Asymmetric Dearomatization of η^2-Arene Complexes: Synthesis of Stereodefined Functionalized Cyclohexenones and Cyclohexenes

Mahendra D. Chordia and W. Dean Harman*

Contribution from Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901

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Abstract: A nonracemic η^2-arene complex (**2**) was prepared from (*R*)-(+)-methyl-2-phenoxypropionate and pentaammineosmium(II) with high coordination diastereoselectivity (>9:1). Complex **2** was then treated with HOTf, an acetal, or a Michael acceptor to generate 4*H*-oxonium complexes at low temperature. These products were then combined with a nucleophile (silylketene acetal or hydride) to form stable alkoxydiene complexes. Further reaction of these complexes with triflic acid yielded isolable enonium complexes, and subsequent hydrolysis formed substituted cyclohexenone complexes. Upon oxidative decomplexation, these materials provided substituted cyclohexenones isolated with high ee's (80−85%). The reaction of cycloenonium complexes with hydride led to the formation of cyclohexenyl ether complexes, and their oxidative decomplexation yielded substituted cyclohexenyl ethers with de and ee values >90%. Treatment of a cyclohexenyl ether complex with triflic acid gave an isolable π-allyl complex. The reaction of this material with a nucleophile followed by decomplexation afforded *cis*-1,4,5-trisubstituted cyclohex-2-enes with ee's ranging from 80 to 90%. The increase in the steric bulk of the alkyl group of the alkoxy chiral auxiliary (methyl vs isopropyl) led to a more complete transfer of chirality.

Introduction

The asymmetric dearomatization of aromatic molecules has considerable potential for the preparation of highly functionalized, stereodefined alicyclic compounds. Thus, reactions such as the asymmetric Birch reduction,[1] enzymatic dihydroxylation,[2] photochemical cycloaddition,[3] and nucleophilic addition to oxazoline-containing naphthalenes[4] have seen widespread application in organic synthesis. Although arenes are easily derivatized through electrophilic and nucleophilic substitution reactions, their conversion to nonaromatic compounds is difficult owing to the loss of aromatic stabilization.

Transition-metal mediated dearomatization methodologies have also shown promise, and two complementary approaches have been developed. Electron-deficient metal centers can form η^6-arene complexes that are activated toward nucleophilc attack at the arene. Examples of such systems include arene complexes of the 12e$^-$ systems Cr $(CO)_3$,[5−9] $[Mn(CO)_3]^+$,[10] $Fe(ArH)^{2+}$,[11] and $Ru(Cp)^+$,[12] and applications of this methodology, including asymmetric variants, have been exploited in organic synthesis.[13−15] In contrast, the 16e$^-$ system $[Os(NH_3)_5]^{2+}$ is electron-rich and forms η^2-arene complexes in which the arene ligand is activated toward a stereospecific reaction with electrophiles.[16] This metal center stabilizes the resulting arenium cations to allow their subsequent stereospecific reaction with nucleophiles. Thus, pentaammineosmium(II) arene complexes have been used as synthons for a broad array of functionalized alicylic compounds, often formed as single diastereomers. However, to date these reactions could only be carried out in racemic form, owing to the fluxional nature of the η^2-arene complexes.[17−20]

Indeed, monosubstituted η^2-pentaammineosmium(II) arene complexes are chiral; however, a facile *intrafacial* linkage isomerization rapidly equilibrates the two enantiomers. Recently we reported that placement of a stereogenic center adjacent to the aromatic ring could influence the coordination site of the pentaammineosmium(II) arene unit.[21] Specifically, a lactate substituent was shown to direct the coordination of the metal through a hydrogen-bond interaction between the ester and the ammine ligands and a steric interaction between the methyl

(1) Mander, L. N. *Synlett* **1991**, 134.
(2) Hudlicky, T.; Tian, X.; Konigsberger, K.; Maurya, R.; Rouden, J.; Fan, B. *J. Am. Chem. Soc.* **1996**, *118*, 10752−10765.
(3) Wender, P. A. *Pure Appl. Chem.* **1990**, *62*, 1597−1602.
(4) Shimano, M.; Meyers, A. I. *J. Org. Chem.* **1995**, *60*, 7445−7455.
(5) Semmelhack, M. F. *Comprehensive Organometallic Chemistry II*; Abel, E. W., Ed.; Pergamon Press: Oxford, 1995; Vol. 12, Chapters 9.1 and 9.2.
(6) Kamikawa, K.; Watanabe, T.; Uemura, M. *J. Org. Chem.* **1996**, *61*, 1375−1384.
(7) Pearson, A. J.; Gontcharov, A. V. *J. Org. Chem.* **1998**, *63*, 152−162.
(8) Price, D. A.; Simpkins, N. S.; MacLeod, A. M.; Watt, A. P. *J. Org. Chem.* **1994**, *59*, 1961−1962.
(9) Quattropani, A.; Anderson, G.; Bernardinelli, G.; Kundig, E. P. *J. Am. Chem. Soc.* **1997**, *119*, 4773−4774.
(10) Sun, S.; Dullaghan, C. A.; Sweigart, D. A. *J. Chem. Soc., Dalton Trans.* **1996**, 4493−4507.
(11) Astruc, D. *Synlett* **1991**, 369−380.
(12) Pearson, A. J.; Park, J. G. *J. Org. Chem.* **1992**, *57*, 1744.
(13) Hegedus, L. S. *Transition Metals in Organic Synthesis*; University Science Books: Mill Valley, 1994; Chapter 10, pp 307−333.
(14) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed.; University Science Books: Sausalito, CA, 1999; Chapter 10, pp 287−313.
(15) Davies, S. G.; McCarthy, T. D. *Comprehensive Organometallic Chemistry II*; Abel, E. W., Ed.; Pergamon Press: Oxford, 1995; Vol. 12, Chapter 9.3.
(16) Harman, W. D. *Chem. Rev.* **1997**, *97*, 1953−1978.
(17) Kopach, M. E.; Kolis, S. P.; Liu, R.; Robertson, J. W.; Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 6199.
(18) Kolis, S. P.; Kopach, M. E.; Liu, R.; Harman, W. D. *J. Org. Chem.* **1997**, *62*, 130.
(19) Kolis, S. P.; Kopach, M. E.; Liu, R.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 6205−6211.
(20) Kolis, S. P.; Chordia, M. D.; Liu, R.; Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2218−2226.
(21) Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 5637−5642.

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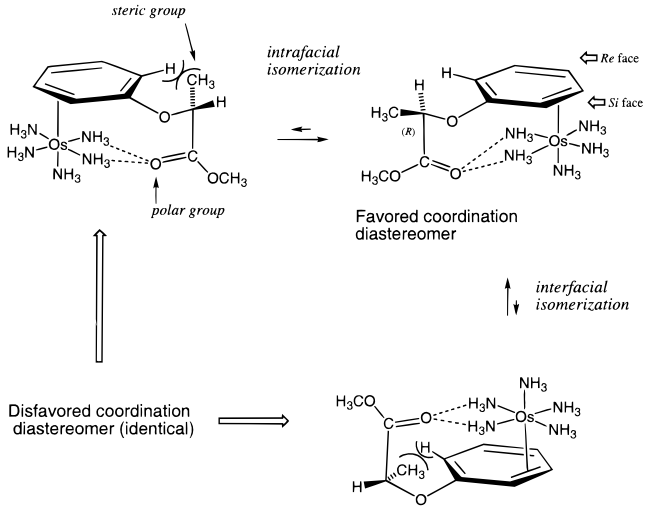


Figure 1. Lactate-mediated stereoselective η^2-arene coordination.

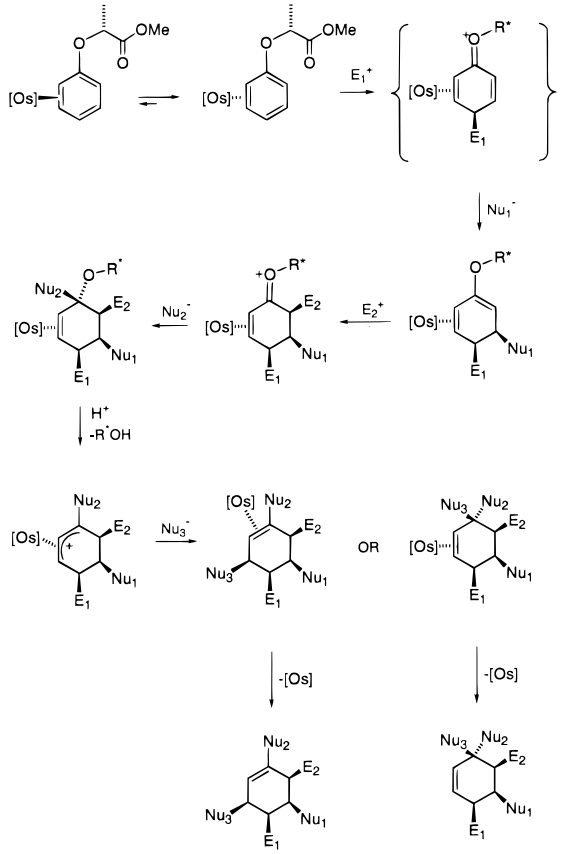


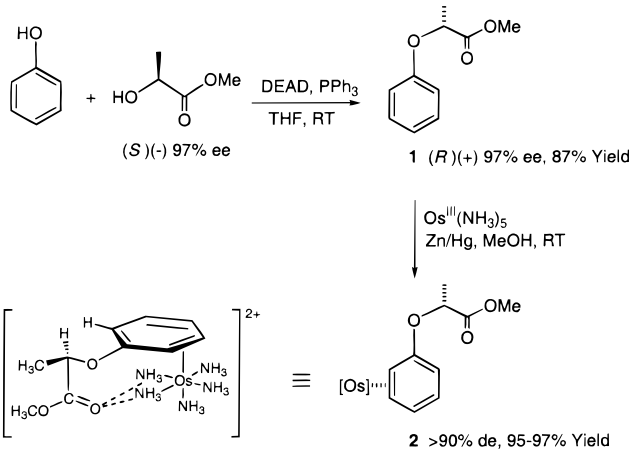
Figure 2. Schematic of lactate-directed dearomatization of arenes.

group and an *ortho* ring hydrogen (Figure 1). In principle, if the chiral auxiliary is applied as a single enantiomer, the metal coordination site will be uniquely defined and correspondingly organic products derived from this system will be formed in enantiomeric excess. The following account describes the application of this idea. Starting with the lactate-derived complex (*R*)-methyl-2-phenoxypropionatepentaammineosmium(II), we sought to prepare a series of functionalized cyclohexenones and cyclohexenes in high enantiomeric excess. A schematic overview of the proposed process is shown in Figure 2.

Results and Discussion

The nonracemic (*R*)-(+)-methyl-2-phenoxypropionate ligand **1** {97% ee, $[\alpha]^{rt}{}_D = 41.2$ (*c* 0.76, $CHCl_3$), lit[22]} was synthesized

Scheme 1



using the Mitsunobu reaction of (*S*)-methyl lactate (97% ee) and phenol with complete inversion in 87% yield (Scheme 1).[23] The enantiomeric excess of **1** was analyzed with chiral HPLC using a Chiralcel-OD column.[24] Reduction of pentaammineosmium(III) with Zn/Hg in the presence of **1** gave [(*R*)- η^2-methyl-2-phenoxypropionate] complex **2** in 95−97% yield. The diastereomer ratio for complex **2** varies somewhat with solvent; however, according to ^{1}H NMR studies, the ratio is always greater than 10:1.

When arene complex **2** was treated with TfOH at −40 °C, protonation occurred at 4-position to generate the 4*H*-oxonium species and this was followed by nucleophilic addition of a silyl ketene acetal (1-methoxy-2-methyl-1-trimethylsiloxypropene; MMTP) opposite to the metal center. Vinyl ether complex **3** was isolated in 76−84% yield. ^{1}H NMR analysis of complex **3** confirmed it to be a single diastereomer (de >90). Subsequent protonation of vinyl ether complex **3** with TfOH formed isolable enonium complex **4** (92−97%) again as a single diastereomer (de >90). Complex **4** was characterized by ^{1}H, ^{13}C, and DEPT NMR data. Hydrolysis of the oxonium led to facile removal of the chiral auxiliary with retention of configuration (thus it can be recycled if necessary), and this was followed by oxidative decomplexation by AgOTf/80 °C or ceric ammonium nitrate (CAN) to afford enone **6** (60−64%). Enone **6** is reported in the literature as a racemic mixture,[25] and ^{1}H and ^{13}C spectral data for **6** are in agreement with the reported data. GCMS analysis gave an M^+ of $m/z = 196$. As can be seen from Table 1 the enantiomeric excess of **6** for a variety of different reaction conditions fell in the range of 73−82%. The highest ee was found to be 82%, representing a reduction of 15% from the aryl-substituted lactate **1**.

