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Toward an Understanding of 1,5-Asymmetric Induction during Nucleophilic Addition to (Arene)chromium Tricarbonyl Complexes: Conformational Preference of the Chromium Tricarbonyl Tripod for Transmission of Chirality

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Asymmetric induction during enolate nucleophile addition to chromium tricarbonyl complexes of 4-alkoxy-1-(trimethylsilyl)benzene derivatives, in which the alkoxy group (R*O) is derived from an optically pure alcohol, is analyzed in terms of the effect of the chiral auxiliary (R*) on the conformation of the tricarbonylchromium tripod. Crystal structure determination on the three complexes **3a** (R* = 2-phenylisobornyl), **3b** (R* = 2-methylisobornyl), and **3c** (R* = 2-(3-[1,3]-dioxalanyl)isobornyl) reveals that the chiral group R* causes a rotation of the $Cr(CO)_3$ group from the normally preferred orientation, the extent and direction of which are dependent on the auxiliary. NMR studies on seven complexes indicate the presence of a single conformation in solution for each, which is assumed to be the same as that shown in the solid state. There is a correlation between the observed asymmetric induction and the $Cr(CO)_3$ tripod rotation, which is believed to be a result of the effect of this conformational distortion on the arene-centered FMO coefficients.

Introduction

Dearomatization of an arene[1] by the one-pot sequence of nucleophilic addition, electrophilic addition, and decomplexation of the corresponding (arene)chromium tricarbonyl complex is a methodology finding many applications in the synthesis of natural products.[2] A particularly useful dearomatization is of (alkoxyarene)chromium tricarbonyls, where carbon nucleophiles add predominantly to the meta position, yielding 5-substituted cyclohexenones.[3] The asymmetric version of this reaction, involving chiral (alkoxyarene)chromium tricarbonyls, yields enantiomerically enriched substituted cyclohexenones, as reported earlier from our laboratories[4] and by Semmelhack.[5] In spite of its potential utility as a mild and rapid route to functionalized chiral carbocycles from suitable arenes,[6] asymmetric induction in these reactions is not completely understood. Nucleophilic addition to chiral complexes of type **1** (Chart 1) presents an interesting example of 1,5-asymmetric induction,[7] rare in the chemical literature.

Background

Our motivation to study these reactions further derived from two results of nucleophilic addition to complexes **1a–c** that have camphor -derived chiral ether auxiliaries. First, the addition of isobutyronitrile anion to the chiral complex **1a**, bearing a methyl para substituent (R′), resulted in very high diastereoselectivity (24:1). Reaction of the synthetically more useful *tert*-butyl lithioacetate with **1a**, but with a $-Si(CH_3)_3$ group in the para position (R′) also gave a remarkably high degree (21:1) of asymmetric induction.[8] Second, the major diastereomers obtained from nucleophilic addition to complexes **1a**,**b** with a methyl para substituent (R′) had opposite stereochemistry at the newly formed center. We were struck by the high diastereoselection at the seemingly similar meta carbons and reversal in selectivity with changes at the remote C2 of the camphyl group.

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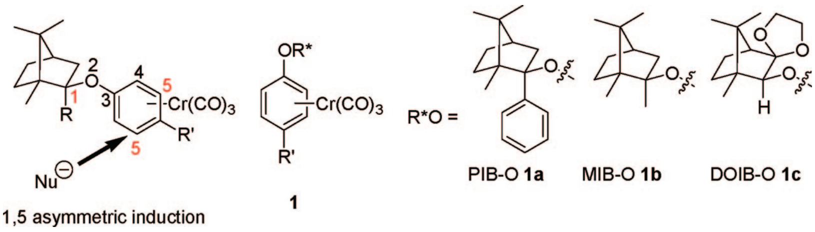
Chart 1.



The origin of diastereoselection in this reaction may arise from steric approach control of the nucleophile influenced by the chiral auxiliary, charge and orbital control related to the orientation of the chromium tricarbonyl tripod with respect to the arene substituents, or a combination of both effects. For achiral (arene)chromium tricarbonyl complexes, the regioselectivity of nucleophilic addition has been attributed to charge and orbital control on the arene, which is significantly influenced by the orientation of the chromium tricarbonyl tripod. This effect will be discussed further here. For complexes that have an electron donor, such as alkoxy, on the arene, the $Cr(CO)_3$ group normally orients itself so that one of the carbonyl groups eclipses the arene C-donor bond (Figure 1, structure **A**).[6a] Extended Hückel calculations indicate that the arene-centered LUMO coefficients are greatest at the meta positions with this orientation,[9a] and this has been offered as an explanation for the preferred addition of nucleophiles meta to the donor substituent. On the other hand, for arenes that have an electron-withdrawing substituent, the $Cr(CO)_3$ tripod orients itself in an anti eclipsed arrangement with respect to the substituent (Figure 1, structure **B**), and the LUMO coefficients are maximum at the ortho and para carbons; for such complexes nucleophile addition occurs at the ortho and para positions. Steric effects are important in that they cause deviations from these ideal structures. Bulky alkyl groups have been shown to cause the $Cr(CO)_3$ tripod to adopt conformation **B**, in contrast to the case for a simple methyl group, which favors **A** (as an electron donor).[6] These orientations are reflected in the nucleophile addition regiochemistry. Related to the present work, diastereoselectivity observed during nucleophile additions to chiral arenemanganese tricarbonyl complexes has been correlated with the LUMO coefficients of the arene complex.[9b]

