Asymmetric Conversion of Arenechromium Complexes to Functionalized Cyclohexenones: Progress toward Defining an Optimum Chiral Auxiliary

Anthony J. Pearson* and Alexander V. Gontcharov

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106

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An investigation into the asymmetric synthesis of 5-substituted cyclohexenones via nucleophile addition to (alkoxyarene)chromium tricarbonyl complexes is described. Diastereoselectivity during the nucleophile addition step was achieved using alkoxy substituents derived from terpenoid substrates as chiral auxiliaries. Selectivities as high as 24:1 were obtained when 2-phenylisoborneol was used as the chiral auxiliary and as high as 17:1 using 3,3-(ethylenedioxy)isoborneol. The absolute stereochemistry of the major products was assigned by Mosher's method, after their conversion to the corresponding cyclohexenol. A study of the temperature dependence of the nucleophile addition to alkoxytoluene complexes revealed a thermodynamic preference for addition ortho to the ether substituent.

Introduction

Dearomatization by means of nucleophile addition to arenes provides useful methodolgy for organic synthesis. The nucleophile addition itself requires activation of the normally inert aromatic ring, and transition metals, such as chromium,[1] iron,[2] and manganese,[3] are quite efficacious in this regard. Early work on nucleophile additions to arenechromium tricarbonyl complexes led to the development of methodology for the conversion of alkylbenzene derivatives to substituted cyclohexadienes and of anisole derivatives to substituted cyclohexenones (Figure 1, R* = Me).[4] Recent work from Kündig's laboratory showed that substituted cyclohexadienes could be obtained with asymmetric induction via nucleophile addition to arene−$Cr(CO)_3$ complexes bearing an *ortho* directing chiral auxiliary.[5] We recognized that a similar approach using alkoxyarenes could also afford 5-substituted cyclohexenones in optically enriched form, provided an appropriate chiral auxiliary could be defined that would lead to practical levels of asymmetric induction (Figure 1).[6]

We began our search for an efficient chiral auxiliary (Figure 1, R*) with a number of readily available chiral alcohols. Then, making some assumptions on the mode of the stereocontrol, we have proceeded to modify the structures of the chiral alcohols aiming at more efficient stereodifferentiation. Our progress is described in this article. More recently, Kündig has developed an approach based on nucleophile additions to nonracemic planar chiral complexes, which were prepared by asymmetric deprotonation of anisolechromium tricarbonyl systems, followed by silylation of the derived anion.[7]

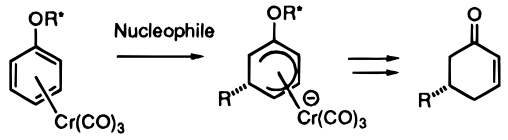

Figure 1. Schematic for asymmetric conversion of (alkoxybenzene)−$Cr(CO)_3$ complexes to substituted cyclohexenones.

Results and Discussion

Figure 2 presents a collection of the chiral alcohols that were chosen for our initial studies. All of them are commercially available in optically pure form except for isoborneol, which is prepared by L-Selectride (Aldrich) reduction of (+)-camphor.[8]

Asymmetric nucleophile additions to two series of alkoxy-substituted chromium complexes were studied: with and without a methyl substituent in the position *para* to the chiral auxiliary. The desired complexes were prepared from fluorobenzene or (*p*-fluorotoluene)chromium tricarbonyl by nucleophilic substitution of fluoride with the corresponding potassium alkoxides (eq 1). These reactions are easily monitored by TLC and were complete within minutes after mixing the reagents.

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

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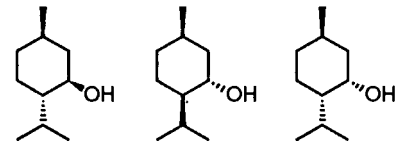
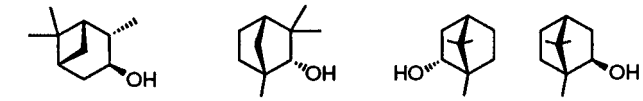
Monocyclic alcohols:



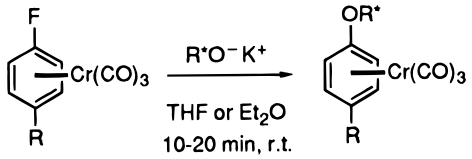
(-)-Menthol (Men-OH) (+)-Isomenthol (IM-OH) (+)-Neomenthol (NM-OH)

Bicyclic Alcohols:



(+)-Isopinocampheol (IPC-OH) (+)-Fenchyl Alcohl (Fen-OH) (-)-Borneol (Bor-OH) Isoborneol (IB-OH)

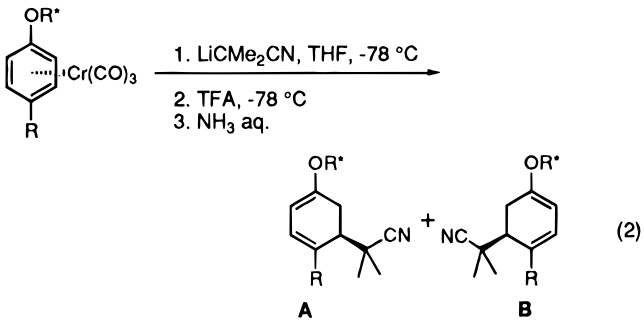
Figure 2. Some mono- and bicyclic chiral alcohols readily available in optically pure form.



(1)

R = H	R* = Men	**1**	83%
R = H	R* = IM	**2**	94%
R = H	R* = NM	**3**	71%
R = H	R* = IPC	**4**	96%
R = Me	R* = IPC	**5**	67%
R = H	R* = Fen	**6**	90%
R = Me	R* = Fen	**7**	89%
R = H	R* = Bor	**8**	90%
R = Me	R* = Bor	**9**	93%
R = Me	R* = IB	**10**	74%

Lithioisobutyronitrile has been shown before to be a nucleophile of optimum reactivity for addition to methoxy-substituted arene-chromium complexes, giving high yields of addition products.[1,4] Therefore, we used it in our studies of asymmetric nucleophilic addition. The whole sequence of transformations outlined in eq 2 is conducted in one pot and leads to the formation of mixtures of diastereomeric dienol ethers. The crude



(2)

mixtures were analyzed by NMR spectroscopy, and the ratios of diastereomers were estimated by integrating the NMR signals most conveniently separated in the spectra. For example, Figure 3 shows the proton NMR spectrum of the diastereomer mixture of dienol ethers **17A** and **17B** obtained from [(fenchyloxy)toluene]chromium complex. In this case, C*H*O protons of the fenchyl fragment are sufficiently separated to allow for accurate integration. In some cases, for example, with isopinocampheoxy-substituted cyclohexadienes **15**, use of an NMR shift reagent was advantageous for signal separation.

Table 1. Diastereomer Ratios and Yields of Cyclohexadienol Ethers

starting complex	product	ratios of diastereomers[a] **A:B**	combined yield, %
1	**11**	1.2:1[b]	80
2	**12**	1:1	74
3	**13**	1:1	77
4	**14**	2.3:1	80
5	**15**	2.7:1	90
6	**16**	3.5:1	67
7	**17**	7.5:1	76
8	**18**	1:1	50
9	**19**	1:1.4[b]	60
10	**20**	1:1.8 [b]	82

[a] Absolute stereochemistry assignment: see text. [b] Absolute stereochemistry not assigned.

In all cases the NMR patterns for the cyclohexadienes were very consistent, presenting no doubts in assigning the signals, even when some side products were present in the crude reaction mixtures. The diastereomer ratios of cyclohexadienol ethers **11**−**20** and their yields are presented in Table 1.

A fairly high degree of asymmetric induction can be achieved with some of these chiral auxiliaries. Thus, fenchyl alcohol as auxiliary afforded 76% de with *p*-methyl substituted complex **7**. No stereoselectivity was observed with monocyclic alcohols as chiral auxiliaries (complexes **1**−**3**) probably due to more facile rotation about the two ether bonds in these complexes.

The presence of a methyl group in the *para* position does not create a serious problem with regioselectivity of nucleophilic addition, but noticeable amounts (ca. 10%) of cyclohexadienes that result from *ortho* addition of the nucleophile were detected by NMR or GC. We will consider the problem of regioselectivity in more detail later, when we discuss the temperature dependence of the selectivities.

The increase in diastereoselectivity when a methyl substituent is present in the position *para* to the chiral auxiliary is fairly significant. We made a similar observation with arenemanganese complexes and explained it by suggesting a nucleophile approach trajectory shifting closer to the chiral auxiliary due to steric repulsion between the nucleophile and the methyl group.[9] On the basis of this observation, one could speculate that a further increase in steric hindrance at the *para* position (e.g., by replacing the methyl group by trimethylsilyl) would increase the diastereoselectivity of nucleophilic addition. Moreover, a trimethylsilyl substituent is known to activate the arene toward the nucleophilic attack at positions *ortho* and *para* to itself, which should help to control the regioselectivity of the additions.