The variation in ee is presumably due to a 5,6-η^2 to 2,3-η^2 (i.e., intrafacial) linkage isomerization for the 4*H*-oxonium under the acidic conditions required for protonation.[21] Supporting this notion, when the concentration of triflic acid or the time allowed before addition of the nucleophile was increased, the ee for the product was lowered (entries 2 and 3 in Table 1). However, increasing the amount of nucleophile or lowering the temperature of the reaction did not have a noticeable effect. Racemization of compound **6** during hydrolysis of oxonium **4** or during decomplexation is also possible, but variation of the

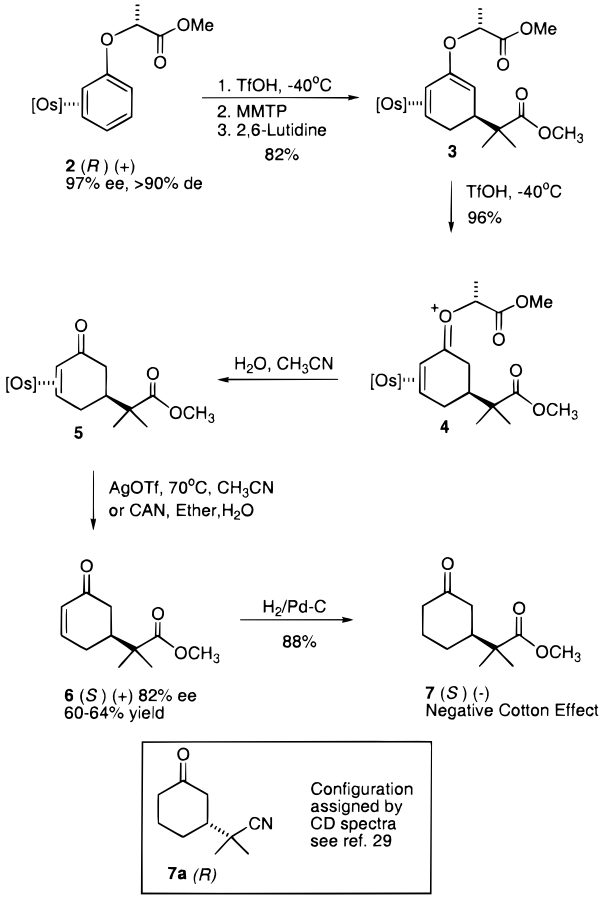
(22) Toda, F.; Tanaka, K. *Tetrahedron Lett.* **1988**, *15*, 1807−1810.
(23) Tottie, L.; Baeckström, P.; Moberg, C.; Tegenfeldt, J.; Heumann, A. *J. Org. Chem.* **1992**, *57*, 6579−6587.
(24) Azzolina, O.; Collina, S.; Vercesi, D. *Farmaco* **1995**, *50*, 725−733.
(25) Pearson, A. J.; Khetani, V. D.; Roden, B. A. *J. Org. Chem.* **1989**, *54*, 5141−5147.

Table 1. Variation in Ee of 5-Substituted-Cyclohexenone **6** with Reaction Conditions

	reaction conditions					
entry	TfOH[a]	temp, °C	time/ min[b]	MMTP[a]	oxidant	% ee of **6**[c]
1	0.7	−40	10	4.5	CAN[d]	78
2	1.5	−40	60	4.0	CAN	73
3	1.0	−40	30	4.5	CAN	74
4	0.7	−60[e]	20	3.5	CAN	76
5	0.6	−40	20	3.5	CAN	74
6	0.5	−40	20	3.5	CAN	78
7	0.5	−40	20	3.5	AgOTf	82
8	0.5	−40	20	3.5	CAN (0.8 equiv)	79

[a] Concentration in [M]. [b] Time in minutes prior to addition of MMTP. [c] ee's were determined by HPLC analysis using a Chiralcel-OD column within ±2% and obtained from 97% ee of starting material. [d] CAN = ammonium cerium(IV) nitrate. [e] 30% of unreacted starting material was recovered.

Scheme 2



oxidant (entries 5−8) also had no significant effect on the product ee. The specific rotation for compound **6** was found to be +9.9 (*c* 0.76, $CHCl_3$). The CD spectrum of compound **6** was obtained in hexanes at 20 °C and showed a negative n−π* Cotton effect at λ_{max} 338 nm. From a comparison of the CD spectrum of (5*R*)-methyl-2-cyclohexenone,[26] the (*S*) configuration was assigned to compound **6**. The assignment was further supported by hydrogenating compound **6** over H_2/Pd at room temperature to cyclohexanone derivative **7** in 88% yield. Spectral data for compound **7** are in agreement with that previously reported for a racemic mixture of this compound.[27] Compound **7** {$[\alpha]^{rt}_D$ −14.7 (*c* 0.8, $CHCl_3$)} also showed a negative n−π*

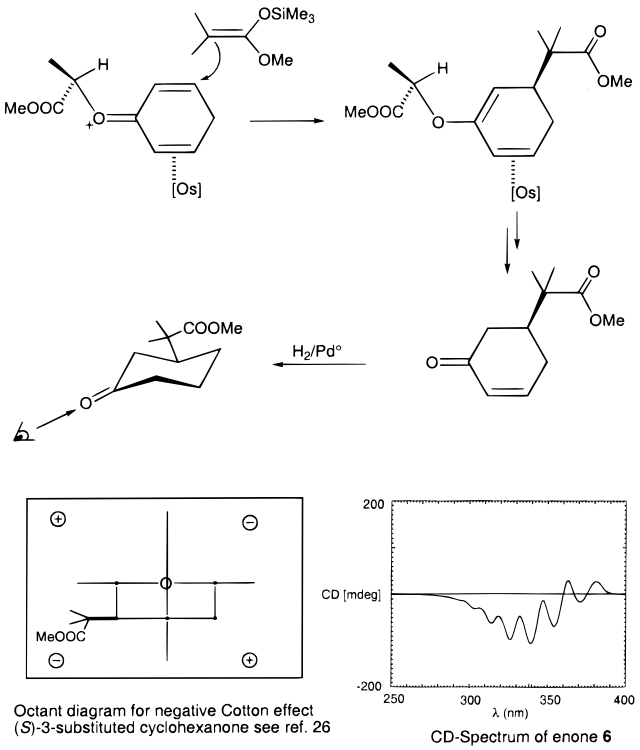


Figure 3. Determination of absolute stereochemistry for 3-substituted cyclohexanones.

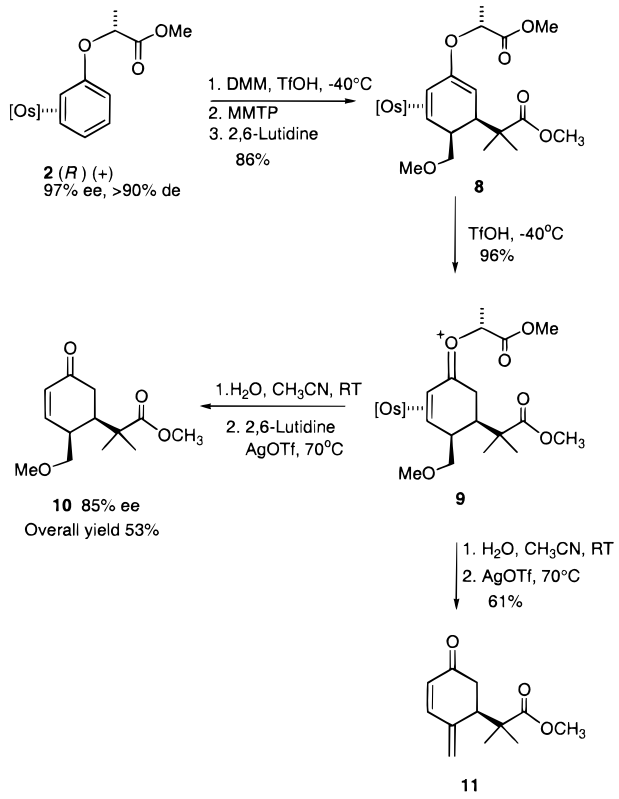
Cotton effect at λ_{max} 298 nm in the CD spectrum, and based on the octant rule[28] and upon a comparison with the related compound **7a**,[29] the (*S*) configuration was confirmed (Scheme 2). Most significantly, the absolute stereochemistry of **7** is fully consistent with our model of the lactate substituent of the arene directing the metal to the *Si* face of the coordinated double bond (see Figures 1 and 3).

In a similar vein, arene complex **2** was first combined with an acetal (dimethoxy methane) and triflic acid; then a silyl ketene acetal (MMTP) was added, resulting in the formation of alkoxydiene complex **8** (86%). This material was then protonated (**9**), hydrolyzed, and decomplexed using AgOTf/70 °C to generate 4,5-disubstituted-cyclohexenone derivative **10** in 53% overall yield from the starting arene complex **2**. When the decomplexation was carried out in the absence of 2,6-lutidine, dienone compound **11** was isolated (61%) as a result of elimination of methanol from the allylic position (Scheme 3). Compounds **10** and **11** were characterized by ^{1}H and ^{13}C NMR and mass spectral data. The 4,5-disubstituted-cyclohexenone derivative **10** {$[\alpha]^{rt}_D$ 184 (*c* 0.31, $CHCl_3$)} was analyzed for enantiomeric excess by chiral HPLC. Upon comparison with racemic enone **10**, the ee of chiral **10** was found to be 85%.

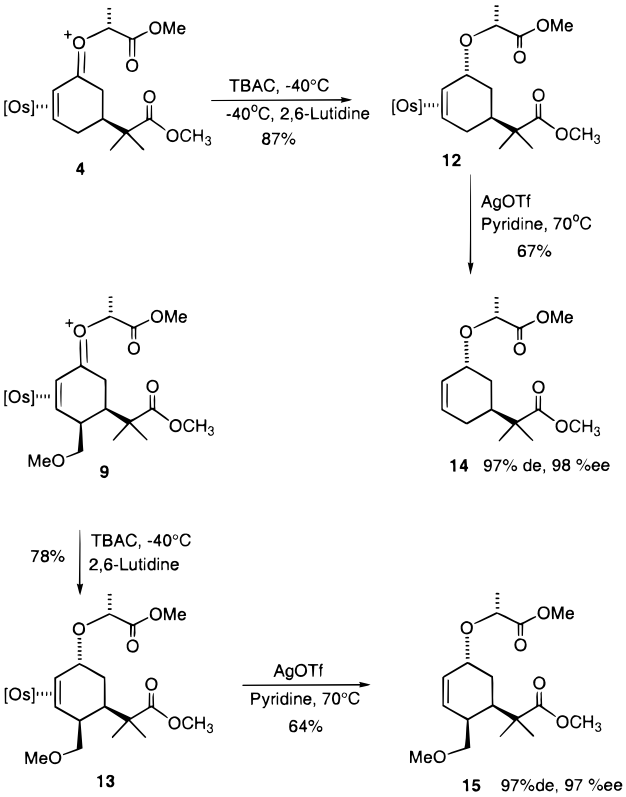
Enonium complexes **4** and **9** were reduced with tetrabutylammonium cyanoborohydride at −40 °C and quenched with 2,6-lutidine to form allyl ether complexes **12** and **13**, respectively (78−87%). These complexes were characterized by ^{1}H and ^{13}C and DEPT NMR data. Oxidative decomplexation by AgOTf/70 °C and pyridine afforded cyclohexenyl ethers **14** (67%) and **15** (64%) (Scheme 4). Compound **14** was assigned the molecular formula $C_{15}H_{24}O_5$ by elemental analysis. Analysis of ^{1}H NMR spectra for both compounds **14** and **15** revealed that these compounds were isolated with de >97%. Chiral HPLC analysis

(26) Gawronski, J. K. *Tetrahedron* **1982**, *38*, 3−26.
(27) RanjanBabu, T. V. *J. Org. Chem.* **1984**, *49*, 2079−2088.
(28) Snatzke, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 14.
(29) Semmelhack, M. F.; Schmalz, H.-G. *Tetrahedron Lett.* **1996**, *37*, 3089.

Scheme 3



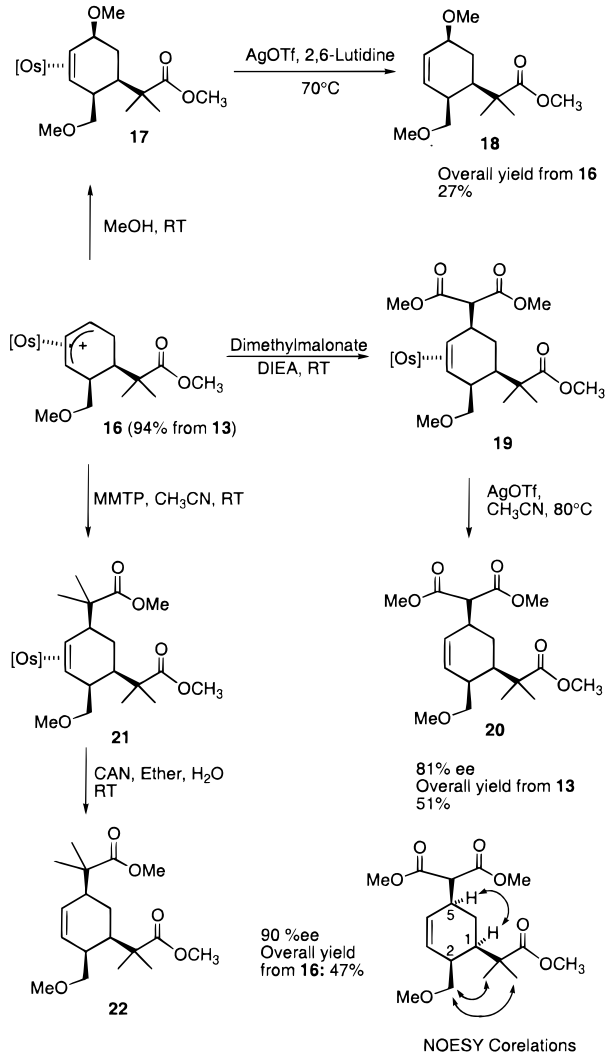
Scheme 4



of compounds **14** and **15** determined that these materials were isolated with an enantiomeric excess of 97−98%.