When steric approach control of the nucleophile is considered, one must consider the stereodirecting effect of the camphyl group, which has been exploited in a number of diastereoselective reactions.[10] The camphyl group has been modified to yield better selectivities in these reactions,[11] and a reversal in asymmetric induction is also noted in a few cases.[12] Interesting examples of reversal in selectivity in certain reactions by simple modification of other chiral auxiliaries have also been reported.[13] In rationalizing the selectivities observed during the reactions of complexes **1**, one or more of the factors mentioned earlier might be involved, and the next logical step would be to probe the structural features and conformational constraints of the complexes.

The present study was carried out with the synthetically useful *tert*-butyl lithioacetate as the nucleophile and arene complexes **3** with a $-Si(CH_3)_3$ group para to the chiral alkoxy group; secondary or tertiary carbanions were not examined. The trimethylsilyl substituent activates the position ortho to itself toward nucleophilic addition and affords better stereo- and regiocontrol than a simple methyl substituent, during both nucleophilic addition and subsequent conversion to a cyclohexenone. Chiral ether auxiliaries (R* = PIB (**3a**), MIB (**3b**), DOIB (**3c**)) were chosen on the basis of our previous experience of variation in and/or reversal of enantioselectivity.[4] In order to assess the factors that the chiral auxiliary might bring to bear in the stereoselection, a few other chiral auxiliaries were used in order to expand the sample set.

Results and Discussion

Nucleophilic Addition to (Arene)chromium Tricarbonyl Complexes. The chiral (alkoxyarene)chromium tricarbonyl complexes **3** were prepared in good yields by S_NAr reactions of the corresponding potassium alkoxide (obtained by treating the chiral isoborneols **2** with potassium hydride) with the fluoroarene complex **4** (Scheme 1). Complex **4** was prepared by the Pauson and Mahaffy procedure[14] of refluxing *p*-fluoro(trimethylsilyl)benzene[15] with chromium hexacarbonyl in a mixture of di-*n*-butyl ether and THF. The chiral isoborneols **2** were prepared by Grignard reagent addition to D-(+)-camphor in the presence of anhydrous cerium chloride[16] (either catalytic or stoichiometric) at room temperature to yield the *exo*-alcohols

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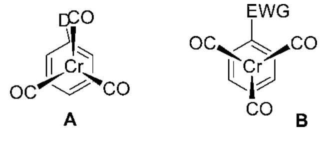
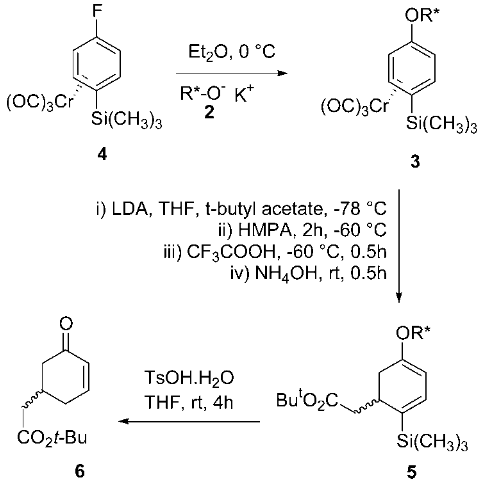


Figure 1. Preferred conformations of arene−$Cr(CO)_3$ complexes with electron-donating (D) and electron-withdrawing (EWG) substituents.

Scheme 1

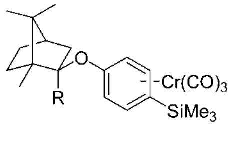


(isoborneols) in good yields.[17] Only the DOIB-OH chiral auxiliary **2c** was prepared differently by the known three-step procedure (see Table 1 for structures of auxiliaries).[18] Each of the complexes **3** was added to a solution of *tert*-butyl lithioacetate in THF, followed by HMPA at −60 °C. The mixture was stirred for 2 h, and trifluoroacetic acid was added at −60 °C, followed by addition of aqueous ammonia solution and warming to room temperature to effect decomplexation. After workup a solution of the product mixture was passed through a plug of alumina to remove chromium compounds. The diastereoselectivity during nucleophilic addition was determined by careful integration of the proton signals that were sufficiently separated (usually the cyclohexadiene protons) in the ^{1}H NMR spectrum of the diastereomeric mixture of cyclohexadienol ethers **5**. The major isomer from diastereoselective nucleophilic addition was determined from the sign of optical rotation (the *S* isomer is dextrorotatory), in chloroform solution, of the corresponding cyclohexenone **6** obtained by hydrolysis/protiodesilylation of the dienol ether mixture. The stereochemistry was further confirmed by recording the CD spectrum in hexane (the *S* isomer shows a negative Cotton effect ($n-\pi^*$) at λ_{max} 338 nm).[19] The results of *tert*-butyl lithioacetate additions to the chiral (arene)chromium tricarbonyl complexes **3** with the ratio of their diastereomeric cyclohexadienol ethers **5** and the corresponding major isomer are collected in Table 1. No ortho addition was detected in the cyclohexadiene products. In some cases traces of decomplexed arene were observed in the ^{1}H NMR spectrum of the crude reaction mixture.

