Although the catalytic activity of complex **246** at 25 °C was much higher (100 turnovers), the enantiomeric excess of 2-phenylbutane was lowered to 68%. 2-Ethyl-1-hexene could also be catalytically hydrogenated using **246** at 25 °C to give 41% ee of 3-methylheptane.

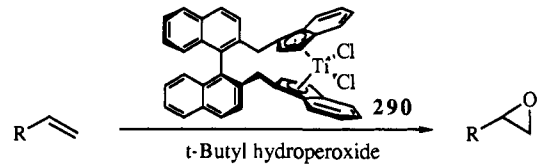
Waymouth and Pino have reported the asymmetric hydrogenation of 2-phenyl-1-butene in 36% ee using the resolved binaphtoate complex of Brintzinger's ethylene-bridged *ansa*-bis(tetrahydroindenyl)zirconium dichloride **279** (Scheme 74)[104] Buchwald reported a 23% ee in this asymmetric hydrogenation using a dihydride derived from the same catalyst **279**.[73] Pino and Waymouth also examined the enantioselectivity in the deuteration of 1-pentene and styrene with derivatives of **279** which gave 23 and 65% ee respectively. Polymerization was a competing reaction in the deuteration of 1-pentene. By isolating hydrooligomerized products they determined that "the enantioface which is prevailing hydrogenated for 1-pentene, styrene, and 2-phenyl-1-butene with these catalysts is the opposite of that which is prevailing polymerized[105] for 1-pentene and propene".[104] This remarkable finding has significance for the mechanisms for asymmetric hydrogenation or stereoregular polymerization of alkenes.

The cyclopentadienylrhodium complexes **209–211** containing a (menthyl- or neomenthyl)cyclopentadienyl ligand also function as hydrogenation catalysts in the presence of triethylamine.[82] 2-Phenyl-1-butene was readily hydrogenated in the presence of these catalysts and 1 atm of hydrogen, but the resulting product was only marginally optically active (<1%). Functionalized alkenes could be hydrogenated using more forcing conditions (5 atm H_2, 50 °C), but in these cases products exhibiting less than 5% optical purity were obtained.

2. Epoxidation

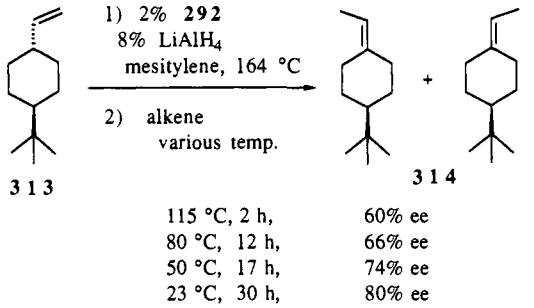
The epoxidation of alkenes in the presence of achiral, polymer-bound bis(cyclopentadienyl)titanium dichloride has been reported to proceed catalytically which is in contrast to the inactivity of free titanocene dichloride.[106] Colletti and Halterman have found that the C_2-symmetrical bis(1-indenyl)titanium dichloride **209** can function as a catalyst for the asymmetric epoxidation of unfunctionalized alkenes in the presence of t-butyl hydroperoxide (Table 4).[107] Both the catalytic activity (40–60 turnovers) and the enantioselectivity

Table 4. Asymmetric Catalytic Epoxidation of Unfunctionalized Alkenes[107]



alkene	(°C) T	no. of turnovers	enantiomeric excess (%)
	80	40	22
	60	14	20
	40	40	18
	23	16	18
	80	60	12
	60	30	7
	80	61	6
	60	44	4
	80	31	3
	60	12	2
	40	10	2

Scheme 75[38]



(12–22% ee) are moderate in this sole example of using chiral cyclopentadienylmetal catalysts for asymmetric epoxidation.