Upon treatment with TfOH, allyl ether complex **13** leads to the formation of allyl complex **16** in 94% yield. This material was characterized by ^{1}H, ^{13}C, and DEPT NMR spectral data. The η^3-allyl complexes of pentaammineosmium have been

Scheme 5

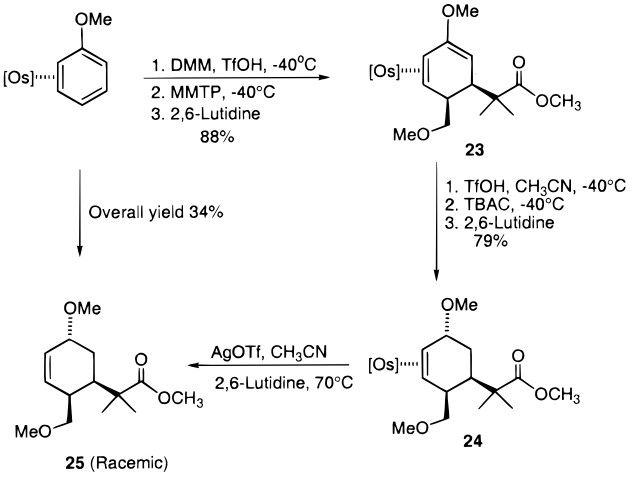


shown to react with a wide range of nucleophiles.[30] As examples, allyl complex **16** was combined with MeOH to regio- and stereoselectively generate allyl methyl ether complex **17**. Oxidative decomplexation of the metal center with AgOTf at 70 °C in the presence of 2,6-lutidine gave the free organic cyclohexenylmethyl ether **18** in 27% overall yield from **16** (Scheme 5). Analogous reactions of allyl complex **16** with carbon nucleophiles such as dimethyl malonate/diisopropylethylamine (DIEA) or silyl ketene acetal (MMTP) followed by oxidation of the metal center gave the trisubstituted cyclohexenes **20** and **22** as a single diastereomer in 51 and 47% yields, respectively (Scheme 5). Compounds **20** and **22** were characterized on the basis of ^{1}H, ^{13}C, and 2D NMR and mass spectral data. NOESY data of compound **20** showed strong corelations between the methylene protons of the methoxymethyl group at C-2 and the *gem*-dimethyl group at C1. Also, correlations between protons at C1 and C5 of the cyclohexenyl ring were observed, confirming the *all-cis* stereochemistry of the cyclohexene skeleton. These data are consistent with both electrophilic and nucleophilic additions occurring opposite to the metal (Scheme 5). Compounds **20** $\{[\alpha]^{rt}_D = 81.9$ (*c* 0.3, $CHCl_3)\}$ and **22** $\{[\alpha]^{rt}_D = 87.2$ (*c* 0.72, $CHCl_3)\}$ were analyzed by chiral HPLC and found to be in 81% and 90% ee, respectively.

The ^{1}H NMR analysis of allyl ether **18** revealed that chemical shifts for the olefinic protons are sufficiently close that NOESY

(30) Harman, W. D.; Hasegawa, T.; Taube, H. *Inorg. Chem.* **1991**, *30*, 453.

Scheme 6



data could not conclusively determine the stereochemistry. Thus, to rule out the possibility of methanol addition *syn* to the osmium (observed for pentaammineosmium(II) furan complexes in acidic media),[31] *trans*-allyl ether complex **24** was prepared from anisole according to Scheme 6. Decomplexation of **24** provided allyl ether **25** in an overall yield of 34% from the anisole complex (Scheme 6). A comparison of ^{1}H NMR spectra revealed that compounds **25** and **18** are diastereomers. This observation indicates that the addition of MeOH to allyl complex **16** occurs *anti* to the metal center (as found for carbon nucleophiles), to form *all-cis* cyclohexenyl ether **18**.

To see if efficient chirality transfer could occur away from the arene ring, our studies included the use of β-substituted Michael acceptors as electrophiles. η^2-Anisole complexes can undergo conjugate addition at C4 with a variety of α,β-unsaturated ketones, aldehydes and esters, and amides in the presence of Brønsted (TfOH) or Lewis acids.[18] In the present study, 2-cyclopentenone and 2-cyclohexeneone were used as electrophiles in the presence of triflic acid at −40 °C with complex **2**. The resulting 4*H*-oxonium complexes were re-aromatized with pyridine as a base to form the appropriate 4-substituted aromatic complexes **26** and **27**, respectively (Scheme 7). Surprisingly, ^{1}H NMR analysis of compounds **26** and **27** revealed that the diastereoselectivities of these two Michael addition reactions are vastly different. Whereas 2-cyclopentenone adds to the arene with poor control of stereochemistry at the benzylic carbon (the diastereomeric ratio of **26** is ∼2:1), addition of 2-cyclohexenone occurs with good control (diastereomeric ratio of **27** is >9:1). In an earlier study,[18] cyclohexanone underwent electrophilic substitution with anisole to give two diastereomers in a 1:1 ratio, but the aromatic product in that study was isolated only *after* the metal had been free to adjust its coordination site. It was first assumed that the low diastereoselectivity observed for cyclopentenone was a result of intrafacial migration by the metal center upon rearomatization (Scheme 7). However, for **2** the chiral auxiliary is highly effective in directing the position of metal coordination, and this fact suggested that the Michael addition was to blame for the poor stereocontrol of **26**. The latter hypothesis was verified by analyzing the decomplexed ligands. Free ligands **28** and **29** were obtained when complexes **26** and **27** were heated at 70 °C in acetonitrile for 3−4 h. Unfortunately, ^{1}H NMR analysis of free organic compounds (**28**, **29**) failed to provide meaningful information about the diastereomeric excess since the newly

(31) Chen, H.; Liu, R.; Myers, W. H.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 509.

Scheme 7

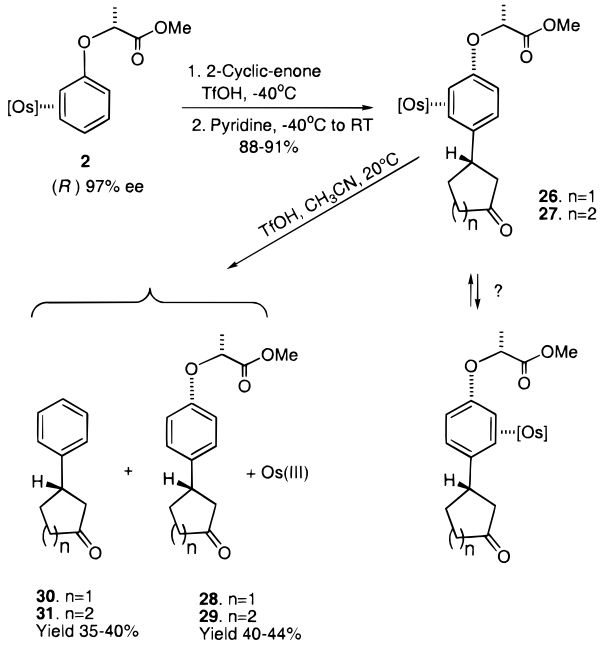
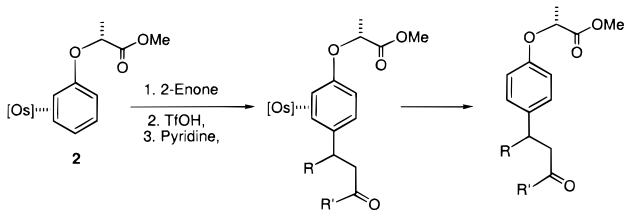


Table 2. Effects of Temperature on Diastereoselectivity of Michael Addition Reactions



entry	Michael acceptor	temp, °C	de of complex[a]	de of free ligand[b]
1	cyclohexenone	−40	9:1	>9:1
2	cyclohexenone	−40	9:1	8.6:1.4
3	cyclohexenone	−60	>9:1	
4	cyclopentenone	−18	2:1	
5	cyclopentenone	−40	2:1	2:1
6	cyclopentenone	−60	2.5:1	
7	cyclopentenone	−80	3:1	3:1
8	3-penten-2-one	−40	2:19	2:1
9	3-penten-2-one	−40	2:1	
10	*t*-4-phenyl-3-buten-2-one	−40	1.14:1	1.14:1

[a] de's were determined by ^{1}H NMR analysis of complexes in acetonitrile-d_3 or acetone-d_6 at room temperature. [b] de's were determined by chiral HPLC analysis.

created chiral center was far from the chiral auxiliary. The HPLC analysis for both compounds **28** and **29** showed that the diastereoselectivity was *identical* to that of their complexes, ruling out any metal migration.

To determine what factors affect the diastereoselectivity for the Michael addition, this reaction was carried out under a variety of different conditions (Table 2) with several different enones. The maximum diastereomer ratio obtained for cyclopentenone was only ∼3:1, achieved by lowering the reaction temperature to −80 °C. Other than temperature, adjusting reaction parameters such as concentration of Michael acceptor, TfOH, addition order, and acid type had virtually no effect on the diastereoselectivity of this reaction. With the exception of cyclohexenone, the enones tested delivered poor diastereoselectivity in their reactions with **2**. By contrast, earlier studies[32] with *N*-methylmaleimide and the anisole complex [Os(NH3)5-

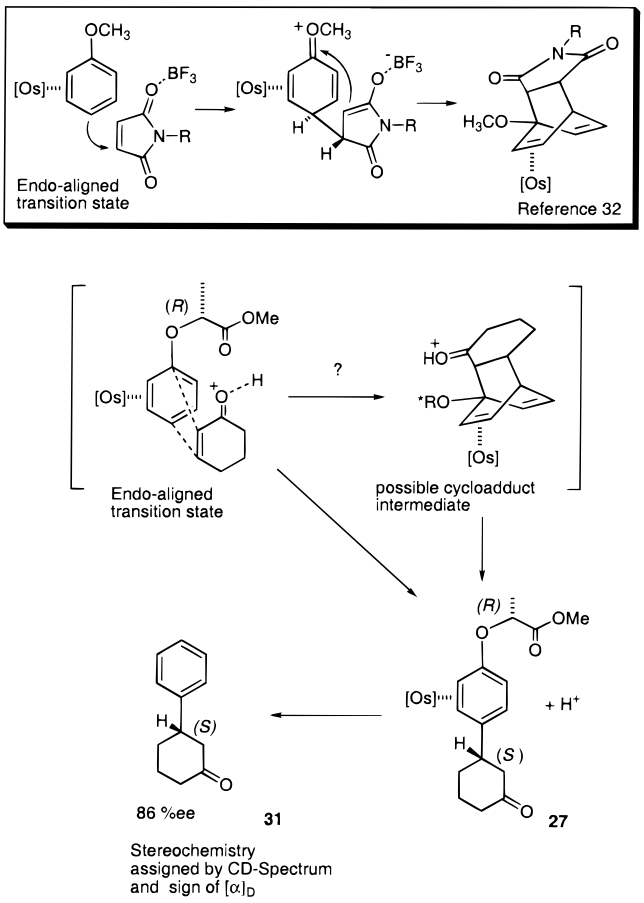


Figure 4. Possible transition state for Michael addition reaction.

(η^2-anisole)]$^{2+}$ demonstrated that this Michael acceptor adds to anisole with high stereocontrol. Using BF_3 as the promoter, the Michael reaction yields a boron enolate which undergoes aldol addition at C1 to deliver an *endo*-cycloadduct exclusively (Figure 4). Unfortunately, for the present study the ease with which the benzylic hydrogen can epimerize prevented analysis of the simple electrophilic substitution product of *N*-methylmaleimide and **2**.