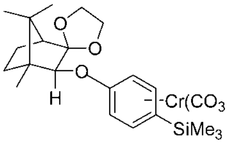
The results of diastereoselectivity from Table 1 show that aryl-substituted chiral auxiliaries give better stereoselection than those with alkyl substituents at C2. This greater selectivity by aryl- over alkyl-substituted auxiliaries has also been noted in other reactions.[20] The complexes **3c**,**d** gave *R* as the major isomer, while the remaining complexes gave the opposite *S* isomer as the major species. In contrast to previous results using unsubstituted or *p*-methyl-substituted complexes (**1**, R′ = H or CH_3), complexes **3a**,**b** gave the same major isomer, the latter albeit with very poor selectivity, indicating that the $-SiMe_3$ substituent also plays an important role in determining stereochemistry. On the other hand, the benzyl derivative **3d** does produce reversed stereochemistry, albeit with low selectivity.

Solid-State Conformations. Before proceeding with the conformational analysis, we shall discuss the conformational classifications of these complexes.[21] Camphor has a rigid bicyclic framework, and the important conformations for these chiral (alkoxy(trimethylsilyl)arene)chromium tricarbonyl complexes should arise from three bond rotations, as shown in Figure 2. The two bond rotations about the ether oxygen (camphyl C2−O and O−arene carbon) both lead to two conformations which would determine the facial preference of the chromium tricarbonyl moiety. Rotation about the camphyl C(2)−O bond would bring the arene ring very close to one of the *gem*-dimethyl groups and is therefore disfavored. The other bond rotation about the arene carbon−oxygen bond would place the $Cr(CO)_3$ group either cis or trans to the endo face of the camphyl moiety, resulting in the two possible conformations cis-endo and trans-endo, respectively. In the case of an arene with a simple methoxy group and *p*-trimethylsilyl group, facial orientation of the tripod is not important. However, because of the stereogenic centers on the auxiliary, the two edges (C edge and C′ edge in Figure 2) of the arene are nonequivalent (diastereotopic). In addition, the electronic effects of the alkoxy group and the trimethylsilyl group would force the $Cr(CO)_3$ tripod to adopt a syn-eclipsed conformation with respect to the alkoxy group (Figure 1, structure **A**). Rotation about the chromium−arene bond, which determines the orientation of the tripod with respect to the chiral auxiliary, i.e., oriented either left (I_l) or right (I_r), leads to four limiting conformations combining these two bond rotations. The left−right notations are taken from Albright et al.'s note on left−right asymmetry in polyene−ML_3 complexes.[22]

Solid-state structures studies on two complexes (**3a**,**b**) which gave the same *S* major isomer from nucleophile addition but with markedly different selectivities and one which gave the *R* isomer (**3c**) were undertaken; complex **3d** did not afford crystals suitable for X-ray studies. ORTEP[23] representations are given in Figures 3−5, and crystal data are summarized in Table 2.



3a R = Ph
3b R= CH_3



3c

While complexes **3a**,**b** each show a single structure, complex **3c** exists in two forms, **3c(A)** and **3c(B)**. The common feature in all the solid -state structures is the face of the arene to which $Cr(CO)_3$ is complexed: i.e., all the complexes have the tripod directed toward the endo face with respect to the camphor

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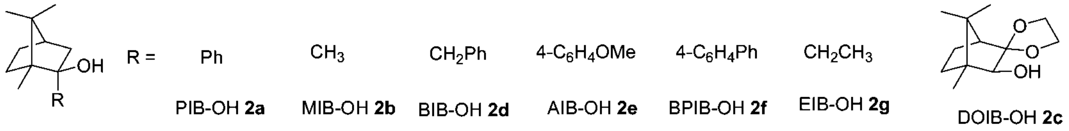
Table 1. Ratio of Diastereoselectivity on Nucleophilic Addition to Chiral (Arene)chromium Tricarbonyl Complexes