[*p*-(Trimethylsilyl)(fenchyloxy)benzene]chromium tricarbonyl (**24**) was prepared as outlined in Scheme 1. Direct complexation of arenes with chromium hexacarbonyl requires fairly harsh reaction conditions (prolonged reflux at 140 °C), which arene **21** cannot withstand, probably because of lability of the TMS group. This prompted us to use a milder method, $Cr(CO)_3$ transfer

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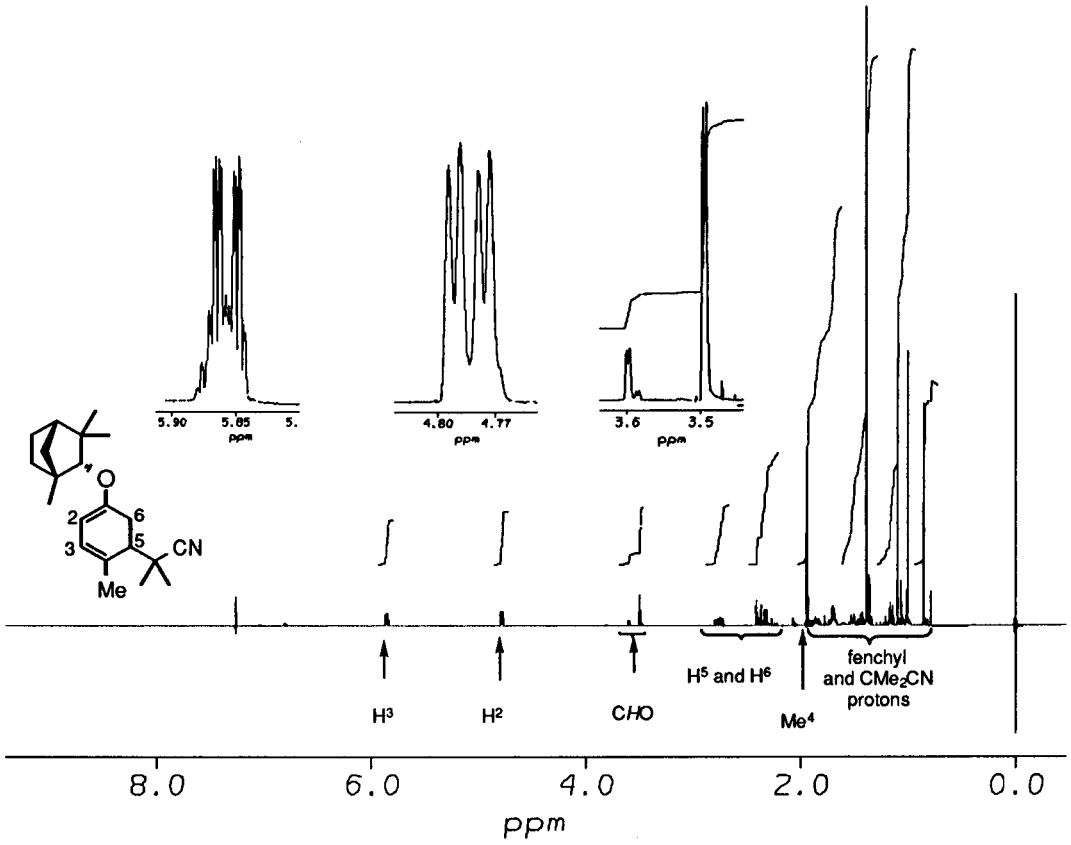
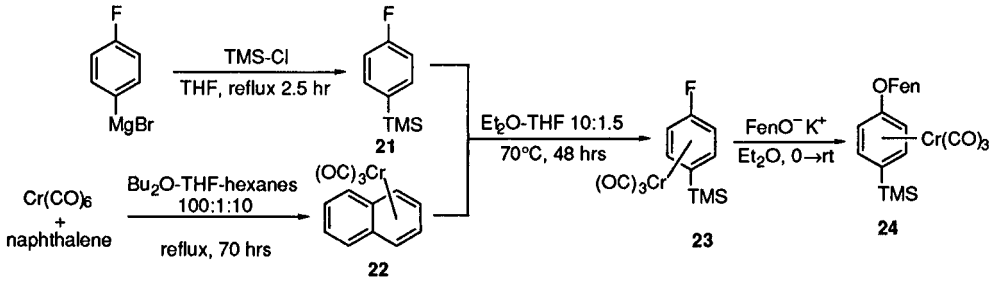


Figure 3. Proton NMR spectrum of crude diastereomer mixture of **17**; (400 MHz, $CDCl_3$/TMS, the spectrum was processed with resolution enhancement).

Scheme 1



from the naphthalene ligand of **22** to the arene, developed by Kündig and co-workers.[10] Arene **21** was prepared by the literature procedure.[11]

Our studies on nucleophilic addition to complex **24** indicated that the trimethylsilyl group is too sterically demanding for the isobutyronitrile anion addition to occur (Table 2). Various methods for activation of the nucleophile were attempted, but no cyclohexadienes were detected after the starting complex was carried through the sequence of transformations. Interestingly, the less sterically demanding acetonitrile anion added easily *meta* to the alkoxy substituent; however, the diastereoselectivity of the addition was very low. This result emphasizes the importance of the steric requirements of the nucleophile in determining diastereoselectivity during its addition.

Dienol ethers **11**−**20** are readily hydrolyzed to the corresponding cyclohexenones (Scheme 2). As reported by Semmelhack,[1,4] hydrolysis in THF/HCl (5 M aqueous) at 100 °C leads to the formation of the thermodynamic product, 2-cyclohexenone **26**. However, our experiments showed that under these conditions THF is not very stable, and a significant amount of 4-chloro-*n*-butanol is formed as a result of THF reaction with HCl, which creates serious difficulties during isolation of the products. We found that methanol can be used instead of THF without any change in the outcome of cyclohexadi-

Table 2. Attempted Nucleophilic Additions to [*p*-(Trimethylsilyl)(fenchyloxy)benzene]chromium Tricarbonyl 24

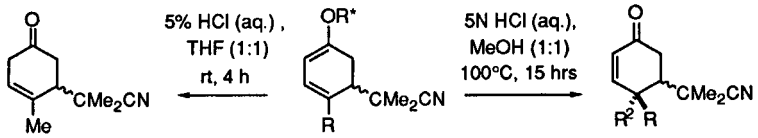
nucleophile	reaction condns	reaction outcome
$LiCMe_2CN$	THF/HMPA, −78 °C, 2 h	no reaction
$LiCMe_2CN$	DME, −78 °C, 2 h	no reaction
$LiCMe_2CN$	THF/TMEDA, −78 °C, 2 h	no reaction
$LiCMe_2CN$	THF, −78 °C, 5 days	extensive decomplexation[a]
$LiCH_2CN$	THF, −78 °C, 2 h	**25** (1.4:1 diast. ratio, 66% yield)[b]

[a] Mixture of products was recovered with *p*-$FenOC_6H_4$-TMS as major. [b] Absolute stereochemistry has not been assigned.

(10) (a) Desobry, V.; Kündig, E. P. *Helv. Chim. Acta* **1981**, *64*, 1288−1297. (b) Kündig, E. P.; Perret, C.; Spichiger, S.; Bernardinelli, G. *J. Organomet. Chem.* **1985**, *286*, 183.

(11) Moerlein, S. M. *J. Organomet. Chem.* **1987**, *319*, 29.

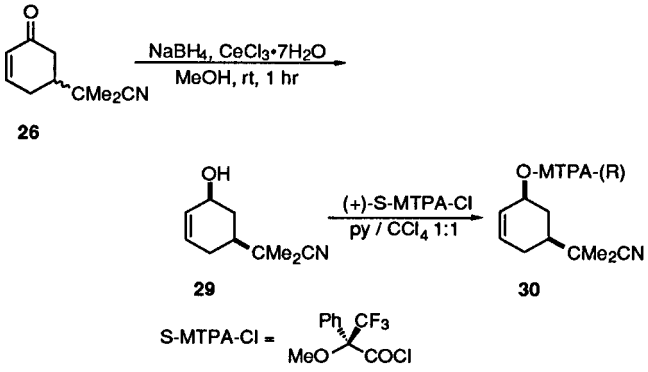
Scheme 2



28 11 - 20

26: R = R2 = H
27: mixture of R = Me, R2 = H and R = H, R2 = Me 1:1

Scheme 3



26 29 30

enol ether hydrolysis. The corresponding chiral alcohols formed in the hydrolysis can also be isolated, so the chiral auxiliary is (partially) recoverable.