For the addition of cyclohexenone to **2**, the assignment of absolute stereochemistry of the newly created benzylic stereocenter could provide information about the transition state of the Michael reaction. Thus, the complex **27** was treated with triflic acid at 20 °C in CH_3CN to bring about the oxidative cleavage of the chiral auxiliary. Taking advantage of an unexpected reaction originally observed for the anisole complex,[33] treatment of substitution complex **27** with triflic acid at 20 °C resulted in the formation of free organic products **29** and 3-phenylcyclohexanone (**31**) {$[\alpha]^{rt}_D = -16.5$ (*c* 0.57, $CHCl_3$)} in about a 1:1 ratio (Scheme 7). In this process, 1 equiv of Os(II) serves as the electron source for the reductive cleavage of the chiral auxiliary. Given that the final state of osmium is Os(III), only half of an equivalent of the aromatic ligand is reduced. Inspection of the CD spectrum (negative n$-\pi^*$ Cotton effect) and comparison of the sign of specific rotation with the literature value[34] {$[\alpha]^{rt}_D = -21$ (*c* 0.96, $CHCl_3$)} determined the configuration for 3-phenylcyclohexanone (**31**) to be (*S*) with 86% ee (HPLC). For cyclopentenone addition product **28**, the absolute stereochemistry of the major stereoisomer was assigned by obtaining 3-phenylcyclopentanone (**30**) from compound **26** and HOTf. Compound **30** gave a negative optical rotation {$[\alpha]^{rt}_D = -45$ (*c* 0.8, $CHCl_3$)}, and on the basis of previously reported data in the literature[35,36] the configuration for the major enantiomer was determined to be (*S*).

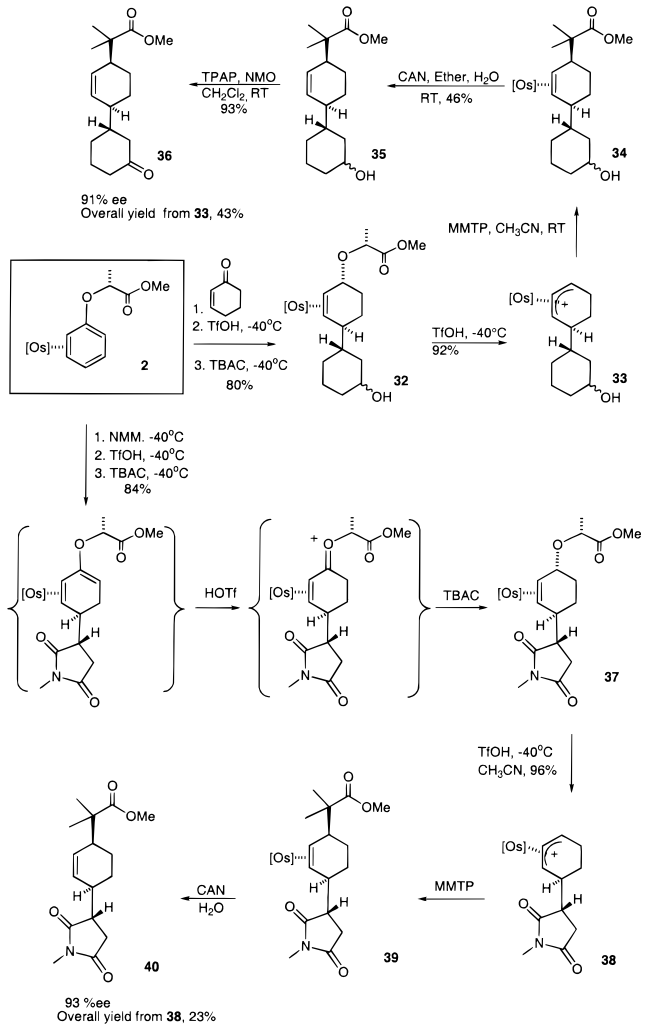
The stereochemistry of the Michael addition reactions with *cyclic* Michael acceptors can be rationalized by invoking an ordered transition state that resembles an *endo* Diels−Alder cycloadduct. In fact it is possible that a cycloadduct (like that isolated for the BF_3-promoted addition of *N*-methylmaleimide and the anisole complex)[32] may be an intermediate in this process. Regardless of whether a cycloadduct is part of the reaction coordinate for the Michael reaction, an *endo* transition state with 2-cyclohexenone or 2-cyclopentenone would furnish the (*S*)-configuration for the benzylic position and could explain the high diastereoselectivity observed, at least for the former case (Figure 4).

Next we sought to combine the stereoselective Michael reactions with those manipulations described earlier for the arene ring. Thus, 2-cyclohexenone and *N*-methylmaleimide were chosen as electrophiles to prepare 4*H*-anisolium complexes at −40 °C. Since these electrophiles were more sterically demanding than the acetal described earlier, the addition of a carbon nucleophile to C3 of the arenium species proved to be difficult. However, hydride addition at C3, protonation at C2, and hydride addition at C1 (individual intermediates not isolated) led to the isolation of cyclohexenyl ether complexes **32** and **37**, respectively. These compounds, upon treatment with triflic acid at 20 °C, formed π-allyl complexes **33** and **38**, respectively, which were then combined with a silyl ketene acetal (MMTP) and oxidatively decomplexed (CAN) to yield 1,4-disubstituted cyclohexenes **35** and **40**. Compound **35** was isolated as a mixture of diastereomers due to the inadvertent reduction of the carbonyl group. Given that this additional stereocenter could complicate analysis of stereocontrol at the ring, the alcohol function of **35** was oxidized back to ketone **36** using TPAP/NMO (TPAP = tetrapropylammonium perruthenate; NMO = *N*-methylmorpholine *N*-oxide). Overall, compounds **36** and **40** were prepared in 31% and 18% chemical yields, respectively, from **2** (yields are unoptimized) (Scheme 8). On the basis of ^1H and ^{13}C NMR and GCMS spectral data, these compounds were prepared as single diastereomers. More significantly, compounds **36** {$[\alpha]^{rt}_D = 42.6$ (*c* 1.2, $CHCl_3$)} and **40** {$[\alpha]^{rt}_D = -7.2$ (*c* 1.6, $CHCl_3$)} were formed in 91% and 93% ee, respectively (HPLC), in reaction sequences that formed three new stereogenic carbons. The overall reaction sequences presented above demonstrate the true breadth of the range of reactions for η^2-arene complexes that can be stereochemically controlled by a single and structurally simple chiral auxiliary.

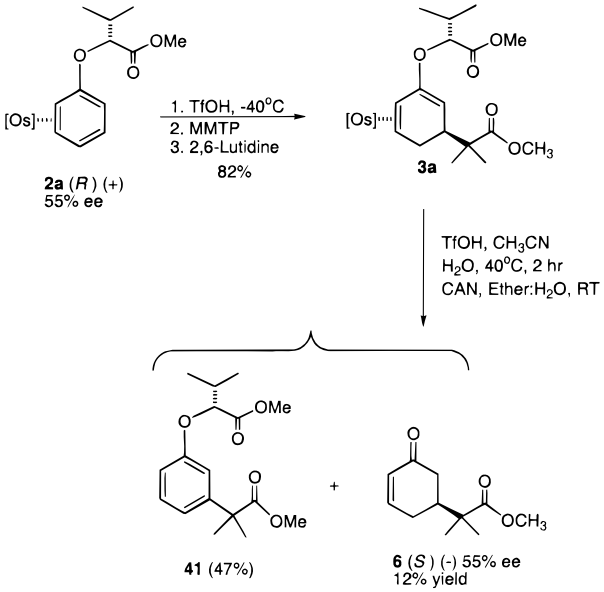
Finally, in an attempt to further optimize the ability of the chiral auxiliary to direct the metal coordination stereochemistry, we set out to modify the alkyl group. In our initial study of chiral anisole complexes of osmium(II), we determined that the polar group of the chiral auxiliary (Figure 1) must incorporate a carbonyl function (i.e., an ester or amide), as it was essential to set up a hydrogen-bonding interaction with the pentaammineosmium unit. However, we did not explore the role of the steric group in any detail (see Figure 1). The isopropyl derivative of **1**, methyl-2-phenoxy-3-methylbutyrate (**1a**), was prepared from (*S*)-(+)-methyl-2-hydroxy-3-methylbutyrate via a Mitsunobu

(32) Kopach, M. E.; Harman, W. D. *J. Org. Chem.* **1994**, *59*, 6506.
(33) Winemiller, W. D.; Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 2096.
(34) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Masaaki, S.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579−5580.
(35) Paquette, L. A.; Gilday, J. P.; Ra, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 6858−6860.
(36) Taura, Y.; Tanaka, M.; Wu, X.; Funakoshi, K.; Sakai, K. *Tetrahedron* **1991**, *47*, 4879−4888.

Scheme 8



Scheme 9



reaction similar to the preparation of **1** except that the synthesis needed to be performed under somewhat harsher conditions (THF reflux, 2 days, 42%). Unfortunately, HPLC analysis of compound **1a** revealed an enantiomeric excess of only 55%. Nonetheless, complexation with Os(III) was carried out to form complex **2a**. Despite the low optical purity of the ligand, NMR analysis revealed that the diastereoselectivity was outstanding and only a single diastereomer was observable by ^{1}H NMR analysis. Thus, a reaction sequence of protonation and addition of MMTP was carried out, similar to that performed on complex **2**, to obtain a single diastereomer of the enone **3a** (^{1}H NMR). However, the bulkier chiral auxiliary apparently retards the acid-catalyzed hydrolysis such that treatment of the reaction mixture with CAN produced rearomatized product **41** (i.e., a net oxidation of the methoxydiene ligand of **3a**) with the alkoxy moiety still intact (47%) (Scheme 9). Thus, the desired enone **6** was obtained in minor amounts (12%). Significantly, chiral HPLC analysis of enone **6** revealed its enantiomeric excess as 55%, identical to the value found for the chiral ligand **1a**. Thus, even though the isopropyl chiral auxiliary is at present of little utility, these experiments indicate that increasing the size of the steric group enhances the fidelity of chirality transfer.

Considerable efforts have been made over the past few years to carry out asymmetric variants of the well-established chromium and manganese arene chemistry.[37−39] Generally, the most successful approaches have invovled the use of chiral auxiliary or a reagent to induce asymmetric *ortho*-lithiation or nucleophilic addition. In these systems, the arene metal fragment is achiral prior to reaction. However, limited success has also been reported in directly inducing asymmetric coordination. For example, Alexakis et al. showed that the chiral *ortho*-substituted benzaldehyde aminals reacted with naphthalenetricarbonylchromium precursor under kinetic conditions to form the asymmetric arene complex with 96% de.[40] Complexation of other arenes containing chiral moieties such as indanes[41] and steroids[42] and terpenoids[43] have also been accomplished with some stereocontrol. What sets the present work apart from the previous examples is that the η^2- binding mode displayed by the pentaammineosmium fragment can adjust its stereochemistry of coordination *without changing the binding face* of the aromatic ring and a single substituent is sufficient to deliver high selectivity. Thus, whereas achieving high control of coordination stereochemistry for η^6-arene complexes relies on kinetic selectivity, the η^2-osmium system is regulated solely by thermodynamics.

Conclusion

This study demonstrates that a simple chiral auxiliary (lactate) attached to an arene may be used to direct the stereospecific coordination to pentaammineosmium(II) and thereby induce high transfer of chirality to C4, C3, and C1 of the arene as well as the benzylic position at C4. With the exception of the benzylic position, enantiomeric excesses fall in the range between 80 and 95% for a wide array of different reactions. *The essential feature of this strategy is that the chiral auxiliary directly interacts only with the metal, not with the chemical reagents.* Because the chiral auxiliary interacts with the metal, its location

(37) Kundig, E. P.; Ripa, A.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1071−1073.

(38) Pearson, A. J.; Zhu, P. Y.; Youngs, W. J.; Bradshaw, J. D.; McConville, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 10376−10377.

(39) Uemura, M.; Miyake, R.; Nakayama, K.; Shiro, M.; Hayashi, Y. *J. Org. Chem.* **1993**, *58*, 1238−1244.

(40) Alexakis, A.; Mangeney, P.; Marek, I.; Rose-Munch, F.; Rose, E.; Semra, A.; Robert, F. *J. Am. Chem. Soc.* **1992**, *114*, 8288−8290.

(41) Ohlsson, B.; Ullenius, C.; Jagner, S.; Grivet, C.; Wenger, E.; Kundig, P. E. *J. Organomet. Chem.* **1989**, *365*, 243−267.

(42) Woo, K.; Carpenter, G. W.; Sweigart, D. A. *Inorg. Chim. Acta* **1994**, *220*, 297−304.

(43) Woo, K.; Willard, P. G.; Sweigart, D. A.; Duffy, N. W.; Robinson, B. H.; Simpson, J. *J. Organomet. Chem.* **1995**, *487*, 111−118.

is primarily on the *opposite* face of the ring from the approach of chemical reagents; thus, the reaction rates are not noticeably affected in comparison to those of anisole, and the degree of stereoselectivity achieved is not a function of the interaction between chiral auxiliary and reagent.

Experimental Section

For general methods, please see the Supporting Information and ref 21. The following abbreviations are used in reporting the spectral details: CV = cyclic voltammetry; DHB = 2,5-dihydroxybenzoic acid; 3-HPA = 3-hydroxypicolinic acid; HATR = horizontal attenuated total reflectance accessory; OTf = trifluoromethanesulfonate; [Os] = pentaammineosmium(II)triflate.