chiral auxiliary/complex **3**	ratio of cyclohexadienol ethers **5**	major isomer **6**
phenylisoborneol (PIB)/**3a**	96:4	*S*
methylisoborneol (MIB)/**3b**	55:45	*S*
3,3-ethylenedioxyisoborneol (DOIB)/**3c**	30:70	*R*
benzylisoborneol (BIB)/**3d**	38:62	*R*
p-methoxyphenylisoborneol (AIB)/**3e**	90:10	*S*
diphenylisoborneol (BPIB)/**3f**	90:10	*S*
ethylisoborneol (EIB)/**3g**	80:20	*S*

framework. While complexes **3a** (30°), **3b** (13.3°), and **3c(A)** (4.0°) have a I_l tripod orientation, **3c(B)** (17.1°) has a I_r orientation (deviation from the syn-eclipsed orientation included in parentheses). The nearly staggered orientation found in complex **3a** and a significant deviation from the expected syn-eclipsed conformation found in complexes **3b** and **3c(B)** indicate that the chiral auxiliary significantly influences the directional orientation of the tripod in the solid state. The tripod orientation has been shown to be sensitive to π−carbonyl interactions[24] between aryl substituents and one or more of the carbonyl ligands. It appears that one of the carbonyl ligands interacts with the phenyl of **3a**, thus forcing the $Cr(CO)_3$ tripod to adopt an I_l orientation. This rotation is smaller for the MIB complex **3b**, which is consistent with the smaller steric energy of methyl versus phenyl, as well as the capability of the latter to participate in π-stacking interactions with CO ligands.

We next set out to determine whether these conformations are preferred in solution. In general (arene)chromium tricarbonyl complexes are found to adopt the same conformation in solution as in the solid state.[25] Crystal-packing effects, as determined by extended Hückel calculations, are not usually important, showing that the preferred gas-phase conformation is similar to that in the solid state.[26] For the present study we used NMR NOE difference experiments[27] to detect any conformational preferences in solution and determine whether correlation with the solid -state structure is plausible. Solid-state or solution conformational analysis of *chiral* (arene)chromium tricarbonyl complexes has been previously reported only for a limited number of compounds[28] and is the focus of the present report aimed at rationalizing the observed diastereoselectivities.

Evidence for Conformational Preference from NOE Analysis. We were not able to differentiate the ^{13}C carbons of the $Cr(CO)_3$ tripod by performing low-temperature NMR experiments. However, we were able to confirm conformational preferences of the arene relative to the chiral auxiliary, as described here. NOE difference experiments were performed on complexes **3a**,**b**,**d** in THF-d_8 and on complex **3e** in $CDCl_3$, while for complex **3c**, the spectra were run both in THF-d_8 and C_6D_6, at room temperature. (Copies of NOE difference spectra are available in the Supporting Information for this paper.) In all the complexes studied, the four arene protons and corresponding carbons appear as separate signals in $CDCl_3$, C_6D_6, and THF-d_8. Because of the diastereotopic nature of the *o/o′* and *m/m′* positions, this nonequivalence does not unambiguously indicate a single rotational isomer about the arene carbon−oxygen bond. Preference for a single rotamer in each case would be indicated by signal enhancement of just one of the two diastereotopic protons on irradiation of a neighboring proton resonance on the chiral camphyl moiety. Assignment of the proton signals, key to the NOE studies, was done by analyzing the ^1H−^1H COSY and ^1H−^{13}C HMQC correlations. As expected, no signal enhancements were observed for the protons meta to the ether on irradiation of any proton on the chiral moiety. The two ortho protons are affected because of their proximity to the chiral auxiliary, which is indeed shown to be the case from the NOE studies. *NOE difference experiments by irradiation of suitably resolved proton signals of the camphyl moiety led to unique enhancements of the diastereotopic ortho proton resonances, and vice versa, indicating a single rotamer about the arene−oxygen bond for all complexes studied!* (Full spectra are included in the Supporting Information.) The preference for a single conformation results from the significant barrier to arene−oxygen bond rotation. While π-symmetry interactions between the arene and the substituent are well-known in uncomplexed arenes, systematic studies of substituent effects in (arene)chromium tricarbonyl complexes also indicate significant double-bond character for the arene carbon−oxygen bond.[29] From the X-ray crystal structures determined in the present work, the C2−O−arene carbon bond angles are measured to be 120.07, 124.32, 120.18, and 120.19° for complexes **3a**,**b**,**c(A)**,**c(B)**, respectively, indicating sp^2 hybridization of oxygen, and thereby leading to significant π-interaction with the arene.

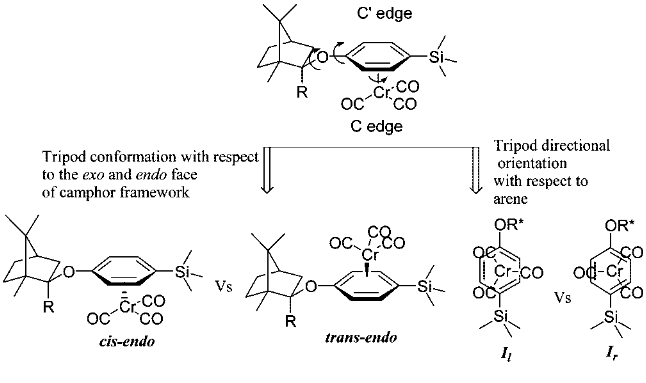


Figure 2. Possible conformations of (alkoxyarene)chromium tricarbonyl complexes.

