Enantiomerically Pure Planar Chiral Organometallic Complexes via Facially Selective π-Complexation

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Robert Paley was born in the Bronx, NY, in 1960. He received his B.Sc. degree from McGill University in 1981 and his Ph.D. degree from the University of Michigan in 1986 under the supervision of Professor Joseph P. Marino. After postdoctoral work with Professor Anthony G. M. Barrett at Northwestern University that included a temporary faculty position as a Lecturer, he became a Visiting Assistant Professor at Swarthmore College and later at the University of New Hampshire. In 1991 Bob secured a tenure track faculty position at Swarthmore College and was promoted to Associate Professor and Chemistry Department Chair in 1997. In 2000 he received a Henry Dreyfus Teacher–Scholar Award. His research interests within synthetic organic chemistry are at the interface of organometallics and asymmetric synthesis.

1. Introduction

The development of methodology to facilitate the control of absolute stereochemistry has long been among the prime goals of modern synthetic organic chemistry. The control of central chirality, particularly with regard to chiral carbon centers, has developed into a fine art that allows the chemist to select from a multitude of reliable procedures. As this field has advanced from the use of stoichiometric methods to catalytic methods, exquisite control over the formation of stereocenters is now commonplace. In contrast, the ability to prepare enantiomerically pure planar chiral material without relying on resolution is just emerging as a contemporary synthetic goal, and it has now become increasingly common to encounter examples of planar chiral organometallics in the literature. Typically these have been utilized to control central chirality in acyclic and cyclic organic systems, either through subsequent diastereoselective transformations of the organic ligand or through the use of these complexes as chiral catalysts for asymmetric transition-metal-mediated processes. As a result, interest in the preparation of enantiomerically pure planar chiral organometallics has grown significantly, and a number of approaches are now available. One of these strategies—diastereoselective π-complexation—has been often utilized, yet a single comprehensive review uniting all enantiomerically pure organometallic planar chiral molecules prepared by this methodology has not previously appeared in the literature. While reviews focusing on the synthesis and use of some of the individual classes of complexes do exist, these have typically not placed an emphasis on a particular strategy or have not focused exclusively upon the synthesis of chiral, nonracemic materials.[1−7]

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1.1. Organization of Review

With the common theme of diastereotopic π-complexation in mind, this review has been organized according to the tactics employed for the differentiation of the diastereotopic faces of the unsaturated organic ligand by the metal fragment. Three such approaches have been identified: (1) diastereoselective complexation induced by substrate chirality, (2) diastereoselective complexation induced by a chiral auxiliary, and (3) diastereoselective complexation by displacing preexisting chirality. Within each strategy, the featured reactions and schemes are arranged in terms of increasing hapticity. While the focus will be on the asymmetric event itself—the π-complexation of the metal fragment to the pro-ligand—subsequent transformations of these products will be mentioned in order to provide context. Complexations that proceed with only marginal diastereoselectivity have been included for the sake of comparison. Synthetic methods, however meritorious, that involve resolution of racemic mixtures (by crystallization, separation via chiral HPLC, or enzymatic methods) or that utilize diastereoselective reactions of prochiral complexes (for example, diastereoselective deprotonation) will not be included here. Finally, the many transient metal–ligand complexes formed during catalytic processes will also be excluded; this review will concentrate on the enantiopure products of stoichiometric transformations.

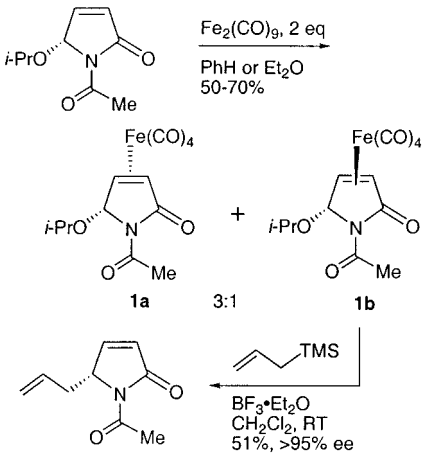
2. Diastereoselective Complexation Induced by Proximal Chirality

Chirality proximal to the unsaturated site on the organic ligand is typically used to direct the approach of the metal fragment to that ligand as the π-complex is formed. In this section the focus is on substrate-based chirality, as distinguished from chiral auxiliaries, which play this role as well but are of course only temporarily attached to the substrate pro-ligand. Proximal chirality may be employed in two contrasting ways: first, by providing steric hindrance to direct the metal fragment *away* from the ligand face or, second, by providing a heteroatomic site for precoordination of the metal fragment to direct it *toward* the adjacent ligand face.

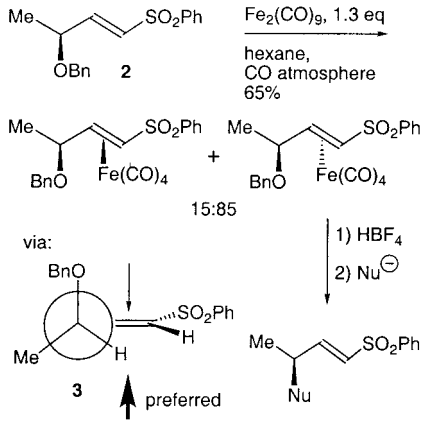
2.1. η^2-Iron Complexes

In the first reported example of an isolable enantiopure η^2-olefin complex prepared by direct complexation, Hiemstra and Speckamp[8] described the complexation of a chiral pyrrolinone. The selectivity of formation of the corresponding η^2-alkene iron tetracarbonyl complexes, **1a** and **1b**, was modestly diastereoselective (3:1), and the major isomer possessed a cis relationship between the $Fe(CO)_4$ fragment and the 5-isopropoxy group (Scheme 1). That the minor product only formed during extended reaction times suggested that the major "antisteric" complexation product could slowly, if incompletely, isomerize to the thermodynamically more stable complex. Thus, the apparent heteroatom-directed delivery to the more hindered alkene face (affording the major isomer) is likely to be a kinetic process. This is in accord with the suggestion put forth by Jackson and co-workers

Scheme 1



Scheme 2



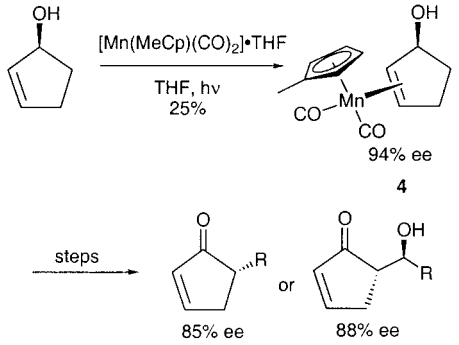
in their earlier exploration of the $Cr(CO)_3$ complexes of racemic indanes.[9] The minor trans complex could be selectively allylated anti to the $Fe(CO)_4$ fragment (>95% ee), though the major cis complex was prone to racemization under similar conditions.

Enders described[10] the diastereoselective complexation of (*S*)-γ-benzyloxy-vinyl sulfone **2**. Treatment of **2** with $Fe_2(CO)_9$ under a CO atmosphere afforded the corresponding η^2-alkene iron tetracarbonyl complexes as a 85:15 mixture (de = 70%) where the major diastereomer could be cleanly separated by fractional crystallization at −25 °C (65% yield; Scheme 2). In this case, analysis by X-ray crystallography revealed that the $Fe(CO)_4$ fragment occupied a position trans to the benzyloxy group, suggesting not a heteroatom-directed process but an approach of the fragment to the less hindered alkene face via conformation **3**. In fact, the outcome of this complexation is not unlike S_N2' organocopper addition to γ-mesyloxy-(*E*)-α,β-unsaturated esters (which *may* proceed via an η^2 and/or η^3 π-complex intermediate).[11] The major complex was elaborated into the corresponding η^3-allyl complex, with loss of the benzyloxy group, by treatment with tetrafluoroboric acid. Nucleophilic addition anti to the metal fragment afforded enantiopure C-3-substituted vinyl sulfones. Similar chemistry has been used to prepare 4-amino-enoates.[12]

2.2. η^2-Manganese Complexes

The lone example of an enantiopure manganese η^2-complex thus far isolated is η^2-manganese complex

Scheme 3

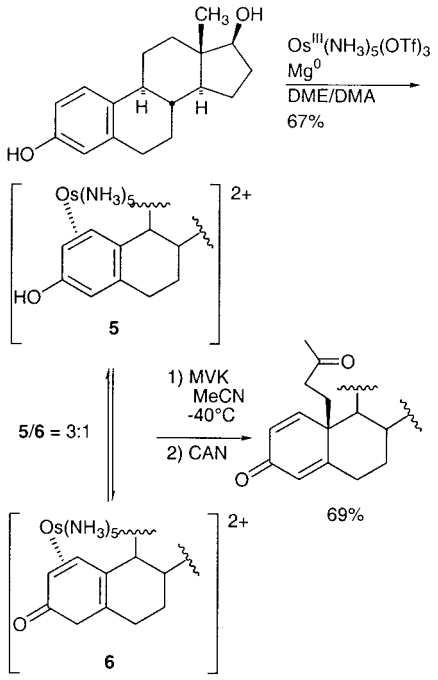


4, described by Schinzer (Scheme 3).[13] The fragment $[Mn(MeCp)(CO)_2]$ was photochemically generated in the presence of enantiopure 2-cyclopenten-1-ol, producing **4** in low yield (25%) but with apparent complete diastereoselectivity. Addition of the metal fragment proceeded syn to the alcohol functionality, again probably as a result of delivery of the metal fragment via coordination to the alcohol. This η^2-manganese complex was shown to participate in highly diastereoselective alkylations and aldol reactions (Scheme 3).

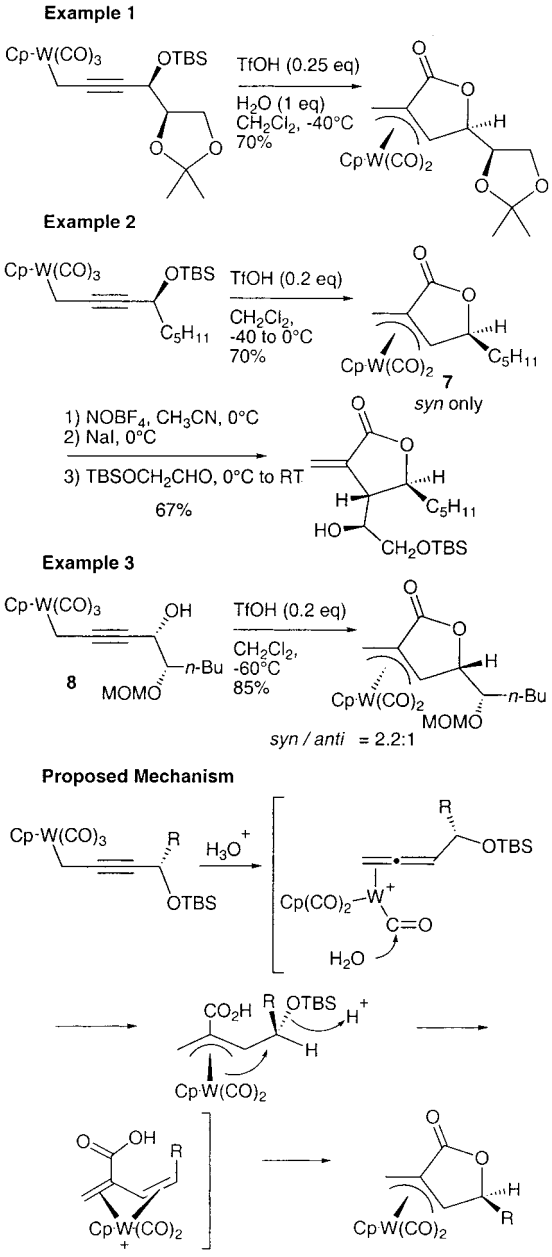
2.3. η^2-Osmium Complexes

Substantial effort has been put forth to modify steroid systems with organometallic fragments for a variety of endeavors; for example, they can be used synthetically for nontraditional and selective approaches to therapeutic agents or to act as markers in receptor studies.[14,15] Harman[16] achieved a regio- and diastereoselective complexation of β-estradiol with a pentaamine osmium(II) fragment that allowed rapid access to a C(19)-alkylated testosterone derivative. Complexation was achieved by reduction of $Os(NH_3)_5(OTf)_3$ with Mg in the presence of excess β-estradiol; the η^2-arene complexes were obtained as

Scheme 4



Scheme 5



a 3:1 equilibrium mixture of the phenolic and dienone tautomers **5** and **6** (67% combined yield), with the organometallic fragment exclusively occupying the α face of the steroid (Scheme 4). In a remarkable transformation, this mixture was reacted with methyl vinyl ketone to afford the C(10) Michael adduct, with the addition proceeding exclusively anti to the $Os(NH_3)_5$ unit. The organometallic fragment was readily removed with ceric ammonium nitrate.

2.4. η^3-Tungsten Complexes

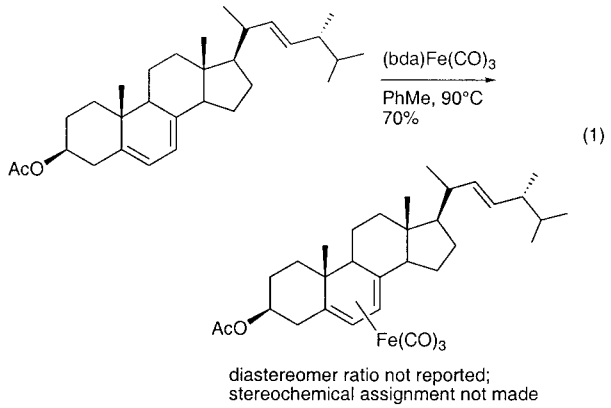
Liu reported the synthesis of several enantiopure tungsten π-allyl complexes derived from the readily prepared α-(silyloxy)-η^1-tungsten propargyl complexes. Treatment of these σ-complexes with a catalytic amount of triflic acid—either in the presence[17] or absence[18,19] of stoichiometric water—afforded the π-allyl complexes (Scheme 5). Interestingly, in each case the *syn*-diastereomer predominated. The role of

water remains unclear; in the initial report,[17] water was deemed essential for syn diastereoselection and a mechanistic rationale was proposed in which nucleophilic addition of water to one of the tungsten carbonyl ligands (of an intermediate η^2-allene cation) was a key step. However, a subsequently reported[18] tungsten π-allyl complex **7** was synthesized under anhydrous conditions and *syn*-diastereoselectivity was still observed. A mechanism that would explain this observation has not yet been offered. A more modest selectivity (2.2:1) was obtained (under anhydrous conditions) in the conversion of an enantiopure α-(hydroxy)-η^1-tungsten propargyl complex, **8**.[19]

Replacement of the two remaining carbonyl ligands on the tungsten atom of the π-allyl complexes with nitrosyl and iodide gives more reactive η^3-complexes which undergo addition to aldehydes. Liu exploited this to achieve the synthesis of enantiopure α-methylene lactones and related natural products; an example of the methodology used for the conversion of **7** is shown in Scheme 5.[19]

2.5. η^4-Iron Complexes

η^4-Iron complexes are among the most frequently prepared planar chiral organometallic species, and consequently there are a number of reports of the synthesis of enantiopure complexes. The first of these complexes to be directly prepared by diastereoselective complexation was actually carried out for the protection of the diene unit found in the steroid B-ring of ergosteryl acetate (eq 1; bda = benzylideneacetone).[20,21] Similarly, the tricarbonyl iron complex of calciferol was also prepared.[22] Some years later, Stephenson[23] reported a diastereospecific conversion of *cis*-5,6-disubstituted-1-methylcyclohexa-1,3-dienes to their corresponding *endo* iron tricarbonyl complexes **9a**−**d** (Scheme 6). This approach utilized the stereodirecting effect of oxygenated groups proximal to the diene unit, presumably via heteroatom delivery of the metal fragment. Similarly, an unstable mono-oxygenated 5-hydroxy analogue (prepared in situ by microbial oxidation) was isolated as its *endo*-complex **10**;[24] Pearson[25] later reported the preparation of the complex, **11**, derived from the 1-trifluoromethyl-5,6-diol analogue. Each of these monocyclic η^4-complexes provided access to the related cationic η^5-complexes in homochiral form.

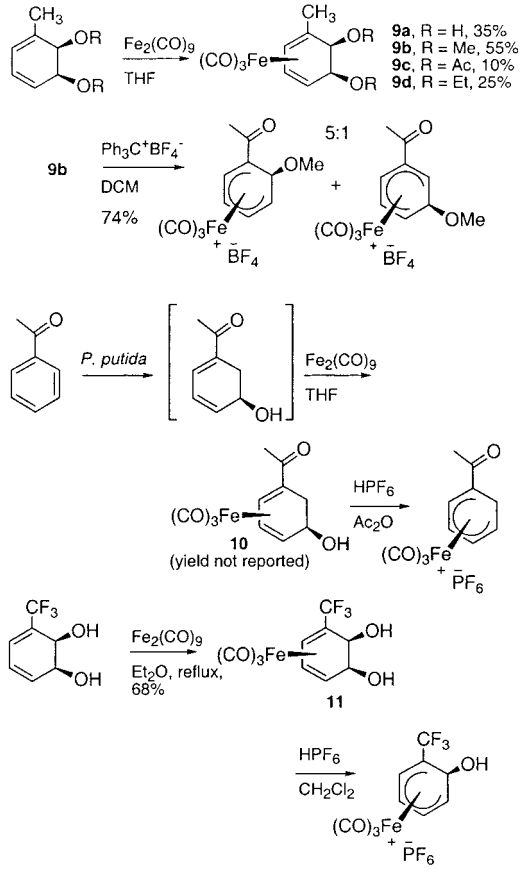


(1)

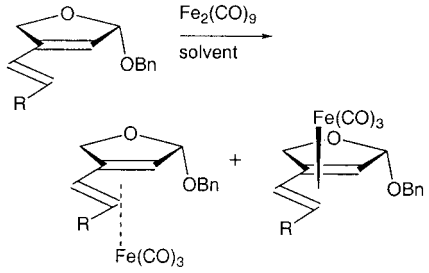
diastereomer ratio not reported;
stereochemical assignment not made

Schmalz[26] prepared enantiopure diene ligands—2-benzyloxy-4-vinyl-2,5-dihydrofurans derived from (+)-L-arabinose—and succeeded in effecting a modestly diastereoselective complexation to them with an iron tricarbonyl fragment (Scheme 7). Here, the diene was imbedded in a cyclic scaffold in order to fix the position of the element of chiral control (the benzyloxy group). As seen in similar cases already described, the major product, **12a**, was likely the result of heteroatomic delivery and installation of the Fe(CO)$_3$ unit syn to the benzyloxy group. The diastereoselectivity of this transformation was solvent dependent, varying from a 3:1 *endo*/*exo* ratio in refluxing ether (for R = CO_2Et) to 1:1.4 in heptane (for R = H); this may be the result of conformational differences in the dihydrofuran ring or of the benzyloxy substituent in different solvents. Furthermore, while the chiral center is located immediately adja-

Scheme 6

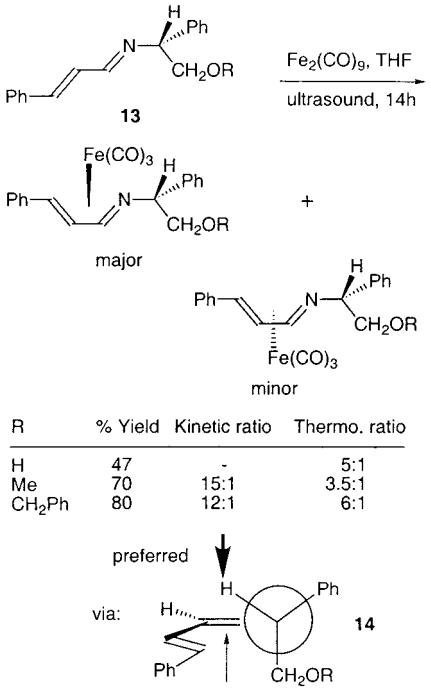


Scheme 7



diene	solvent	% yield	12a /12b
R = H	Et_2O	77	2.2 : 1
R = H	*n*-heptane	85	1 : 1.4
R = H	toluene	75	1.3 : 1
R = CO_2Et	Et_2O	90	3.0 : 1

Scheme 8

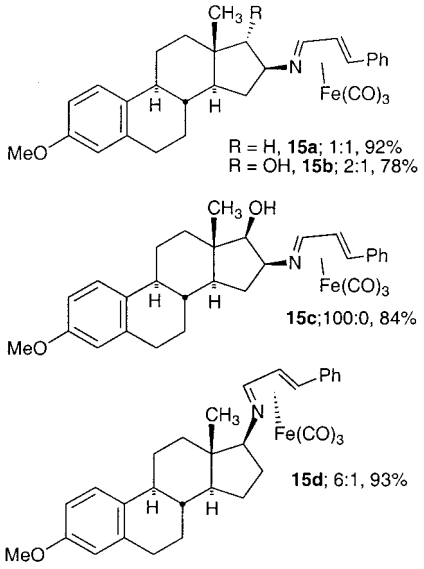


cent to the diene, the benzyloxy group may not be suitably positioned to effect a more dramatic differentiation of the diastereotopic diene faces. Fortunately, the diastereomeric iron diene complexes were readily separable by chromatography and each could be transformed into various derivatives under carefully controlled conditions without loss of optical integrity.[27]

Enantiopure 1-aza-1,3-butadienes have also been diastereoselectively complexed with an iron tricarbonyl fragment. The rationale for preparing enantiopure η^4-(1-aza-1,3-butadiene)tricarbonyliron complexes stems from their use as transfer reagents for asymmetric and catalytic installation of the $Fe(CO)_3$ fragment into prochiral 1,3-dienes.[3] Knölker[28] reported the diastereoselective complexation of α-alkyl-*N*-benzyl analogues, **13** (Scheme 8). In these cases, however, solutions of the initially formed (kinetic) complex mixtures equilibrated upon standing to thermodynamic mixtures possessing poorer diastereomer ratios. An examination of the kinetics of this epimerization suggested an intramolecular mechanism that was postulated to proceed via a 16-electron η^1-imine intermediate. An examination of the published X-ray crystal structure suggests that the major (kinetic) product of the complexation proceeded through low-energy conformation **14**, which bears a striking resemblance to the conformation, **3**, presumed to lead to the major product in Enders' preparation of η^2-alkene iron tetracarbonyl complexes (section 1.1).[10]

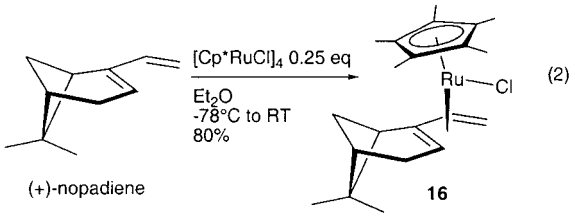
Imhof[29] described the formation of *N*-steroidal-1-aza-1,3-butadienes **15** (Chart 1; selected examples shown); by modification of the substituent pattern on the steroid D-ring, diastereoselectivities were improved from stereorandom (1:1, for **15a**) to complete selectivity (for **15c**); the absolute stereochemistry of the iron fragment was only determined for complex **15d** using X-ray crystallography. Unlike those reported by Knölker,[28] these complexes were thermally stable. However, Imhof's attempt to use the diene precursor to complex **15c** as an $Fe(CO)_3$ transfer reagent in order to achieve an enantioselective synthesis of the corresponding complex of prochiral 1-methoxy-1,3-cyclohexadiene was entirely unsuccessful; unfortunately a racemic mixture was obtained.