Hydrolysis of 4-methyl-substituted cyclohexadienes (**15**, **17**, **19**, **20**) under these conditions led to formation of an approximately 1:1 mixture of cyclohexenones epimeric at C(4). Mild hydrolysis in this case (5% HCl/THF, rt) afforded the single kinetic hydrolysis product, 3-cyclohexenone **28**.

Determination of the Absolute Stereochemistry of Cyclohexenone 26. Reduction of cyclohexenone **26**, obtained by the hydrolysis of cyclohexadiene **14** (with IPC as a chiral auxiliary), with sodium borohydride in the presence of cerium(III) chloride provided exclusively equatorial alcohol **29** (Scheme 3). No traces of the epimeric alcohol or of the 1,4-reduction product were detected. The absolute stereochemistry of **29** was determined by the method developed by Mosher:[12] conversion into an α-methoxy-α-(trifluoromethyl)phenylacetate (MTPA) ester **30**, which was analyzed by NMR spectroscopy.

After our preliminary report,[6] an alternative method for assignment of absolute stereochemistry of cyclohexenone **26** was carried out by Semmelhack.[13] Hydrogenation of **26** gave the corresponding cyclohexanone, the stereochemistry of which was established from its CD spectrum based on the "octant rule". We were pleased to find that Semmelhack's and our assignments were in agreement.

The absolute stereochemistries of cyclohexenones from the remaining complexes were assigned on the basis of comparison of their optical rotations. Also, we made an assumption that no selectivity reversal occurs when the methyl group is introduced into the position *para* to the chiral auxiliary, thereby establishing the absolute stereochemistry of methyl-substituted derivatives.

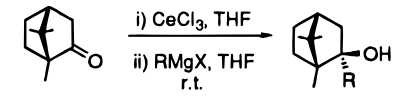
(12) (a) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. (b) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(13) Semmelhack, M. F.; Schmalz, H.-G. *Tetrahedron Lett.* **1996**, *37*, 3089.

Table 3. Results of $LiCMe_2CN$ Addition to Arenechromium Complexes with Tertiary Alcohols as Chiral Auxiliaries

starting complex	product	diastereomer ratios **A:B**	combined yield, %
34	39	1:1.8	89
35	40	1:9.5	81
36	41	ca. 4:1	95
37	42	24:1	63
38	43	1:1	91

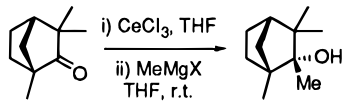
Having thus established that chiral alcohols can be used as chiral auxiliaries in the asymmetric conversion of arene-chromium complexes to functionalized cyclohexenones, we turned our attention to modifications of the auxiliary so as to increase the diastereoselectivity of the nucleophilic addition.

Camphor-Derived Alcohols as Chiral Auxiliaries. As far as the synthetic chiral auxiliaries are concerned, we considered one of their major requirements to be the simplicity of their synthesis (besides, of course, high stereoselectivities) because the chiral auxiliary in our transformation is used stoichiometrically. The known alcohols **31**−**33** were prepared by addition of the corresponding Grignard reagent to a preformed complex of the ketone with cerium(III) chloride.[14] Addition of PhMgX to fenchone gives an inseparable mixture of *endo*- and *exo*-alcohols, so we elected not to study the fenchyl analogue of **32**.



(+)-Camphor

31 R = Me (MIB-OH) 81%
32 R = Ph (PIB-OH) 87%



(-)-Fenchone

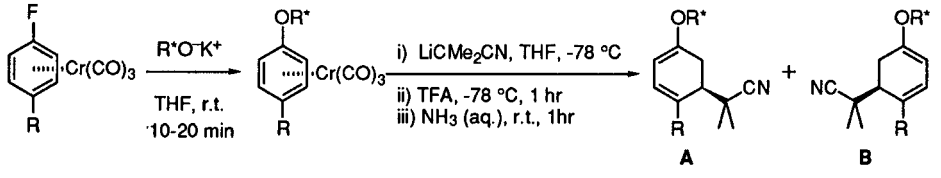
33 (MeF-OH) 85%

The results of addition of isobutyronitrile anion to complexes **34**−**38** are presented in Table 3. Generally, the increase in steric hindrance at the 2-position of isoborneol leads to enhancement of the diastereoselectivity of nucleophilic addition, which reaches a very high level (24:1, 92% de) with phenylisoborneol (PIB) as a chiral auxiliary (Scheme 4).

An interesting observation comes from comparing the selectivities obtained with chiral auxiliaries having the norbornane skeleton. Thus, neither borneol nor isoborneol promoted any significant diastereoselectivity. Introduc-

(14) Dimitrov, V.; Bratovanov, S.; Simova, S.; Kostova, K. *Tetrahedron Lett.* **1994**, *35*, 6713.

Scheme 4



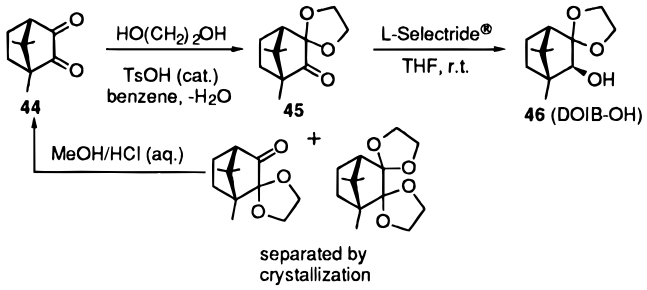
34	68%	R* = MIB	R = H	**39**
35	60%	R* = MIB	R = Me	**40**
36	59%	R* = PIB	R = H	**41**
37	89%	R* = PIB	R = Me	**42**
38	72%	R* = MeF	R = Me	**43**

ing some substituents at either the 3-position (as in fenchyl alcohol) or at the 2-position (as with the tertiary alcohols discussed above) led to a substantial increase in the effectiveness of the chiral auxiliary. The same major diastereomer was formed with all these chiral auxiliaries except one, 2-methylisoborneol. Substitution at both the 2- and 3-positions (as in methylfenchyl ether **38**) leads to complete loss of diastereoselectivity. It appears that these observations correlate with an intuitive picture of conformational behavior of the arene complexes and steric approach control of the diastereoselectivity.

Molecular mechanics calculations on the (fenchyloxy)arene and (isobornyloxy)arene complexes indicate that there are two important conformations of approximately the same energy, with the barrier between them of 3 kcal/mol, and which differ from each other by 180° rotation about the arene−oxygen bond.[15] Projections of these two conformations for chiral auxiliaries with variously substituted norbornane skeleta are shown in Figure 4. One can speculate that introduction of substituents at C-2 or C-3 of the chiral auxiliary should lead to an energy difference between the conformers due to the steric repulsion between that substituent and the chromium tricarbonyl fragment. An assumption that addition of the nucleophile to the complex occurs in the thermodynamically preferred conformation would explain the experimentally observed diastereoselectivity for the complexes with bornyl, isobornyl, fenchyl, and phenylisobornyl as chiral auxiliary. The only case that falls out of the trend is [(methylisobornyl)oxy]arene complexes (**34**, **35**), for which we could not find any plausible explanation. Interestingly, complex **34** showed a unique temperature dependence of the selectivity, which we shall discuss later. Also, it is difficult to predict the conformational behavior of (methylfenchyl)oxy-substituted complex **38**, and with substituents present at both 2- and 3-positions, the energy of the two conformers may again have become equal.

We attempted to calculate the energy differences between these conformers for complexes **34**−**38** by carrying out MMX calculations for arene complexes with a series of chiral auxiliaries. However, we discovered some grounds to doubt the reliability of the MMX force field for this kind of calculation because it does not take into account several steric and electronic factors inherent in arene transition metal complexes. One of them is the preference for chromium tricarbonyl to adopt the conformation where one of the carbonyls is eclipsed with the alkoxy substituent,[16] which is not reflected in the MMX parameters. We noted that the minimization process often drives the tricarbonylmetal unit into the opposite eclipsed or some staggered conformation. We do not know the energetic cost of this conformational change, but it would not be surprising if it could account for the energy difference we seek.

Scheme 5



The lowest box in the Figure 4 illustrates a similar analysis of the conformational preference for (3-substituted isobornyloxy)arene complexes that predicts the diastereoselectivity of nucleophilic addition to be opposite to that observed with the fenchyloxy auxiliary. It was encouraging to find that experimental results with such chiral auxiliaries are consistent with this analysis. Below we describe the synthesis of these complexes and the results of nucleophilic addition to them.