(*R*)-(+)-Methyl-2-phenoxypropionate (1).[23] Triphenylphosphine (28.8 g, 0.11 mol), phenol (10.4 g, 0.11 mol), and (*S*)-methyl lactate (11.0 g, 0.105 mol, 97% ee) were dissolved in dry THF (100 mL), and to this mixture was added dropwise solution of diethyl azodicarboxylate (DEAD) (20.0 g, 0.115 mol) in dry THF (25 mL) over period of 30 min at room temperature. The reaction mixture was stirred at room temperature for 18 h during which time a white precipitate appeared in the mixture; then the solvent was removed under reduced pressure. The residue obtained was treated with 1:1 ether/hexanes (200 mL) to form a white precipitate of triphenylphosphine oxide. The mixture was then filtered through a bed of silica gel−Celite, and the residual solid was washed with 1:1 ether/hexanes (2 × 25 mL). The combined filtrate was evaporated under reduced pressure, and the resulting syrup was purified by column chromatography (silica gel) using initially hexanes and then hexanes/ethyl acetate (20:1) to isolate compound **1** as a thick transparent oil (87%). The ^{1}H NMR spectrum of compound **1** was identical to that reported in the literature.[22] Compound **1** was analyzed for ee by HPLC with a Chiralcel OD-H column (90:10 hexanes/2-propanol; 0.8 mL/min): (*S*)-(minor) t_R = 5.7 min, (*R*)-(major) t_R = 13.3 min 97% ee, $[\alpha]^{rt}_D$ 41.2 (*c* 0.76, $CHCl_3$).

2,3-η^2-[Os(NH$_3$)$_5$-2′-methylphenoxypropionate](OTf)$_2$ (2). Using the previously reported[21] procedure for racemic complexes, the nonracemic complex **2** was prepared (95−97%). The coordination diastereoselectivity of different batches of the complex was assessed through ^{1}H NMR in CD_3CN and always found to be >90%.

{Os(NH$_3$)$_5$[3,4-η^2-2-(Methyl-2′-oxypropionate)-6-(1-carbomethoxy-1-methylethyl)-1,3-cyclohexadiene]}(OTf)$_2$ (3). The 2-methylphenoxypropionate complex **2** (351 mg, 0.466 mmol) was dissolved in CH_3CN (3.23 g) and cooled to −40 °C. First TfOH (128 mg, 0.85 mmol) in CH_3CN (1.1 g) at −40 °C was added (a color change from orange-red to dark blue was observed), and then after 20 min MMTP (869 mg, 4.99 mmol) in CH_3CN (1.1 g) at −40 °C was added. The reaction mixture was allowed to stand at −40 °C for 16 h, over which time the dark blue color slowly discharged to brown. The reaction was then quenched by addition of cold (−40 °C) 2,6-lutidine (227 mg, 1.76 mmol) in CH_3CN (0.87 g). After standing at −40 °C for an additional 15 min, the mixture was allowed to warm to room temperature and added to stirring ether (100 mL), yielding a yellow oil. The ether layer was decanted and the oil was redissolved in CH_3CN (∼2.5 g). Addition of this solution to stirred ether/CH_2Cl_2 (2:1, 300 mL) gave a pale yellow precipitate, which was collected by filtration followed by drying in vacuo (331 mg, 82%) (note: the solid returns to an oil if it is not filtered quickly from the precipitating solution): ^{1}H NMR (CD_3CN) δ 4.62 (q, J = 6.8 Hz, 1H), 4.17 (bs, 3H, *t*-NH_3), 4.14 (d, J = 3.9 Hz, 1H), 3.78 (d, J = 8.5, 1H), 3.69 (s, 3H), 3.67 (m, 1H), 3.60 (s, 3H), 3.07 (br s, 12H) 2.97 (m, 1H), 2.50 (m, 1H), 1.68 (ddd, J = 2.2,2.4,8.7, 1H), 1.46 (d, J = 6.8, 3H), 1.13 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (CD_3CN) δ 178.2 (CO), 174.5 (CO), 160.5 (C), 121.5 (q, J = 300 Hz, CF_3), 89.9 (CH), 70.5 (CH), 52.8 (CH_3), 51.8 (CH_3), 48.0 (C), 46.1 (CH), 43.4 (CH), 41.1 (CH), 26.2 (CH_2), 22.0 (CH_3), 18.4 (CH_3); CV $E_{p,a}$ = 0.70 V (NHE).

[Os(NH$_3$)$_5$(2,3-η^2-1-Methyl-2′-oxypropionate-5-(1-carbomethoxy-1-methyl ethyl)cyclohex-2-ene-1-oxonium)](OTf)$_3$ (4). Complex **3** (350 mg, 0.428 mmol) was dissolved in CH_3CN (3.2 g) and cooled to −40 °C. Cold TfOH (−40 °C, 95 mg, 0.63 mmol) in CH_3CN (1.1 g) was added, and the light yellow solution immediately darkened. After 10 min the reaction mixture was removed from the cold bath and added to stirring ether (∼250 mL) at room temperature, giving a precipitate which was collected by filtration and dryed in vacuo as a gray solid, **4** (395 mg, 96%): ^{1}H NMR (CD_3CN) δ 5.90 (dt, J = 3.0, 7.2 Hz, 1H), 5.66 (q, J = 6.9 Hz, 1H), 5.24 (d, J = 7.2 Hz, 1H), 5.14 (br s, 3H), 3.97 (br s, 12H), 3.83 (s, 3H), 3.65 (s, 3H), 3.05 (br t, J = 15.9 Hz, 1H), 2.11 (dd, J = 10.2, 20.7 Hz, 1H), 1.84 (m, 1H), 1.77 (dd, J = 7.2 Hz, 1H), 1.72 (d, J = 6.9 Hz, 3H), 1.16 (s, 6H), 0.93 (m, 1H); ^{13}C NMR (CD_3CN) δ 201.7 (CO), 177.6 (CO), 170.7 (CO), 78.9 (CH), 61.7 (CH), 57.2 (CH), 55.1 (CH_3), 52.9 (CH_3), 45.6 (C), 38.3 (CH), 31.0 (CH_2), 26.5 (CH_2), 23.4 (CH_3), 22.7 (CH_3), 17.3 (CH_3).

[Os(NH$_3$)$_5$(2,3-η^2-5-(1-Carbomethoxy-1-methylethyl)cyclohex-2-ene-1-one)](OTf)$_2$ (5). Complex **4** (200 mg, 0.233 mmol) was dissolved in CH_3CN (3.1 g), and water (205 mg) was added in a pressure tube. The pressure tube was sealed and heated under a nitrogen atmosphere in an oil bath at 70 °C for 2 h. The reaction mixture was then allowed to cool to room temperature and without isolation used for decomplexation. Complex **5** in racemic form has been isolated and characterized previously.[21]

(*S*)-(−)-2-Methyl-2-(5-oxocyclohex-3-enyl)propionic Acid Methyl Ester (6). We have reported[21] the decomplexation of racemic **5** with CAN to give racemic **6**, but an alternate procedure using AgOTf as an oxidizing agent is as follows: Complex **5** (302 mg, 0.392 mmol) was dissolved in CH_3CN (4.3 g) in a pressure tube, and AgOTf (207 mg, 0.807 mmol) was added to it. The tube was sealed, and the mixture was heated on an oil bath at 80 °C for 3 h. The mixture, after cooling to room temperature, was transferred to a round-bottom flask and concentrated under reduced pressure, and the thick residue thus obtained was added to stirring ether (25 mL). The resulting slurry was filtered through a bed of silica gel to remove solid, and the residue was washed with additional ether (25 mL). The combined ethereal filtrate was washed with water and brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave an oil. Purification of the residue by column chromatography (silica gel) gave compound **6** as a colorless oil (49 mg, 64%) {$[\alpha]^{rt}_D$ = 9.9 (*c* 0.76, $CHCl_3$)}. The ee of enone **6** was analyzed by HPLC using a Chiralcel OD-H column (90:10 hexanes:2-propanol 0.8 mL/min): (*S*)-(major) t_R = 8.6 min, (*R*)-(minor) t_R = 11.0 min, 82% ee. The CD spectrum for the compound was obtained in hexanes and showed a negative Cotton effect (n−π*) at λ_{max} 338 nm.

(*S*)-(−)-2-Methyl-2-(3-oxocyclohexyl)propionic Acid Methyl Ester (7). A solution of enone **6** (19 mg, 0.094 mmol) in methanol (1.5 mL) was stirred in the presence of Pd/C (10 mg, 10%) under an H_2 atmosphere at room temperature for 2 h. The reaction was monitored by subjecting small aliquots to GCMS analysis. After reduction was complete, the reaction mixture was diluted with ether (10 mL) and filtered through a bed of silica gel and Celite to remove Pd/C. Solvents were removed from the filtrate under reduced pressure to yield **7** as a colorless oil (17 mg, 88%). The compound was characterized by ^{1}H and ^{13}C NMR and IR spectral data, which were identical to those reported in the literature for the racemic compound:[25] GCMS (EI) *m*/*z* 198 (M^+) {$[\alpha]^{rt}_D$ −14.7 (*c* 0.8, $CHCl_3$)}. The CD spectrum for the compound was obtained in hexanes and showed a negative Cotton effect (n−π*) at λ_{max} 298 nm.

Disubstituted Vinyl Ether Complex 8. Chiral complex **2** (362 mg, 0.48 mmol) and dimethoxymethane (63 mg, 0.83 mmol) were dissolved in CH_3CN (4.11 g), and the resulting solution was cooled to −40 °C. First TfOH (173 mg, 1.15 mmol) in CH_3CN (1.32 g) at −40 °C was added (a color change from orange-red to dark blue was observed), and then after 20 min MMTP (880 mg, 5.05 mmol) in CH_3CN (1.47 g) at −40 °C was added. The mixture was then allowed to stand at −40 °C. Over 16 h, the dark blue color of reaction mixture discharged to brown. The reaction was then quenched by addition of cold (−40 °C) 2,6-lutidine (227 mg, 1.76 mmol) in CH_3CN (0.87 g). After standing at −40 °C for an additional 15 min, the mixture was allowed to warm to room temperature and added to stirring ether (100 mL), yielding a yellow oil. The ether layer was decanted, and the oil was redissolved in CH_3CN (3.5 g). Addition of this solution to stirring ether:hexanes/CH_2Cl_2 (1:1:0.5, ∼370 mL) followed by quick filtration and drying in vacuo gave **8** as a pale yellow solid (372 mg, 86%) (note: the solid returns to an oil if it is not filtered quickly from the precipitating solution): ^{1}H NMR (CD_3CN) δ 4.55 (q, J = 6.8 Hz, 1H), 4.43 (d, J =

6.8, 1H), 4.05 (br s, 3H), 3.90 (d, J = 8.4, 1H), 3.67 (d, J = 7.2 Hz, 1H), 3.63 (s, 3H), 3.59 (s, 3H), 3.43 (dd, J = 4.4, 5.1 Hz,1H), 3.29 (s, 3H), 3.20 (dd, J = 7.2 Hz, 1H), 3.13 (br s, 12H), 2.55 (t, J = 6.8 Hz, 1H), 1.41 (d, J = 6.8, 3H), 1.23 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (CD_3CN) δ 179.8 (CO), 174.2 (CO), 161.6 (C), 121.8 (q, J = 310 Hz, CF_3), 94.3 (CH), 74.8 (CH_2), 71.4 (CH), 59.3 (CH_3), 53.2 (CH_3), 52.5 (CH_3), 48.2 (2 × CH), 45.4 (C), 44.2 (CH), 40.4 (CH), 26.4 (CH_3), 21.4 (CH_3), 18.8 (CH_3); CV $E_{p,a}$ = 0.71 V (NHE).

2*H*-Oxonium Complex 9. Complex **8** (364 mg, 0.405 mmol) was dissolved in CH_3CN (4.25 g) and cooled to −40 °C. Cold TfOH (−40 °C, 194.3 mg, 1.29 mmol) in CH_3CN (1.23 g) was added and the light yellow solution immediately darkened. After 10 min, the reaction mixture was removed from the cold bath and added to stirring ether (∼250 mL) to form a precipitate which was collected by filtration and dried in vacuo. Product **9** was isolated as an off gray solid (407 mg, 96%): ^{1}H NMR (CD_3CN) δ 5.78 (dd, J = 2.4, 7.2 Hz, 1H), 5.59 (q, J = 6.8 Hz, 1H), 5.19 (d, J = 7.2 Hz, 1H), 5.09 (br s, 3H), 3.90 (br s, 12H), 3.76 (s, 3H), 3.63 (t, J = 2.8 Hz, 1H), 3.58 (s, 3H), 3.51 (dd, J = 2.8, 10.4, 1H), 3.21 (s, 3H), 2.57 (m, 1H), 2.47 (m, 1H), 1.80 (d, J = 6.8 Hz, 3H), 1.22 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (CD_3CN) δ 203.8 (CO), 178.0 (CO), 170.3 (CO), 125.8 (C), 121.7 (q, J = 300 Hz, CF_3), 79.1 (CH), 73.6 (CH_2), 65.3 (CH), 59.0 (CH), 57.1 (CH_2), 55.0 (CH_3), 52.9 (CH_3), 45.0 (C), 40.9 (CH), 38.1 (CH), 31.3 (CH_2), 24.5 (CH_3), 23.3 (CH_3), 17.2 (CH_3).