Chart 1. Tricarbonyl Iron Complexes of *N*-Steroidal-aza-1,3-butadienes



2.6. η^4-Ruthenium Complexes

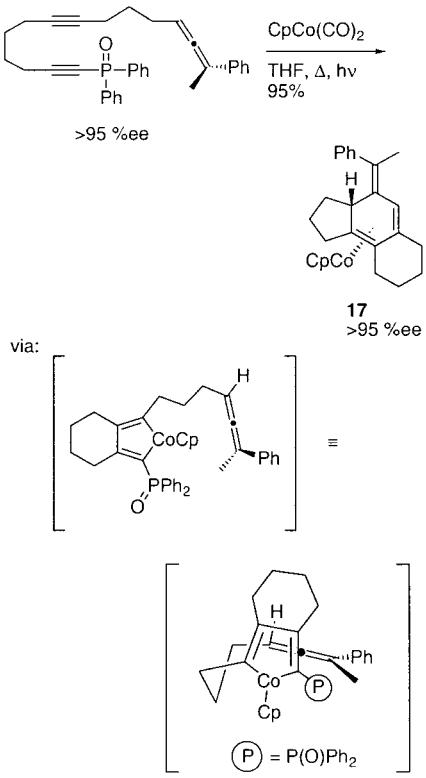
The use of a chiral ligand directly derived from a natural product is a frequently encountered strategy for effecting a diastereoselective π-complexation of a metal fragment, though often it is difficult to predict what level of selectivity may be observed. The lone reported example of an enantiopure η^4-ruthenium complex utilized this approach. Koelle[30] installed a Cp*RuCl fragment onto the less hindered face of (+)-nopadiene by simple treatment with $[Cp^*RuCl]_4$ in Et_2O at −78 °C; the diastereomer shown (**16**, eq 2) was the only one observed by the ^1H NMR spectrum.



2.7. η^4-Cobalt Complexes

The cobalt-mediated cyclotrimerization of alkynes (with $CpCo(CO)_2$) is a well-established methodology for the generation of arene systems, but intermediate cobalt-containing complexes are not typically isolated from procedures of this type.[31] However, variations of this [2+2+2] cycloaddition chemistry which employ two alkynes and an alkene can afford η^4-cobalt complexes, and thus, opportunities exist to develop asymmetric versions in which enantiopure planar chiral complexes may be prepared. Though this

Scheme 9



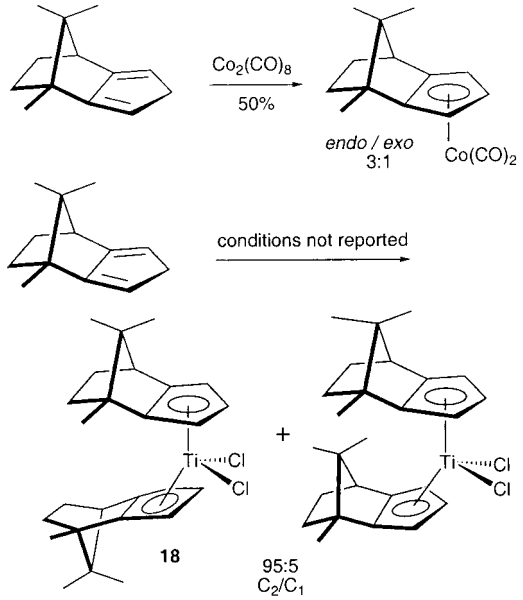
chemistry, as described by Malacria, appears to be intended as an approach for the preparation of the demetalated unsaturated organic ligands, complexes of this type could in principle find other applications. It was recently demonstrated[32] that an intramolecular cobalt(I)-mediated [2+2+2] cyclization of an enantiopure allene−diyne can proceed with total transfer of chirality from the initial axially chiral allene to the product η^4-cobalt diene complex, **17**, which possesses central and planar chiralities. The origin of the selectivity presumably results from an approach of the putative cobaltacyclopentadiene to the less hindered allene face during the key [4+2] cycloaddition process. The length of the carbon-atom tether also forces the cobaltacyclopentadiene to adopt a single conformation in order to bring about an overlap between the allene and terminal diene orbitals (Scheme 9).

Related chemistry that utilized enantiopure chiral phosphine oxides at the termini of linear enediynes proved to be less successful in terms of diastereoselectivities.[33]

2.8. η^5-Complexes

Largely driven by the pursuit of effective group 4 transition-metal catalysts for asymmetric reactions and/or olefin polymerization, the array of planar chiral, nonracemic η^5-cyclopentadienyl complexes that have been prepared by diastereoselective complexation is truly impressive. Two prior review articles by Halterman[4,34] covered the synthesis and complexation of many ligand types, featuring those with equivalent, homotopic, and enantiotopic π-faces as well as those capable of exhibiting planar chirality as a result of possessing diastereotopic faces. The

Scheme 10



production of racemic and meso complexes were also included. In keeping with the theme of this review, the focus will be narrowed here to include only ligands with diastereotopic cyclopentadienyl faces that lead to chiral, nonracemic complexes.

A number of researchers have provided seminal contributions to this field: the laboratories of Paquette,[35−42] Erker,[43−46] Halterman,[47−50] and Marks[51−56] have been the most actively involved since the latter portion of the 1980s. However, the initial report of the complexation to chiral η^5-ligands possessing diastereotopic π-faces was that of Vollhardt and Halterman,[57] who demonstrated that the selective complexation of a (+)-camphor-derived cyclopentadienyl ligand was possible (Scheme 10). A cobalt(I) dicarbonyl fragment was preferentially installed on the less hindered *endo* (α) face of the ligand to afford the corresponding complex. Also, C_2-symmetric titanocene dichloride **18** was prepared from the same ligand, along with a minor amount of the unsymmetric, C_1, isomeric metallocene. Again, this result is due to the overwhelming preference for complexation on the less hindered face of each of the ligand units of the complex.

In the ensuing years, Paquette and co-workers greatly developed this field by preparing chiral ligands capable of exhibiting a high degree of facial discrimination upon complexation as well as by rationalizing the origin of these selectivities. The seminal work in this field was actually performed with the achiral isodicyclopentadienyl (IsodiCp) ligand,[35] when it was observed that metalation of the lithium salt of the anion derived from IsodiCp exhibited remarkable temperature sensitivity, leading to differing complexation π-facial selectivities. To develop an understanding of the role played by sterics and/or stereoelectronic factors while also seeking to prepare possible catalysts for asymmetric transformations, the complexation of related chiral, nonracemic ligands was undertaken. The *general* trends observed tend to be similar to those seen in the achiral IsodiCp series; that is, for reactions at room

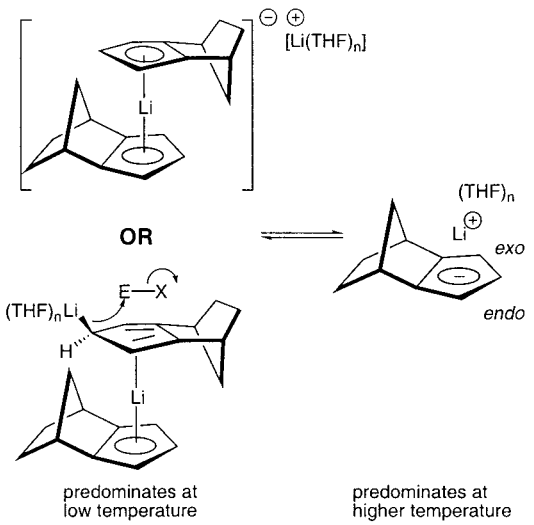
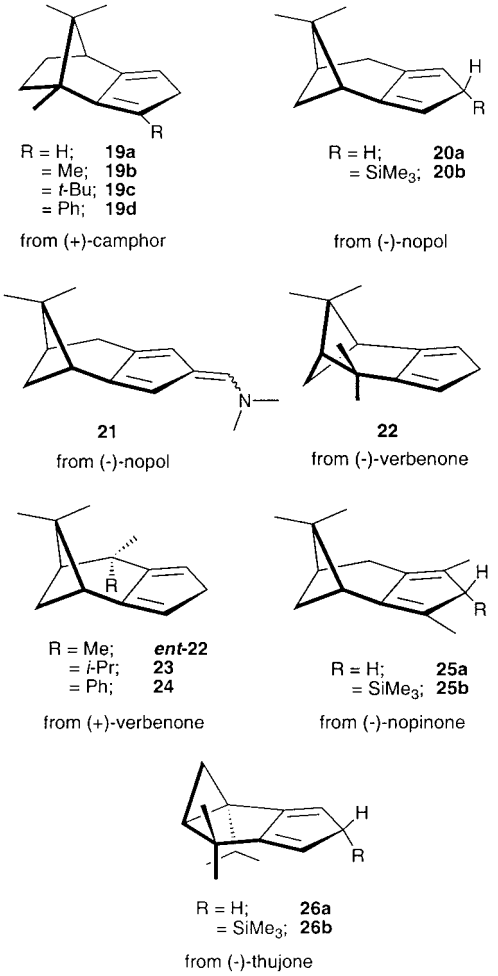


Figure 1. Location of the lithium cation in the aggregation states of the deprotonated achiral isodicyclopentadienyl (IsodiCP) ligand.

temperature or higher, sterics controlled the product distribution and the metal complexation tended to preferentially occur syn to the less hindered face. On the other hand, low-temperature complexations appeared to be anti-steric, giving the more hindered facial diastereomer. Eventually these results, particularly regarding the complexation of the lithium salts of the anionic ligands, were rationalized on the basis of the aggregation state and location of the lithium counterion (Figure 1). At lower temperatures the monomer−dimer equilibrium shifts toward the fast-reacting dimer, where one lithium counterion occupies a position on the less hindered face of each ligand. Capture of the metal must then occur from the more hindered opposite face (*endo*, in the case of the achiral IsodiCp ligand as shown in Figure 1). On the other hand, at higher temperatures the monomer−dimer equilibrium shifts toward the monomer and complexation simply occurs from the less hindered *exo* face. A number of natural products were elaborated into chiral cyclopentadienyl ligands (**19**-**26**; Chart 2), and these, or the anions derived from them, were converted into a series of planar chiral metal complexes, as summarized in Table 1.[36−42] Entries 7−10 reveal that facial selectivities can be reversed (at least for ligand **20a**) by changing reaction temperature. Later, in a remarkable finding, Paquette[40] discovered that selectivities could be reversed by first preparing the trimethylsilyl derivative of the chiral cyclopentadienyl ligand; the silyl group exhibited a preference for occupying the less hindered face of the ligand. Then, treatment with the metal complexing agent without prior deprotonation of the ligand afforded the *more* hindered complex (Scheme 11).

While Table 1 catalogs examples of enantiopure metallocene complexes possessing two different η^5-cyclopentadienyl ligands, Table 2 lists metallocene complexes prepared by use of ca. 0.5 equiv of the metal source with respect to the chiral ligand (except in the case of entry 11). That is, Table 2 lists planar chiral metallocenes having two identical η^5-cyclopentadienyl ligands. All of these complexes are furthermore denoted as "unbridged" due to the absence of a

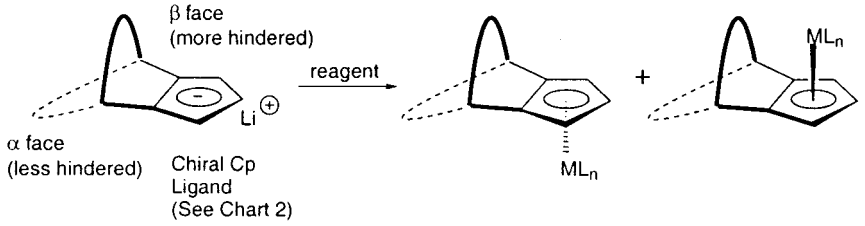
Chart 2. Cyclopentadienyl Ligands Derived from the Chiral Pool. Each Ligand Is Drawn with the More Hindered Face as the Top (*β*) Face



connecting chain between the two η^5-ligands. Those complexes in Table 2 can exist as a C_2-symmetric isomer (from complexation of the metal to the same face of each η^5-ligand) or as a C_1-symmetric isomer (from complexation of the metal to opposite faces of each η^5-ligand). Clearly, if the complexation to one face is significantly favored, the C_2-isomer should be preferentially formed. Indeed, Table 2 reveals that this is overwhelmingly the case in most of the reported examples. It is interesting to note that a C_2-metallocene isomer that would be formed from complexation to the less preferred face of each η^5-ligand has never been observed.

Rather than focusing on preparing ligands with cyclopentadienyl units fused to bicyclic systems derived from the chiral pool, Erker[43−46] developed indenyl ligands rendered chiral (and thus capable of exhibiting planar chirality upon metal complexation) by single-position attachment of a natural product-derived unit. In this case three metallocene isomers are possible, which Erker dubbed "racem-like" (Table 3, structures **A** and **B**) and "meso-like" (structure **C**). Selectivity is apparently determined by sterics, depending on the preferred conformation of the chiral unit with respect to the indene. While the initial efforts in this series, as listed in Table 3, involved the use of cholesterol units attached to the indene

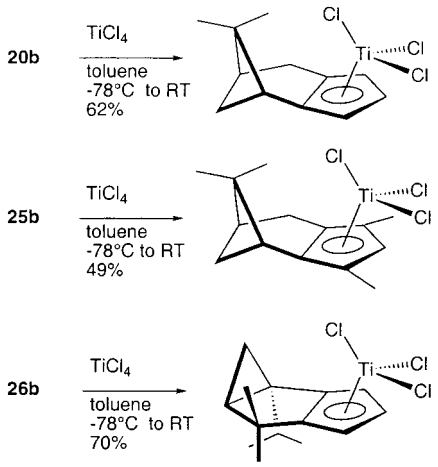
Table 1. Diastereoselective Synthesis of Enantiopure Planar Chiral Unbridged Metallocene Complexes Containing Different Cyclopentadienyl Ligands



entry	Cp	reagent, conditions[a]	%	ML$_n$	α/β	ref
1	**21**[b]	[(*p*-Xyl)(Cp)Fe]$^+$PF$_6^-$, *hν*, then $^-$OH	*c*	CpFe	73:27	36
2	**21**[b]	[CpRu(MeCN)$_3$]$^+$PF$_6^-$,Δ, then $^-$OH	*c*	CpRu	93:7	36
3	**19a**	CpTiCl$_3$, RT	58	CpTiCl$_2$	7:1	37
4	**19a**	CpZrCl$_3$·2THF, Δ	58	CpZrCl$_2$	2:1	37
5	**19a**	Cp*ZrCl$_3$, Δ	60	Cp*ZrCl$_2$	1.4:1	37
6	**19a**	*exo*-isodiCpTiCl$_3$, −78 °C to RT	36	*exo*-isodiCpTiCl$_2$	α only	38
7	**20a**	CpTiCl$_3$, −78 °C to Δ	55	CpTiCl$_2$	1:5	39
8	**20a**	CpTiCl$_3$, RT to Δ	45−50	CpTiCl$_2$	3:1	39
9	**20a**	CpZrCl$_3$·2THF, tol, −78°C to Δ	66	CpZrCl$_2$	β only	39
10	**20a**	CpZrCl$_3$·2THF, tol, RT to Δ	56	CpZrCl$_2$	3.5:1	39
11	**20a**	Cp*ZrCl$_3$, tol, RT to Δ	69	Cp*ZrCl$_2$	2:1	39
12	**20a**	CpTiCl$_3$, 50 °C	69	CpTiCl$_2$	α only	40
13	**22**	CpTiCl$_3$, RT	45	CpTiCl$_2$	α only	40
14	**22**	CpZrCl$_3$·2THF, tol, Δ	65	CpZrCl$_2$	1:1	41
15	**22**	Cp*ZrCl$_3$, tol, RT to Δ	55	Cp*ZrCl$_2$	α only	41
16	**22**	neomen-CpTiCl$_3$, −78 °C to RT	62	neomen-CpCl$_2$	α only	38
17	*ent*-**22**	neomen-CpTiCl$_3$, −78 °C to RT	58	neomen-CpCl$_2$	α only	38
18	*ent*-**22**	CpTiCl$_3$, −78 °C to RT	42	CpTiCl$_2$	α only	38
19	*ent*-**22**	*exo*-isodiCpTiCl$_3$, −78 °C to RT	68	*exo*−isodiCpTiCl$_2$	α only	38
20	**25a**	CpTiCl$_3$, −78 °C	*c*	CpTiCl$_2$	α only	40
21	**26a**	CpTiCl$_3$. −78 °C	63	CpTiCl$_2$	10:3	40

[a] All reactions carried out in THF unless otherwise noted. [b] Reaction performed on neutral cyclopentadiene, not lithium cyclopentadienide. [c] Chemical yield not reported.

Scheme 11



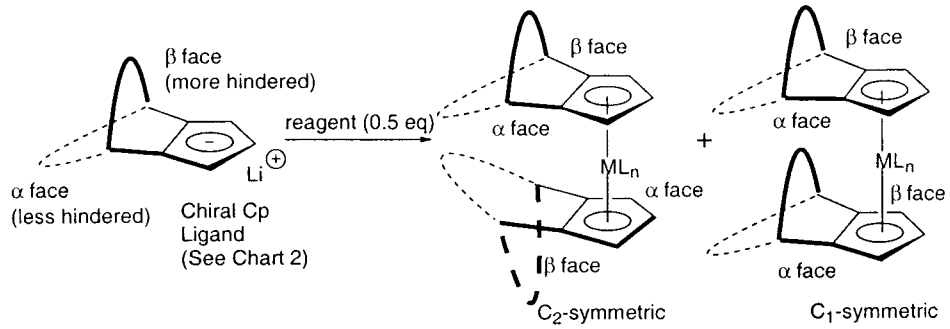
(entries 1 and 2), the best complexation selectivities were eventually obtained with the neomenthyl analogue (entries 3 and 10). Negishi[58] effectively exploited the readily isolated major metallocene of entry 3 as a catalyst for enantioselective alkene alkylalumination. These ligands were also employed by Whitby,[59] who used them to prepare mixed-ligand monoindenyl zirconium complexes (**27** and **28**, Scheme 12) and then employed them as catalysts in enantioselective carbomagnesiation reactions.

More recently, Schumann and Halterman reported the diastereoselective synthesis of additional bis(indenyl) complexes of this type.[48] Inspection of Table 3 reveals that the additional methyl substituents on the dimethylneomenthyl ligand used by Erker (entry 10) had resulted in an enhanced diastereoselectivity in the complexation event (compared to entries 3 or 5, for example), and this suggested that further studies were warranted. Once the (−)-3-menthyl-4,7-dimethylindene ligand became synthetically available,[49] complexations to it were explored because it was reasoned that the menthyl's three equatorial substituents should render it "conformationally better defined" than the neomenthyl group. As it turned out, however, complexation diastereoselectivities were only modest (entries 11−14, Table 3).