One of the easiest ways to introduce functionality at C-3 of camphor is its mild oxidation with selenium dioxide, which leads to camphorquinone **44** in high yield (Scheme 5).[17] Reaction of **44** with ethylene glycol gave a mixture of two monodioxolane derivatives and the corresponding bis-dioxolane, from which ketone **45** was easily separated by crystallization, whereas the two other products can be recycled by converting them back into camphorquinone.[18] Reduction of **45** with L-Selectride gave a high yield of 3,3-(ethylenedioxy)isoborneol (DOIB-OH) **46**. Nucleophilic addition to the complexes derived from **46** (see Scheme 4 for general structures: **47**, R* = DOIB, R = H; **48**, R* = DOIB, R = Me) afforded diastereomer ratios **A**:**B** of 1:7.3 and 1:17, respectively (dienes **49** and **50** analogous to Scheme 4). The latter is a remarkable and synthetically useful level of asymmetric induction and the absolute stereochemistry of the major diastereomer agrees with our prediction.

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(17) von Rupe, H.; di Vignano, T. A. *Helv. Chim. Acta* **1937**, *20*, 1078.

(18) (a) Fleming, I.; Woodward, R. B. *J. Chem Soc. C* **1968**, 1289. (b) Oppolzer, W.; Chapuis, C.; Dupuis, D.; Guo, M. *Helv. Chim. Acta* **1985**, *68*, 2100.

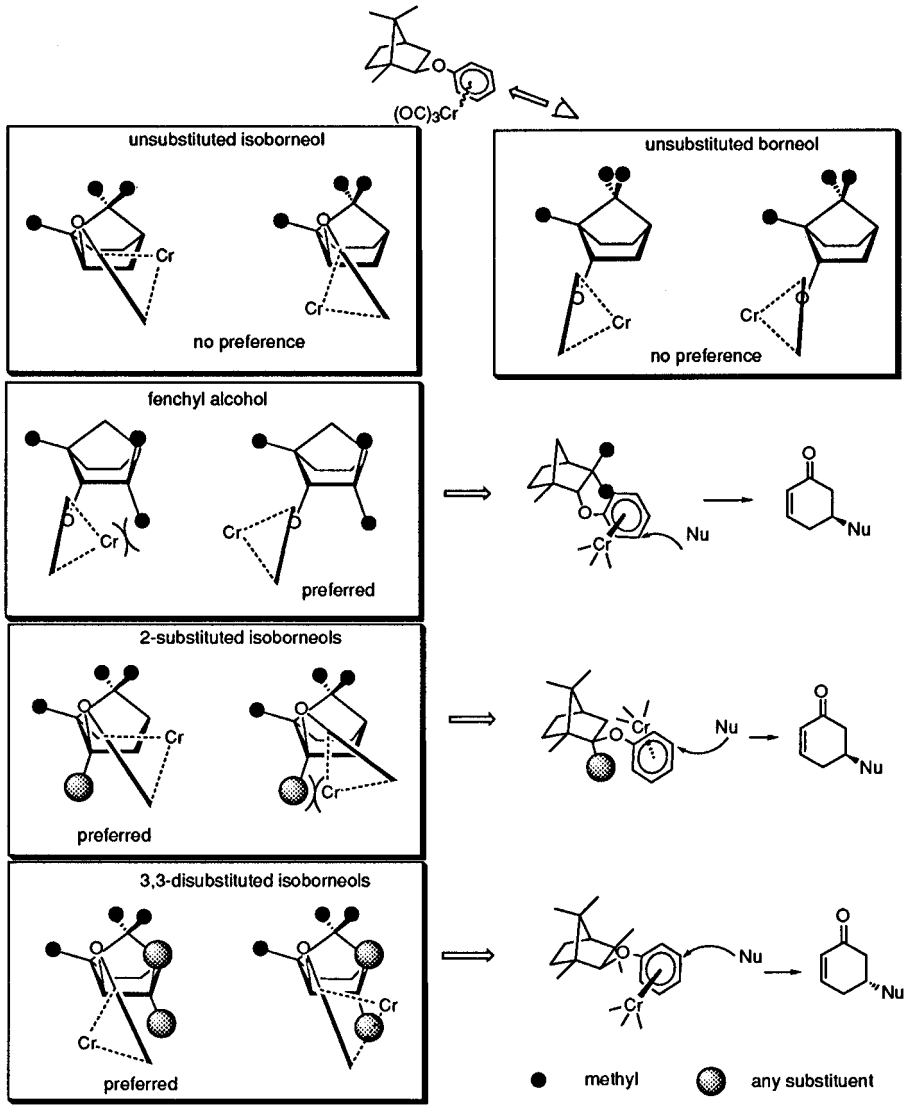
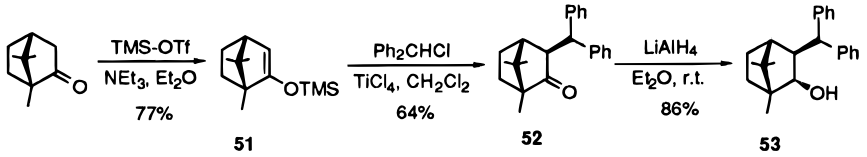


Figure 4. Analysis of preferred conformations of arenechromium complexes with various chiral auxiliaries.

Scheme 6



A related chiral auxiliary **53** was prepared by a procedure developed by Oppolzer[19] (Scheme 6). Alkylation of the enolsilane **51** afforded **52**, reduction of which afforded 3-*exo*-diphenylmethylisoborneol (DPMIB-OH, **53**). Addition of $LiCMe_2CN$ to the corresponding chromium complex **54** (R = Me, R* = DPMIB) proceeded with 83% de (11:1 diastereomer ratio). The results with 3-substituted isoborneols are collected in Table 4.

There is, however, a problem with most of the modified chiral auxiliaries we studied: hydrolysis of the dienol ethers under harsh conditions does not return the chiral auxiliary unchanged. With tertiary alcohols, water elimination usually occurs leading to the corresponding alkenes. DOIB-OH (**46**) is easily hydrolyzed to the corresponding α-hydroxy ketone, while DPMIB-OH does not undergo any changes during the hydrolysis. There may be two solutions to this chiral auxiliary recovery problem. A mild hydrolysis (as in Scheme 2) could be carried out first, which would lead to the nonconjugated 3-cyclohexenone and the chiral auxiliary, which would be unchanged under these conditions. After separation, the 3-cyclohexenone could be rearranged to the thermodynamically more stable 2-cyclohexenone. The above

Table 4. Diastereoselectivity of $LiCMe_2CN$ Addition to Arenechromium Complexes 47, 48, and 54

starting complex	yield of the complex, %	R*	R	diastereomer ratios **A:B**	combined yield, %
47	76	DOIB	H	1:7.6	86
48	71	DOIB	Me	1:17	65
54	91	DPMIB	Me	1:11	76

(19) Oppolzer, W.; Kurth, M.; Reichlin, D.; Chapuis, C.; Mohnhaupt, M.; Moffatt, F. *Helv. Chim. Acta* **1981**, *64*, 2802.

Table 5. Temperature Dependence of the Selectivity in Nucleophilic Addition to (Alkoxybenzene)chromium Complexes

Arene complex	R*	Reaction conditions	Diastereomer : ratios	Combined yield, %
6	Fen	THF, 0 °C	1.5:1	55 [a]
	Fen	THF, -30 °C	2.7:1	80
	Fen	THF, -78 °C	3.5:1	67
36	PIB	THF, -30 °C	1.8:1	80
	PIB	THF, -78 °C	4.0:1	95
34	MIB	THF, -35 °C	1.2:1	80
	MIB	THF, -78 °C	1:1.8	89

[a] 1:9 ratio of *ortho*/*meta* addition products was detected. The diastereomer ratio of *ortho* isomers was 5:1 (absolute stereochemistry has not been assigned).

transformation has been shown to work for [(methylisobornyl)oxy]cyclohexadiene (**39**). Alternatively, the products of the chiral auxiliary transformation during the hydrolysis could be converted back into the chiral alcohol. Thus, 3-oxoisoborneol, a product of DOIB-OH hydrolysis, can be reoxidized to camphorquinone, from which a two-step procedure affords the chiral auxiliary DOIB-OH as described above. Another problem with all the chiral auxiliaries studied so far is that the mixtures of diastereomeric dienol ethers have proven to be impossible to separate. The products are usually oils, fairly nonpolar, and have very similar retention factors on silica gel. Future work will focus on identifying systems that provide a solution to this problem.

Temperature Effects in Asymmetric Nucleophile Additions to Arenechromium Complexes

Although the level of asymmetric induction Semmelhack and Schmaltz achieved was appreciably lower than ours,[13] they showed that thermodynamically controlled nucleophilic addition gives a significantly higher level of asymmetric induction than the kinetically controlled reaction. Thus, in one case, the selectivity increased from 14% ee to 48% ee when the temperature of the reaction was raised from −78 to 0 °C. With these rather unexpected results in mind, we decided to study the temperature dependence of diastereoselectivity of nucleophilic additions to some of our complexes.