2-(2-Methoxymethyl-5-oxocyclohex-3-enyl)-2-methylpropionic Acid Methyl Ester (10). Complex **9** (347 mg, 0.331 mmol) was dissolved in CH_3CN (3.5 g) and water (100 mg) was added. The solution was stirred at room temperature for 1 h during which time the color lightened from dark brown to yellow. Without isolation, the resulting mixture was transferred to a pressure tube and 2,6-lutidine (107 mg, 1.0 mmol) followed by AgOTf (125 mg, 0.486 mmol) was added. The pressure tube was sealed and heated in an oil bath at 70 °C for 4 h. The mixture was then allowed to cool to room temperature, concentrated under reduced pressure, and added to a mixture of ether and water (1:1, 40 mL). The ethereal layer was separated, washed with dilute $NaHCO_3$ solution and brine, and then dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave a pale yellow oil. Further purification of crude material on a preparative TLC plate (500 μm, silica gel, 15:85 ethyl acetate/hexanes) yielded compound **10** as a colorless oil (51 mg, 64%): $[\alpha]^{rt}_D$ 184 (c 0.31, $CHCl_3$); IR (neat, HATR) cm^{-1} 1725, 1678, 1459, 1389, 1249, 1193, 1134; ^{1}H NMR ($CDCl_3$) δ 6.97 (dd, J = 5.7, 9.9 Hz, 1H), 6.04 (d, J = 10.2 Hz, 1H), 3.68 (s, 3H), 3.52 (d, J = 5.7 Hz, 2H), 3.24 (s, 3H), 2.77 (m, 2H), 2.40 (m, 2H), 1.26 (s, 3H), 1.22 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 200.2 (CO), 177.2 (CO), 152.2 (CH), 129.3 (CH), 70.7 (CH_2), 58.7 (CH_3), 51.8 (CH_3), 44.2 (C), 44.0 (CH), 38.2 (CH_2), 37.1 (CH_2), 24.8 (CH_3), 23.2 (CH_3); GCMS (EI) m/z 240 (M^+), 209, 176, 165, 149, 121, 107. The enone **10** was analyzed for ee by HPLC with a Chiralcel OD-H column (90:10 hexanes/2-propanol; 0.8 mL/min): (major) t_R = 7.5 min, (minor) t_R = 9.7 min, 85% ee (compared with racemic **10**).

2-Methyl-2-(2-methylene-5-oxocyclohex-3-enyl)propionic Acid Methyl Ester (11). Complex **9** (155 mg, 0.148 mmol) was dissolved in CH_3CN (4.3 g) and water (100 mg) was added. The solution was stirred at room temperature for 1 h during which time the color faded from dark brown to yellow. Without isolation, the resulting mixture was transferred to a pressure tube and AgOTf (40 mg, 0.156 mmol) was added. The pressure tube was then sealed and heated in an oil bath at 70 °C for 2 h. The mixture was cooled and concentrated under reduced pressure, giving a thick syrup, which was added to a mixture of water and ether (1:1, 40 mL). The ethereal layer was separated, washed with water (5 mL) and brine, and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure afforded a colorless oil (19 mg, 61%): ^{1}H NMR ($CDCl_3$) δ 7.57 (d, J = 10.2 Hz, 1H), 5.92 (d, J = 10.2 Hz, 1H), 5.47 (br s, 1H), 5.30 (br s, 1H), 3.64 (s, 3H), 3.19 (dd, J = 3.0, 6.9 Hz, 1H), 2.63 (AB d, J = 3.0, 6.6 Hz, 2H), 1.13 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 197.7 (CO), 176.9 (CO), 147.8 (C), 140.5 (CH), 127.6 (CH), 123.3 (CH), 51.8 (CH_3), 46.8 (C), 46.7 (CH), 39.0 (CH_2), 23.2 (CH_3), 23.0 (CH_3); GCMS (EI) m/z 208 (M^+), 177, 149, 107.

Allyl Ether Complex 12. Complex **3** (392 mg, 0.389 mmol) was dissolved in CH_3CN (2.81 g) and cooled to −40 °C. A cold solution of tetrabutylammonium cyanoborohydride (TBAC) (−40 °C, 221 mg, 0.784 mmol) in CH_3CN (1.30 g) was added and the mixture left in a cold bath for 2 h, during which time a color change to pale yellow was observed. To this mixture was added a cold solution (−40 °C) of 2,6-lutidine (0.107 g, 1.0 mmol, in CH_3CN 1.11 g); after 10 min at −40 °C the mixture was allowed to warm to room temperature and precipitated in stirring ether:CH_2Cl_2 (2:1, 300 mL) to form a light yellow precipitate. Collection of the precipitate by filtration at reduced pressure followed by drying in vacuo afforded solid **12** (291 mg, 87%): ^{1}H NMR (CD_3CN) δ 4.97 (d, J = 7.9 Hz, 1H), 4.10 (q, J = 6.8, 1H), 4.07(br s, 3H), 3.68 (m, 1H), 3.67 (s, 3H), 3.60 (s, 3H), 3.50 (dd, J = 6.0, 9.3 Hz,1H), 3.17(br s, 12 H), 3.07 (m, 1H), 2.55 (m, 1H), 2.14 (bs, 1H), 1.76 (m, 1H), 1.51 (dd, J = 3.3, 15.8 Hz, 1H), 1.35 (d, J = 6.8, 3H), 1.06 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (CD_3CN) δ 178.8 (CO), 174.9 (CO), 121.8 (q, J = 315 Hz, CF_3), 78.9 (CH), 72.0 (CH), 52.8 (CH_3), 52.6 (CH), 52.4 (CH_3), 47.2 (CH), 45.7 (C), 35.9 (CH_2), 30.4 (CH_2), 29.1 (CH_2), 23.2 (CH_3), 21.4 (CH_3), 18.3 (CH_3); CV $E_{p,a}$ = 0.66 V (NHE).

Allyl Ether Complex 13. Repeating the same procedure on complex **9** (471 mg, 0.449 mmol) as that for complex **4**, allyl ether complex **13** was obtained as a pale yellow solid (318 mg, 78%): ^{1}H NMR (CD_3CN) δ 5.11 (br q, J = 7.2 Hz, 1H), 4.14 (q, J = 6.8, 1H), 4.06 (br s, 3H), 3.68 (m, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 3.35−3.52 (m, 3H), 3.32 (s, 3H), 3.23 (br s, 12 H), 2.92−3.14 (m, 2H), 1.82 (m, 1H), 1.59 (m, 1H), 1.36 (d, J = 6.8, 3H), 1.25 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (CD_3CN) δ 179.5 (CO), 175.2 (CO), 121.9 (q, J = 300 Hz, CF_3), 80.9 (CH), 76.1 (CH_2), 72.7 (CH), 59.3 (CH_3), 56.4 (CH), 52.8 (CH_3), 52.6 (CH_3), 47.5 (CH), 45.4 (C), 43.6 (CH), 42.7 (CH), 30.1 (CH_2), 26.9 (CH_3), 24.4 (CH_3) 18.6 (CH_3); CV $E_{p,a}$ = 0.66 V (NHE).

2-[5-(1-Methoxycarbonylethoxy)cyclohex-3-enyl]-2-methylpropionic Acid Methyl Ester (14). Pyridine (139 mg, 1.76 mmol) and then AgOTf (122 mg, 0.474 mmol) were added to a solution of complex **12** (211 mg, 0.233 mmol) in CH_3CN (2.67 g) in a pressure tube. The pressure tube was then sealed and heated in an oil bath at 70 °C for 2.5 h. The mixutre was then allowed to cool to room temperature, and solvent was evaporated under reduced pressure to yield a thick residue, which was added to a mixture of ether and water (1:1, 50 mL). The ethereal layer was separated, washed with a dilute $NaHCO_3$ solution and brine, and dried over anhydrous Na_2SO_4. Evaporation of solvent under reduced pressure afforded a crude pale yellow oil. Further purification on a preparative TLC plate (500 μm, silica gel, 10:90 ethyl acetate/hexanes, 2 runs) yielded compound **14** as a colorless oil (45 mg, 67%): $[\alpha]^{rt}_D$ +151.2 (c 0.82, $CHCl_3$); IR (neat, HATR) cm^{-1} 2984, 2971, 2950, 1750, 1728, 1434, 1368,1198, 1131; ^{1}H NMR ($CDCl_3$) δ 5.95 (ddd, J = 2.1,5.4, 9.6 Hz, 1H), 5.79 (m,1H), 4.11 (q, J = 6.9 Hz, 1H), 3.95 (br s, 1H), 3.73 (s, 3H), 3.65 (s, 3H), 2.11 (m, 1H), 1.73−2.07 (m, 4H), 1.38 (d, J = 6.8, 3H), 1.17 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.9 (CO), 174.0 (CO), 132.3 (CH), 124.9 (CH), 72.7 (CH), 71.2 (CH), 51.8 (CH_3), 51.5 (CH_3), 44.6 (C), 35.8 (CH), 29.8 (CH_2), 27.2 (CH_2), 22.8 (CH_3), 21.4 (CH_3), 19.0 (CH_3); GCMS (EI) m/z 284 (M^+), 197, 181, 165, 149, 121, 102, 79. Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.27; H, 8.85. The diastereoselectivity for the compound was determined by ^{1}H NMR and found to be 97%. Compound **14** was analyzed for ee by HPLC with a Chiralcel OD-H column (98:2 hexanes/2-propanol; 0.8 mL/min): (minor) t_R = 6.4 min, (major) t_R = 8.2 min, 98% ee (compared with racemic **14**).

2-[5-(1-Methoxycarbonylethoxy)-2-methoxymethylcyclohex-3-enyl]-2-methylpropionic Acid Methyl Ester (15). Repeating the same procedure on complex **13** (185 mg, 0.205 mmol) as that for complex **12**, compound **15** was obtained as a colorless oil (43 mg, 64%): $[\alpha]^{rt}_D$ 226.5 (c 0.68, $CHCl_3$); IR (neat, HATR) cm^{-1} 2984, 2950, 2890, 1751, 1727, 1448, 1435,1198, 1131; ^{1}H NMR ($CDCl_3$) δ 5.95 (dd, J = 5.1, 10.2 Hz, 1H), 5.84 (dd, J = 4.5, 9.9 Hz, 1H), 4.11 (q, J = 6.6 Hz, 1H), 3.94 (br s, 1H), 3.71 (s, 3H), 3.64 (s, 3H), 3.38 (dd, J = 5.7, 9.3 Hz, 1H), 3.25 (dd, J = 6.6, 15.9 Hz, 1H), 3.20 (s, 3H), 2.52 (m, 1H), 2.22 (dq, J = 2.7, 5.1 Hz, 1H), 1.89 (bd, J = 5.2, 1H), 1.80 (dd, J = 5.2, 9.3 Hz, 1H), 1.36 (d, J = 6.6 Hz, 3H), 1.24 (s, 3H), 1.16 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.1 (CO), 173.9 (CO), 135.2 (CH), 125.7 (CH), 72.8 (CH), 71.8 (CH), 71.6 (CH), 58.6 (CH_3), 51.8 (CH_3), 51.4 (CH_3), 44.0 (C), 39.5 (CH), 37.6 (CH_2), 27.2 (CH_2), 25.4 (CH_3), 23.4 (CH_3),

18.9 (CH_3); GCMS (EI) *m*/*z* 328 (M^+); HRMS (MALDI, 3-HPA) exact mass calcd for $(C_{17}H_{28}O_6Na)^+$ requires *m*/*z* 351.1784, found *m*/*z* 351.1787. The diastereoselectivity for the compound was determined by ^{1}H NMR and found to be 97%. Compound **15** was analyzed for ee by HPLC with a Chiralcel OD-H column (98:2 hexanes/2-propanol; 0.8 mL/min): (minor) t_R = 7.3 min, (major) t_R = 8.4 min, 97% ee (compared with racemic **15**).

Allyl Complex 16. Complex **13** (225 mg, 0.25 mmol) in CH_3CN (4.2 g) was cooled to −40 °C, and TfOH (77 mg, 0.51 mmol) in CH_3CN (1.5 g) at −40 °C was added to it. The solution immediately turned from yellow to dark brown. After standing at −40 °C for 15 min, the solution was removed from the cold bath and added to stirring ether (∼300 mL), forming a brown precipitate. Filtration of the precipitate under reduced pressure followed by washing with ether (100 mL) and drying in vacuo yielded off gray solid **16** (223 mg, 94%): ^{1}H NMR (CD_3CN) δ 5.70 (br s, 1H), 5.60 (m, 1H), 5.30 (br s, 3H), 5.24 (t, J = 6.0, 1H), 4.05 (br s, 12H), 3.81 (dd, J = 7.8, 10.5, 1H), 3.64 (s, 3H), 3.57 (dd, J = 3.6,10.5, 1H), 3.30 (s, 3H), 1.50 (br d,J = 6.8, 1H), 1.38 (m, 1H), 1.17 (s, 6H); ^{13}C NMR (CD_3CN) δ 178.5 (CO), 122.0 (q, J = 315 Hz, CF_3), 89.1 (CH), 84.8 (CH), 80.5 (CH), 72.0 (CH_2), 59.1 (CH_3), 52.9 (CH_3), 45.0 (C), 43.9 (CH), 36.8 (CH), 24.6 (CH_2), 23.9 (CH_3), 23.4 (CH_3).