Additional planar chiral monoindenyl complexes have been prepared by Schumann and Halterman[50] and are cataloged in Table 4. Especially noteworthy here are the synthesis of late-transition-metal complexes (group 9 metals as well as molybdenum). Diastereoselectivities are fair to moderate; the best case is that of the Co(dppe) complex (entry 12), possibly due to the larger steric requirement of the dppe ligand as compared to that of COD.

Another significant category of chiral, nonracemic cyclopentadienyl ligands are the *ansa*-metallocenes, where a connecting bridge exists between the two cyclopentadienyl ligands of the complex. This group of complexes may be further divided into two classes—those that derive their chirality from a chiral unit attached to one of the cyclopentadienyl ligands or those possessing chirality along the *ansa*-chain. In the former category, Marks and co-workers[51−56] prepared a huge number of silyl-bridged *ansa*-metal-

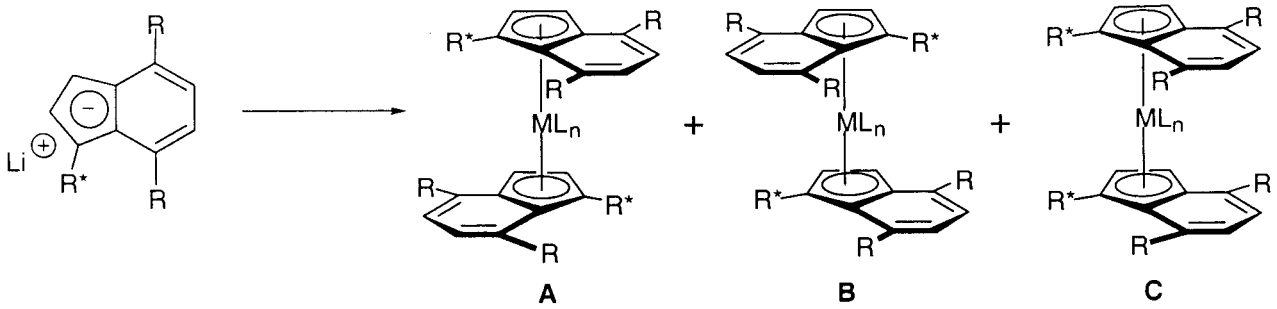
Table 2. Diastereoselective Synthesis of Enantiopure Planar Chiral Unbridged Metallocene Complexes Containing Identical Cyclopentadienyl Ligands



entry	Cp	reagent/conditions[a]	%	ML$_n$	C$_2$/C$_1$ ratio	ref
1	**19a**[b]	$TiCl_4$, Et_2O, RT	23	$TiCl_2$	100:0	42
2	**19a**	$TiCl_3$·3THF, DME, Δ	43	$TiCl_2$	9:1(α,β)	37
3	**19a**	$ZrCl_4$, DME, Δ	50	$ZrCl_2$	13:1 (α,β)	37
4	**19b**	$TiCl_3$, THF, −78 °C to Δ	37	$TiCl_2$	9:1(α,β)	47
5	**19b**	$ZrCl_4$, Et_2O, RT	42	$ZrCl_2$	4:1(α,β)	47
6	**19c**	$ZrCl_4$, Et_2O, RT	30[c]	$ZrCl_2$	"complex"	47
7	**19d**	$ZrCl_4$, Et_2O, RT	15	$ZrCl_2$	6:1(α,β)	47
8	**20a**[b]	$TiCl_4$, Et_2O, 0 °C to RT	39	$TiCl_2$	100:0	42
9	**20a**	$TiCl_3$·3THF, DME, −78 °C to Δ	71	$TiCl_2$	100:0	39
10	**20a**	$ZrCl_4$, DME, −78 °C to Δ	67	$ZrCl_2$	45:1 (α,β)	39
11	**20a**[d]	$Fe(CO)_5$, C_8H_{18}, −78 °C to Δ[e]	70	$Fe_2(\mu{-}CO)_2CO_2$	100:0	42
12	**22**	$TiCl_3$·3THF, DME, Δ	45	$TiCl_2$	100:0	41
13	**22**	$ZrCl_4$, DME, Δ	65	$ZrCl_2$	100:0	41

[a] 0.5 eq of metal halide used, unless otherwise noted. [b] Metal cation not specified. [c] Crude yield of complex mixture; major diastereomer purified in 16% yield. [d] Reaction performed on neutral cyclopentadiene, not lithium cyclopentadienide. [e] Norbornene used as an additive.

Table 3. Diastereoselective Synthesis of Enantiopure Planar Chiral "Unbridged Bisindenyl Metallocene" Complexes

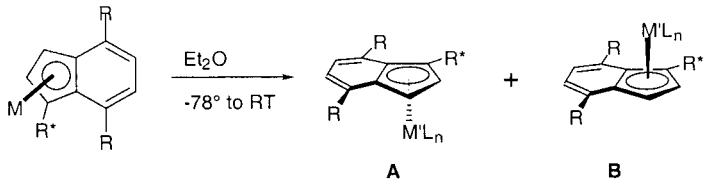


entry	R	R*[a]	reagent, solvent[b]	ML$_n$	A/B/C	%[c]	ref
1	H	3α-cholestanyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	55:40:5	74(21,53,−)	43
2	H	3β-cholestanyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	16:21:63	31(−,−,16)	43
3	H	(+)-neomenthyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	93:2:5	(61,−,−)	44
4	H	(+)-neoisomenthyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	82:7:11	(25,−,−)	44
5	H	(+)-neomenthyl	$ZrCl_4$,PhMe	$ZrCl_2$	70:6:24	(60,−,−)	45
6	H	(+)-neoisomenthyl	$ZrCl_4$,PhMe	$ZrCl_2$	62:11:26	(21.−.−)	45
7	H	(+)-menthyl	$ZrCl_4$,PhMe	$ZrCl_2$	28:6:66	(13,−,7)	45
8	H	(+)-isomenthyl	$ZrCl_4$,PhMe	$ZrCl_2$	53:11:31	(17,−,14)	45
9	H	(−)-neoisopinocamphenyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	52:<1:48	21	46
10	CH_3	(−)-neomenthyl	$ZrCl_4(THF)_2$,PhMe/THF	$ZrCl_2$	98:1:1	(28,−,−)	45
11	CH_3	(−)-menthyl	$ZrCl_4$,PhMe	$ZrCl_2$	44:0.56	(25,−,33)	48
12[d]	CH_3	(−)-menthyl	$ZrCl_4$,PhMe	$ZrCl_2$	47:0:53	87	48
13	CH_3	(−)-menthyl	$FeCl_2(THF)_{1.5}$,THF	Fe	63:13:24	49	48
14	CH_3	(−)-menthyl	$NiCl_2$(DME),THF	Ni	54:9:37	47	48

[a] All menthyl (and analogous) ligands are attached to the indene at the cyclohexyl 1′ position (menthol numbering). [b] All reactions were performed at −78°C to RT except entries 1 and 2 (−78 to −60 °C). [c] Combined overall yield; isolated yield of **A**, **B**, **C** (respectively) in parentheses. [d] The potassium salt, not the lithium salt, was used.

locene complexes, most of which uniquely involve lanthanide metals (Table 5). Many of these complexes have been exploited for use as hydroamination or hydrogenation catalysts, while their zirconium-based analogues have been utilized as catalysts for olefin polymerization. Chart 3 catalogs these chiral ligands (**29**−**34**), and the data in Table 5 reveal that complexation was generally highly diastereoselective as

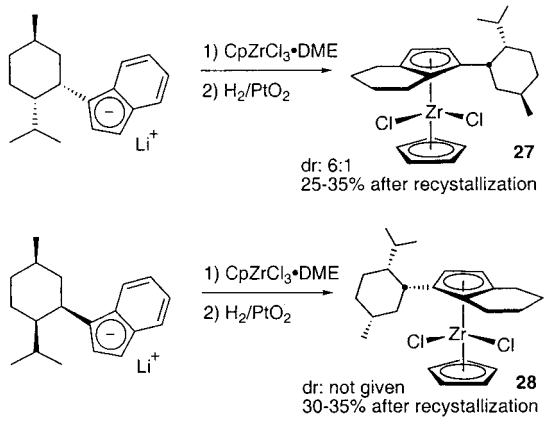
Table 4. Diastereoselective Synthesis of Enantiopure Planar Chiral Monoindenyl Complexes[50]



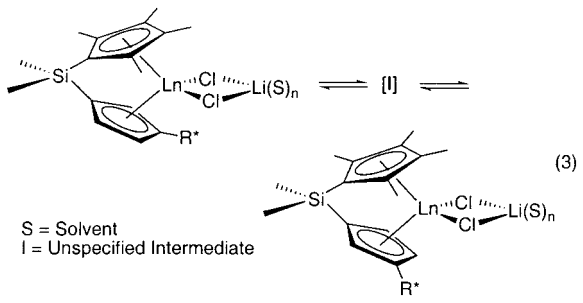
entry	R	R*[a]	M	reagent	M′L_n	A/B	%[b]
1	CH_3	(−)-menthyl	Li	$[RhCl(COD)]_2$	Rh(COD)	69.5:29.5	98(40,21)
2	CH_3	(−)-menthyl	$SnBu_3$	$[RhCl(COD)]_2$	Rh(COD)	68:22	79
3	CH_3	(−)-menthyl	Li[c]	$[RhCl(COD)]_2$	Rh(COD)	58:42	93
4	CH_3	(−)-menthyl	Na	$[RhCl(COD)]_2$	Rh(COD)	33:67	70
5	CH_3	(−)-menthyl	K	$[RhCl(COD)]_2$	Rh(COD)	25:75	89
6	*i*-Pr	(−)-menthyl	Li	$[RhCl(COD)]_2$	Rh(COD)	69:31	75
7	H	(+)-neomenthyl	Li	$[RhCl(COD)]_2$	Rh(COD)	40:60	100(18,29)
8	CH_3	(−)-menthyl	Li	$[RhCl(C_2H_4)_2]_2$	$Rh(C_2H_4)_2$	67:33	78
9	CH_3	(−)-menthyl	K	$[RhCl(CO)_2]_2$	$Rh(CO)_2$	40:60	75
10	CH_3	(−)-menthyl	Li	$[IrCl(COD)]_2$	Ir(COD)	69:31	83(43,16)
11	CH_3	(−)-menthyl	K	$[IrCl(COD)]_2$	Ir(COD)	55:35	75
12	CH_3	(−)-menthyl	Li[d]	$CoCl_2$(dppe)	Co(dppe)	86:14	33
13	CH_3	(−)-menthyl	Li	$Mo(CO)_6$[e]	$Mo(CO)_3$	71:29	95

[a] All menthyl (and analogous) ligands are attached to the indene at the cyclohexyl 1′ position. [b] Combined overall yield; isolated yield of **A**, **B** (respectively) in parentheses. [c] 12-crown-4 was used as an additive. [d] Two equivalents of lithiated indene used per metal reagent. [e] Reaction carried out from −78 to +65 °C.

Scheme 12



a result of successful steric-based differentiation of the cyclopentadienyl faces by the attached chiral unit. Interestingly, most of the complexes were configurationally labile in diethyl ether solutions at room temperature. While many initally formed complexes could be purified by low-temperature recrystallization from diethyl ether, contact with the solvent at room temperature prior to isolation *or* stirring in diethyl ether for extended periods caused an epimerization to take place via an unspecified intermediate **I** (eq 3). The solvent-dependent equilibrium ratios for some



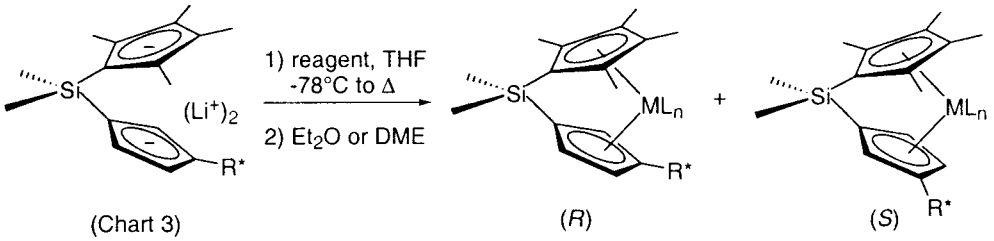
(3)

of the lanthanide complexes—a result of formal dissociation of the chiral η^5-unit followed by recoordination to the opposite face—are listed in Table 6.[51]

Among the class of *ansa*-metallocenes bearing chirality along the linker instead of one of the cyclopentadienyl units, Bercaw's $K_2[BnBp]^{2-}$ ligand, **35**,[60] is one of the more architecturally fascinating. Here, Marks' achiral silylene ($SiMe_2$) linker was replaced by the C_2-symmetric 1,1′-binaphth-2,2′-diolate group, and formation of a single diastereomeric complex was promoted by avoidance of a steric interaction between the naphthol rings and trimethylsilyl substituents on the cyclopentadienyl rings. Indeed, the desired enantiopure yttrocene complexes were formed in good yields without detection of any minor diastereomeric complexes (Scheme 13). This metallocene was readily converted into its corresponding alkyl derivative, (BnBp)YCH($SiMe_3$)$_2$, which was a precatalyst for alkene hydrogenation and polymerization.

A number of chiral, nonracemic ligand systems have been reported with identical indene units linked by chiral bridges. The complexations to provide the corresponding *ansa*-metallocenes have met with mixed success—some conversions have been plagued by low yields, others by poor complexation selectivity. The best results obtained with this class of ligands are undoubtedly those obtained by Halterman (**36**)[61] and by Bosnich (**37**, "(*R*,*R*)-cyclacene"),[62] shown in Scheme 14. The ligands were cleverly designed to allow the indene units to project out from a C_2-symmetric cycloalkane scaffold. An acceptable yield was also obtained by Halterman with bisindenyl system **38**.[63] In this case, the author speculated that the initial complexation event to one of the indene units was not selective; however, because of the steric interactions built into this ligand system, only one of the diastereomeric metallocenes could be produced. It is possible that the "wrong" facial isomer underwent

Table 5. Diastereoselective Synthesis of Enantiopure Planar Chiral Silyl-Bridged *ansa*-Metallocene Cyclopentadienyl Complexes



(Chart 3) (*R*) (*S*)

entry	ligand	reagent[a]	% yield	(*R*)/(*S*)	ML_n	ref
1	**29**	$SmCl_3$	47[b]	*c*	$Sm(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
2	**29**	$LaCl_3$	47[b]	>90:10	$La(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
3	**29**	$NdCl_3$	65[b]	*c*	$Nd(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
4	**29**	YCl_3	63[b]	>90:10	$Y(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
5	**29**	$LuCl_3$	57[b]	>90:10	$Lu(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
6	**29**	$SmCl_3$	54[b]	*c*	$Sm(\mu\text{-}Cl)_2Li(DME)$	51
7	**30**	$SmCl_3$	60[b]	*c*	$Sm(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
8	**30**	YCl_3	64[b]	>90:10	$Y(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
9	**30**	$LuCl_3$	70[b]	>90:10	$Lu(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
10	**30**	$SmCl_3$	88[b]	*c*	$Sm(\mu\text{-}Cl)_2Li(DME)_2$	51
11	**30**	$LuCl_3$	89[b]	<10:90	$Lu(\mu\text{-}Cl)_2Li(DME)_2$	51
12	**31**	YCl_3	48[b]	<10:90	$Y(\mu\text{-}Cl)_2Li(OEt_2)_2$	51
13	**29**	$ZrCl_4$[d]	62	60:40	$ZrCl_2$	52
14	**30**	$ZrCl_4$[d]	67	8:1	$ZrCl_2$	52
15	**30**	$HfCl_4$[d]	73	*c*	$HfCl_2$	53
16	**32**	YCl_3	35	100:0	$Y(\mu\text{-}Cl)_2Li(OEt_2)_2$	54
17	**32**	$LuCl_3$	54	100:0	$Lu(\mu\text{-}Cl)_2Li(OEt_2)_2$	54
18	**33**[e]	$Zr(NMe_2)_4$[f]	65	85:15	$ZrCl_2$	55
19	**34**	$YCl_3(THF)_3$[g]	74[b]	100:0[b]	$Y(\mu\text{-}Cl)_2Li(OEt_2)_2$	56
20	**34**	$LuCl_3$[g]	71[b]	100:0[b]	$Lu(\mu\text{-}Cl)_2Li(OEt_2)_2$	56

[a] All reactions carried out in THF, from −78 °C to reflux, unless otherwise noted. [b] Yield (or (*R*)/(*S*) ratio) after isolation by recrystallization. [c] (*R*)/(*S*) ratio not observable by ^1H NMR. [d] RT to Δ. [e] Neutral cyclopentadiene used not the dianion. [f] Reaction performed in toluene at 120 °C, followed by treatment with $Me_2NH{\cdot}HCl$ in DCM from −78 °C to RT. [g] Reaction performed in Et_2O, −78 °C to RT.

Chart 3. *ansa*-Metallocene Ligands Possessing a Chiral Unit Attached to One of the Two Cp Ligands

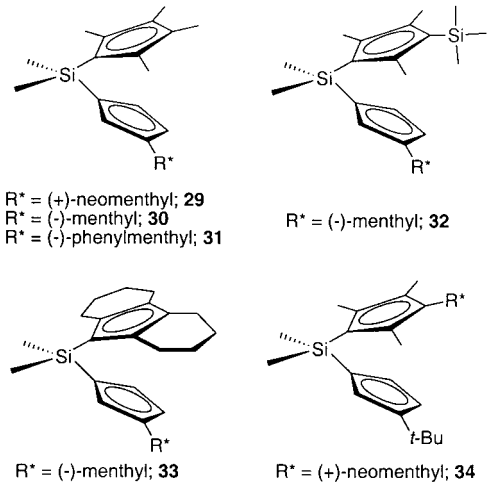
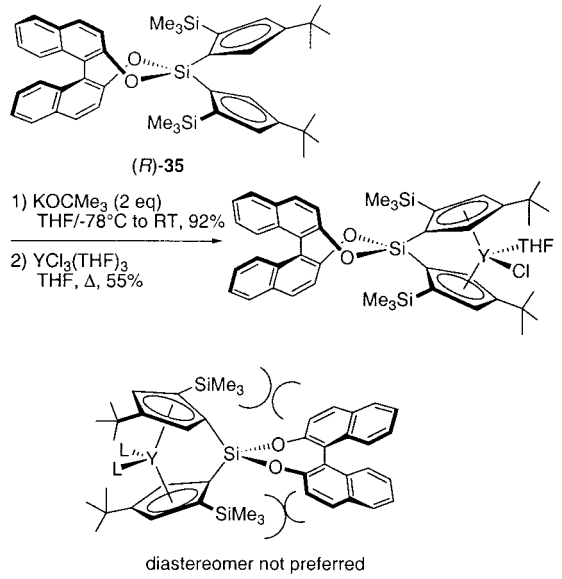


Table 6. Solvent-Dependent Diastereomer Ratios at Equilibrium (25 °C) for $Me_2Si(\eta^5\text{-}C_5Me_4)(\eta^5\text{-}C_5H_3R^*)Ln(\mu\text{-}Cl)_2Li(ether)_2$ Complexes[51]