The results of our studies are presented in Tables 5 (for alkoxybenzene complexes) and 6 (for alkoxytoluene complexes). Interestingly, in none of the cases we studied did raising the temperature of the reaction lead to an increase of the diastereoselectivity of nucleophilic addition. Apparently, none of our chiral auxiliaries can create a difference in the product diastereomer stabilities sufficient to give any significant improvement in diastereomer distribution at higher temperatures (in fact, the opposite trend is observed).

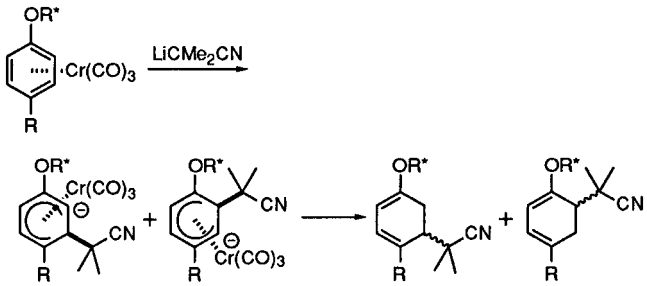
The temperature dependence experiments with alkoxytoluene complexes allowed us to make an interesting observation of regioselectivity change when the reaction control switches from kinetic to thermodynamic. *Ortho*-addition becomes dominant at higher temperatures, although significant amounts of *meta*-addition products are also formed (Table 6, Scheme 7). Despite the fact that regioselectivity of nucleophilic addition to anisolechromium complexes has been extensively studied over the years, this observation is the first report of kinetic regioselectivity being different from thermodynamic. The selectivity we observed with alkoxytoluene

Table 6. Temperature Dependence of the Selectivity in Nucleophilic Additions to (Alkoxytoluene)chromium Complexes[a]

R	R*	Reaction conditions	*ortho*/*meta* Ratio	Diastereomer ratios: *meta*	*ortho*	Combined yield, %
Me	Me	THF/HMPA, -5 °C	1.6:1	—	—	54
Me	Me	THF/HMPA, -78 °C	1:5.9	—	—	55
Me	IPC	THF, 0 °C	2.6:1	1.6:1	4.6:1	84
Me	IPC	THF/HMPA, -5 °C	4.1:1	1.5:1	5.2:1	70
Me	IPC	THF/HMPA, -30 °C	1:4.4	1.6:1	1.5:1	78
Me	IPC	THF/HMPA, -78 °C	1:8.5	2.7:1	n. d.	90
Me	Fen	THF, -5 °C	3.6 :1	2.8:1	2.9:1	68
Me	Fen	THF, -30 °C	1:5.9	n. d.	2.5:1	73
Me	Fen	THF/HMPA, -78 °C	1:19	7.5:1		76
Me	PIB	THF, -30 °C		8:1		83
Me	PIB	THF, -78 °C		24:1		63
TMS	Fen	THF, -5 °C	3.3:1	1.3:1	1:3.1	79
TMS	Fen	THF, -5 °C [b]	11:1		1:3.3	92
TMS	Fen	THF, -30 °C [b]		no reaction [c]		

[a] All the reactions were run for 2-2.5 hours unless noted otherwise; [b] reaction was run for 22-24 hours; [c] only starting material and the product of its decomplexation were isolated.

Scheme 7. *Ortho*- vs *Meta*-Addition to (Alkoxytoluene)chromium Complexes



complexes at low temperatures is consistent with the known strong *meta*-directing effect of the alkoxy substituent during these reactions. In the absence of the *para*-substituent, the combination of electronic and steric effects probably makes the corresponding *meta* cyclohexadienyl product also thermodynamically more stable. It is possible that the introduction of the methyl substituent *para* to the alkoxy inverts the relative stabilities of the two addition products. It seems improbable that the electronic effect of the methyl group would be strong enough to outweigh the electronic effect of alkoxy group, so one would expect only a slight weakening of the preference for the *meta* addition if the electron donating effect of the methyl group is taken into consideration. The only other obvious effect of the methyl group is steric, and it has to be compared with the steric effect of alkoxide. From the Newman projections of the C^6-C^1 bond of cyclohexadienyl ligand (Figure 5) one can see that the added nucleophile (at C^6 position) is involved in a close to gauche interaction with the substituent at C^1 (Me in the case of *meta*-addition and alkoxide in the case of *ortho*-addition). By its order of magnitude, gauche interaction might be sufficient to account for the observed *ortho*/*meta* selectivity (e.g., 0.8 kcal/mol in butane,[20] whereas about 0.4 kcal/mol energy difference between the isomers is required to produce 2:1 isomer distribution).

(20) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*; Plenum Press: New York, 1984; pp 104−105.

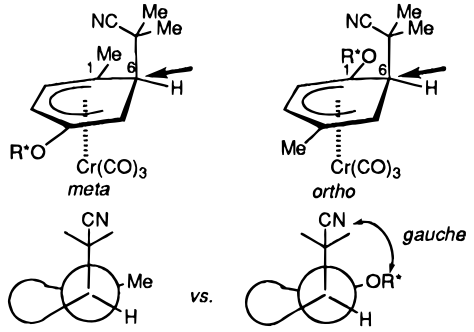


Figure 5. Steric interactions of the substituents in cyclohexadienylchromium complexes.

Conclusions

Terpenoid chiral alcohols and some of their simple derivatives can serve as efficient chiral auxiliaries during nucleophilic addition to arenechromium complexes. These alcohols can be easily attached to the arene by nucleophilic substitution of fluoride in (fluoroarene)chromium complexes with the corresponding potassium alkoxides. Addition of nucleophiles to the resulting chiral complexes occurs with high diastereoselectivity (up to 92% de), and after protonation of the addition product, subsequent demetalation, and hydrolysis, 5-substituted cyclohexenones of high enantiomeric purity are produced. Steric approach control appears to be the dominant factor in determining the stereochemical outcome of nucleophilic addition.

Experimental Section

General procedures and characterization methods are as described elsewhere.[9]

η^6-(Fluorobenzene)- and η^6-(4-fluorotoluene)chromium tricarbonyls were synthesized by refluxing fluorobenzene or fluorotoluene with chromium hexacarbonyl in dibutyl ether according to the reported procedures.[21] Yields were 50% and 56%, respectively.

General Procedure for Synthesis of η^6-(Phenyl alkyl ether)chromium Tricarbonyl Complexes. A solution of the alcohol (3 mmol) in 4 mL of dry diethyl ether was added to a stirred suspension of potassium hydride (3 mmol) in 6 mL of ether cooled to 0 °C. After gas evolution had stopped, the mixture was allowed to stir for 30 min at room temperature, and then a solution of (PhF)$Cr(CO)_3$ (2.9 mmol) in 10 mL of ether was added dropwise. The progress of the reaction was monitored by TLC. It was usually complete within minutes. The reaction was worked up with 3 mL of a saturated aqueous solution of NH_4Cl. The layers were separated. The water layer was extracted with ether, and the combined organic phases were dried with $MgSO_4$. Evaporation of solvent gave the crude product, which was either crystallized from CH_2Cl_2−hexanes or purified by flash chromatography on silica gel (hexanes−CH_2Cl_2 as eluent).

η^6-[[[(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohex-2-yl]oxy]benzene]chromium tricarbonyl (**1**) was prepared from (1*R*,2*S*,5*R*)-(−)-menthol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 83% as yellow crystals; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (2H), 5.18−5.13 (m, 2H), 4.86 (1H), 3.86 (dt, 1H, J = 4.2, 10.6 Hz), 2.26−2.18 (m, 1H), 2.18−2.07 (m, 1H), 1.76−1.67 (m, 2H), 1.50−1.37 (m, 2H), 1.11−0.98 (m, 2H), 0.96 (d, 3H, J = 6.6 Hz), 0.91 (d, 3H, J = 7.2 Hz), 0.78 (d, 3H, J = 6.9 Hz); FTIR (KBr pellet) 1954 (vs), 1887 (vs), 1862 (vs) cm^{-1}.

η^6-[[[(1*S*,2*R*,5*R*)-2-Isopropyl-5-methylcyclohex-2-yl]oxy]benzene]chromium tricarbonyl (**2**) was prepared from (1*S*,2*R*,5*R*)-(+)-isomenthol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 94% as yellow crystals; mp 75.5−77 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57−5.51 (m, 2H), 5.14−5.07 (m, 2H), 4.87−4.81 (m, 1H), 4.31 (m, 1H), 1.00 (d, 3H, J = 6.6 Hz), 0.92 (d, 3H, J = 6.0 Hz), 0.90 (d, 3H, J = 6.3 Hz), 1.95−0.84 (m, remaining H's); FTIR (CH_2Cl_2) 1965, 1882 cm^{-1}.