We have also observed some interesting trends for the ^{13}C shifts of the ortho and meta carbons of the complexed arenes (see Figure 6 and Table 3), which appear to correlate with the sense of rotation of the $Cr(CO)_3$ tripod. These ^{13}C NMR peaks were assigned by combining the data from NOE difference experiments, ^1H−^{13}C correlation, and ^1H−^1H COSY NMR spectra. The data for each complex, together with the corresponding major isomer (*R* or *S*) from *tert*-butyl lithioacetate addition, along with directional orientation of the tripod (I_l or I_r) from the solid state where available, are collected in Table 3.

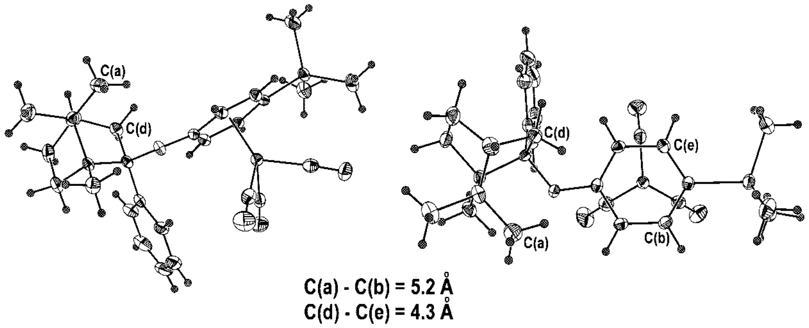


Figure 3. X-ray crystal structure of complex **3a** (two views; 50% probability thermal ellipsoids).

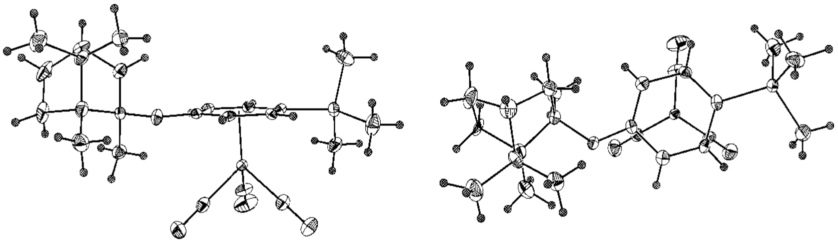
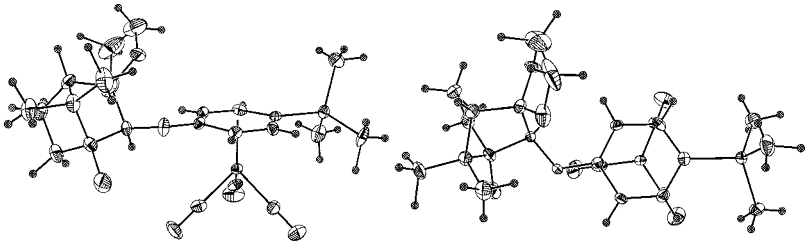
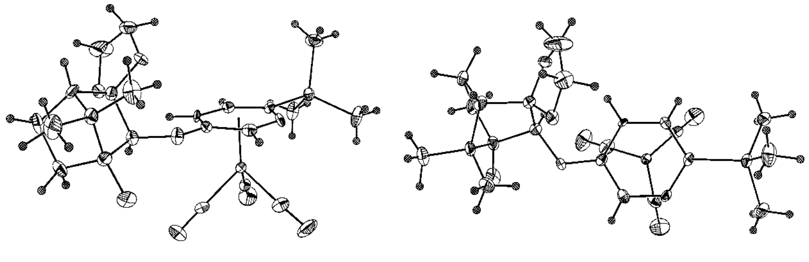


Figure 4. X-ray crystal structure of complex **3b** (two views; 50% probability thermal ellipsoids).



Conformation A



Conformation B

Figure 5. X-ray crystal structure of complex **3c** (two conformations in the unit cell, two views each; 50% probability thermal ellipsoids).