3. Alkene Isomerization

The catalytic isomerization of terminal to internal alkenes using catalytic amounts of reduced bis(cyclopentadienyl)titanium complexes has been known for several years. Initial treatment of titanocene dichloride with $LiAlH_4$ at elevated temperatures has been postulated to effect the partial reduction to give an unidentified titanium species which can insert into an allylic carbon–hydrogen bond to give an intermediate π-allyltitanium hydride species which can undergo reductive elimination to give the free isomerized alkene.[108] Chen and Halterman have recently found that the *meso*-vinylcyclohexane **313** can be enantioselectively isomerized into the chiral ethylidenecyclohexane **314** in the presence of reduced *ansa*-bis(indenyl)-titanium dichloride **292** (Scheme 75). In this case the titanium dichloride **292** was treated at high temperature with $LiAlH_4$, followed by introduction of the alkene at lower temperatures. The catalyst gave 50 turnovers with enantioselectivity of the resulting alkene **314** near 80% ee at lower reaction temperatures.[38]

4. Ketone Reduction

The use of titanocene dichloride to catalyze the reduction of ketones in the presence of alkylmagnesium bromide reagents possessing a β-hydride was reported over 10 years ago.[109] Attempts to carry out this reduction asymmetrically using chiral bis(cyclo-

Scheme 76[87]

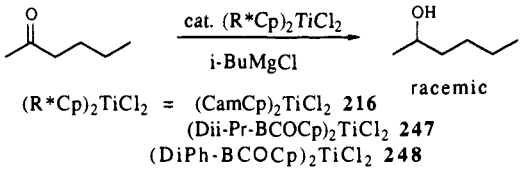
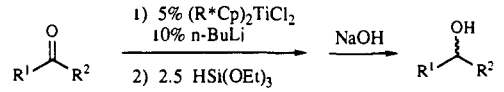


Table 5. Hydrosilyation of Ketones



ketone	(R*Cp)TiCl$_2$	% ee
2-octanone	Bis(indenyl)TiCl$_2$ **292**	1
2-octanone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **247**	6
2-octanone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **248**	1
acetophenone	Bis(indenyl)TiCl$_2$ **292**	7
acetophenone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **247**	12
acetophenone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **248**	5
2-acetonaphthone	Bis(indenyl)TiCl$_2$ **292**	20
2-acetonaphthone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **247**	13
2-acetonaphthone	(Dii-Pr-BCOCp)$_2$TiCl$_2$ **248**	6

pentadienyl)titanium dichloride catalysts have failed. Although the reaction of 2-hexanone with isobutylmagnesium bromide in the presence of catalytic amounts of the chiral titanocene **216** containing a chiral cyclopentadienyl ligand derived from camphor did give the desired secondary alcohol, the product was racemic (Scheme 76).[87] Similar attempts using titanocene dichlorides **247** and **248** containing the C_2-symmetrical bicyclooctane-fused cyclopentadienes also gave products of low enantiomeric purity. In these cases, the reaction without the chiral metallocene "catalyst" also gave significant amounts of reduction to secondary alcohols along with the expected tertiary alcohol addition products.[67]

Buchwald recently reported the use of titanocene dichloride as a catalyst for the hydrosilylation of ketones under very mild conditions which after hydrolysis of the initially formed silyl ether forms a secondary alcohol.[110] Chen and Halterman have examined this reduction using a number of different chiral bis(cyclopentadienyl)- and *ansa*-bis(indenyl)titanium dichlorides **247**, **248**, and **292**. After activation of the metallocene dichlorides according to Buchwald's procedure, a number of prochiral ketones can be reduced at room temperature by triethoxysilane. As seen in Table 5, the enantioselectivities of the reduction catalyzed by complexes **247–292** were low.[67]

5. Aldol Reactions

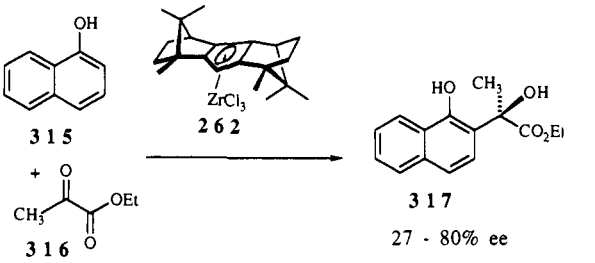
Erker has recently published the use of the (DibornaCp)$ZrCl_3$ complex **262** as effectively catalyzing the aldol-like carbon–carbon coupling reaction of 1-naphthol (**315**) with ethyl pyruvate (**316**) in the presence of 1% of **262** to give a good yield of the chiral ethyl acetate **317** in 27–80% ee enantiomeric excess (Scheme 77).[47]