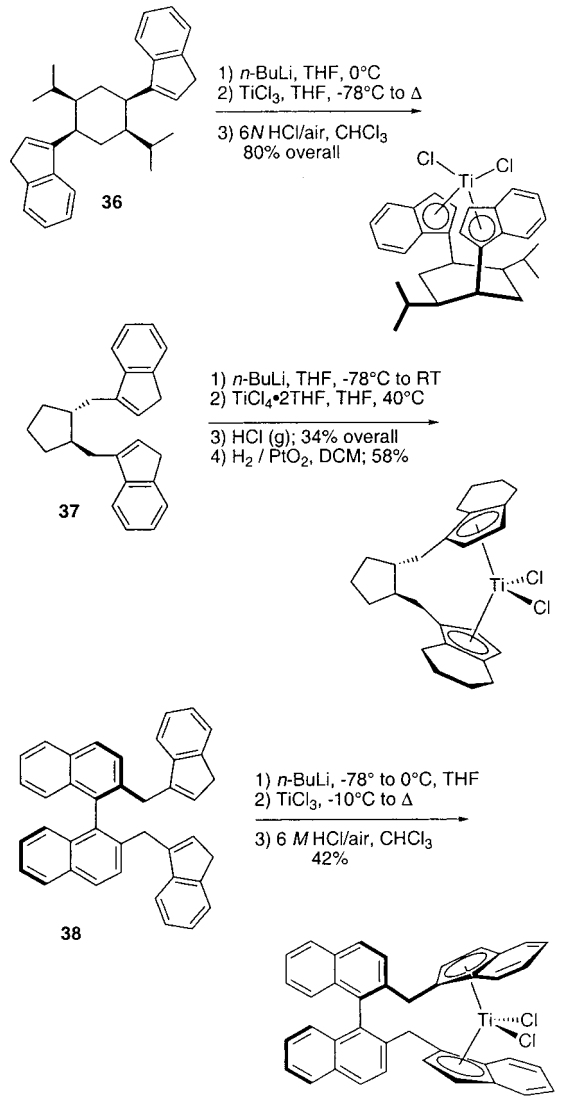
entry	complex (ligand/metal)	equilibrium diastereomer ratio (*R*:*S*)	solvent
1	**29**/La	75:25	THF
2	**29**/Nd	74:26	THF
3	**29**/Sm	74:26	THF
4	**29**/Sm	34:66	Et_2O
5	**29**/Y	74:26	THF
6	**29**/Y	46:54	Et_2O
7	**29**/Lu	74:26	THF
8	**29**/Lu	51:49	Et_2O
9	**30**/Sm	20:80	THF
10	**30**/Sm	>95:5	Et_2O
11	**30**/Y	20:80	THF
12	**30**/Y	90:10	Et_2O
13	**30**/Lu	20:80	THF
14	**30**/Lu	85:15	Et_2O
15	**31**/Y	6:94	THF
16	**31**/Y	83:17	Et_2O

intermolecular metalation to form oligomeric material. Unfortunately, a C_2-symmetric cycloalkane scaffold design does not guarantee success, as complexation of Rieger's ligand (**39**)[64] afforded a complex mixture of diastereomers (Scheme 15). While Green's tartrate-derived system (**40**)[65] did produce a single *meso*-like diastereomer metallocene, complex yields were low. Finally, Bosnich's "(*S*,*S*)-chiracene" ligand **41**[66] (Scheme 16) yielded mixed results: the *meso*-like titanocene derivative **42** was obtained with some selectivity (**42**/**43**/**44**, M = Ti; 4.2:2.5:1) but was not easily purifed. Photolysis (THF, RT) caused an isomeric redistribution of the isomers where **43** became the dominant species present (**43**/**42**, M = Ti; 5.9:1, 77% yield); however, it could only be purified by resolution with the sodium salt of (*R*)-binaphtholate via chromatography on silanized silica. The

Scheme 13

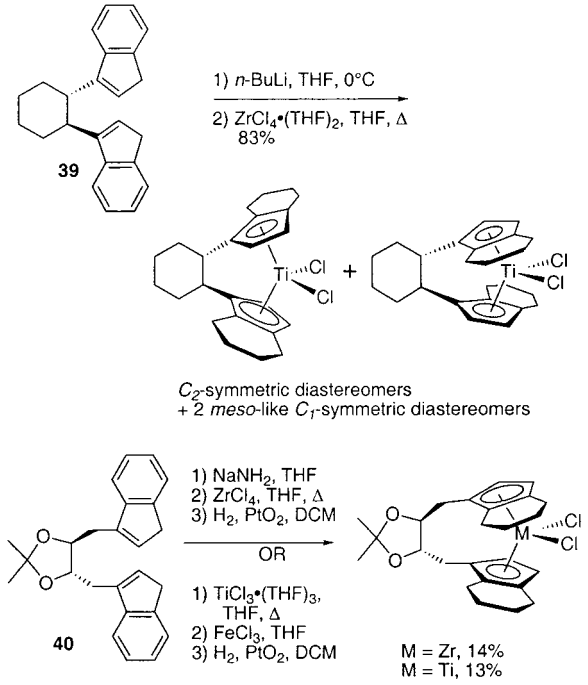


Scheme 14

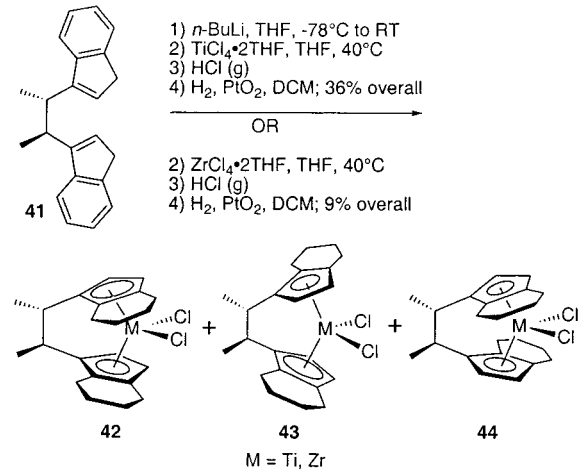


overall yield was 25%. For the zirconium analogue, the same complexes were obtained as a mixture with more impressive selectivity (M = Zr; 18.8:1:1) but in a low (9%) yield (recrystallization of the major, *meso*-like isomer, was possible).

Scheme 15



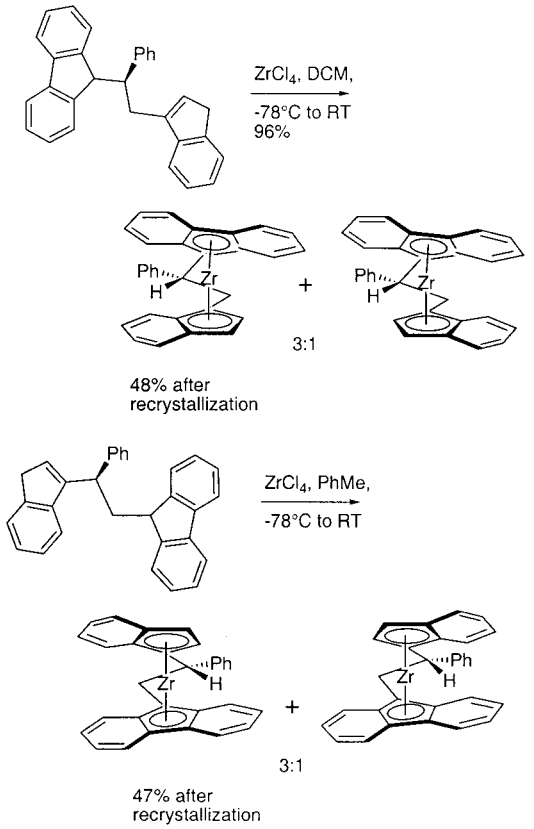
Scheme 16



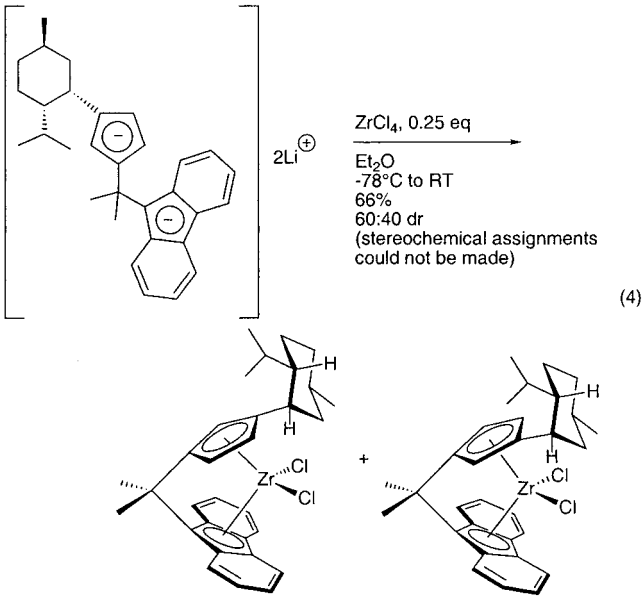
Rieger[67] and Jany[68] also prepared ligands bearing chirality on the *ansa*-linkage; in these cases, however, one of the cyclopentadienyl units was an indene (thus possessing diastereotopic faces) and the other a fluorene unit (with homotopic faces) (Scheme 17). Complexation selectivities of 3:1 were obtained for each ligand; purification was possible for each product (by recrystallization). After hydrogenation to afford the tetrahydroindenyl derivative, the complexes were studied for use as olefin polymerization catalysts.

In a separate category, reminiscent of the approach used by Erker and others to diastereoselectively complex indenyl ligands, a neomenthyl-modified cyclopentadiene unit linked to a fluorene was prepared and used to synthesize the corresponding planar chiral *ansa*-zirconocene (equation 4).[69] Unfortunately the diastereoselectivity was only modest (60:40), and the major isomer could neither be isolated nor identi-

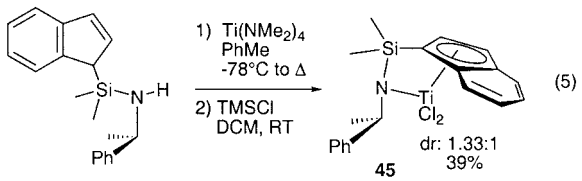
Scheme 17



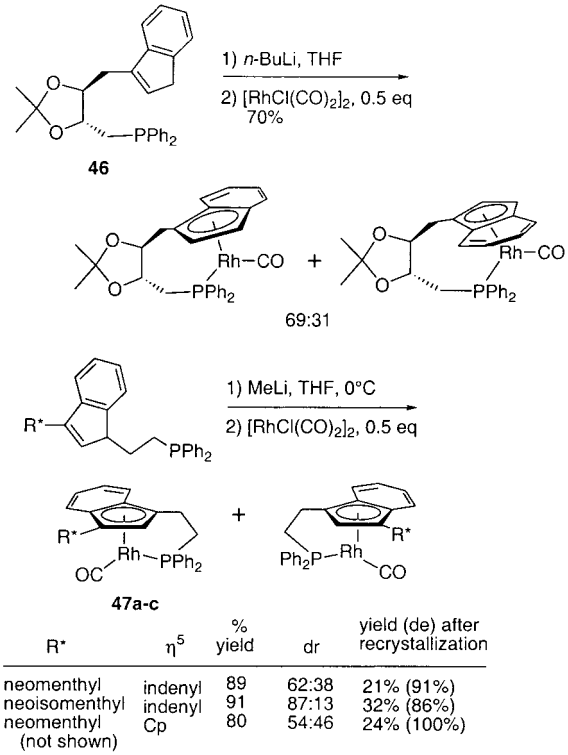
fied unambiguously, as the mixture crystallized with the same diastereomer ratio.



There are also a series of bidentate "half-sandwich" η^5-complexes that have been prepared in enantiopure form. Waymouth[70] described the synthesis of indenyl−amido complex **45** (eq 5), which could be isolated



Scheme 18



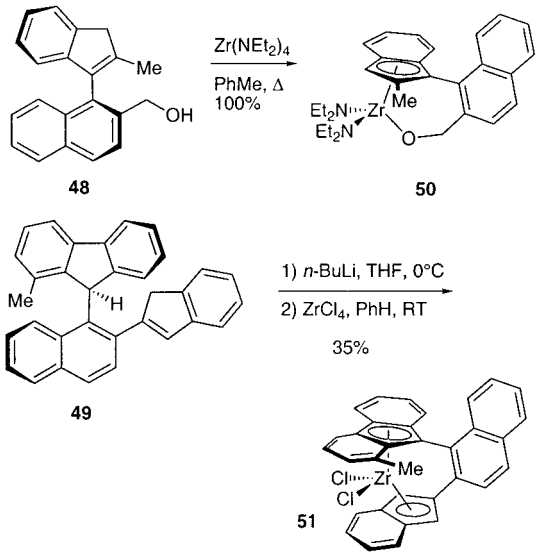
R*	η^5	% yield	dr	yield (de) after recrystallization
neomenthyl	indenyl	89	62:38	21% (91%)
neoisomenthyl	indenyl	91	87:13	32% (86%)
neomenthyl (not shown)	Cp	80	54:46	24% (100%)

as a single diastereomer following recrystallization. The complexation was only modestly selective however—1.33:1. The complex was also active as an olefin polymerization catalyst.

Tani studied the use of hybrid bidentate ligands to effect a highly diastereoselective installation of a Rh(I)CO fragment. Taking inspiration from the work of Green as well as that of Erker as discussed earlier, these ligands consist of an indene unit tethered to a phosphine group; a chiral group is either placed along the tether or attached directly to the indene. Initial results using a ligand, **46**,[71] (Scheme 18) which contained an L-tartrate-derived group as a chiral tether were promising, with production of the diastereomeric Rh(I) complexes in a 69/31 ratio. In a later version of this approach,[72] modification of the indene with an enantiopure neoisomenthol unit afforded the best results, producing the diastereomers of complex **47b** in an 87:13 ratio. However, the pure diastereomer could not be obtained; recrystallization of the mixture did not enhance the diastereomer ratio beyond 93:7. Use of neomenthyl instead of neoisomenthyl was less efficient (**47a**, 62:38), while employing a neomenthyl-modified cyclopentadienyl template was still less effective (**47c**, 54:46). In this latter case, however, the major diastereomer was obtained pure by recrystallization. The planar chirality of these complexes was subsequently used to control the chirality about the metal, as the oxidative addition reaction of complexes **47a** and **47b** with alkyl halides proceeded with impressive selectivity in the product rhodium(III) acyl complexes.

In addition to the previously discussed efforts of Bercaw (Scheme 13) and Halterman (Scheme 14), Baker and Wallace also demonstrated—on two occasions—that axial chirality can be effectively utilized to install planar chirality (Scheme 19). Es-

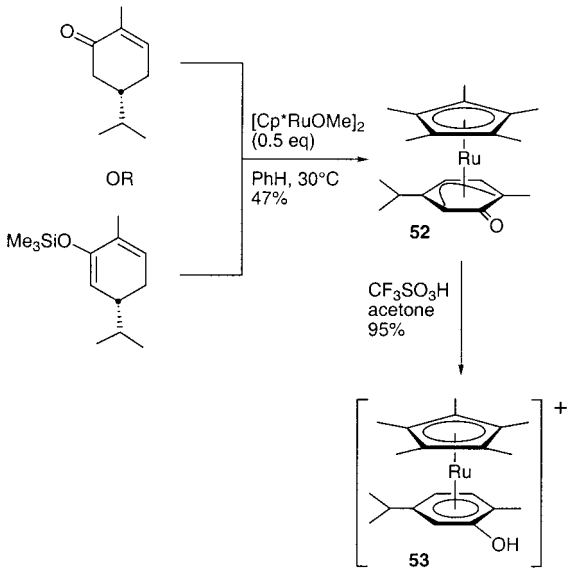
Scheme 19



sential to the success of this strategy was their ability to prepare ligands **48** and **49**, each in enantiopure (>99% ee) form. Simple treatment of ligand **48** with $Zr(NEt_2)_4$ quantitatively provided the bidentate η^5-indenyl-alkoxide metal complex **50**;[73] inspection of the ^{1}H NMR spectrum of the crude product indicated the presence of a single diastereomer. Likewise, deprotonation of **49** with excess *n*-BuLi followed by treatment with $ZrCl_4$ afforded the corresponding *ansa*-metallocene **51**.[74] While the enantiomeric excess of this complex was not determined, it presumably would also be >99%, as treatment with acetic acid led to the recovery of enantiopure ligand **49**, indicating no loss of optical integrity due to racemization (i.e., rotation about the chiral axis).

Finally, a relatively limited number of enantiopure η^5-complexes *not* derived from cyclopentadienyl-type precursors have also been prepared. Most are derived from steroid precursors and as such have been categorized separately in this review article (see below). A distinct example—the diastereoselective π-complexation of a natural product, carvone—has

Scheme 20



been studied by Koelle.[75] In particular, it was found that treatment of (*R*)-(−)-7,8-dihydrocarvone or its derived trimethylsilyl enol ether with $[Cp^*RuOMe]_2$ caused a dehydrogenation resulting in the formation of the corresponding η^5-oxocyclohexadienyl species **52** (Scheme 20). Although the substrate's central chirality was ultimately destroyed during this transformation, the preferred approach of the Cp*Ru fragment would still be expected to be anti to the isopropyl group of the terpene. Indeed, this was shown to be true as the enantiomeric purity of complex **52** was determined to be 100%. Treatment of **52** with triflic acid produced η^6-phenol cation **53** without loss of enantiomeric purity.

2.9. Efforts to Derivatize Steroids: η^5- and η^6-Complexes

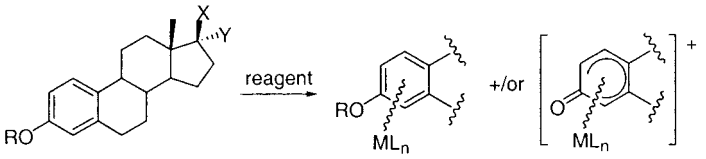
The complexations described in this section have been placed apart from those grouped by complex hapticity and bound metal. There is a substantial body of work that has focused on steroid A-ring modification with organometallic fragments, and while these efforts have usually produced the corresponding η^6-complexes, the formation of η^5-complexes or even mixtures of η^5- and η^6-complexes have occasionally resulted. Thus, from an organizational standpoint, it is more prudent to present these results separately, in tabular form. An exception has made for Harman's markedly distinct η^2-osmium complexes that have already been discussed (section 2.3).

The considerable effort put forth to modify steroids with organometallic moieties has largely been aimed at biological studies or for rapid and nontraditional synthetic entry into steroid derivatives with therapeutic properties, and review articles which highlight these endeavors are available.[14,15] The synthetic aspect of this work has almost exclusively focused on preparing organometallic complexes of β-estradiol and its derivatives; the resulting planar chiral complexes are summarized in Table 7.[76−86] Inspection of the α/β ratios listed in Table 7 do not seem to reveal any obvious pattern; in several cases (entries 6, 8−11) respectable selectivity was obtained and the major diastereomer was the α-isomer (of the η^6 and/or η^5 complex). While these results suggest that complexation selectivity might be predictable (due to a presumed nonbonding interaction between the C(13) methyl and an β-organometallic fragment that would be expected to raise the energy of the β-isomer), in fact many of the other complexations entered in Table 7 proceed either with only marginal diastereoselectivity, are stereorandom (entries 3, 4, 14), or even proceed with opposite selectivity (entries 1, 2, 13). Thus, any attempt to predict selectivities of complexation for any as-yet-uncomplexed steroidal substrate should probably be avoided; any diastereoselectivity obtained would likely be fortuitous.

2.10. η^6-Chromium Complexes

Chromium(0) tricarbonyl arene complexes are perhaps the most-widely studied of the organotransition-metal compounds by virtue of their ease of prepara-

Table 7. Formation of η^5- and η^6-Complexes from Modification of Steroidal A-Rings



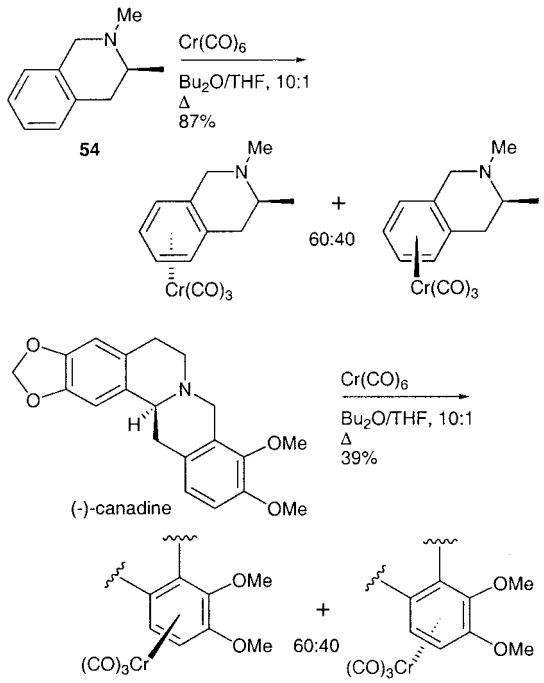
entry	R	X	Y	reagent	η^6 α:β	η^5 α:β	ML_n	%y	η^6/η^5	ref
1	H	OH	H	$Cr(CO)_6$	1:1.2		$Cr(CO)_3$	27		76
2	TBS	OH	H	$Cr(CO)_6$	1:1.4		$Cr(CO)_3$	70		76
3	Me	OTBS	H	$Cr(CO)_6$	1:1		$Cr(CO)_3$	85		77
4	Me	*a*	*a*	$Cr(CO)_6$	1:1		$Cr(CO)_3$	88		77
5	$(CH_2)_3OH$	OH	H	$Cr(CO)_6$	1.3:1		$Cr(CO)_3$	57		78
6	H	OH	H	$[RuCl(Cp^*)]_2$	α only	1.4:1	RuCp*	ca. 100	1:1.5	79
7	Me	O	O	$[CpRu(MeCN)_3]^+PF_6^-$	2.3:1		$[RuCp]^+$	53		80
8	H	OH	H	$[Cp^*RhS_n]^{2+}(BF_4)_2^-$	6.4:1	7.3:1	$[RhCp^*]^{2+}$	100	1.7:1	81
9	H	OH	H	$[Cp^*Ru(MeCN)_3]^+OTf^-$	5.6:1		$[RuCp^*]^+$	65		82
10	$(CH_2)_3OH$	OH	H	$[Cp^*Ru(MeCN)_3]^+OTf^-$	9:1		$[RuCp^*]^+$	77		82
11	H	OH	Ph	$[Cp^*Ru(MeCN)_3]^+OTf^-$	2.3:1		$[RuCp^*]^+$	37		83
12	H	OH	H	$[Cp^*Ir(acet)_3]^{2+}(BF_4)_2^-$, NEt_3		9:1	$[IrCp^*]^+$	82		84
13	Me	O	O	$[Mn(CO)_5]^+BF_4$	1:1.5		$Mn(CO)_3$	51		85
14	Me	OMe	H	$[Mn(CO)_5]^+BF_4$	1:1		$Mn(CO)_3$	91		85
15	H	OH	H	$[Cp^*Ru(OMe)]_2$ /TfOH	1.5:1		$[RuCp]^+$	45		86
16	H	OH	H	$[Cp^*Ru(OMe)]_2$		4:1	RuCp	73		86
17	H	O	O	$[Cp^*Ru(OMe)]_2$ /TfOH	2:1		$[RuCp]^+$	60		86
18	H	O	O	$[Cp^*Ru(OMe)]_2$		3:1	$RuCp^+$	72		86

[a] X = Y = $-OCH_2CHO-$.

tion, stability, functional group compatibility, and value for stereoselective manipulation of aryl side chains. There have been numerous published examples of diastereoselective complexations using *racemic* substrates; many of these have already been described in review articles.[5,6] The selective complexation of the $Cr(CO)_3$ fragment to one of the diastereotopic arene faces of *enantiopure* substrates is commonly carried out through the use of chiral auxiliaries; that strategy will be discussed in section 3 of this review article. Of the alternate approaches, simple discrimination of the two faces of unsymmetrically substituted ring-fused arenes may be somewhat selective and has been utilized on occasion. Perhaps more efficient has been the strategy of delivering the $Cr(CO)_3$ fragment to one arene diastereoface by a presumptive precomplexation of it to a heteroatom, suitably positioned at or near a chiral center on one of the side chains of an *ortho*-disubstituted benzene derivative. The application of each of these approaches toward installation of planar chirality will be summarized below.