It is interesting to note that for each arene complex **3**, the major diastereomer arises from nucleophile addition at the more deshielded meta carbon. While it is tempting to speculate that this is consistent with a charge-controlled reaction, the differences in shieldings are quite small (e.g., $\Delta\delta = 0.8$ for complex **3a**) and it is likely that perturbation of the arene-based LUMO coefficients is also an important feature. On the other hand, the correlations between carbon shieldings and sense of rotation of the $Cr(CO)_3$ tripod may provide a rapid method for assigning this structural feature in a series of related complexes and, therefore, predicting the stereochemical outcome of nucleophile

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Table 2. Crystal Data for Complexes 3a–c

	3a	3b	3c
formula	$C_{28}H_{34}CrO_4Si$	$C_{23}H_{32}CrO_4Si$	$C_{24}H_{32}CrO_6Si$
space Group	$P2_12_12_1$	$P2_1$	$P2_1$
a (Å)	10.7012(14)	7.7412(6)	9.0373(13)
b (Å)	10.8019(14)	10.9198(8)	10.5947(15)
c (Å)	22.171(3)	14.3413(10)	25.708(4)
β (deg)		103.8960(10)	96.084(2)
V (Å^3)	2562.8(6)	1176.82(15)	2447.6(6)
Z	4	2	4
D_x (Mg m^{-3})	1.334	1.277	1.348
λ (Å)	0.71073	0.71073	0.71073
θ range (deg)	2.1–30.0	4.4–27.7	3.1–26.6
μ (mm^{-1})	0.53	0.56	0.55
T (K)	150(1)	150(1)	150(1)
size (mm)	0.3 × 0.2 × 0.2	0.44 × 0.22 × 0.20	0.22 × 0.14 × 0.06
abs cor	empirical	empirical	empirical
T_{min}, T_{max}	0.901, 1.000	0.861, 1.000	0.924, 1.000
no. of measd rflns	18 645	9061	22 225
no. of indep rflns	6827	4724	9263
no. of rflns with $I > 2\sigma(I)$	4856	4723	8142
R_{int}	0.055	0.016	0.052
h	−15 to +12	−10 to +9	−11 to +11
k	−15 to +15	−14 to +13	−13 to +13
l	−31 to +26	−18 to +18	−32 to +31
fefinement	F^2	F^2	F^2
R ($F^2 > 2\sigma(F^2)$)	0.039	0.051	0.063
R_w (F^2)	0.063	0.112	0.117
S	0.90	1.40	1.08
$\Delta\rho_{max}$ (e Å^{-3})	0.29	0.43	0.42
$\Delta\rho_{min}$ (e Å^{-3})	−0.27	−0.70	−0.59
Flack param	0.019 (14)	0.07 (3)	0.01 (2)

addition, especially for cases where crystal structures are unavailable, such as in this case complex **3d**. One edge of the arene is more deshielded than the other. In complexes **3a**,**b**,**e** it is the C′ edge, while in complexes **3c**,**d** it is the C edge (see Figure 2). The effect of the solvent appears to be negligible, as complex **3c** revealed the same pattern in both THF-d_8 and C_6D_6 solvents. Complexes **3a**,**b** showed the same pattern in their ^{13}C shieldings, while complex **3c** showed a reverse pattern. Complex **3e** showed a pattern similar to that of complexes **3a**,**b**, implying an I_l orientation of the tripod. It may be noted that generally an arene carbon that is eclipsed by a Cr−CO bond is deshielded more than one that is not. This argument has been invoked when comparing the Cr−CO bond eclipsing among the ortho, meta, and para positions. In the present case, the edge of the arene bearing one carbonyl group is deshielded more than the edge that is proximate to two CO ligands. Complex **3d** showed a pattern similar to that of complex **3c**, but opposite to that of **3a**,**b**, and may be assigned the I_r tripod orientation. It is noteworthy that the major stereoisomer from nucleophile addition to **3d** has *R* stereochemistry, but the ee is only 24%.

The pattern of ^{13}C chemical shifts, in conjunction with the cis-endo preference of $Cr(CO)_3$, points to conformational preference in this series of chiral (arene)chromium tricarbonyl complexes but needs further study for general application as a method to determine tripod orientation in solution. The anisotropic ring carbon chemical shifts have long been deliberated inconclusively.[30] Carbon shieldings, as well as coupling constants in organometallic compounds, have been analyzed to determine fluxionality and conformations of σ- and π-bonded complexes.[31] In (arene)chromium chemistry ^{13}C NMR data has so far been applied to determine the syn-eclipsed or anti-eclipsed conformational ratio of $Cr(CO)_3$ with respect to substituents on the arene. The carbon shieldings of (naphthalene)chromium complexes with varied ligands have been correlated with reactivity toward nucleophilic addition.[32]

Origin of Diastereoselection. The nucleophile addition reactions studied in this work are considered to be kinetically controlled. With all other reaction parameters constant (*tert*-butyl lithioacetate as nucleophile and the same reaction conditions), the diastereoselectivity must be solely dependent on the properties of the starting chiral complex and the asymmetric induction occurs at the nucleophilic addition step. From the X-ray crystal structure data, there does not appear to be a uniformly significant difference in steric environments at the two arene meta positions. For example, the neighboring methylene and methyl groups of the isoborneol substituent on complex **3a** produce very similar steric environments at the respective meta positions (see distances reported in Figure 3). Note that the phenyl substituent on the chiral auxiliary is actually syn to the $Cr(CO)_3$ group and, therefore, cannot exert any steric approach control, because the nucleophile approach is anti to the metal. However, as discussed above, the chiral auxiliary causes a rotation of the $Cr(CO)_3$ tripod away from its ideal position (also shown in Figures 3−5, second view for each structure). Complexes **3a**,**b** have a I_l conformation, while one of the two solid-state structures of complex **3c** displays the I_r orientation of the tripod.