B. Stoichiometric Diastereoselective Reactions

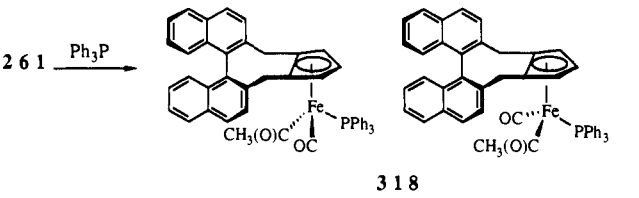
1. Creation of Stereogenic Metal

The earliest asymmetric reaction utilizing chiral cyclopentadienylmetal complexes was the diastereoselective conversion of a nonstereogenic metal atom coordinated to a chiral cyclopentadienyl ligand. In general these reactions gave low stereoselectivities and were used mainly as stereochemical markers in mechanistic studies (see section II).

Scheme 77[46]



Scheme 78[111]



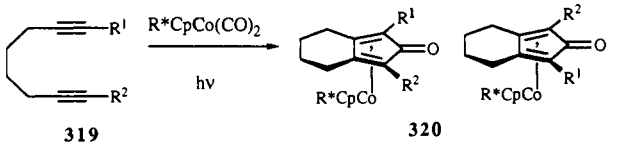
Colletti and Halterman have examined the influence of the BpDMCp ligand on the stereochemistry at iron in acetyl iron **318** formation from methyliron **261** in the presence of triphenylphosphine[111] (Scheme 78). The acetyl complex **318** was formed kinetically under thermal conditions as a nearly 50:50 mixture of diastereomers. When these diastereomeric acetyliron complexes were equilibrated, their ratio changed to 70:30. Alternative formation of the acetyliron complex **318** under oxidative conditions gave rise to a 60:40 mixture of diastereomers.

2. Cobalt-Mediated Reactions

On the basis of the known conversion of diynes in the presence of achiral cyclopentadienylcobalt dicarbonyl to (cyclopentadienyl)(cyclopentadienone)cobalt complexes,[112] Halterman and Vollhardt examined the diastereoselectivity of this reaction using unsymmetrical diynes and chiral cyclopentadienylcobalt dicarbonyl complexes. When the chiral cyclopentadienylcobalt dicarbonyl **203** containing the phenylmenthylcyclopentadienyl ligand was photolyzed in the presence of substituted 1,6-diynes **319**, diastereomeric cyclopentadienone complexes **320** were formed in up to 67:33 selectivity (Table 6).[8] When the analogous reactions were performed using cyclopentadienylcobalt dicarbonyl **255** containing the dimethyl-substituted bicyclooctane-fused cyclopentadienyl ligand, higher diastereoselectivities up to 74:26 were observed.[87]

Prochiral α,δ,ω-enediyne **321** was cyclized in the presence of the chiral cyclopentadienylcobalt dicarbonyl **203** containing the phenylmenthylcyclopentadiene ligand to yield a mixture of 58:42 diastereomeric [2 + 2 + 2] trimerization products **322**.[87] Only two out of the possible four diastereomeric products were observed in this reaction. It was established that the tertiary hydrogen atom was located exo to the cobalt fragment (Scheme 79). Removal of the chiral metal fragment from complex **322** would result in enantiomeric tricyclic organic products of 16% ee.

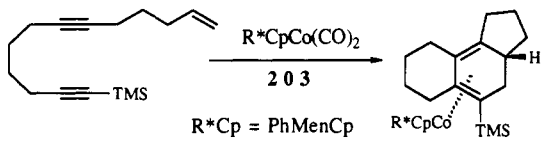
Table 6. Diastereoselective Cyclopentadienylcobalt–Cyclopentadienone Complex Formation[112,87]