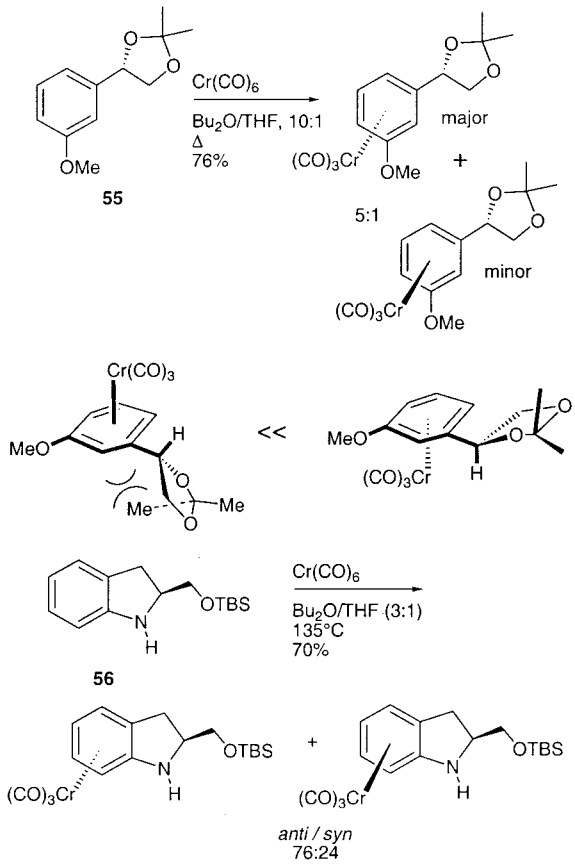
Some of the earliest examples of simple, "unaided" complexations were those on steroid derivatives by Jaouen and by Gill; these are included in Table 7.[76−78] Selectivities were poor. In a similar vein, Davies[87] reported the complexation of tetrahydroisoquinoline **54** (Scheme 21) using the standard thermodynamic conditions ($Cr(CO)_6$ in refluxing dibutyl ether/THF); the corresponding complex was obtained as an inseparable 60:40 mixture of diastereomers (87% yield). The major isomer was established to be the one with the organometallic fragment anti to more hindered face. In a related case, the more electron-rich arene unit of (−)-canadine was regioselectively complexed in a 39% yield;[88] the ratio of diastereomers was also 60:40. The rigidity of each of these fused-ring molecules precluded heteroatom delivery; diastereoselectivity was likely the result of a thermodynamic preference for the least hindered face.

Scheme 21



In a case with far greater conformational flexibility, Jones[89] found that the complexation of aryl acetonide **55** proceeded with a respectable degree of selectivity (5:1) under thermodynamic conditions (Scheme 22). Since the related diol undergoes complexation with no selectivity, one can speculate that the acetonide *gem*-dimethyl groups are essential for the selectivity observed for **54**. Indeed, β-face complexation would force the acetonide to adopt a conformation that would place one of the methyl groups directly under the arene ring. Complexation to the α-face yields a

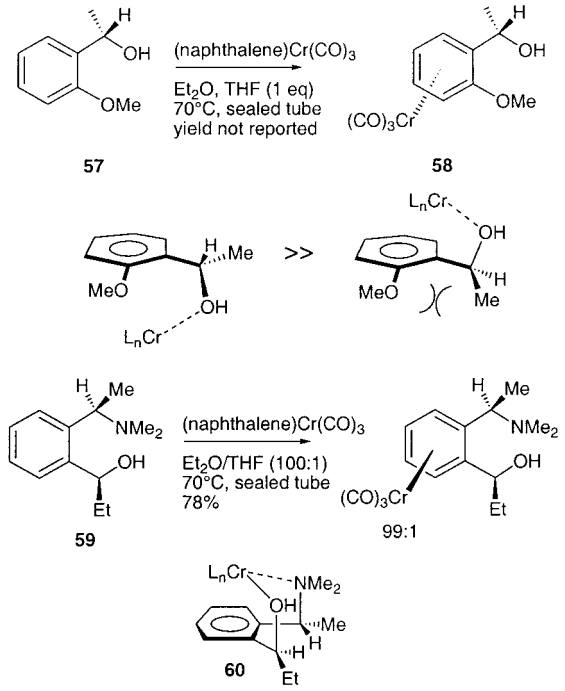
Scheme 22



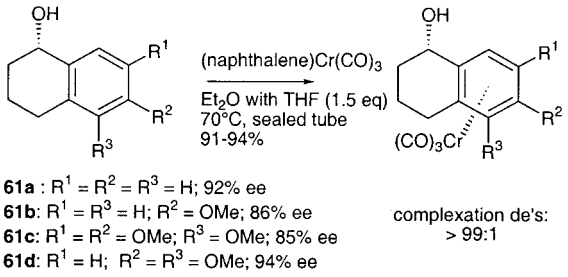
product that would lack this destabilizing nonbonded interaction, as the *gem*-dimethyl groups point well away from the arene ring as well as the $Cr(CO)_3$ fragment. In another case, Agbossou prepared the chromium complexes derived from silyloxymethylindoline **56** with a modest 76:24 selectivity in favor of the anti isomer. These complexes were then modified to aminophosphine phosphinites for use as ligands in enantioselective rhodium-catalyzed hydrogenations of ketones.[90]

On the other hand, heteroatom delivery of the organometallic fragment has been a more successful tactic for diastereoselective formation of η^6-chromium arene complexes. A conformational preference in chiral benzyl alcohol **57** allowed Uemura to utilize heteroatom delivery to selectively prepare complex **58**.[91] Use of (naphthalene)$Cr(CO)_3$ as the $Cr(CO)_3$ transfer reagent (Et_2O with 1 equiv of THF, 70 °C, sealed tube) afforded a single diastereomer (Scheme 23); for comparison, use of $Cr(CO)_6$ under thermodynamic conditions (Bu_2O/heptane/THF (10:1:1)) with *racemic* **57** produced the complex as a 78:22 mixture. Outstanding 99:1 facial selectivity was achieved for the complexation of aryl amino alcohol **59**,[92] a result of not one but two heteroatoms which could align in a highly favored, sterically unhindered conformation (**60**, Scheme 23) in order to deliver the $Cr(CO)_3$ to the preferred face. In the case of the more conformationally restricted cyclic benzyl alcohols **61a**−**d**, Schmalz[93] was able to effect an exceptionally diastereoselective complexation using [(naphthalene)$Cr(CO)_3$] as the organometallic transfer reagent; other conditions (using $Cr(CO)_6$) gave decreased selectivities and/or yields. Clearly the proximity of the alcohol to the arene ring allowed for nearly exclusive delivery of the $Cr(CO)_3$ fragment to the more hindered face of each substrate.

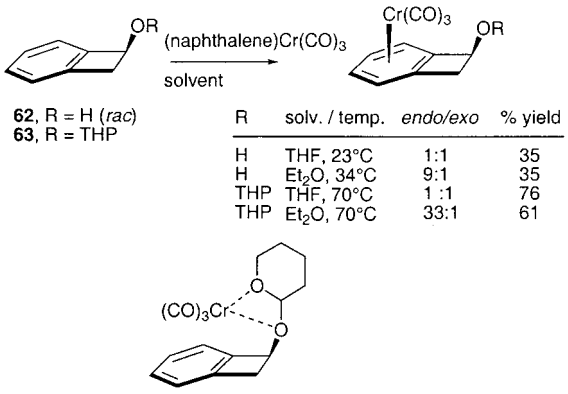
Scheme 23



Scheme 24



Scheme 25

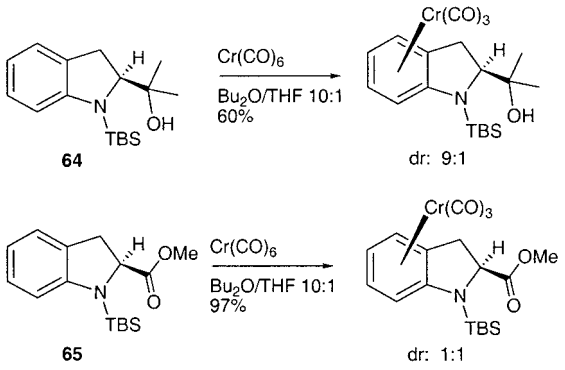


Scheme 24

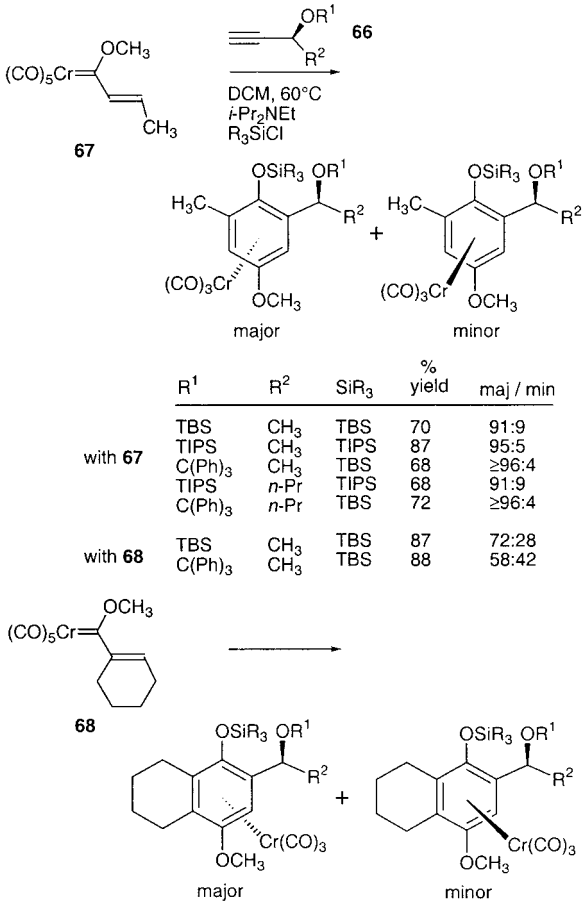
Scheme 25

The later results of Kündig[94] suggest that the particular solvent used in the complexation can have a direct impact on the diastereomer ratio. For example, neither the ring-fused arene cyclobutanol **62** nor its THP derivative **63** could be selectively complexed in THF (Scheme 25). However, in diethyl ether dramatic improvements in selectivity were obtained, as **62** and **63** were complexed with diastereomer

Scheme 26



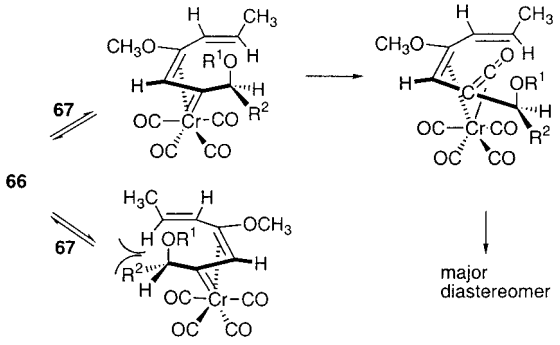
Scheme 27



	R^1	R^2	SiR_3	% yield	maj / min
with **67**	TBS	CH_3	TBS	70	91:9
	TIPS	CH_3	TIPS	87	95:5
	$C(Ph)_3$	CH_3	TBS	68	≥96:4
	TIPS	*n*-Pr	TIPS	68	91:9
	$C(Ph)_3$	*n*-Pr	TBS	72	≥96:4
with **68**	TBS	CH_3	TBS	87	72:28
	$C(Ph)_3$	CH_3	TBS	88	58:42

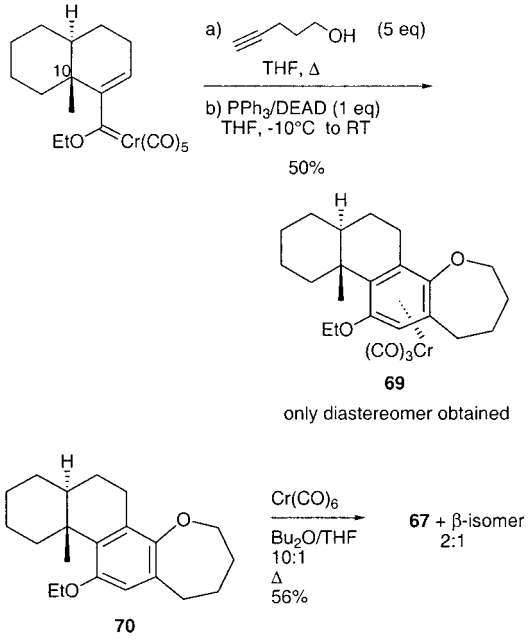
ratios of 9:1 and 33:1, respectively. It was speculated that the THF must have competed with the substrate oxygen atom(s) for chromium coordination sites, negating the intramolecular heteroatom delivery of the $Cr(CO)_3$ fragment that would result in a facially selective complexation. In noncoordinating Et_2O, the chromium atom was able to bind to the substrate as desired to deliver the $Cr(CO)_3$ fragment selectively. Conversion of alcohol **62** into its THP derivative **63** "extended the reach" of this substituent, allowing the $Cr(CO)_3$ fragment to be delivered to the syn face with an even greater selectivity (33:1). Finally, the selective complexation (9:1) of indoline **64** by Jones[95] is attributable to heteroatom delivery, as the related carbomethoxy indoline **65** is complexed without selectivity (Scheme 26).

Scheme 28

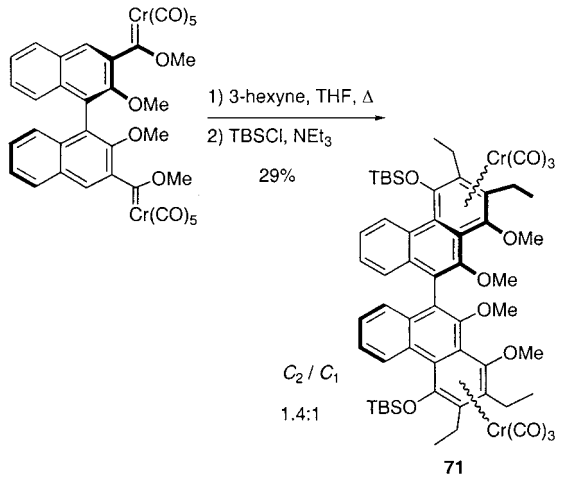


The Dötz benzannulation provides an alternate approach toward the synthesis of η^6-chromium *para*-dioxygenated arene complexes and has been recently reviewed.[96] Instead of complexing a preformed aromatic system, this transformation constructs the complexed arene ring from an alkyne and an unsaturated alkoxy pentacarbonyl chromium carbene complex. In principle, preferential coordination of the $Cr(CO)_3$ fragment to one of the two arene faces of the ultimate product could be directed by chirality situated on either reaction partner. Indeed, efforts have been reported involving either strategy. Dötz used carbene complexes bearing chiral auxiliaries—this approach will be discussed in section 3.5 of this review. On the other hand, Wulff[97] described the highly diastereoselective syntheses of a number of arene $Cr(CO)_3$ complexes using enantiopure propargyl ethers, **66** (Scheme 27). Stereoselectivity was enhanced with larger protecting groups on the propargylic oxygen (such as TIPS or trityl), provided that *trans*-propenyl carbene complex **67** was utilized rather than the cyclohexenyl analogue **68**. Evidence pointed to allylic strain in one of the two possible η^1,η^3-vinyl carbene complexed intermediates as a likely origin of stereoselectivity (Scheme 28). Subsequent studies by Wulff[98] revealed that the use of chiral cyclohexenyl carbenes with simple alkynes also was a viable strategy for diastereoselective complexation;, however, these studies were performed on racemic substrates. Quayle[99] did in fact use a chiral, nonracemic cyclohexenyl carbene in a tandem Dötz—Mitsunobu sequence—a single diastereomeric η^6-chromium arene complex (**69**) was obtained as a consequence of the steric congestion about the β-face caused by the C(10) methyl group (Scheme 29). Interestingly, the benzannulation approach proceeded with significantly higher selectivity than simple complexation of oxepin **70**. Finally, Dötz[100] used axial chirality to induce asymmetry in a slightly diastereoselective preparation of bis-η^6-chromium arene complexes **71**. Four diastereomeric products, each possessing elements of planar and axial chirality, were possible, though only two were formed. While the major C_2-symmetrical diastereomer could be readily separated and distinguished from the minor C_1-symmetrical product, the exact stereochemical assignment has not been made (Scheme 30).

Scheme 29



Scheme 30

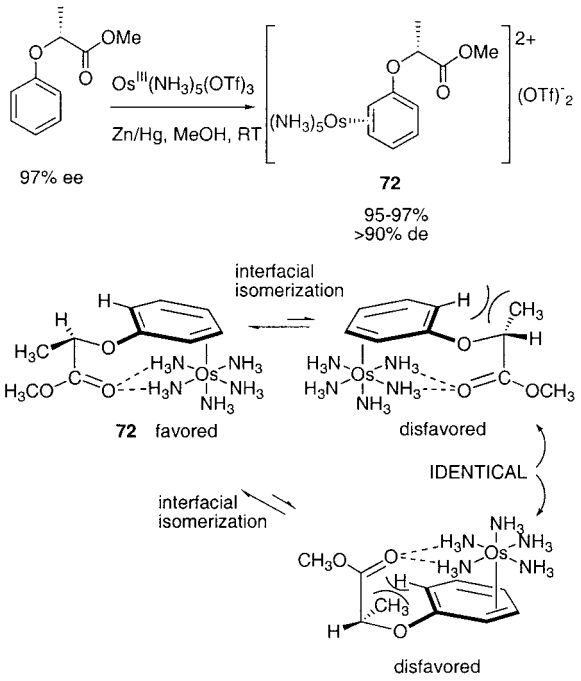


3. Diastereoselective Complexation Induced by Chiral Auxiliaries

3.1. η^2-Osmium Complexes

Harman developed rich chemistry of η^2-osmium arene complexes in which the aromatic ligand is dearomatized and thus becomes activated toward reactions with electrophiles, producing a variety of functionalized compounds.[101] Unfortunately, due to the fluxional nature of the complexes as a result of intrafacial linkage isomerizations, this chemistry had long been limited to the preparation of racemic material. However, the recent disclosure[102] that a chiral lactate auxiliary, attached through a phenolic oxygen, can direct a diastereoselective complexation (Scheme 31) no longer limits the scope of this methodology—it can now be used to prepare stereodefined cyclohexenes and cyclohexenones with high enantiomeric purity (Scheme 32). Though there is some variability in the outcome of the complexation event, typical diastereomer ratios for this high-yielding process were greater than 10:1. The lactate

Scheme 31



auxiliary directed the coordination of the metal fragment to primarily one face, giving complex **72**, through a combination of hydrogen-bond interactions (between the lactate ester carbonyl and the metal ammine ligands) and steric interactions (between the lactate methyl group and an *ortho* ring hydrogen on the arene). These steric interactions are likely to also reduce the fluxionality of the complex.