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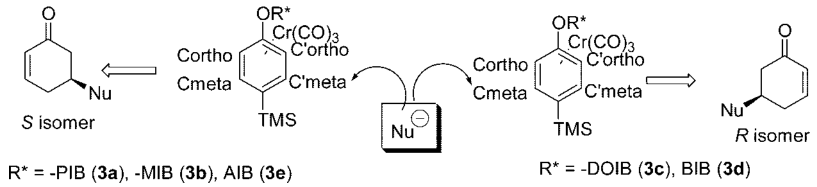

Figure 6

Table 3. ^{13}C NMR Chemical Shifts Correlated (Tripod Orientation from X-ray Crystal Structures and Major Isomer from *tert*-Butyl Lithioacetate Addition)

Complex	Solvent	C_{meta}	C_{ortho}	C'_{meta}	C'_{ortho}	Tripod (I_l /I_r)	Major isomer
-PIB **3a**	THF-d_8	101.5	83.7	102.3	84.5	I_l	*S*
-MIB **3b**	THF-d_8	101.4	83.0	102.2	83.1	I_l	*S*
-AIB **3e**	$CDCl_3$	98.8	82.7	99.4	84.3	-	*S*
-DOIB **3c**	THF-d_8	102.2	82.4	101.2	79.7	I_r & I_l	*R*
-DOIB **3c**	C_6D_6	100.7	81.1	99.3	78.3	I_r & I_l	*R*
-BIB **3d**	THF-d_8	100.9	84.9	100.1	84.7	-	*R*

Interestingly, reaction of **3a** with $LiCH_2CO_2Bu^t$ followed by hydrolysis affords enone **6** (Scheme 1) as the *S* enantiomer in 92% ee, while **3b** gives (*S*)-**6** in only 10% ee; in contrast **3c** affords (*R*)-**6** in 40% ee. The latter result is consistent with the presence of both conformations **A** and **B**, possibly with rapid oscillation between the two: **A** would give (*S*)-**6** with <<10% ee, while **B** would give (*R*)-**6** with <90% ee (possibly ca. 50% on the basis of the torsion angle). However, it is not possible to evaluate these effects quantitatively, because we do not know the relative rates of nucleophile addition to each conformation. These results indicate a connection between the $Cr(CO)_3$ conformation and stereoselectivity during nucleophile addition, suggesting that the chiral auxiliary may transmit its effect through the $Cr(CO)_3$ group, which in turn perturbs the arene-centered MO coefficients. Diastereoselectivity was reported from our laboratory in studies of nucleophile addition to chiral (arene)manganese tricarbonyl complexes.[9] The effect of direction of $Mn(CO)_3$ tripod orientation on the MO coefficients of the arene was determined, and the arene meta carbon with the larger coefficient was the favored site for nucleophile addition. The same effect likely explains the selectivities observed for the (arene)chromium tricarbonyl complexes studied here. However, it should be pointed out that the dioxolane moiety of **3c** will exert a much greater steric effect at the neighboring meta position than would the methylene group of **3a**,**b**. However, as discussed above, complex **3d**, which has a chiral auxiliary that is closely related to those of **3a**,**b**, appears to adopt a tripod orientation that is opposite to that of **3a**,**b** and leads to the opposite stereochemical preference during nucleophile addition.

Conclusions

Diastereoselectivity was observed with complexes **3** during reaction with *tert*-butyl lithioacetate. This selectivity of nucleophilic addition at the meta carbons of (alkoxyarene)chromium tricarbonyls represents a case of conformational transmission of chirality from the camphyl group apparently via the $Cr(CO)_3$ tripod to the site of nucleophilic attack. The data with regard to conformational preferences, NMR studies, solid-state structure, and selectivity of nucleophilic addition all point to the orientation of the tripod as a structural element in determining diastereoselectivity. The nucleophile adds to the arene meta carbon, which is fairly remote from the chiral environment, with the two diastereotopic meta positions being sterically more or less similar. How the chemical shift nonequivalence of the arene carbons relates to the directional orientation of the tripod and to diastereotopicity of the arene is an interesting problem for further study.

Experimental Section

The preparation of chiral (alkoxyarene)chromium tricarbonyl complexes has been detailed elsewhere,[4b] and the same procedure was followed for making the substrates used in the present study. Full descriptions are reported in the Supporting Information for this paper, as are the general experimental procedures for obtaining spectroscopic data. The general method for enolate addition to these complexes is described here, and two examples are presented in detail. Full descriptions for all other complexes are given in the Supporting Information.