319 320

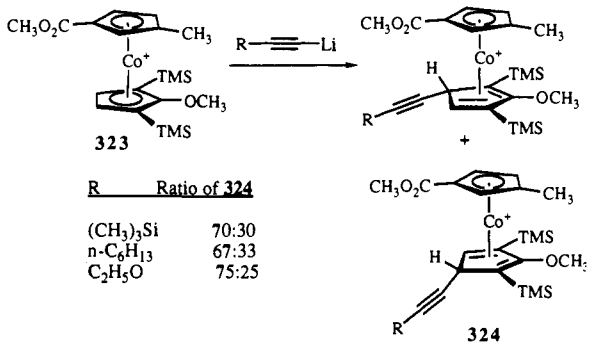
diyne 319			
R^1	R^2	R*CpCo(CO)$_2$	diastereomeric ratio of **320**
TMS	H	PhMenCp **203**	52:48
TMS	CH_3	PhMenCp **203**	67:33
TMS	C_2H_5	PhMenCp **203**	60:40
CH_3	H	PhMenCp **203**	61:39
C_2H_5	H	PhMenCp **203**	56:44
TMS	C_2H_5	TartCp **245**	50:50
TMS	H	DiMe-BCOCp **255**	74:26

Scheme 79[8,87]



321 322

Scheme 80[4]



323

R	Ratio of 324
$(CH_3)_3Si$	70:30
n-C_6H_{13}	67:33
C_2H_5O	75:25

324

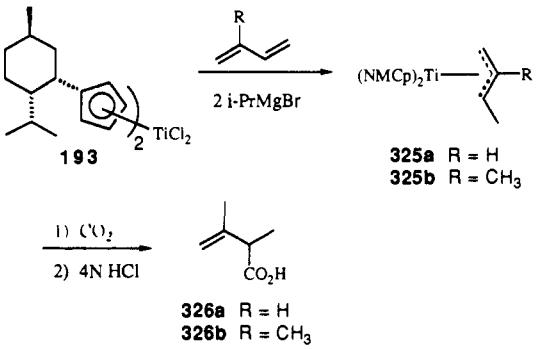
A final diastereoselective reaction involving chiral cyclopentadienylcobalt complexes was the stereoselective addition of acetylides to the bottom ring in the chiral cobalticinium complex **323** to form **324** (Scheme 80).[4] The origin of the stereoselectivity in this reaction was postulated to be the first case of interannular, possibly electronically transmitted asymmetric induction in an organometallic compound.

3. Allyltitanium Reactions

Allylmetal reagents have been successfully used in a number of synthetically interesting transformations which has led to the development of allyl complexes of chiral titanocenes. Sato has reported that the π-allyltitanocene complex **325** containing chiral neomenthylcyclopentadienyl ligands reacts with carbon dioxide to form 2-methyl-3-butenoic acids **326a** and **326b** which exhibit 19 and 11% optical purities, respectively (Scheme 81).[113] The allyltitanium complex **325** was formed from the reaction of 1,3-butadiene with reduced titanocene dichlorides **193**.

Collins has reported an enantioselective allylation of aldehydes using the chiral allyltitanium reagent **327**.[114] Addition of 1 equiv of *n*-PrMgBr to resolved ethylene-bridged *ansa*-bis(tetrahydro-1-indenyl)titanium dichloride **277** followed by addition of 1 equiv of either allyl- or crotylmagnesium bromide gave the desired allyltitanium complex **327** (R = H, CH_3) usually as an unisolated intermediate. Treatment of allyltitanium **327** with various aldehydes followed by acid workup gave good yields of homoallylic alcohols **328** and **329** (Table 7). The enantioselectivity of the allyl addition reaction (**327** R = H) to give the homoallylic alcohols **328** was as high as 40% when 2-phenylpropionaldehyde was used. In the crotyl-addition reactions (**327**, R = CH_3) the diastereoselectivity ranged from 2.5:1 up to 40:1 favoring the anti-diastereomer **329a** over the syn-isomer **329b**. The enantioselectivities in these latter addition reactions was as high as 55% ee.