2-(5-Methoxy-2-methoxymethylcyclohex-3-enyl)propionic Acid Methyl Ester (18). Allyl complex **16** (215 mg, 0.226 mmol) was dissolved in methanol (2.43 g) and stirred at room temperature for 30 min, with a color change from brown to red observed during stirring. The solution was then transferred to a cold bath (−40 °C) and quenched with a solution of 2,6-lutidine (157 mg, 1.47 mmol) in methanol (1.0 g) at −40 °C. The mixture was kept at −40 °C for an additional 30 min, then warm to room temperature, and added to stirring ether (200 mL) to give a red-orange slurry. Filtration of the slurry, followed by washing with ether (50 mL) and drying in vacuo, afforded a solid (157 mg). This solid without characterization was subjected to decomplexation as follows: The solid was dissolved in CH_3CN (1.5 g) and 2,6-lutidine (107 mg, 1.0 mmol) in a pressure tube, and AgOTf (56 mg, 0.216 mmol) was then added to the solution. The tube was sealed and heated in an oil bath at 70 °C for 2 h. The pressure tube was then cooled to room temperature, and the solution was transferred to a round-bottom flask. Evaporation of solvents under reduced pressure afforded a crude material, which was added to a mixture of ether:water (1:1, 30 mL). The ethereal layer was separated and the aqueous layer extracted with ether (10 mL). The combined ethereal layer was washed with water and brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure yielded a pale yellow oil. Further purification on a preparative TLC plate (500 μm, silica gel, 1:9 ethyl acetate/hexanes) gave colorless oil **18** (16 mg, 27%): ^{1}H NMR ($CDCl_3$) δ 5.79 (m, 2H), 3.84 (br s, 1H), 3.67 (s, 3H), 3.46 (dd, J = 5.7, 9.0 Hz, 1H), 3.38 (s, 3H), 3.26 (dd, J = 6.0, 9.5 Hz, 1H), 3.23 (s, 3H), 2.54 (br q, J = 4.8 Hz, 1H), 1.95−2.01 (m, 2H), 1.51 (m, 1H), 1.24 (s, 3H), 1.19 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.0 (CO), 132.0 (CH), 128.7 (CH), 77.7 (CH), 72.5 (CH_2), 58.5 (CH_3), 55.5 (CH_3), 51.6 (CH_3), 44.6 (C), 42.8 (CH), 37.5 (CH), 27.0 (CH_2), 24.8 (CH_3), 22.9 (CH_3); GCMS (EI) *m*/*z* 211, 155, 123, 102, 91, 79, 45; HRMS (MALDI, 2,5-DHB) exact mass calcd for $(C_{14}H_{24}O_4Na)^+$ requires *m*/*z* 279.1564, found *m*/*z* 279.1572.

2-[5-(1-Methoxycarbonyl-1-methylethyl)-4-methoxymethylcyclohex-2-enyl]malonic Acid Dimethyl Ester (20). The allyl ether complex **13** (188 mg, 0.208 mmol) in CH_3CN (2.2 g) was cooled to −40 °C, and TfOH (50 mg, 0.335 mmol) in CH_3CN (1.1 g) at −40 °C was added to it. After the mixture was allowed to stand at −40 °C for 15 min, a cold (−40 °C) solution of dimethyl malonate (211 mg, 1.59 mmol) and DIEA (118 mg, 0.91 mmol) in CH_3CN (1.7 g) was added. The reaction mixture was left in a cold bath for 16 h. The mixture was then allowed to warm to room temperature and transferred to a pressure tube, and AgOTf (60 mg, 0.234 mmol) was added. The pressure tube was sealed and heated in an oil bath at 80 °C for 4 h. The reaction mixture was transferred to a round-bottom flask and the solvent removed under reduced pressure to give a residue. The residue was diluted with ether (25 mL) and washed with a dilute NaOH solution (10 mL × 2) to remove the excess of dimethyl malonate, then with water, and finally with brine. The ethereal layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a thick colorless oil. Further purification of the oil by column chromatography (silica gel) using gradient eluents hexanes, ethyl acetate/hexanes (5:95), and ethyl acetate/hexanes (20:80) gave compound **20** as a colorless oil (38 mg, 51%): $[\alpha]^{rt}_D$ 81.9 (*c* 0.3, $CHCl_3$); IR (neat, HATR) cm^{-1} 2953, 1753, 1727, 1434, 1256, 1192, 1150; ^{1}H NMR ($CDCl_3$) δ 5.79 (ddd, J = 2.4, 5.5, 10.0 Hz, 1H), 5.57 (dd, J = 2.5, 10.2 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.66 (s, 3H), 3.41 (dd, J = 5.9, 9.2 Hz, 1H), 3.29 (d, J = 8.6 Hz, 1H), 3.23 (s, 3H), 3.20 (dd, J = 6.1, 9.4 Hz, 1H), 2.93 (m, 1H), 2.54 (dt, J = 5.1 Hz, 1H), 2.01 (ddd, J = 1.7, 4.5, 12.5 Hz, 1H), 1.67 (dd, J = 5.5, 12.7 Hz, 1H), 1.46 (dd, J = 2.7, 5.3 Hz, 1H), 1.22 (s, 3H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.0 (CO), 168.8 (CO), 168.7 (CO), 131.7 (CH), 128.0 (CH), 72.8 (CH_2), 58.5 (CH_3), 56.5 (CH), 52.3 (CH_3 × 2), 51.6 (CH_3), 44.6 (CH), 44.5 (C), 38.2 (CH), 37.2 (CH), 25.1 (CH_2), 24.8 (CH_3), 23.0 (CH_3); GCMS (EI) *m*/*z* 356 (M^+), 325, 293, 223, 191, 163, 133, 119, 91, 45. HPLC analysis with a Chiralcel OD-H column (99:1 hexanes/2-propanol; 0.8 mL/min): (major) t_R = 6.2 min (minor) t_R = 7.5 min 81% ee.

2-[5-(1-Methoxycarbonyl-1-methylethyl)-2-methoxymethylcyclohex-3-enyl]-2-methylpropionic Acid Methyl Ester (22). A MMTP (178 mg, 1.02 mmol) solution in CH_3CN (1.4 g) was added to the allyl complex **16** (203 mg, 0.214 mmol) in CH_3CN (2.5 g) at room temperature, and the resulting mixture was stirred at room temperature for 3 h. The mixture was then added to stirring ether (300 mL), forming a precipitate, which was collected as a brown solid by filtration and drying under reduced pressure. The solid was then subjected to decomplexation without characterization as follows: The solid was dissolved in water (10 mL), and ether (15 mL) was added to form a biphasic mixture. To this mixture was added CAN (150 mg, 0.274 mmol), and the solution wasstirred for 30 min at room temperature. The ethereal layer was separated and the aqueous layer was extracted with ether (10 mL). The combined ethereal layer was washed with dilute $NaHCO_3$, water, and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to yield an oil. Further purification of the oil by column chromatography (silica gel) using hexanes:ethyl acetate (9:1) as eluent gave compound **22** as a colorless oil (33 mg, 47%): $[\alpha]^{rt}_D$ 87.2 (*c* 0.72, $CHCl_3$); IR (neat, HATR) cm^{-1} 2978, 2951, 2934, 1727, 1464, 1434, 1389,1190, 1140; ^{1}H NMR ($CDCl_3$) δ 5.77 (dq, J = 2.6, 10.3 Hz, 1H), 5.49 (br d, J = 10.3 Hz, 1H), 3.67 (s, 3H), 3.65 (s, 3H), 3.40 (dd, J = 5.9, 9.2 Hz, 1H), 3.23 (s, 3H), 3.19 (dd, J = 6.1, 9.2 Hz, 1H), 2.51 (m, 2H), 1.97 (dt, J = 4.4, 10.3 Hz, 1H), 1.43 (m, 2H), 1.21 (s, 3H), 1.17 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.2 (CO), 178.0 (CO), 131.4 (CH), 128.1 (CH), 73.0 (CH_2), 58.5 (CH_3), 51.6 (CH_3), 51.5 (CH_3), 45.3 (CH), 45.0 (C), 44.8 (C), 44.5 (CH), 37.2 (CH_2), 24.5 (CH_3), 23.0 (CH_3), 22.1 (CH_3), 21.8 (CH_3 × 2); GCMS (EI) *m*/*z* 326 (M^+), 294, 197, 181, 165, 149, 121, 102, 79; HRMS (MALDI 2-DHB) exact mass calcd for $(C_{18}H_{30}O_5Na)^+$ requires *m*/*z* 349.1991, found *m*/*z* 349.1991. HPLC analysis with a Chiralcel OD-H column (99:1 hexanes/2-propanol; 0.8 mL/min): (major) t_R = 6.2 min (minor), t_R = 7.5 min 90% ee.

For complexes **23** and **24** please see Supporting Information.

2-(5-α-Methoxy-2-methoxymethylcyclohex-3-enyl)propionic Acid Methyl Ester (25). Lutidine (108 mg, 1.0 mmol) followed by AgOTf (97 mg, 0.378 mmol) was added to a solution of complex **24** (182 mg, 0.218 mmol) in CH_3CN (2.67 g) in a pressure tube. The pressure tube was sealed and heated on an oil bath at 70 °C for 2.5 h. The mixture was then allowed to cool and transferred to a round-bottom flask. Evaporation of solvent under reduced pressure afforded a residue, which was added to a mixture of ether/water (1:1, 30 mL). The ethereal layer was separated and the aqueous layer extracted with ether (10 mL); the combined ethereal layer was washed with water and brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure yielded a pale yellow oil. Further purification on a preparative TLC plate (500 μm, silica gel, 1:9 ethyl acetate/hexanes) gave pale yellow oil **25** (28 mg, 49%): ^{1}H NMR ($CDCl_3$) δ 5.93 (m, 2H), 3.72 (d, J = 4.2, 1H), 3.66 (s, 3H), 3.41 (dd, J = 5.7, 9.3 Hz, 1H), 3.34 (s, 3H), 3.29 (dd, J = 6.3, 9.3 Hz, 1H), 3.23 (s, 3H), 2.54 (br q, J = 5.7 Hz, 1H), 2.16 (m, 1H). 1.95 (br d, 1H), 1.72 (m, 1H), 1.25 (s, 3H), 1.20 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.1 (CO), 134.6 (CH), 126.4 (CH), 73.4 (CH), 71.8 (CH_2), 58.6 (CH_3), 56.1 (CH_3), 51.5 (CH_3), 44.1 (C), 39.5 (CH), 37.7 (CH), 25.3 (CH_2), 24.9 (CH_3), 23.6 (CH_3); GCMS *m*/*z* 256, 212, 156, 124, 103, 92.

General Procedure for Preparation of Complexes 26 and 27. A cold (−40 °C) solution of TfOH (0.2 mmol) in CH_3CN (2.5 g) was added to cold (−40 °C) solution of complex **2** (0.15 mmol) and the respective cycloalkenone (0.3 mmol). The mixture turned from orange-red to dark blue immediately upon addition, after standing at (−40 °C) for 30 min. Cold (−40 °C) pyridine (1.0 mmol) in CH_3CN (1.0 g) was added. The solution slowly turned to orange-brown over a period of 30 min. The solution was then warmed to room temperature and added to a stirring mixture of ether/CH_2Cl_2 (2:1, ∼300 mL). The yellow solid precipitated was collected by filtration and dried under reduced pressure (88−91%).

Complex 26: ^{1}H NMR (acetone-d_6) δ 6.38 (d, J = 6.8 Hz, 1H major), 6.24 (d, J = 7.6 Hz, 1H minor), 5.39 (m, 1H major + 2H minor), 5.26 (d, J = 8.3 Hz, 1H major), 4.99 (dd, 1H major and 1H minor), 4.81 (q, J = 6.6 Hz, 1H), 4.25 (bs, 3H), 3.81 (s, 3H), 3.11 (bs, 12H), 2.82 (m, 1H), 2.40−2.17 (m, 5H), 1.65 (d, J = 6.8 Hz, 3H).

Complex 27: ^{1}H NMR (CD_3CN) δ 6.32 (d, J = 6.8 Hz, 1H), 5.29 (d, J = 6.4 Hz, 1H), 5.19 (d, J = 6.8 Hz, 1H major), 4.89 (d, J = 6.4 Hz, 1H), 4.71 (q, J = 6.9 Hz, 1H), 4.15 (bs, 3H), 3.71 (s, 3H), 2.99 (bs, 12H), 3.00−2.60 (m, 2H), 2.40−2.00 (m, 4H), 1.80−1.60 (m, 3H), 1.54 (d, J = 6.8 Hz, 3H).