η^6-[[[(1*S*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohex-2-yl]oxy]benzene]chromium tricarbonyl (**3**) was prepared from (1*S*,2*S*,5*R*)-(+)-neomenthol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 71% as yellow crystals; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54−5.49 (m, 2H), 5.21−5.14 (m, 2H), 4.89−4.84 (m, 1H), 4.47 (m, 1H), 2.18−2.09 (m, 1H), 0.98 (d, 3H, J = 6.6 Hz), 0.87 (d, 3H, J = 6.6 Hz), 0.83 (d, 3H, J = 6.6 Hz), 1.08−1.33, 1.06−1.83 (m's, remaining H's); FTIR (CH_2Cl_2) 1965, 1880 cm^{-1}.

η^6-[[[(1*S*,2*S*,3*S*)-2,6,6-Trimethylbicyclo[3.1.1]hept-3-yl]oxy]benzene]chromium tricarbonyl (**4**) was prepared from (+)-isopinocampheol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 96% as yellow crystals; mp 122−126 °C; EI HRMS m/z 366.0926, calcd for $C_{19}H_{22}O_4Cr$ 366.0923; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.59−5.49 (m, 2H), 5.18−5.12 (m, 1H), 5.08−5.03 (m, 1H), 4.89−4.83 (m, 1H), 4.27 (ddd, 1H, J = 0.5, 5.0, 8.0 Hz), 2.59−2.48 (m, 1H), 2.42−2.32 (m, 1H), 2.31−2.19 (m, 1H), 2.02−1.94 (m, 1H), 1.93−1.83 (m, 2H), 1.25 (s, 3H), 1.19 (d, 3H, J = 7.4 Hz)1.10 (d, 1H, J = 9.9 Hz), 0.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 233.4, 142.4, 95.3, 94.5, 85.2, 80.4, 78.7 (2C), 47.2, 44.2, 41.1, 38.1, 35.7, 32.6, 27.2, 23.9, 20.6; FTIR (CH_2Cl_2) 1965, 1883 cm^{-1}.

η^6-[4-[[(1*S*,2*S*,3*S*)-2,6,6-Trimethylbicyclo[3.1.1]hept-3-yl]oxy]-toluene]chromium tricarbonyl (**5**) was prepared from isopinocampheol (Aldrich) and (*p*-fluorotoluene)chromium tricarbonyl: yield 67% as yellow crystals; mp 123−124 °C; EI HRMS m/z 380.1061 [M$^+$], calcd for $C_{20}H_{24}O_4Cr$ 380.1080; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.43−5.36 (m, 2H), 5.20−5.15 (m, 1H) 5.10−5.06 (m, 1H), 4.23−4.16 (m, 1H), 2.58−1.91 (m, 1H), 2.41−2.31 (m, 1H), 2.66−2.15 (m, 1H), 2.07 (s, 3H), 2.01−1.94 (m, 1H), 1.91−1.81 (m, 2H), 1.24 (s, 3H), 1.16 (d, 3H, J = 7.2 Hz), 1.09 (d, 1H, J = 10.1 Hz), 0.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 233.9, 140.2, 101.7, 95.6, 94.9, 81.2, 79.6, 78.8, 47.1, 44.2, 41.1, 38.1, 35.7, 32.7, 27.2, 23.9, 20.6, 19.8; FTIR (CH_2Cl_2) 1961, 1878 cm^{-1}.

η^6-[[[(1*R*,2*R*)-1,3,3-Trimethylbicyclo[2.2.1]hept-2-yl]oxy]benzene]chromium tricarbonyl (**6**) was prepared from (1*R*)-*endo*-(+)-fenchyl alcohol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 90% as yellow crystals; mp 103−105 °C; EI HRMS m/z 366.0892, calcd for $C_{19}H_{22}O_4Cr$ 366.0923; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.56−5.47 (m, 2H), 5.23−5.18 (m, 1H), 5.11−5.06 (m, 1H), 4.88−4.82 (m, 1H), 3.68 (s, 1H), 1.87−1.37 (m, 5H), 1.24 (d, 1H, J = 5.8 Hz), 1.18 (s, 6H), 1.13−1.02 (m, 1H), 0.85 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 233.3, 144.0, 94.9, 94.0, 91.0, 85.4, 80.9, 79.0, 49.6, 48.9, 41.4, 40.2, 29.7, 26.3, 25.6, 20.4, 20.1; FTIR (CH_2Cl_2) 1965, 1883 cm^{-1}.

η^6-{4-[[(1*R*,2*R*)-1,3,3-Trimethylbicyclo[2.2.1]hept-2-yl]oxy]-toluene}chromium tricarbonyl (**7**) was prepared from fenchyl alcohol (Aldrich) and (*p*-fluorotoluene)chromium tricarbonyl: yield 89% as yellow crystals; mp 104−105 °C; EI HRMS m/z 380.1066 [M$^+$], calcd for $C_{20}H_{24}O_4Cr$ 380.1080; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39−5.31 (m, 2H), 5.28−5.23 (m, 1H), 5.13−5.08 (m, 1H), 3.59 (d, 1H, J = 1.6 Hz), 2.07 (s, 3H), 1.86−1.37 (m, 5H), 1.23−1.16 (m, 1H), 1.17 (s, 3H), 1.15 (s, 3H), 1.12−1.00 (m, 1H), 0.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 233.9, 141.8, 102.1, 95.2, 94.2, 91.2, 82.1, 80.0, 49.6, 48.9, 41.3, 40.0, 30.4, 26.3, 25.6, 20.3, 20.0, 19.8; FTIR ($CHCl_3$) 1965, 1886 cm^{-1}.

η^6-{[[(1*S*,2*R*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl]oxy]benzene}chromium tricarbonyl (**8**) was prepared from [(1*S*)-*endo*]-(−)-borneol (Aldrich) and (fluorobenzene)chromium tricarbonyl: yield 90% as yellow crystals; mp 128−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58−5.45 (m, 2H), 5.15−5.10 (m, 1H), 4.99−4.94 (m, 1H), 4.88−4.82 (m, 1H), 4.12 (ddd, 1H, J = 1.7, 3.2, 9.3 Hz), 2.34−2.23 (m, 1H), 2.07−1.96 (m, 1H), 1.82−1.68 (m, 2H), 1.28 (s, 3H), 1.2 (d, 3H), 0.9 (s, 3H); ^{13}C NMR, DEPT (75 MHz, $CDCl_3$) δ C: 233.4, 143.0, 49.6, 47.6, CH: 95.4, 94.8, 85.0, 84.3, 80.3, 78.4, 45.0, CH_2: 36.3, 27.6, 36.3, CH_3: 19.6, 18.9, 13.6; FTIR (CH_2Cl_2) 1963, 1881 cm^{-1}.

η^6-{4-[[(1*S*,2*R*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl]oxy]-toluene}chromium tricarbonyl (**9**) was prepared from [(1*S*)-

(21) Mahaffy, C. A. L.; Pauson, P. L. *Inorg. Synth.* **1979**, *19*, 154.

endo]-(−)-borneol (Aldrich) and (*p*-fluorotoluene)chromium tricarbonyl: yield 93% as yellow crystals; mp 146−148 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.44−5.36 (m, 2H), 5.17−5.13 (m, 1H) 5.01−4.97 (m, 1H), 4.05 (m, 1H), 2.27 (m, 1H), 2.06 (s, 3H), 2.04−1.94 (m, 1H), 1.81−1.67 (m, 2H), 1.37−1.14 (m, 3H), 0.91 (s, 6H), 0.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 233.9, 141.0, 101.4, 95.8, 95.2, 84.4, 81.0, 79.2, 49.6, 47.5, 45.0, 36.3, 27.6, 26.6, 19.8, 19.5, 18.9, 13.5; FTIR (CH_2Cl_2) 1961, 1881 cm^{-1}.

η^6-{4-[[(1*R*,2*R*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl]oxy]-toluene}chromium tricarbonyl (**10**) was prepared from isoborneol (synthesized by L-Selectride reduction of (+)-camphor (Acros) as described in the literature) and (*p*-fluorotoluene)chromium tricarbonyl: yield 74% as yellow crystals; mp 147−150 °C dec; EI HRMS *m*/*z* 380.1089 (M^+), calcd for $C_{20}H_{24}O_4Cr$ 380.1080; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.43−5.36 (m, 2H), 5.16−5.12 (m, 1H), 5.05−5.01 (m, 1H), 3.76 (dd, 1H, J = 2.4, 4.9 Hz), 2.06 (s, 3H), 1.96−1.51 (m, 4H), 1.18−0.85 (m, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 233.9, 140.2, 101.4, 95.9, 95.3, 86.2, 80.9, 79.1, 49.4, 47.0, 45.3, 39.3, 33.9, 27.2, 20.1, 19.9, 19.8, 11.5; FTIR (CH_2Cl_2) 1962, 1878 cm^{-1}.