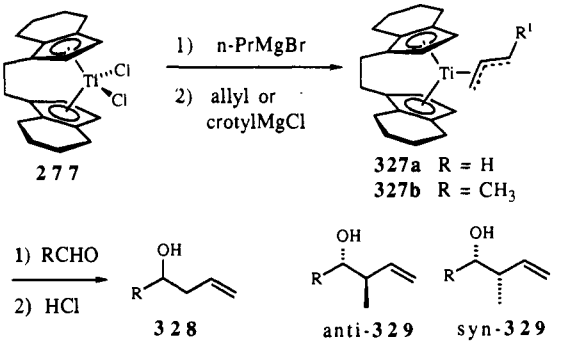
Scheme 81[113]



193 325a R = H, 325b R = CH_3

326a R = H
326b R = CH_3

Table 7. Enantioselective Allylation of Aldehydes



277 327a R = H, 327b R = CH_3

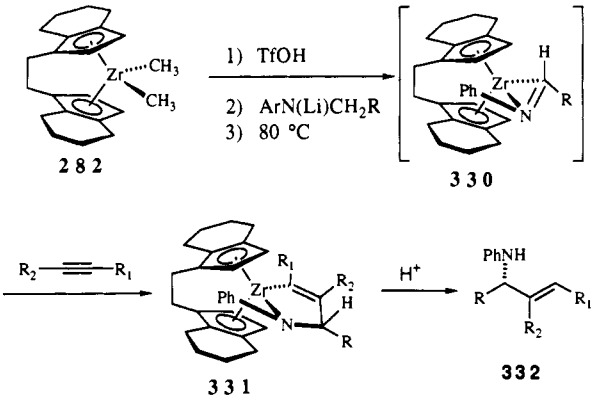
328 anti-329 syn-329

aldehyde	reagent	anti:syn (329 only)	% ee
$PhCH_2CHO$	**235b**	2.5:1	10
c-$C_6H_{11}CHO$	**235b**	8.0:1	34
t-BuCHO	**235b**	36:1	55
PhCHO	**235b**	40:1	22
$PhCH_2CHO$	**235a**		42
c-$C_6H_{11}CHO$	**235a**		20
t-BuCHO	**235a**		5
PhCHO	**235a**		5

4. Allylic Amines

Buchwald has reported the development of a stoichiometric method for the preparation of allylic amines in high enantioselectivity from a chiral zirconocene imine complex and an alkyne.[115] As shown in Scheme 82, enantiomerically pure *ansa*-zirconocene dimethyl complex **282** (derived from Brintzinger's ethylene-bridged *ansa*-bis(tetrahydro-1-indenyl)zirconium dichloride **279**) was converted into virtually diastereomerically pure imine complex **330** by the method shown. This unisolated intermediate further reacted with various alkynes to give stable metallapyrroline complex **331**, again with virtually complete diastereoselectivity. Treatment of **331** with acid liberated the chiral allylic

Scheme 82[115]



amines **332** in good yield in >95% ee for most examples. When unsymmetrical alkynes were used one regioisomeric product was favored.

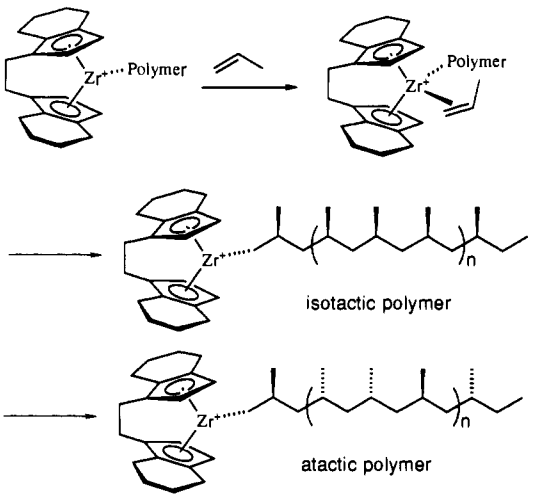
C. Catalytic Stereoregular Polymerizations

The most intensively studied reaction which utilizes chiral cyclopentadienylmetal complexes has been the stereoregular polymerization of propene to form highly isotactic poly(propylene). The application of group 4 metallocenes as Ziegler–Natta catalysts for the polymerization of alkenes has been known since 1957.[116] When unsubstituted, achiral bis(cyclopentadienyl)titanium, -zirconium, and -hafnium catalysts were used with various catalyst activators such as MAO [methylaluminoxane, $(Al(CH_3)O)_n$], atactic poly(propylene) was produced.[117] In 1984 Ewen published the first use of a chiral metallocene as a catalyst in the polymerization of propene.[118] Using a mixture of meso- and *dl*-isomers of Brintzinger's ethylene-bridged *ansa*-bis(1-indenyl)-titanium dichloride **276**, Ewen reported that a mixture of 63% isotactic and 37% atactic poly(propylene) was produced. This report was quickly followed by Kaminsky and Brintzinger's use of ethylene-bridged bis-(tetrahydro-1-indenyl)zirconium dichloride **279** to give highly isotactic poly(propylene) with high molecular weight and narrow molecular weight range.[119] Since these reports appeared, several groups have intensively examined this polymerization reaction, resulting in several review articles.[76b,120,64] Of particular interest has been the development of cationlike homogeneous zirconocene catalysts which do not require cocatalysts for polymerization.[121]