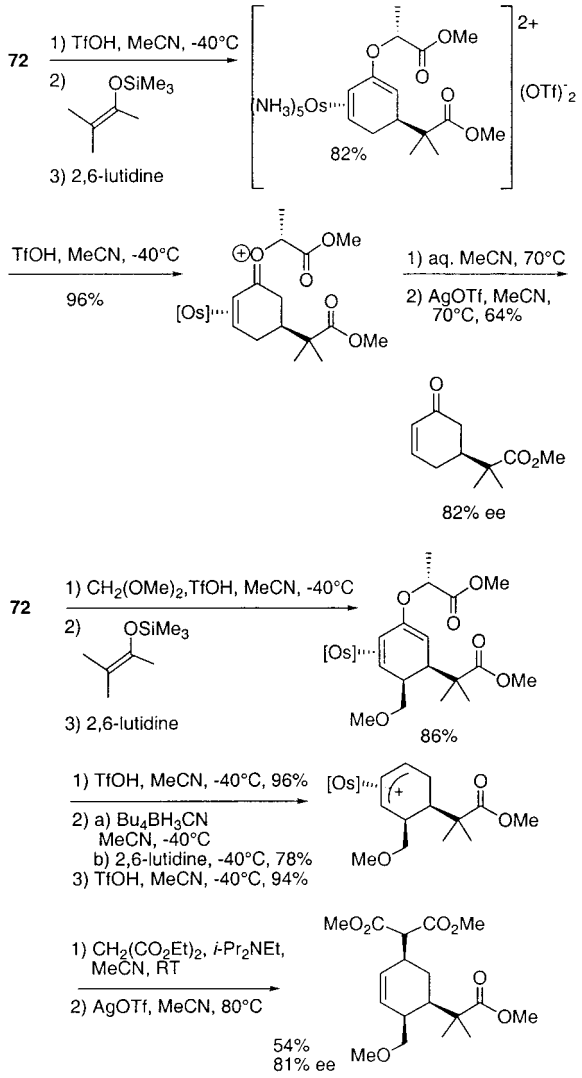
3.2. η^3-Tungsten Complexes

Liu demonstrated that enantiopure π-allyl tungsten complexes can be prepared from achiral tungsten propargyl complexes by use of a chiral auxiliary.[103] The intermediate η^2-allene cation (see Scheme 5, section 2.4) formed by protonation of the η^1-propargyl species was treated with sodium oxazolidinonate, which intercepted one of the metal-bound carbonyl ligands. Rearrangement of the presumed tungsten−aminocarbonyl intermediate upon warming, via insertion of the carbonyl into the central carbon of the allene, afforded diastereomeric π-allyl tungsten complexes in a 3.8:1 ratio (Scheme 33). Separation and further elaboration of these complexes provided π-allyl-γ-lactone complexes; interestingly, this approach afforded the *anti*-π-complexes and not the *syn*-isomers discussed earlier (section 2.4). This distinction turned out to be unimportant, as *syn*- or *anti*-π-allyl-γ-lactone complexes were shown to lead to the same homoallylic alcohol upon condensation with an aldehyde.

3.3. η^4-Iron Complexes

One of the earliest reports of diastereoselective complexation was that of Helquist and co-workers,[104] who prepared an enantiomerically pure enone ligand, **73**, with a side chain possessing a chelating phosphite group (Scheme 34). This ligand was designed to effect selectivity by virtue of conformational preferences

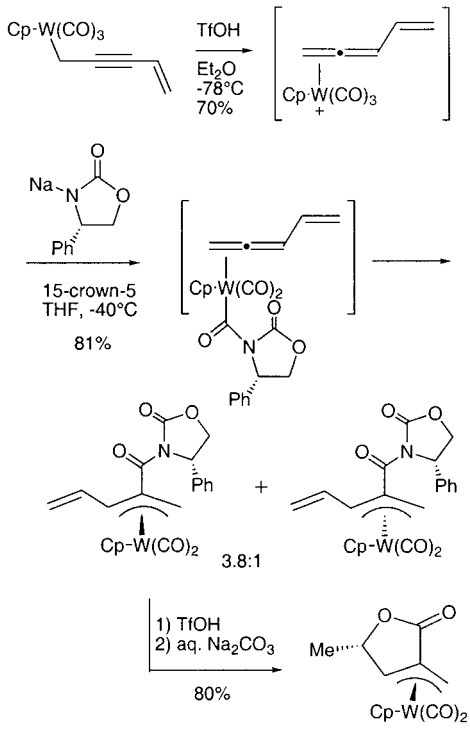
Scheme 32



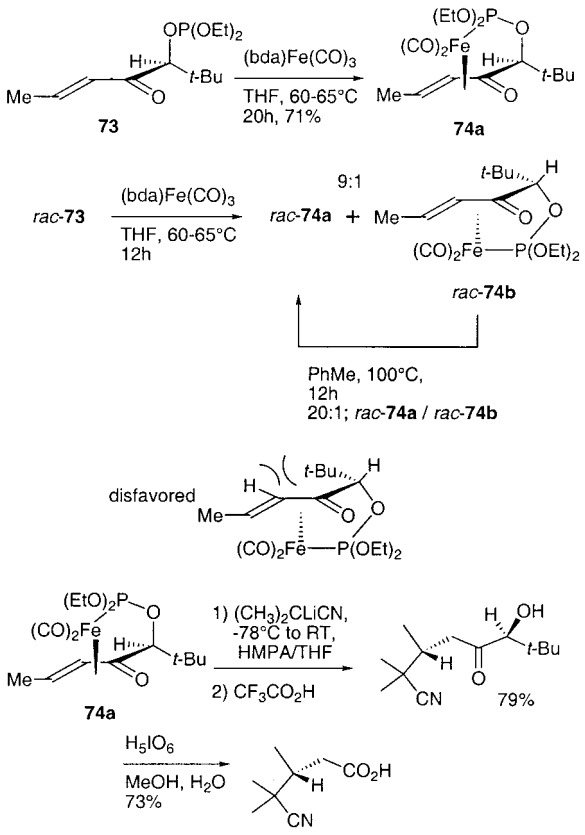
imposed by the chirality of the side chain; the concept is related to that used by Harman some years later, as described in Scheme 31. Treatment of ligand **73** with (bda)$Fe(CO)_3$ (60−65 °C, THF, 20 h; bda = benzylideneacetone) did indeed place the $Fe(CO)_3$ fragment onto a single diastereoface to produce enantiopure **74a**. Its diastereomer, **74b**, could only be detected upon shorter reaction times (12 h, starting with *rac*-**73**), and after isolation it could be isomerized to *rac*-**74a** by additional heating. Thus, this complexation was under thermodynamic control. The enantiopure product could be further transformed via diastereospecific addition of α-lithioisobutyronitrile; the chiral auxiliary was later removed by an oxidative cleavage.

There have been a number of published methods which have sought to utilize chiral auxiliaries in order to effect diastereoselective complexations of diene and azadiene systems. The benchmark paper in this area is that of Pearson and co-workers, published in 1994.[105] Although removal of the employed auxiliaries was not discussed, reported facial selectivities were good to excellent. For the azadiene series, the chiral hydrazine SAMP was elaborated into the corresponding *N*-amino-1-aza-dienes **75** by treatment with cinnamaldehyde or benzylideneacetone (Scheme 35). In the former case, **75a**, an acceptable diastereomer ratio (6:1) was obtained with $Fe_2(CO)_9$ in refluxing Et_2O; use of other solvents resulted in diminished selectivities. When conformational constraints where enhanced, as in substrate **75b** (as a result of placement of a C(2)-methyl group capable of restricting N−N bond rotation), complex-

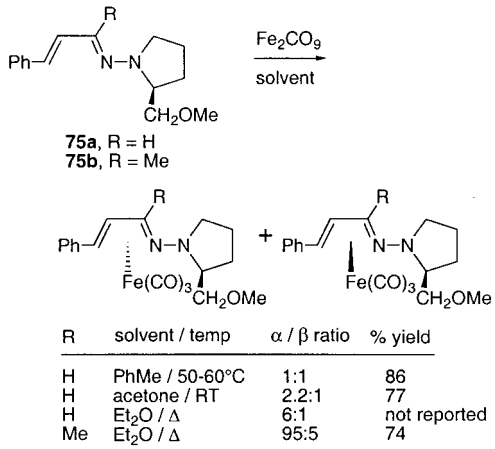
Scheme 33



Scheme 34

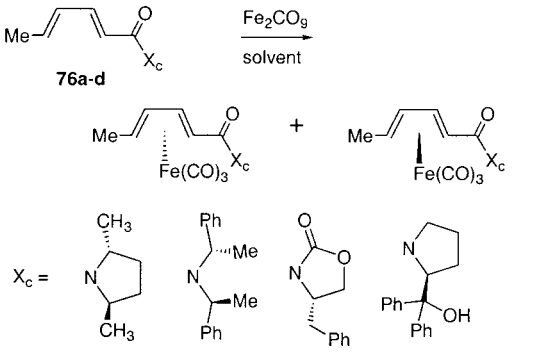


Scheme 35



R	solvent / temp	α / β ratio	% yield
H	PhMe / 50-60°C	1:1	86
H	acetone / RT	2.2:1	77
H	Et_2O / Δ	6:1	not reported
Me	Et_2O / Δ	95:5	74

Scheme 36



X_c	solvent / temp	α / β ratio	% yield
a	Et_2O / Δ	4.6:1	95
b	Et_2O / Δ	1.5:1	46
c	Et_2O / Δ	2:1	78
d	Et_2O-DCM / Δ	>99:1	40 (84, brsm)

ation selectivity dramatically increased to 95:5. The ease of separation of the diastereomers, either by chromatography or recrystallization, was not discussed. For the diene series, an array of a chiral dienamides, **76a**−**d**, were prepared (Scheme 36). For substrates **76a**−**c**, diastereomer ratios of the corresponding complexes were poorer (1.5:1 to 4.6:1) by comparison to the analogous azadienes. This was likely a result of the increased distance between the auxiliary's chiral center and the diene as compared to azadienes **75**. Fortunately, excellent diastereocontrol was obtained with the sterically demanding (*S*)-2-(diphenylhydroxymethyl)pyrrolidine auxiliary; **76d** was complexed in a >99:1 ratio, though it was not possible to improve the yield beyond 40% (or 84% based on 48% recovered starting material).

Our own contribution to this field has been the diastereoselective complexation of an iron tricarbonyl unit to a series of enantiopure sulfinyl dienes.[106] Unlike Schmalz's ligands,[26] the sulfinyl dienes are acyclic and thus likely to possess increased conformational mobility which in principle could prove detrimental to efforts to differentiate the diene diastereofaces. To restrict this mobility, we took advantage of 1,3-allylic strain in order to define the optimal location for the sulfoxide group along the diene. Thus, sulfinyl dienes of Type I (Scheme 37)

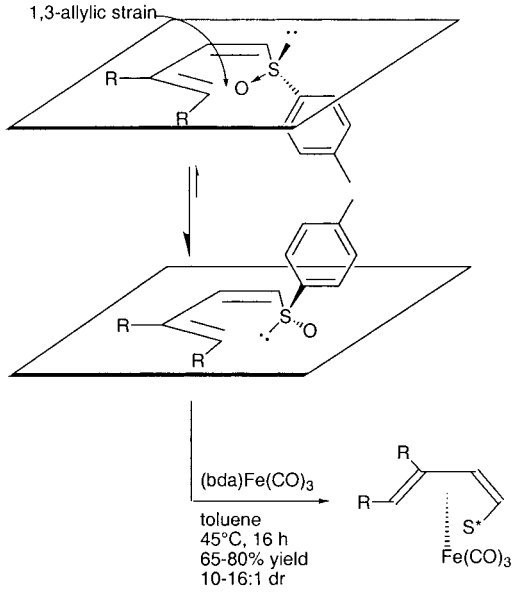
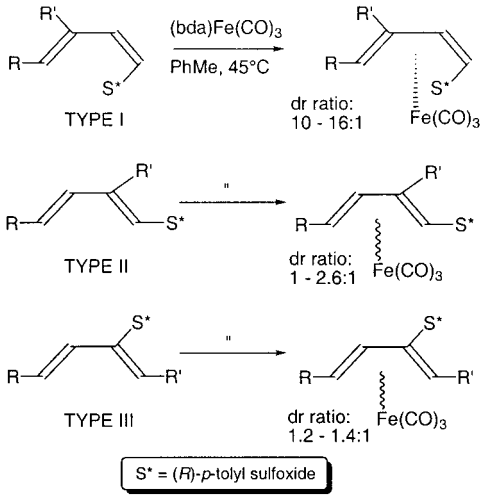


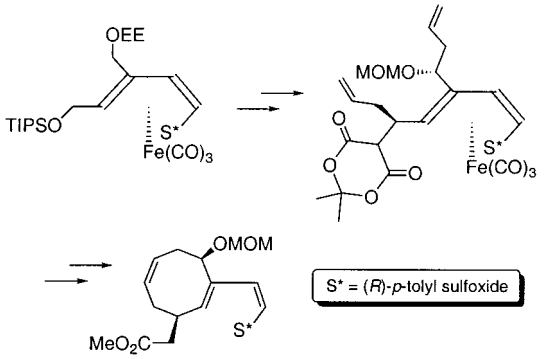
Figure 2. Likely conformers of a (*Z*)-1-sulfinyldiene involved in the diastereoselective complexation with an $Fe(CO)_3$ fragment.

Scheme 37

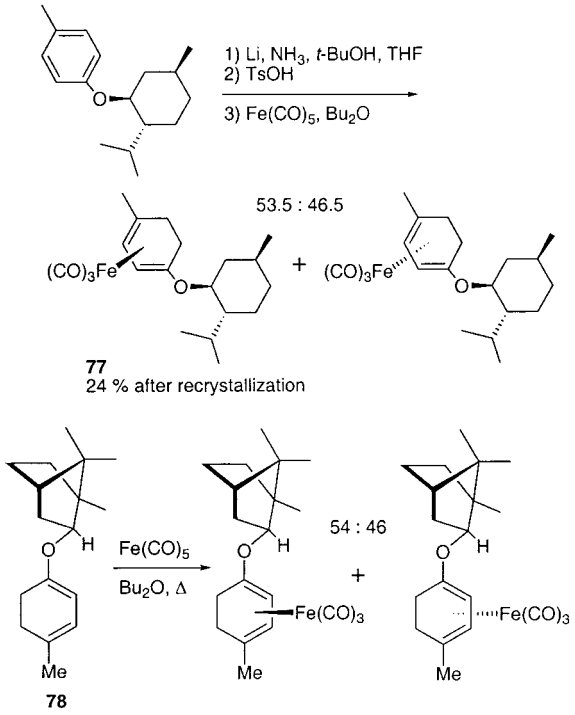


displayed impressive complexation diastereoselectivity (10:1 to 16:1), where as those of Type II or III did not. Though Types II and III sulfinyl dienes are certainly capable of allylic strain when R′ ≠ H, it seems likely that the bulky *p*-tolyl unit of the sulfoxide would not be positioned close enough to the diene system to effect the desired level of selectivity. On the other hand, (*Z*)-1-sulfinyldienes (Type I) would likely adopt a low-energy conformation (Figure 2) which would place the *p*-tolyl group in a position which would significantly block the approach to one of the diene faces (the β face, as we have defined it). While unsubstituted (*Z*)-1-sulfinyldienes (Type I, R = H) or their 4-substituted analogues (Type I, R = $CH(OEt)_2$) can be efficiently complexed using $Fe(CO)_5$/NMO, 3,4-disubstituted-(*Z*)-1-sulfinyldienes (Type I; R, R′ ≠ H) required the use of $(bda)Fe(CO)_3$ as the complexing reagent to obtain good (ca. 80%) chemical yields. In virtually all cases, the diastereomeric complexes were easily separable by silica gel chromatography, and it was demonstrated that complexations with $(bda)Fe(CO)_3$ were under kinetic

Scheme 38



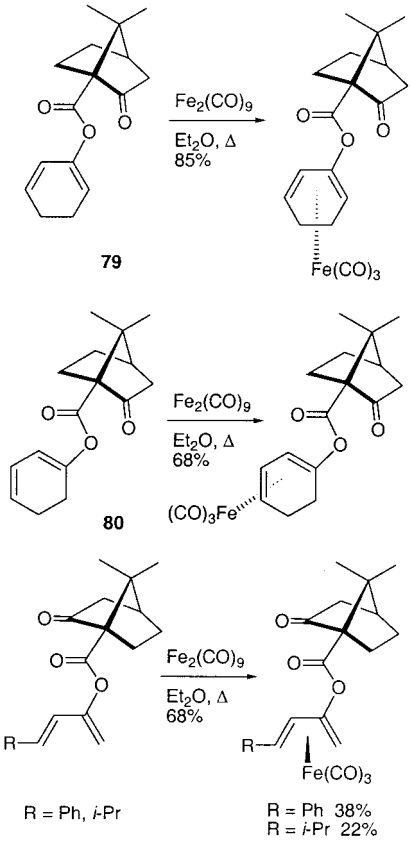
Scheme 39



control. The 3,4-disubstituted-(*Z*)-1-sulfinyldienes were used as templates for the construction of six- through nine-membered carbocyclic rings via ring-closing metathesis chemistry.[107] Additional stereocenters were installed along the periphery of the diene as the metathesis substrate was being assembled (Scheme 38; only approach to eight-membered analogue shown). This strategy for asymmetric synthesis is one of a small but growing collection of examples featuring the use of sulfoxides in combination with organotransition-metal chemistry.[108] Here the approach is an indirect one—the sulfoxide controls the installation of the planar chirality, and once installed the iron fragment controls the formation of additional chiral centers.

Efforts using auxiliaries to effect similar selectivity on cyclic diene systems have unfortunately been less successful (Scheme 39). For example, Potter's report[109] of the complexation of a diene, equipped with an enantiopure menthyl auxiliary, was barely diastereoselective (53.5:46.5). The major product **77** was separated from the minor isomer by recrystallization, giving a poor overall yield of 24%. Similarly, Ong's complexation of an analogous substrate, **78**,[110] where

Scheme 40

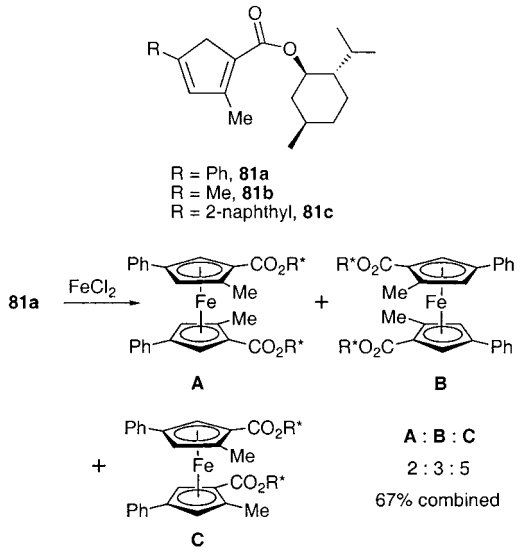


the menthyl group had been replaced by a 4-isobornyl auxiliary (derived from (+)-camphene), required "several tedious" recrystallizations in order to obtain a diastereomerically pure complex from a 54:46 mixture. A subsequent effort using heteroatom-possessing auxiliaries derived from (−)-proline and (−)-alanine (in order to take advantage of heteroatom-delivery of the organometallic fragment) were only marginally better—the best example afforded a 62:38 diastereomer ratio.[111] In each of these cases it is apparent that the origin of the poor selectivity is a result of the lack of conformational restrictions about the linkage to the auxiliary. Without a more careful design for minimizing these degrees of freedom, any diastereoselectivity would be expected to be merely fortuitous. A marked improvement was in fact obtained by Yeh[112] with the use of a (+)-ketopinoxy auxiliary—coordination of the incoming $Fe(CO)_3$ fragment to the auxiliary's ketone prior to complexation was suggested as the cause of the complete preference for delivery to the less hindered diene face of **79** and **80** (Scheme 40). For acyclic systems, the transformation was not as successful. The 2-carboxy-1,3-dienes suffered from instability, and though single diastereomeric complexes were formed, yields were poor (22−38%). Finally, placement of the auxiliary at the terminal position of the diene system led to virtually no facial discrimination by the $Fe(CO)_3$ fragment.