η^6-[4-Fluoro(trimethylsilyl)benzene]chromium Tricarbonyl (23). (Naph-thalene)chromium tricarbonyl (1.2 mmol), *p*-fluoro(trimethylsilyl)benzene (1.5 mL), dry THF (1.5 mL), and dry ether (10 mL) were placed into a 50 mL high-pressure tube, which was then filled with nitrogen by freeze-pump-thaw cycle and sealed under atmospheric pressure. The reaction mixture was heated at 70 °C for 2 days (the color changes from red to yellow). The product was isolated by column chromatography on flash silica gel with hexanes−ether 10:1 as eluent: yield 72% as yellow crystals; mp 97−98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.49 (m, 2H), 5.26 (m, 2H), 0.25 (s, 9H); ^{13}C NMR δ 232.0, 147.7 (d, J_{CF} = 267 Hz), 98.2 (d, J = 6.4 Hz), 95.0, 78.7 (d, J = 90 Hz), −1.1; FTIR (CH_2Cl_2) 1976, 1900 cm^{-1}.

η^6-[4-[[(1*R*,2*R*)-1,3,3-Trimethylbicyclo[2.2.1]hept-2-yl]-oxy](trimethylsilyl)benzene]chromium Tricarbonyl (24). The complex was synthesized from η^6-[*p*-fluoro(trimethylsilyl)-benzene]chromium tricarbonyl and fenchyl alcohol (Aldrich) according to the procedure used for other chromium complexes reported above: yield 98% as yellow crystals; mp 96−98 °C; EI HRMS *m*/*z* 438.1315 [M^+], calcd for $C_{22}H_{30}O_4CrSi$ 438.1318; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54 (m, 2H), 5.15 (m, 1H), 5.05 (m, 1H), 3.74 (s, 1H), 1.90−1.40 (m, 5H), 1.25−1.2 (1H)1.19 (s, 6H), 1.09 (m, 1H), 0.87 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 233.6, 145.5, 100.3, 99.4, 92.9, 90.5, 80.4, 78.5, 49.6, 48.9, 41.5, 40.3, 30.3, 26.3, 25.6, 20.5, 20.2, −1.1; FTIR (CH_2Cl_2) 1962, 1881 cm^{-1}.

η^6-{[[(1*R*,2*R*)-1,2,7,7-Tetramethylbicyclo[2.2.1]hept-2-yl]oxy]-benzene}chromium tricarbonyl (**34**) was prepared from (1*R*,2*R*)-1,2,7,7-tetramethylbicyclo[2.2.1]heptan-2-ol (vide infra) and (fluorobenzene)chromium tricarbonyl: yield 68% as yellow crystals; mp 148−149 °C dec; EI HRMS *m*/*z* 380.107 34 (M^+), calcd for $C_{25}H_{26}O_4Cr$ 380.107 97; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (m, 2H), 5.05 (m, 2H), 4.85 (m, 1H), 2.47 (ddd, 1H, J = 3.0, 4.4, 13.1 Hz), 1.78 (t, 1H, J = 4.7 Hz), 1.72 (m, 1H), 1.51−1.41 (m, 3H), 1.06 (m, 1H), 1.51 (s, 3H), 0.95 (s, 3H), 0.90 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 233.6, 139.1, 95.5, 94.5, 90.2, 85.0, 82.6, 81.6, 54.3, 48.7, 45.7, 43.8, 30.5, 26.3, 21.0, 20.8, 20.4, 10.1; FTIR (CH_2Cl_2) 1965, 1881 cm^{-1}.

η^6-{4-[[(1*R*,2*R*)-1,2,7,7-Tetramethylbicyclo[2.2.1]hept-2-yl]-oxy]toluene}chromium tricarbonyl (**35**) was prepared from (1*R*,2*R*)-1,2,7,7-tetramethylbicyclo[2.2.1]heptan-2-ol (vide infra) and (*p*-fluorotoluene)chromium tricarbonyl: yield 60% as yellow crystals; decomp. ca. 135 °C without melting; EI HRMS *m*/*z* 394.120 89 (M^+), calcd for $C_{21}H_{26}O_4Cr$ 394.123 62; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.36 (m, 2H), 5.12 (m, 1H), 5.04 (m, 2H), 2.49 (m, 1H), 2.06 (s, 3H), 1.78 (m, 1H), 1.67 (m, 1H), 1.54−1.36 (m, 3H), 1.47 (s, 3H), 1.13−0.97 (m, 1H), 0.92 (s, 3H), 0.90 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 234.1, 136.7, 101.6, 95.9, 94.6, 89.9, 83.7, 82.3, 54.3, 48.8, 45.8, 43.7, 30.6, 26.3, 21.0, 20.9, 20.1, 19.8, 10.2; FTIR (CH_2Cl_2) 1962, 1884 cm^{-1}.

η^6-{[[(1*R*,2*S*)-2-Phenyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]-oxy]benzene}chromium tricarbonyl (**36**) was prepared from (1*R*,2*S*)-2-phenyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (vide infra) and (fluorobenzene) chromium tricarbonyl: yield 59% as yellow crystals; mp 136−140 °C dec; EI HRMS *m*/*z* 442.123 01 (M^+), calcd for $C_{25}H_{26}O_4Cr$ 442.123 61; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.46−7.30 (m, 5H), 5.29−5.16 (m, 2H), 4.90−4.77 (m, 3H), 2.50 (ddd, 1H, J = 2.3, 4.3, 14.2 Hz), 2.29 (d, 1H, J = 14.2 Hz), 1.98 (t, 1H, J = 4.3 Hz), 1.77 (m, 1H), 1.35−1.19 (m, 2H), 1.17 (s, 3H), 0.99 (s, 3H), 0.96 (s, 3H), 0.94−0.73 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 233.6,139.6, 137.9, 128.5 (2C), 127.76, 127.81, 125.1, 93.1, 93.2, 92.5, 87.4, 84.8, 83.6, 55.4, 50.4, 45.6, 39.6, 30.4, 26.2, 21.6, 21.1, 9.83; FTIR (CH_2Cl_2) 1964, 1876 cm^{-1}.

η^6-4-{[[(1*R*,2*S*)-2-Phenyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]oxy]toluene}chromium tricarbonyl (**37**) was prepared from (1*R*,2*S*)-2-phenyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (vide infra) and (*p*-fluorotoluene)chromium tricarbonyl: yield 89% as yellow crystals; mp 132−134 °C dec; EI HRMS *m*/*z* 456.139 74 (M^+), calcd for $C_{26}H_{28}O_4Cr$ 456.139 27; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.46−7.28 (m, 5H), 5.10−4.80 (m, 4H), 2.52 (ddd, 1H, J = 3.1, 4.2, 14.2 Hz), 2.26 (d, 1H, J = 14.2 Hz), 1.99 (s, 3H), 1.99 (t, 1H, J = 4.9 Hz), 1.89−1.66 (m, 1H), 1.36−1.17 (m, 2H), 1.15 (s, 3H), 0.97 (s, 3H), 0.95 (s, 3H), 0.90−0.73 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 234.1, 139.6, 134.8, 128.5, 128.4, 127.8, 127.7, 125.2, 117.8, 103.9, 93.2, 92.8, 85.7, 84.5, 55.3, 50.4, 45.6, 39.3, 30.4, 26.2, 21.2, 21.0, 19.7, 9.8; FTIR (CH_2Cl_2) 1959, 1875 cm^{-1}.

η^6-4-{[[(1*R*,2*S*)-1,2,3,3-Tetramethylbicyclo[2.2.1]hept-2-yl]-oxy]toluene}chromium tricarbonyl (**38**) was prepared from (1*R*,2*S*)-1,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-ol (vide infra) and (*p*-fluorotoluene)chromium tricarbonyl: yield 72%; mp 158−160 °C dec; EI HRMS *m*/*z* 394.124 17 (M^+), calcd for $C_{25}H_{26}O_4Cr$ 394.123 62; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.37−5.07 (m, 4H), 2.30−2.11 (m, 1H), 2.07 (s, 3H), 1.86−1.34 (m, 3H), 1.26 (s, 3H), 1.19−1.08 (m, 2H), 1.05 (s, 3H), 1.04 (s, 3H), 1.03 (s, 3H), 1.03−0.92 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 234.0, 138.3, 102.5, 94.9, 94.3, 92.2, 87.4, 85.4, 54.1, 49.7, 43.8, 40.8, 29.0, 27.2, 25.8, 24.2, 19.8, 19.0, 17.2; FTIR (CH_2Cl_2) 1961, 1878 cm^{-1}.