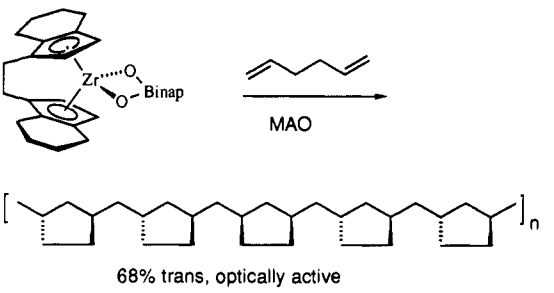
The interesting point in these polymerization studies for more synthetically inclined chemists is that the high degree of stereoregularity in the polymerization is due to a high degree of enantiofacial recognition in introducing propene into the growing polymer chain. The postulated mechanism shown in Scheme 83 for the incorporation of propene requires repeated insertion of propene both with a high degree of enantiofacial selectivity and high regioselectivity for head to tail orientation leads to isotactic poly(propylene). If the incorporation of propene is not stereoselective, atactic polymer is formed. In these catalytic polymerizations, it is not necessary to have an enantiomerically enriched catalyst since the polymer produced is essentially achiral due to its meso symmetry.

Waymouth has recently reported the polymerization of 1,5-hexadiene which can give four different stereoregular polymers, meso-diisotactic, racemo-diisotactic, meso-disyndiotactic, and racemo-disyndiotactic. Of these types, the racemo-diisotactic polymer contains no mirror planes of symmetry and is chiral. When 1,5-hexadiene was polymerized with an enantiomerically pure ethylene-bridged *ansa*-bis(tetrahydroindenyl)zirconium catalyst in the presence of MAO, an optically active polymer was formed. (Scheme 84).[122]

Scheme 83



Scheme 84[122]



VI. Summary

During the past approximately 15 years, chiral cyclopentadienylmetal complexes have been prepared from three general types of cyclopentadienyl ligands: ligands containing diastereotopic faces which may give diastereomeric complexes upon metalation, ligands containing enantiotopic faces which give rise to racemic monocyclopentadienylmetal complexes, and ligands containing equivalent, homotopic faces which inherently produce a single stereoisomeric complex upon metalation. Several good examples have been developed for each type of cyclopentadienylmetal complex. Several asymmetric applications of chiral cyclopentadienylmetal complexes as catalysts for asymmetric hydrogenation, alkene epoxidation, alkene isomerization, ketone reduction, and stereoselective alkene polymerization and as stoichiometric reagents for stereoselective cobalt-mediated reactions, allyltitanium addition reactions with aldehydes, and the highly selective formation of allylic amines are shown. Given the increasing rate at which new applications of chiral cyclopentadienylmetal complexes are now appearing, we can surely anticipate future significant developments in this still young area of stereoselective chemistry.

Note Added in Proof

Several recent papers describing new chiral cyclopentadienylmetal complexes and their applications have appeared: (a) Rheingold, A. L.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Organometallics* **1992**, *11*, 1869. (b) Conticello, V. P.; Brard, L.; Giardello, M. A.; Tsuji, Y.; Stern, C. L.; Sabat, M.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 2761. (c) Gagné, M. R.; Brard, L.; Contecello, V. P.; Giardello, M. A.; Stern, C. L.; Marks, T. J. *Organometallics* **1992**, *11*, 2003. (d) Lee, I.-M.; Gauthier, W. J.; Ball, J. M.; Iyengar, B.; Collins, S. *Organometallics* **1992**, *11*, 2115.

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VII. References

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