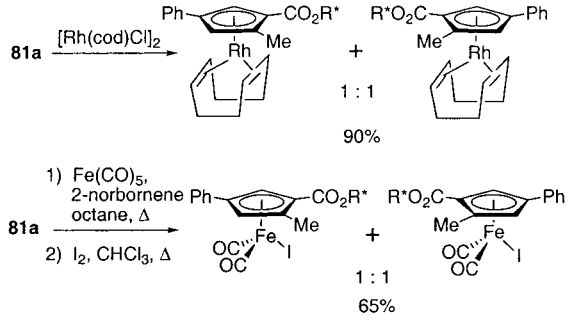
3.4. η^5-Complexes (Iron, Cobalt, Rhodium, Ruthenium)

In stark contrast to the excellent complexation diastereoselectivities frequently exhibited by cyclo-

Scheme 41



Scheme 42

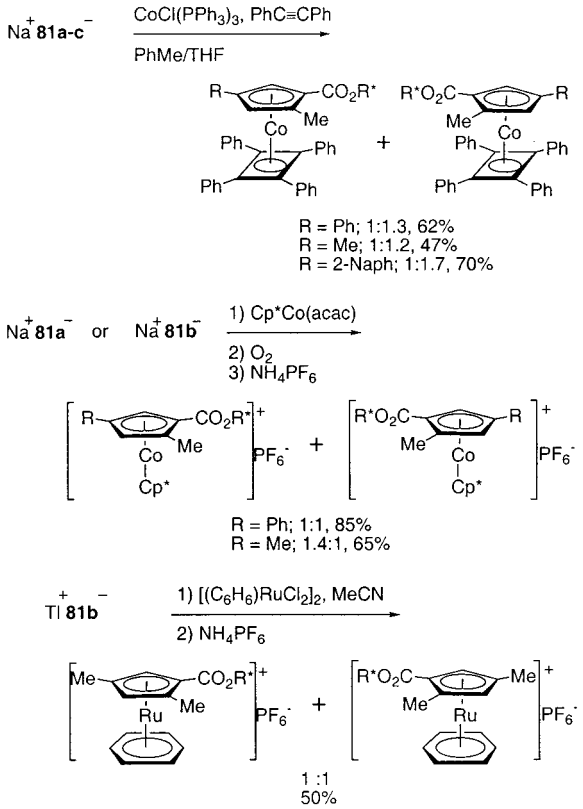


pentadiene ligands modified via direct attachment of *nonremovable* chiral units (menthoxy, isomenthoxy, etc.; section 2.8), cyclopentadiene ligands bearing *removable* auxiliaries generally have not been complexed with a high degree of facial selectivity. A group of these metal complexes has been prepared by Takahashi and co-workers, utilizing enantiopure 1-menthoxycarbonyl-2-methyl-4-substituted-1,3-cyclopentadiene ligands **81a**−**c** (Schemes 41−43).[113−119] Complexation of these ligands with a number of metal sources typically occurred with respectable chemical yields though with poor or random facial selectivity. However, the complexes (R* = (−)-menthyl) were typically purified by either preparative HPLC or fractional recrystallization, affording diastereomerically pure complexes in modest or very low yields. A comparison of these diastereomeric ratios with those in section 2.8 suggests that the increased distance between the chiral auxiliary and the cyclopentadienyl ligand (as a result of two atoms which link them) must substantially reduce conformational restrictions which would allow for the differentiation of the ligand diastereofaces. This increased conformational freedom is likely the direct cause of the observed loss of selectivity.

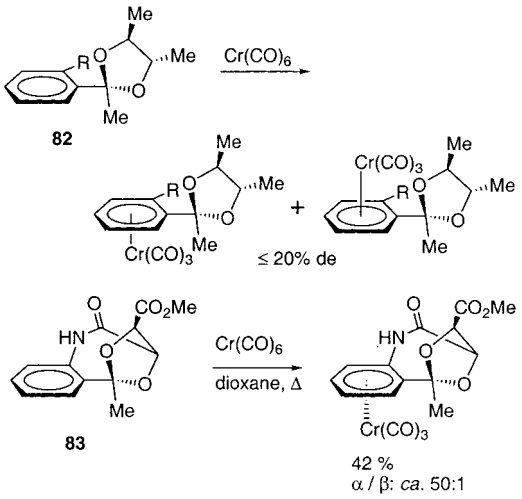
3.5. η^6-Chromium Complexes

The earliest attempt to utilize a removable chiral unit for the purpose of effecting a diastereoselective complexation of a $Cr(CO)_3$ fragment to an arene was

Scheme 43

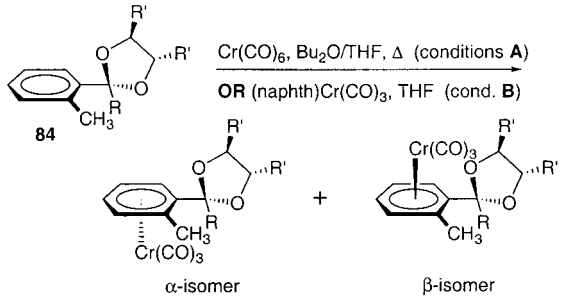


Scheme 44

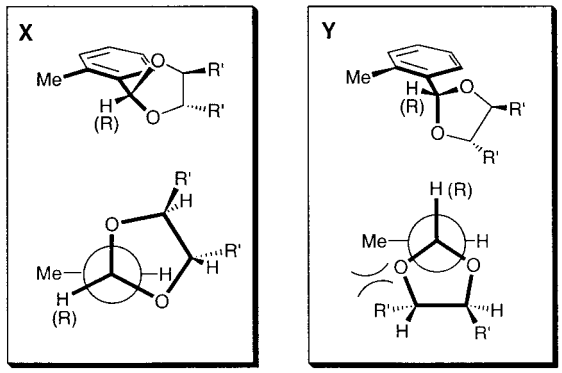


that of Solladié-Cavallo in 1979.[120] Ortho-substituted aryl ketals **82** derived from (*S*,*S*)-(+)-butanediol were prepared and subjected to $Cr(CO)_6$; details in this paper were rather sketchy, but none of the complexations proceeded with diastereomer ratios of better than 60:40 (Scheme 44). Even with the conformational restriction imposed on the ketal unit by the ortho alkyl group, the facial differentiation with this particular auxiliary was not significant. Levine[121] later reported a highly diastereoselective complexation (50:1) by using a substantially conformationally restricted substrate **83** derived from (+)-dimethyl tartrate. The lactam formed between the *o*-amine group and one of the tartrate ester groups effectively forced the ketal unit to occupy a position that efficiently blocked one of the arene faces. Unfortu-

Scheme 45



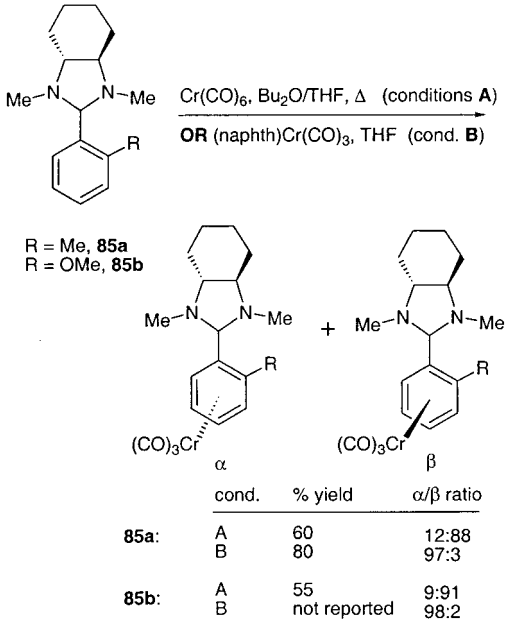
arene	R	R'	cond.	α/β ratio	yield, %
84a	Me	CH_2OH	A	53:47	77
84a	Me	CH_2OH	B	69:31	not determined
84b	Me	CO_2Et	A	67:33	69
84c	Me	$CON(Me)_2$	B	57.5: 42.5	not determined
84d	H	$CON(Me)_2$	B	74:26	61



nately, attempts to remove the chiral auxiliary or hydrolyze the amide bond under acidic conditions were unsuccessful.

Aubé returned to using systems more closely related to those of Solladié-Cavallo and reported some modest success.[122] Rather than being limited to ortho-substituted aryl ketals derived from (*S*,*S*)-(+)-butanediol, Aubé surveyed related chiral acetals and ketals decorated with an array of other functionalities (Scheme 45). The best diastereomeric ratio (74:26) was observed using kinetic conditions with substrate **84d**, which featured a chiral acetal derived from *N*,*N*,*N*′,*N*′-tetramethyltartramide. Two views of a likely staggered conformation, **X** (R = H), suggest a kinetic preference for α-delivery of the $Cr(CO)_3$ fragment as result of the position of the acetal unit which raises the $\Delta G^{\ddagger}$ of *β*-delivery by hindering the approach to the *β*-face. Consideration of another likely conformation obtained by rotation about the sp^3-carbon−arene bond, **Y** (R = H), reveals a steric interaction between one of the amide groups (R′) and the ring methyl (or the arene ring itself). This nonbonding interaction raises the energy of conformation **Y** as well as the energy of the corresponding transition state for *β*-delivery of the $Cr(CO)_3$ fragment. (Delivery to the α-face would require overcoming a still higher $\Delta G^{\ddagger}$ in this conformation.) Taken together, these rationalizations point to a mild kinetic preference for α-delivery, and these arguments seem to be strengthened by the loss of selectivity observed with the chiral ketal (**84c**). Though equipped with the same chiral auxiliary, the replacement of the hydrogen atom with a methyl group leads to transition states corresponding to **X** and **Y** which, in all likelihood, are more similar in energy since they possess similar nonbonding interactions. Thus, the preference for α- over *β*-delivery is diminished. In any case, that only modest diastereoselectivity is observed, even in the best case studied (**84d**), suggests that transition state energies are not dramatically different to cause highly selective approach of the organometallic fragment to a single arene face under kinetic conditions. The relevant chiral center(s) in this particular auxiliary is(are) simply too far removed from the arene face to effect significant facial discrimination; this problem is exacerbated by an inability to "lock" the auxiliary into a specific conformation that would greatly bias fragment approach to one arene face.

Scheme 46



	cond.	% yield	α/β ratio
85a:	A	60	12:88
	B	80	97:3
85b:	A	55	9:91
	B	not reported	98:2

The real breakthrough in this area was the report by Alexakis of the use of a chiral aminal possessing C_2 symmetry, as summarized in Scheme 46.[123] Kinetic complexation of arene **85a** and **85b** with (naphthalene)$Cr(CO)_3$ (THF, RT) proceeded with excellent diastereoselectivities (94−96% de) in favor of the α-isomer and in good yield. Interestingly, the selectivity was reversed under thermodynamic conditions [$Cr(CO)_6$, Bu_2O/THF, 140 °C], affording the *β*-isomer with somewhat reduced selectivity (76−82% de) and yield. The authors offered no explanation for the observed behavior, though it is tempting to speculate based on the reported X-ray crystal structure of the major thermodynamic product derived from **85b**. If one assumes that the conformation found in solution closely resembles that found in the solid state, then three structural features appear to be relevant. First, the arene substituent (methyl or methoxy) is positioned to avoid contact with the auxiliary, and second, the arene plane is not perpendicular to the auxiliary but rather is positioned at an angle which minimizes contact with its pseudoaxial methyl group (Figure 3). Third, one of the *N*-methyl groups is a pseudoequatorial position about the five-membered aminal ring and points away from the arene *β*-face, while the

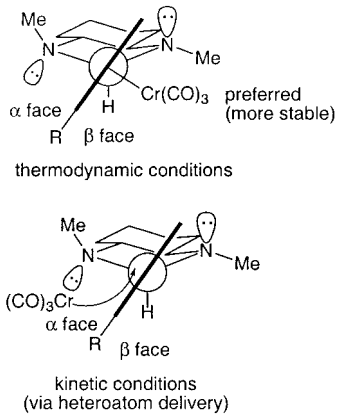
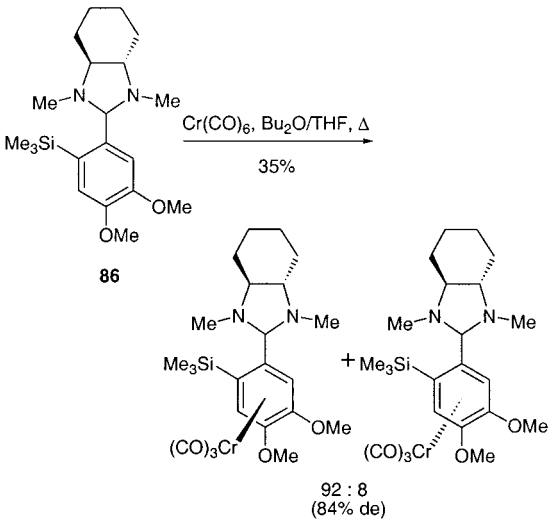


Figure 3. Possible outcomes in the diastereoselective complexation of an aryl aminal with a $Cr(CO)_3$ fragment.

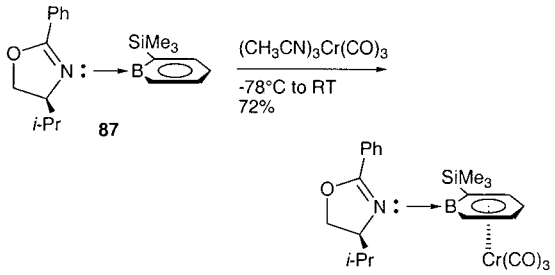
Scheme 47



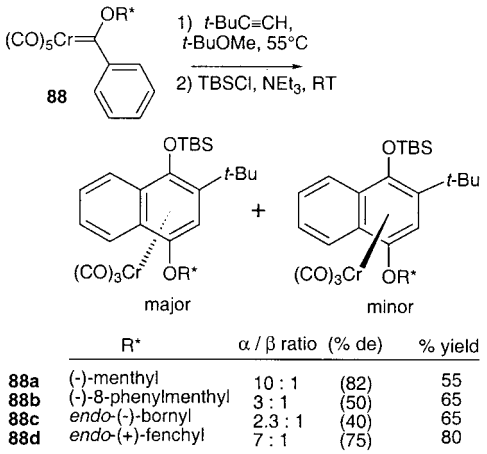
other *N*-methyl group is pseudoaxial and is positioned near the arene α-face. These three features permit the two faces of the arene to be differentiated while minimizing rotation about the bond connecting the arene to the auxiliary. Under thermodynamic conditions, the *β*-isomer would be more stable and is thus preferentially formed; the α-isomer would be of higher energy as a result of the nonbonding interaction with the pseudoaxial methyl. On the other hand, under kinetic conditions, heteroatom delivery of the $Cr(CO)_3$ fragment is likely to operate; the nitrogen atom whose methyl serves to sterically destabilize the α-isomer under thermodynamic conditions is now well-positioned to deliver the metal fragment to the α-face. Kündig used this methodology in a recently published synthesis of (−)-lasubine(I);[124] arene **86** was complexed under thermodynamic conditions with good diastereoselectivity (84% de). Removal of the aminal auxiliary proceeded uneventfully via acid hydrolysis (HCl/THF, 95%; Scheme 47)

In an effort to prepare an enantiopure Lewis acid based on planar chirality, Fu reported a unique approach to the diastereoselective complexation of an arene.[125] Here the arene unit was an *o*-trimethylsilyl borabenzene, and the chiral auxiliary (an oxazoline) was attached by an N−B dative bond (Scheme 48). Rotation about this bond was minimized by the steric

Scheme 48



Scheme 49



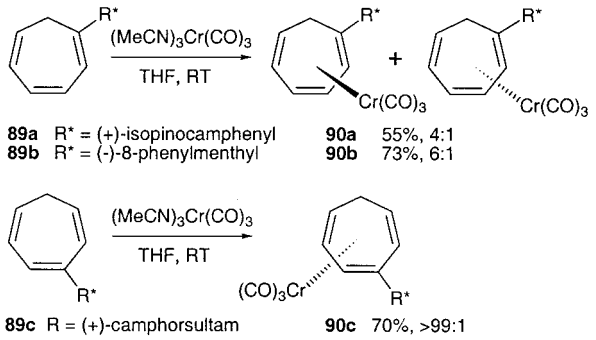
	R*	α / β ratio	(% de)	% yield
88a	(-)-menthyl	10 : 1	(82)	55
88b	(-)-8-phenylmenthyl	3 : 1	(50)	65
88c	*endo*-(-)-bornyl	2.3 : 1	(40)	65
88d	*endo*-(+)-fenchyl	7 : 1	(75)	80

interaction between the trimethylsilyl group and the isopropyl of the oxazole; the borabenzene−oxazoline adduct **87** appeared to be a single atropisomer by ^1H NMR spectroscopy. As a result, the phenyl group of the oxazoline auxiliary occupied a position over the *β*-face of the arene and kinetic complexation afforded α-face complexation exclusively. It was noted that selectivity decreased when the complexation was carried out at higher temperatures (9:1 at RT) or with different chiral oxazolines (or tertiary amines).

As mentioned in section 2.10, η^6-chromium arene complexes can be prepared by utilizing the Dötz benzannulation and facial selectivity can be obtained by chiral modification of either reaction partner. Dötz reported some success in this area via attachment of chiral auxiliaries to the chromium carbene complex (Scheme 49).[126] The highest diastereoselectivities were obtained with menthyloxy and *endo*-fenchyl carbenes **88a** and **88d** (10:1 and 7:1, respectively), and while it again seems likely that differentiation occurred at the stage of formation of the η^1,η^3-vinyl carbene complexed intermediates (see Scheme 28), the conformational flexibility of the chiral auxiliaries made any rationalization or prediction difficult. Indeed, Dötz pointed out that stereoelectronic factors may play some as-yet-undetermined role, since benzannulation with vinyl analogues of aryl carbenes **88** failed to proceed with significant diastereoselectively.

Finally, Rigby described[127] the auxiliary-directed diastereoselective complexation of cycloheptatrienes **89** to afford η^6-chromium tricarbonyl triene complexes **90** (Scheme 50), which were shown to participate in higher-order cycloaddition reactions. Trienes **89a** and **89b**, each possessing a chiral auxiliary

Scheme 50



positioned at the triene terminus, were converted to the corresponding complexes (**90a** and **90b**) with good selectivity (4:1 and 6:1, respectively). The major diastereomers could each be isolated by recrystallization. On the other hand, triene **89c**, with an auxiliary attached to an internal position of the triene, afforded a single diastereomeric chromium tricarbonyl complex, **90c**. Due to the apparent lack of restriction imposed on the conformation of the auxiliaries with respect to the triene units, the authors were unable to rationalize the origin of the complexation diastereoselectivities.

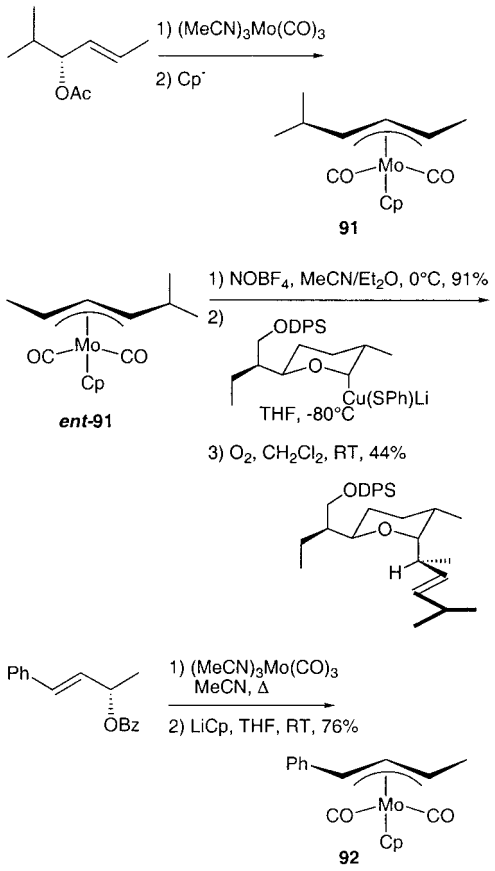
4. Diastereoselective Complexation by Displacing Preexisting Chirality

Most of the enantiopure planar chiral transition-metal complexes in this category possess unsymmetrical η^3-allyl ligands, and these have typically been prepared from allylic bromides or acetates or vinylic epoxides. For these cases, the ability to prevent or minimize isomerization of the η^3-allyl complex via $\sigma-\pi-\sigma$ rearrangements is essential for isolation as enantiomerically and/or diastereomerically homogeneous material; as will be discussed, this may be achieved in some cases by careful control of reaction conditions. In keeping with the theme of this review article, transiently formed metal complexes derived from enantiomerically pure substrates (e.g., those likely formed along the reaction pathway of palladium-catalyzed allylic alkylations) will not be included here nor will those prepared from preexisting complexes of different hapticity (e.g., η^3-iron complexes derived from η^2- or η^4-complexes).

4.1. η^3-Molybdenum Complexes

Faller was the first to investigate the transformation of an enantiopure allylic acetate into the corresponding η^3-molybdenum complex.[128] Though chemical yield was not reported, it was unequivocally established that complex **91** (Scheme 51) was formed with retention of chemistry. Kocienski[129,130] later reported that the enantiomeric complex, derived from the enantiomeric allylic acetate, was actually obtained as an 85:15 mixture of *exo*/*endo* rotamers (rotation about the Mo$-\pi$-allyl bond). The derived cationic nitrosyl complex was utilized in a synthetic sequence and was thus treated with α- or β-glucosyl copper reagents to regio- and diastereoselectively afford *C*-glycosides. Similarly, the only other reported

Scheme 51

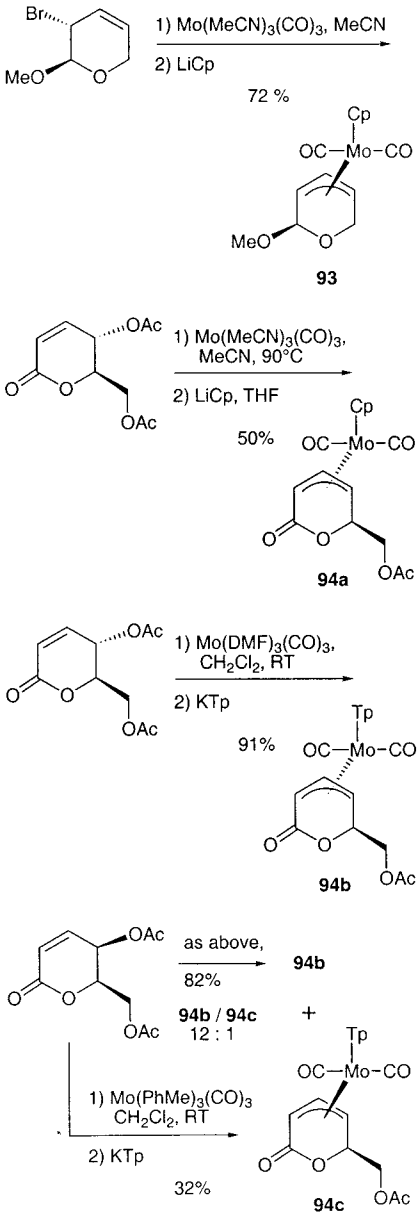


enantiopure acyclic η^3-molybdenum complex, **92**,[131] was prepared with retention from the corresponding allylic benzoate and obtained as a 13:1 mixture of *exo*/*endo* rotamers. However, treatment of the derived cationic nitrosyl complex with a organocopper(I) nucleophile was nonregioselective.