General Procedure for Nucleophilic Addition/Electrophilic Addition/Demetalation Sequence. To a solution of diisopropylamine (1.7 mL, 12.5 mmol, 5 equiv) in anhydrous THF (12.5 mL) at 0 °C was added dropwise *n*-butyllithium (1.6 M in hexanes; 5.0 mL, 12.5 mmol, 5 equiv). After 15 min, the resulting LDA solution was cooled to −78 °C and a solution of *tert*-butyl acetate (1.9 mL, 2.5 mmol, 5 equiv) in THF (12.5 mL) was added dropwise. After an additional 30 min a solution of the (arene)chromium tricarbonyl complex (2.5 mmol, 1 equiv) in 12.5 mL of THF was added, followed immediately by the addition of anhydrous HMPA (5.4 mL, 31 mmol, 12.5 equiv). The resulting heterogeneous, yellow reaction mixture was warmed to −60 °C and maintained at this temperature for the duration of the reaction. After 4 h trifluoroacetic acid (5.2 mL, 67.5 mmol, 27 equiv) was added in one portion and the reaction mixture immediately became deep red. After 0.5 h the reaction mixture was removed from the cooling bath and diluted with concentrated aqueous ammonia (5 mL). Finally, after an additional 0.5 h the now heterogeneous green reaction mixture was diluted with additional aqueous concentrated ammonia and extracted with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and then filtered and concentrated in vacuo, usually affording a green oil. The product was then purified by column chromatography using a hexane/ethyl ether eluent system. Using this procedure, complex **3a** afforded dienol ether **5a**, which was purified by flash column chromatography (20:1 hexanes/ether); the diastereomers were not separated by this method, so that stereoselectivity could be determined by ^{1}H NMR spectroscopy. Yield: 72%. R_f: 0.48 (20:1 hexane/ether). Data for major diastereomer: ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) δ 7.51−7.49 (1H, m), 7.40−7.20 (4H), 5.91 (1H, d, $J = 5.7$ Hz), 4.17 (1H, dd, $J = 5.7$, 2.2 Hz), 2.75−2.64 (1H, m), 2.48 (1H, dt, $J = 14.4$, 3.6 Hz), 2.37 (1H, dd, $J = 16.6$, 6.7 Hz), 2.24 (1H, dd, $J = 14.5$, 12.0 Hz), 2.17 (1H, d, $J = 14.3$ Hz), 2.07 (1H, d, $J = 16.6$ Hz), 1.92−1.82 (2H), 1.83−1.67 (1H, m), 1.56 (9H, s), 1.56−1.42 (1H, m), 1.36−1.08 (2H), 1.07 (3H, s), 0.92 (2 × 3H, s), 0.01 (9H, s, $-\mathrm{Si(C\underline{H}_3)_3}$); ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) δ 172.6 ($-\mathit{C}\mathrm{OOC(CH_3)_3}$), 150.7 (C1′), 141.6 (C1″), 133.6 (C3′), 130.3 (C4′), 128.4, 127.7, 127.1, 126.7, 125.6 (preceding five signals correspond to C−H aromatic carbons), 99.9 (C2′), 89.8 (C2), 80.3 (C6′), 54.6 (C1), 50.4 (C7), 45.5 (C4), 40.4 (C3), 36.1 (C5′$-\mathit{C}\mathrm{H_2COO}-$), 32.5 (C5), 31.7 (C5′), 30.2 (C6), 28.3 ($-\mathrm{COOC(}\mathit{C}\mathrm{H_3)_3}$), 26.4 ($-\mathrm{COO}\mathit{C}\mathrm{(CH_3)_3}$), 21.6 (C8 or C9), 21.2 (C8 or C9), 10.1 (C10), −1.4 ($-\mathrm{Si(}\mathit{C}\mathrm{H_3)_3}$). Diastereomer ratio from ^{1}H NMR: 21:1. The major isomer was determined to be *S* from optical rotation and the CD spectrum of the derived cyclohexenone.

Using the same procedure, complex **3c** afforded a diastereomeric mixture of dienol ethers **5c**. Yield: 65%. R_f: 0.71 (20:1 hexane/ether). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$;): partial data for major diastereomer, δ 6.18 (1H, d, $J = 5.8$ Hz), 4.89 (1H, dd, $J = 5.8$, 2.0 Hz), 4.02−3.71 (4H), 3.79 (1H, s), 2.80−2.73 (1H, m), 1.45 (9H, s), 0.88 (3H, s), 0.84 (3H, s), 0.09 (9H, s, $-\mathrm{Si(}\mathit{C}\mathrm{H_3)_3}$); partial data for minor diastereomer, δ 6.18 (1H, d, $J = 6.0$ Hz), 1.47 (9H, s). Diastereomer ratio from ^{1}H NMR: 70:30. The major isomer was determined to be *R* from optical rotation of the corresponding cyclohexenone.

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Supporting Information Available: Text, figures, and tables giving experimental procedures, characterization data, X-ray crystallographic data, and NMR data for all of the complexes studied in this paper and the assignment of signals and analysis of the NOEs; crystal data are also given as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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