General Procedure for Decomplexation of Complexes 26 and 27. A solution of the complex (0.2 mmol) in CH_3CN (5.0 g) in a pressure tube was heated at 80 °C for 3−4 h. The pressure tube was then allowed to cool, the white solid formed in the reaction mixture was removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting crude material was dissolved in water (15 mL) and extracted with ether (20 mL). The ethereal layer was separated, washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated to yield a clear oil. Purification of the crude oil by column chromatography (silica gel) using hexanes/ethyl acetate (9:1) afforded compounds **28** and **29** in 74% and 71% yields, respectively.

2-[4-(3-Oxocyclopentyl)phenoxy]propionic acid methyl ester (28): IR (neat, HATR) cm^{-1} 1737, 1611, 1511, 1240, 1204, 1133, 977; ^{1}H NMR ($CDCl_3$) δ 7.15 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 4.75 (q, J = 6.6 Hz, 1H), 3.76 (s, 3H), 3.34 (m, 1H), 2.64 (dd, J = 7.8, 18.3 Hz, 1H), 2.21−2.49 (m, 4H), 1.83−2.00 (m, 1H), 1.61 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 218.2 (CO), 172.5 (CO), 156.08 (C), 135.9 (C), 127.6 (CH), 115.0 (CH), 72.5 (CH), 52.3 (CH_3), 45.9 (CH_2), 41.4 (CH), 38.9 (CH_2), 31.3 (CH_2), 18.6 (CH_3); GCMS (EI) m/z 262, 203, 175, 147, 120.

2-[4-(3-Oxocyclohexyl)phenoxy]propionic acid methyl ester (29): IR (neat, HATR) cm^{-1} 1756, 1737, 1709, 1511, 1447, 1240, 1223, 1206; ^{1}H NMR ($CDCl_3$) δ 7.10 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.73 (q, J = 6.9 Hz, 1H), 3.75 (s, 3H), 2.93 (m, 1H), 2.24−2.61 (m, 4H), 2.02−2.15 (m, 2H), 1.71−1.85 (m, 2H), 1.60 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 211.0 (CO), 172.6 (CO), 156.2 (C), 137.4 (C), 127.5 (CH), 115.1 (CH), 72.5 (CH), 52.3 (CH_3), 49.0 (CH_2), 43.8 (CH), 41.1 (CH_2), 32.8 (CH_2), 25.4 (CH_2), 18.5 (CH_3); GCMS (EI) m/z 276, 233, 217, 159, 133, 120, 91.

General Procedure for Oxidation of Complexes 26 and 27 with TfOH. Neat TfOH (50 mg, 0.33 mmol) was added to a stirred solution of the complex (0.2 mmol) in CH_3CN (3.0 g) at room temperature. The solution was turned dark immediately and was stirred for 30 min and diluted with ether/water (1:1, 50 mL). The ethereal layer was separated and washed with dilute $NaHCO_3$, water, and brine. Drying over Na_2SO_4 followed by evaporation under reduced pressure yielded a pale yellow oil. The crude oil was purified by column chromatography (silica gel) using hexanes/ethyl acetate (95:5) to give 3-phenylcyclopentanone **(30)** (36%) from complex **26** and 3-phenylcyclohexanone **(31)** (40%) from complex **27**. Further elution of the column with hexanes/ethyl acetate (85:15) gave compounds **28** and **29** from complexes **26** and **27** (40 and 44%), respectively. Compounds **30** and **31** were characterized by ^{1}H NMR and GCMS analysis and were in agreement with previously reported data.[34−36] For chiral purity, HPLC analysis of compound **31**, $[\alpha]^{rt}_D$ −16.5 (c 0.57, $CHCl_3$), was performed on a Chiralcel OD-H column (99:1 hexanes/2-propanol; 0.8 mL/min): (major) t_R = 6.2 min (minor) t_R = 7.5 min, and ee found to be 86%. The CD spectrum of compound **31** gave a negative Cotton effect (n−π*). Compound **30** could not be separated by chiral HPLC under a variety of conditions and hence the optical purity is not determined. On the basis of the sign of specific rotation, $[\alpha]^{rt}_D$ −45 (c 0.8, $CHCl_3$), the (*S*) configuration was assigned to the major enantiomer.

General Procedure for the Synthesis of Compounds 32 and 37. TfOH (0.3 mmol) at −40 °C in CH_3CN (1.5 g) was added to a cold (−40 °C) solution of complex **2** (0.25 mmol) and the respective Michael acceptor (cyclohexenone or *N*-methylmaleimide) (0.3 mmol) , with a color change from orange-red to dark blue immediately upon addition. The solution was allowed to stand for 15 min, and a cold (−40 °C) solution of tetrabutylammonium cyanoborohydride (0.5 mmol) was added in CH_3CN (1.5 g). Over a period of 2−3 h the color of the solution faded to yellow orange. The solution was then quenched by addition of lutidine (1.0 mmol) in CH_3CN (1.5 g) at −40 °C. After 30 min the solution was removed from the cold bath and allowed to warm to room temperature. Addind a stirring mixture of ether/CH_2Cl_2 (2:1, 300 mL) precipitated a yellow solid which was collected by filtration followed by drying under reduced pressure.

Partial characterization of complex **32** (80%): ^{1}H NMR (acetone-d_6) δ 5.12 (m, 1H), 4.17 (q, J = 6.9 Hz, 1H), 4.14 (bs, 3H), 3.66 (s, 3H), 3.58 (m, 1H), 3.29 (bs, 12H), 2.85 (s, 3H), 1.36 (d, J = 6.6 Hz, 3H).

Partial characterization of complex **37** (84%): ^{1}H NMR (CD_3CN) δ 5.20 (m, 1H), 4.71 (bs, 3H), 4.26 (q, J = 6.6 Hz, 1H), 3.74 (bs, 12H), 3.67 (s, 3H), 1.37 (d, J = 6.6 Hz, 3H).

Generation of Allyl Complexes 33 and 38. Complexes **32** and **37** upon treatment with TfOH as in the case of the synthesis of complex **16** gave complexes **33** and **38**, respectively (92−96%).

Partial characterization of complex **33**: ^{1}H NMR (CD_3CN) δ 6.05 (bs, 3H), 5.90 (m, 2H), 5.64 (t, J = 6.3, 1H), 4.74 (bs, 12H), 3.60 (m, 1H),1.65−1.89 (m, 8H).

Complex **38** used without characterization in the next reaction.

Addition of Nucleophiles to Allyl Complexes 33 and 38 Followed by Decomplexation. MMTP (1.0, mmol) was added to solution of the allyl complex **33** or **38** (0.1 mmol) in CH_3CN at room temperature, and the solution was stirred for 3−4 h. The reaction mixture was then removed from the glovebox, transferred to a flask, and concentrated under reduced pressure. The residue was then dissolved in water (10 mL) and ether/ethyl acetate (1:1, 20 mL). To this biphasic reaction mixture was added CAN (0.15 mmol), and the solution was stirred at room temperature for 30 min. The organic layer was separated, and the aqueous layer was extracted with ether/ethyl acetate (1:1, 10 mL). The combined organic layer was washed with water, dilute $NaHCO_3$, and brine. Drying over Na_2SO_4 followed by evaporation under reduced pressure gave a thick oil. Further purification by column chromatography (silica gel) using hexanes/ethyl acetate as gradient eluents with increased polarity led to isolation of cyclohexene derivatives **35** and **40** from **33** and **38**, respectively.

2-Methyl-2-(3′-hydroxybicyclohexyl-2-en-4-yl)propionic acid methyl ester 35 (46%): IR (neat, HATR) cm^{-1} 3359, 2930, 2858, 1726, 1453, 1258, 1133; ^{1}H NMR ($CDCl_3$) δ 5.70 (dt, J = 3.6, 10.5 Hz, 1H), 5.52 (br d, J = 10.5 Hz, 1H), 3.61 (s, 3H), 3.54 (m, 1H), 2.41 (m, 1H), 1.90−2.08 (m, 2H), 1.74−1.87 (m, 2H), 1.18−1.71 (m, 9H), 1.13 (s, 3H), 1.10 (s, 3H), 0.86−0.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 178.3 (CO), 132.2 (CH), 127.8 (CH), 71.1 (CH), 51.6 (CH_3), 45.4 (C), 42.5 (CH), 40.9 (CH), 40.1 (CH_2), 38.9 (CH), 35.7 (CH_2), 29.7 (CH_2), 24.1 (CH_2), 23.9 (CH_2), 22.3 (CH_3), 21.9 (CH_3), 21.3 (CH_2); GCMS (EI) m/z 262, 203, 180, 161, 121, 102, 79; HRMS (MALDI 2-DHB) exact mass calcd for $(C_{17}H_{28}O_3Na)^+$ requires m/z 303.1936, found m/z 303.1931.

2-Methyl-2-[4-(1-methyl-2,5-dioxopyrrolidin-3-yl)cyclohex-2-enyl]-propionic acid methyl ester 40 (23%): $[\alpha]^{rt}_D$ −7.2 (c 1.6, $CHCl_3$); IR (neat, HATR) cm^{-1} 2950, 1723, 1695, 1435, 1384, 1279, 1261, 1125; ^{1}H NMR ($CDCl_3$) δ 5.76 (dt, J = 8.7, 2.7 Hz, 1H), 5.70 (dt, J = 10.2, 2.1 Hz, 1H), 3.66 (s, 3H), 2.96 (s, 3H), 2.89 (m, 1H), 2.69 (dd, J = 18.3, 9.0, 1H), 2.58 (m, 1H), 2.43 (dd, J = 18.3, 4.8, 1H), 2.42 (m, 1H), 1.53 (m, 3H), 1.35 (m, 1H), 1.16 (s, 3H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.8 (CO), 177.8 (CO), 176.6 (CO), 130.0 (CH), 129.9 (CH), 51.7 (CH_3), 45.6 (CH), 44.3 (C), 41.3 (CH), 35.1 (CH), 31.9 (CH_2), 24.7 (CH_3), 22.8 (CH_3), 22.7 (CH_2), 22.3 (CH_3), 21.4 (CH_3); GCMS (EI) m/z 293 (M^+), 233, 192, 105; HRMS (MALDI) exact mass calcd for $(C_{16}H_{23}NO_4Na)^+$ requires m/z 316.1525, found m/z 316.1536. Compound **40** was analyzed for ee by HPLC on a Chiralcel OD-H

column (85:15 hexanes/2-propanol; 1.0 mL/min): (major) t_R = 10.2 min, (minor) t_R = 13.7 min. 93% ee (compared with racemic **40**).

2-Methyl-2-(3′-oxobicyclohexyl-2-en-4-yl)propionic Acid Methyl Ester 36. Compound **35** (14.0 mg, 0.05 mmol) and *N*-methylmorpholine *N*-oxide (12.0 mg, 0.1 mmol) were dissolved in dry CH_2Cl_2 and TPAP (3.0 mg, 0.008 mmol) was added. The mixture was stirred at room temperature and monitored by TLC analysis until the polar starting material was consumed (∼4 h). The reaction mixture was then diluted with ether (10 mL) and washed with dilute HCl, water, and brine. The ethereal layer was dried over Na_2SO_4 and evaporated under reduced pressure to yield a transparent oil (13 mg, 93%): $[\alpha]^{rt}_D$ 42.6 (*c* 1.2, $CHCl_3$); IR (neat, HATR) cm^{-1} 3021, 2942, 2866, 1717, 1454, 1255, 1135; ^1H NMR ($CDCl_3$) δ 5.75 (br d, J = 10.0 Hz, 1H), 5.56 (br d, J = 10.0 Hz, 1H), 3.65 (s, 3H), 1.20−2.20 (m, 15H), 1.12 (s, 3H), 1.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 211.8 (CO), 178.0 (CO), 130.9 (CH), 128.6 (CH), 51.7 (CH_3), 46.1 (CH), 45.3 (C), 43.4 (CH), 42.5 (CH), 41.5 (CH_2), 38.7 (CH_2), 29.2 (CH_2), 25.5 (CH_2), 23.7 (CH_2), 22.3 (CH_3), 22.0 (CH_3), 21.0 (CH_3); GCMS (EI) *m*/*z* 278 (M^+); HRMS (MALDI) exact mass calcd for $(C_{17}H_{26}O_6Na)^+$ requires *m*/*z* 301.1780, found *m*/*z* 301.1773. Compound **36** was analyzed for ee by HPLC on a Chiralcel OD-H column (90:10 hexanes/2-propanol; 0.8 mL/min): (minor) t_R = 6.3 min, (major) t_R = 6.6 min, 91% ee (compared with racemic **36**).

For compounds **2a**, **3a**, and **41**, please see the Supporting Information.

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Supporting Information Available: ^1H and ^{13}C NMR spectral data and HPLC chromatograms for selected compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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