To date, Liebeskind and co-workers have solely been responsible for investigations involving enantiopure η^3-molybdenum complexes derived from cyclic precursors. These studies have revealed that changes in Mo(0) source, temperature, leaving group, solvent, and substrate sterics may each impact the key oxidative addition step and thus can effect the stereochemistry of the product complex. Initial work revealed distinct pathways for the reaction of an allylic bromide and an allylic acetate using Mo(MeCN)$_3$(CO)$_3$ followed by CpLi; the former[132] proceeded with inversion (producing **93**) and the latter[133] with retention to give **94a**. Use of KTp rather than CpLi similarly afforded **94b**[134] in better yield. However, use of a diastereomeric allylic acetate under identical conditions led to a surprising result: the inversion product **94b** predominated (12:1). The minor diastereomer, retention product **94c**, was prepared independently by treatment with the more labile Mo(toluene)(CO)$_3$ (Scheme 52).

To investigate these observations in the absence of steric or conformational effects brought about by the choice of substrate, additional studies were carried out using "sterically unbiased" allylic acetate **95** (Scheme 53).[134] The inversion product (**96a**) again dominated (66:34) using Mo(DMF)$_3$(CO)$_3$, and this

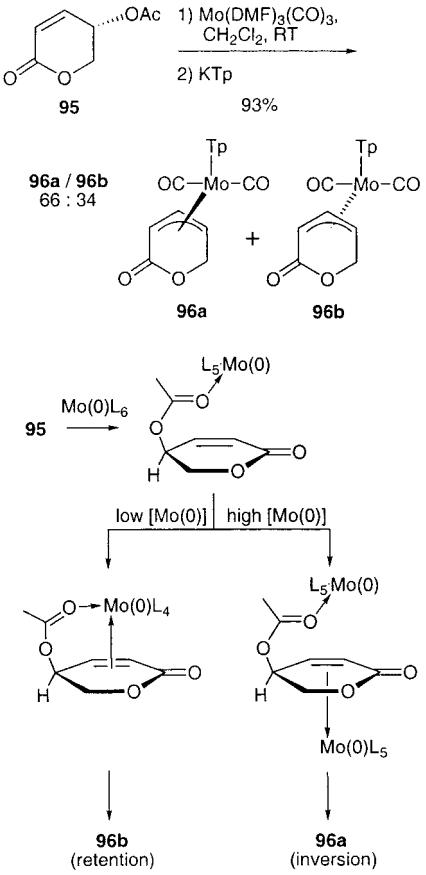
Scheme 52



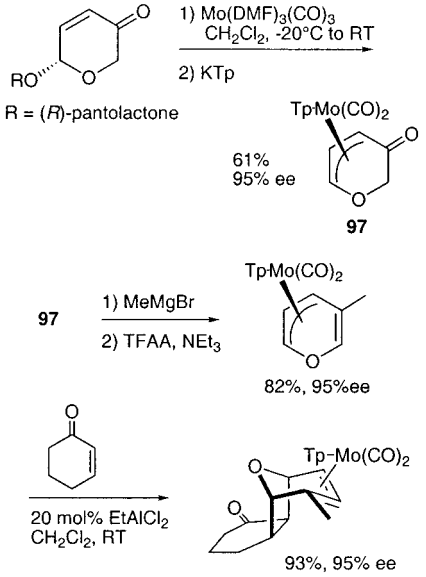
selectivity could be improved by lowering the reaction temperature (from RT to −40 °C) or using an excess of the Mo(0) source. On the other hand, the retention product (**96b**) could be obtained with excellent enantiopurity by utilizing (toluene)$Mo(CO)_3$ (ee's > 95%) or by a slow inverse addition of $Mo(DMF)_3(CO)_3$ to the substrate (94% ee). It was speculated that the pathway leading to the retention product was preferred with low Mo(0) concentration or the presence of a Mo(0) species capable of low coordination numbers such as the labile (toluene)$Mo(CO)_3$. A chelated intermediate was proposed which would be capable of leading to the retained stereochemistry upon oxidative addition.

Complexes of this type were envisioned to be "enantiomerically pure scaffolds" for the synthesis of homochiral organic molecules. To this end, enantiopure η^3-molybdenum complex **97** was prepared[135] (via inversion) and ultimately modified for use as a partner in [5+2] cycloaddition reactions with a number of electron-deficient alkenes. The resulting

Scheme 53



Scheme 54

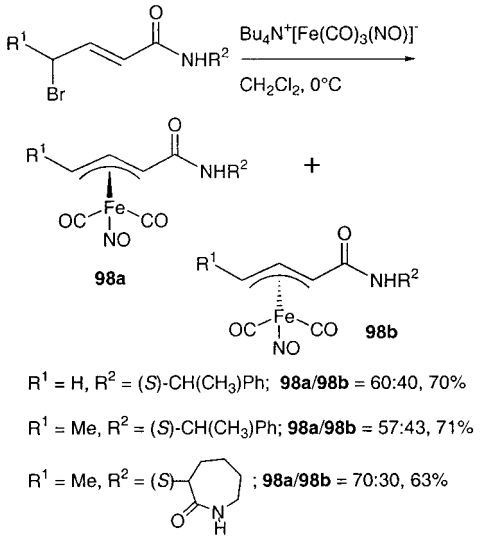


oxabicyclo[3.2.1]octenes were typically produced with an excellent degree of enantiopurity (Scheme 54).

4.2. η^3-Iron Complexes

The two types of enantiopure η^3-iron complexes that have been directly prepared by displacement of a preexisting chiral center—η^3-allyldicarbonylnitrosyl iron complexes reported by Nakanishi[136] and Ley's η^3-allyltricarbonyliron lactone complexes[137,138]—have

Scheme 55



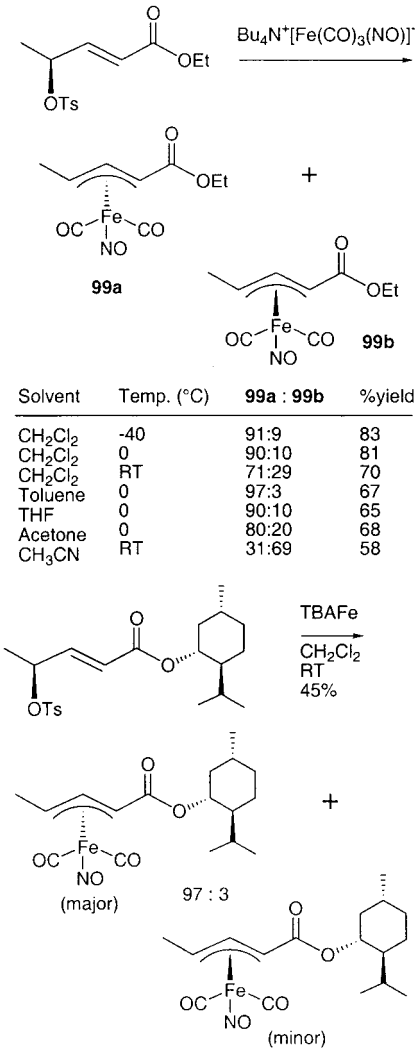
each been the subject of recent reviews and thus will only be briefly covered here.

Enantiopure η^3-allyldicarbonylnitrosyl iron complexes have been prepared via two similar approaches. In the first method, diastereomeric γ-bromo-α,β-unsaturated amides were utilized; the amide nitrogen was incorporated into a chiral auxiliary. Treatment with tetrabutylammonium tricarbonylnitrosylferrate (TBAFe) afforded the η^3-iron complexes in good yield but with only slight diastereoselectivities. Major and minor diastereomeric complexes, **98**, were readily separated by chromatography. Ester analogues could also be prepared and separated, but complex formation was completely nonselective (Scheme 55).[139]

A superior approach eschewed the use of chiral auxiliaries and instead simply relied on the synthesis of enantiomerically pure allylic tosylates. Enantiomeric ratios of the product complexes, **99**, varied with temperature and solvent with the best results (97:3) obtained by treatment of the allylic tosylate with TBAFe in toluene at 0 °C. The inversion product was preferred in all solvents except acetonitrile, where a 69:31 enantiomeric ratio favored the retention product (Scheme 56).[140] Complex preparation with the analogous allylic bromides did not proceed with the degree of enantioselectivity observed with the tosylates, as only a 38% ee was obtained. The authors speculated that the diminished selectivity using the bromide analogues could be a result of "the intervention of a radical process" but offered no experimental data to support this. Interestingly, when a menthyl ester auxiliary was employed along with an allylic tosylate, the "matched" case proceeded with excellent diastereoselectivity (97:3).[140] This was an improvement from the 71:29 ratio obtained under the same conditions (CH_2Cl_2, RT) without the presence of the auxiliary.

The unique π-allyltricarbonyliron lactone complexes prepared and studied by Ley and co-workers have been converted into a wealth of diverse products and have been utilized in natural product synthesis. Enantiopure complexes are readily available from the corresponding vinylic epoxides, and in cases where

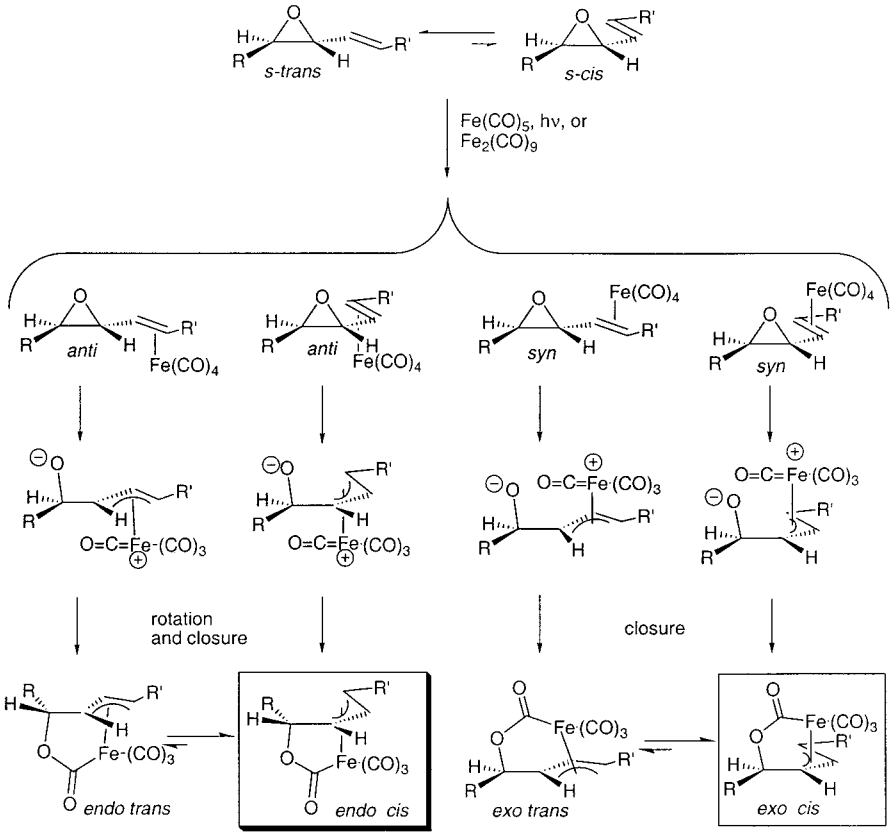
Scheme 56



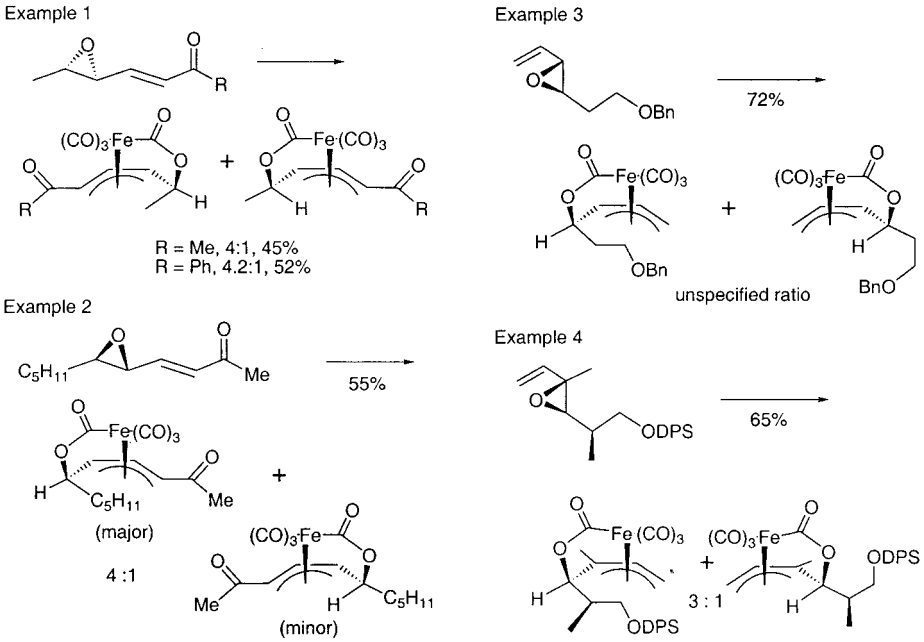
Solvent	Temp. (°C)	**99a** : **99b**	%yield
CH_2Cl_2	-40	91:9	83
CH_2Cl_2	0	90:10	81
CH_2Cl_2	RT	71:29	70
Toluene	0	97:3	67
THF	0	90:10	65
Acetone	0	80:20	68
CH_3CN	RT	31:69	58

diastereoselective complexation is possible, diastereoselectivities tend to be moderate (typically 3:1−4:1). The rationale for the origin of this diastereoselectivity has been proposed to derive from a preferential complexation of an $Fe(CO)_4$ fragment to the alkene anti to the epoxide.[138] Since the initial vinyl epoxide is conformationally flexible, four diastereomeric π-complexes would be produced as a consequence of anti or syn complexation to the *s-trans* or *s-cis* conformers. Isomerization of these initial π-complexes to alkoxy-π-allyl species would then enable interception of an iron-bound carbonyl ligand by the alkoxide to afford diastereomeric lactone complexes. Fortunately, equilibria between the two possible trans π-allyl complexes and their more stable cis π-allyl analogues simplifies the outcome significantly. Thus, for trans vinyl epoxides (as shown in Scheme 57), the major diastereomer typically is the one designated as *endo cis* (the C1-substituent points toward the iron atom); the minor diastereomer corresponds to the *exo cis* isomer (the C1-substituent points away from the iron atom). For cis vinyl epoxides this outcome is reversed—the *exo cis* isomer is the major product. The enantiomerically pure π-allyltricarbonyliron lactone complexes prepared by Ley and co-workers are summarized in Schemes 58[141−145] and 59.[146−149] Finally, an enantiopure *exo*-

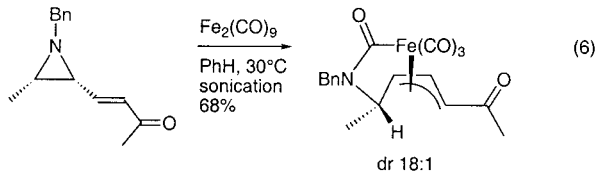
Scheme 57



Scheme 58



π-allyltricarbonyliron lactam has recently been prepared from the corresponding cis vinyl aziridine; the complex diastereomer ratio was 18:1 (eq 6).[150]

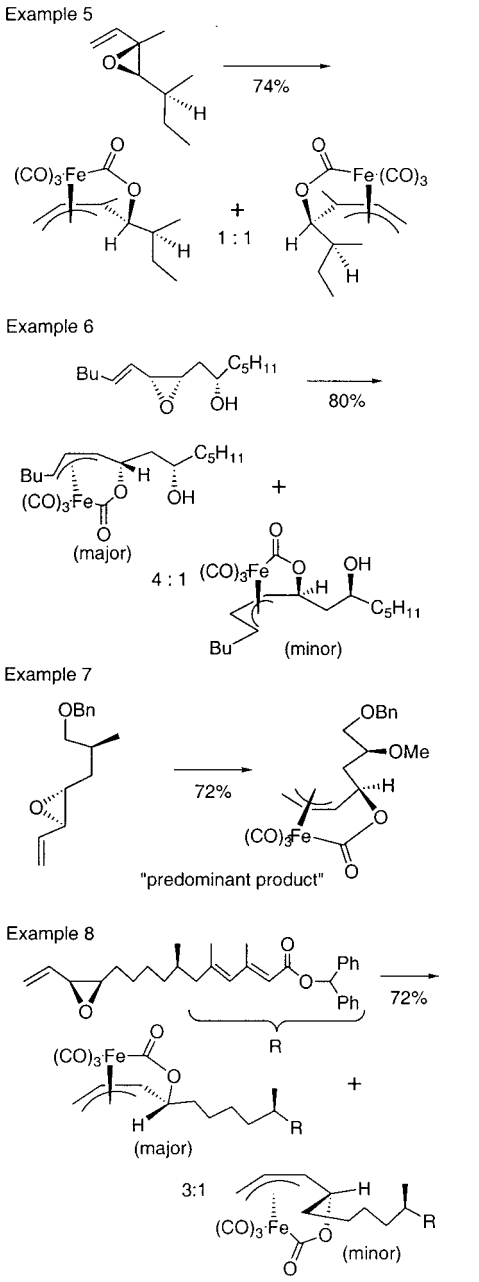


(6)

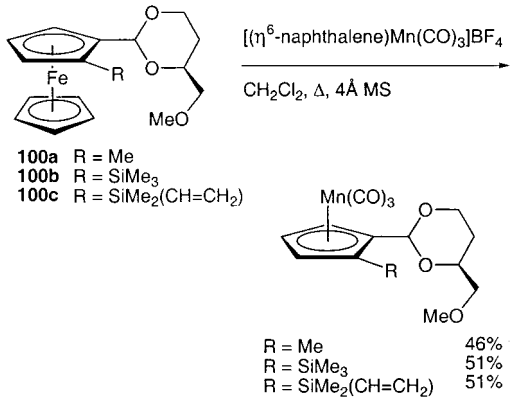
4.3. η^5-Manganese Complexes

Chung and Sweigart[151] reported an entirely unique approach to the synthesis of planar chiral organometallics from compounds with a preexisting chirality. Whereas the previous work summarized in section 4 of this review has generally used a stereogenic carbon center as the origin of asymmetry for the complexation event, Chung and Sweigart employed planar chirality. Known nonracemic planar

Scheme 59



Scheme 60



chiral ferrocenes, **100**, were treated with a $Mn(CO)_3$ transfer reagent to afford the planar chiral η^5-manganese complexes with complete inversion of absolute configuration (Scheme 60). Remarkably, no $CpMn(CO)_3$ was obtained in this reaction, implying that the incoming $Mn(CO)_3$ fragment preferentially complexes to the more substituted of the two ferrocenyl cyclopentadienyl units.

5. Concluding Remarks

Here examples of enantiopure planar chiral organometallic complexes prepared by the methodology of diastereoselective complexation have been brought together for the first time. Many of these complexes have been used as scaffolds for subsequent selective transformations, and after intentional demetalation enantiomerically pure or enantiomerically enriched organic compounds have been obtained. Other complexes have instead been utilized as catalysts for asymmetric transformations and/or polymerizations. Despite the diversity of these complexes, common themes governing the selectivity of complexation by the metal fragment emerge. For rigid systems high selectivity is most commonly observed in situations where (1) a heteroatomic delivery group is proximal to the π-ligand or (2) steric bulk directs coordination toward one face of the ligand at the expense of the other. For nonrigid (acyclic) systems, these effects are enhanced if nonbonding interactions (such as allylic strain) serve to minimize conformational degrees of freedom. In general, for substrates that are not carefully designed, the degree of selectivity is unpredictable and often diastereorandom.

This presentation and discussion has served to highlight a growing field, and one is optimistic that it will assist and stimulate further efforts in this area.

6. Acknowledgments

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