η^6-{[[Spiro[(1*R*,2*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-3,2′-[1,3]dioxolan]-2-yl]oxy]benzene}chromium tricarbonyl (**47**) was prepared from spiro[(1*R*,2*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-3,2′-[1,3]dioxolan]-2-ol (vide infra) and (fluorobenzene)chromium tricarbonyl: yield 70% as a yellow amorphous solid slowly crystallizing at low temperature; mp 109−111 °C; EI HRMS *m*/*z* 424.0989 (M^+), calcd for $C_{21}H_{24}O_6Cr$ 424.0978; ^{1}H NMR (200 MHz, C_6D_6) δ 4.96−4.89 (m, 1H), 4.76−4.60 (m, 3H), 3.98−3.89 (m, 1H), 3.83 (s, 1H), 3.40−3.29 (m, 1H), 3.26−3.09 (m, 3H), 1.71−1.60 (m, 1H), 1.44−1.14 (m, 4H), 1.27 (s, 3H), 1.06 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (50 MHz, C_6D_6) δ 233.9, 143.5, 115.0, 95.4, 94.0, 90.1, 84.7, 81.1, 78.3, 64.4, 63.7, 52.2, 49.9, 48.2, 34.0, 21.1, 21.1, 20.5, 11.3; FTIR ($CHCl_3$) 1966, 1888 cm^{-1}.

η^6-{4-[[Spiro[(1*R*,2*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-3,2′-[1,3]dioxolan]-2-yl]oxy]toluene}chromium tricarbonyl (**48**) was prepared from spiro[(1*R*,2*S*)-1,7,7-trimethylbicyclo[2.2.1]-heptane-3,2′-[1,3]dioxolan]-2-ol (vide infra) and (*p*-fluorotoluene)chromium tricarbonyl: yield 71% as yellow amorphous solid; EI HRMS *m*/*z* 438.1133, calcd for $C_{22}H_{26}O_6Cr$ 438.1135; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.43−5.17 (m, 4H), 4.06−3.76 (m, 4H), 3.73 (s, 1H), 2.05 (s, 3H), 1.72−1.48 (m, 3H), 1.40−1.24 (m, 2H), 1.10 (s, 3H), 0.95 (s, 3H), 0.85 (s, 3H); ^{13}C (50 MHz, $CDCl_3$) δ 234.0, 141.5, 114.9, 101.3, 96.2, 94.9, 90.2, 82.4, 79.1, 64.5, 63.9, 51.9, 49.7, 48.0, 33.9, 21.1, 20.7, 20.2, 19.8, 11.1; FTIR (CH_2Cl_2) 1960, 1876 cm^{-1}.

η^6-{4-[[(1*R*,2*R*,3*S*)-3-Benzhydryl-1,7,7-trimethylbicyclo[2.2.1]-hept-2-yl]oxy]toluene}chromium tricarbonyl (**54**) was prepared from (1*R*,2*R*,3*S*)-3-benzhydryl-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-ol and (*p*-fluorotoluene)chromium tricarbonyl: yield 91% as yellow crystals; dec ≥ 190 °C without melting; EI HRMS *m*/*z* 546.1858 (M^+), calcd for $C_{33}H_{34}O_4Cr$ 546.1862; ^{1}H NMR (200 MHz, C_6D_6) δ 7.20−6.65 (m, 10H), 4.40−4.18 (m, 5H), 3.79 (d, J = 7.8, 1H), 2.62 (dd, J = 7.8, 12.9, 1H), 1.55 (s, 3H), 1.47−1.38 (m, 3H), 1.37 (s, 3H), 1.12 (s, 3H), 1.16−0.84 (m, 2H), 0.61 (s, 3H); ^{13}C NMR (50 MHz, C_6D_6) δ 234.7, 146.0, 145.2, 140.6, 129−125 (11 carbon signals, overlapped with the

solvent signal), 103.3, 93.0, 91.7, 90.1, 84.4, 80.1, 54.9, 52.4, 51.3, 48.4, 47.6, 33.3, 30.2, 21.9, 19.3, 12.8; FTIR (CH_2Cl_2) 1957, 1873 cm^{-1}.

General Procedure for Nucleophilic Additions of Isobutyronitrile Carbanion to Arylchromium Complexes with Subsequent *in Situ* Conversion to the Corresponding Cyclohexadienes. A THF solution of isobutyronitrilelithium was prepared by adding 1 mmol of isobutyronitrile to a solution of 1 mmol of LDA in 2 mL of THF (prepared from diisopropylamine and butyllithium according to the standard procedure[22]) at −78 °C and stirring the resulting mixture at that temperature for 30 min. A solution of the (arene)chromium tricarbonyl complex (0.2 mmol) in 2 mL of THF was added dropwise. The reaction mixture was stirred for 2 h. Then 400 μL of trifluoroacetic acid was added (this caused immediate color change to red), and stirring was continued for another hour, the temperature still being maintained at −78 °C. Decomplexation of the cyclohexadiene chromium complex was accomplished by treating the reaction mixture with a concentrated aqueous solution of NH_3 for approximately 2 h at room temperature. The organic products (together with chromium containing products (most likely $[Cr(CO)_3(NH_3)_3]$) were extracted with diethyl ether. The ether solution was washed with water, dried with $MgSO_4$, and evaporated. A mixture of diastereomeric cyclohexadienes was isolated by TLC on a silica gel plate with hexanes−ether 10:1 as eluent.

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-2-yl]oxy]cyclohexa-1,3-dienes (11). Mixture of diastereomers (1:1.2): combined yield 80% as a colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ major diastereomer: 5.98 (ddd, 1H, J = 9.4, 6.5, 2.3 Hz), 5.21 (dd, 1H, J = 9.6, 3.7 Hz), 4.83 (d, 1H, J = 6.3 Hz), 3.82−3.69 (m, 1H), 2.50−2.08 (m, 7H), 2.58−2.36 (m, 4H), 1.25−1.07 (m, 1H), 0.93−0.76 (remaining H's); minor diastereomer (partial data): 5.23 (dd, 1H, J = 9.4, 3.3 Hz).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*S*,2*R*,5*R*)-2-isopropyl-5-methylcyclohex-2-yl]oxy]cyclohexa-1,3-dienes (12). Mixture of diastereomers (1:1): total yield 68% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.98 (ddd, 1H + 1H, J = 2.2, 6.1, 9.6 Hz), 5.21 (dd, 1H, J = 2.6, 9.6 Hz), 5.20 (dd, 1H, 3.5, 9.6 Hz), 4.91 (d, 1H, J = 6.5 Hz), 4.89 (d, 1H, J = 6.6 Hz), 4.23 (m, 1H + 1H), 2.50−2.20 (m, 3H + 3H), 1.95−0.98 (m, 9H + 9H), 0.93−0.78 (4s's and 6 d's).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-2-yl]oxy]cyclohexa-1,3-dienes (13). Mixture of diastereomers (1:1): total yield 77% as a colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ 5.97 (ddd, 1H, J = 2.2, 6.1, 9.7 Hz), 5.97 (ddd, 1H, J = 1.9, 5.9, 9.8 Hz), 5.19 (dd, 1H, J = 3.6, 9.7 Hz), 5.19 (dd, 1H, J = 3.8, 9.5 Hz), 4.77 (d, 1H + 1H, J = 5.4 Hz), 4.26−4.23 (m, 1H + 1H), 2.54−1.98 (m, 4H + 4H), 1.75−1.40 (m, 5H + 5H), 0.92−0.63 (m, remaining H's).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*S*,2*S*,3*S*)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]oxy]cyclohexa-1,3-dienes (14). Mixture of diastereomers (2.3:1): total yield 40% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer 6.00 (ddd, 1H, J = 2.0, 6.1, 9.6 Hz), 5.25 (dd, 1H, J = 3.6, 9.6 Hz), 4.78 (d, 1H, J = 6.1 Hz), 4.22 (dt, 1H, J = 8.7, 4.3 Hz), 2.50−2.18 (m, 6H), 1.88−1.65 (m, 3H), 1.22−1.13 (m, 1H), 1.12 (s, 3H), 1.10 (d, 3H, J = 7.7 Hz), 0.90, 0.86 (2 s's, 3H each), 0.79 (s, 3H); minor diastereomer (partial data) 5.99 (m, 1H), 5.26 (dd, 1H, J = 3.3, 9.6 Hz), 4.80 (d, 1H, J = 6.0 Hz), 4.17 (dt, 1H, J = 8.6, 4.3 Hz), 1.7 (d, 1H, J = 8.0 Hz), 0.91, 0.87 (2 s's, 3H each).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[(1*S*,2*S*,3*S*)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]oxy]cyclohexa-1,3-dienes (15). Mixture of diastereomers (2.7:1): total yield 80% as a colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ major diastereomer 5.86−5.81 (m, 1H), 4.73 (dd, 1H, J = 2.4, 6.0 Hz), 4.19−4.11 (m, 1H), 2.68−2.55 (m, 1H), 2.41−2.17 (m, 4H), 1.83 (s, 3H), 1.82−1.75 (m, 2H), 1.53−1.60 (m, 2H), 1.22−1.12 (m, 1H), 1.11 (s, 3H), 1.09 (s, 6H), 1.07(d, 3H, J = 7.5 Hz), 0.79(s, 3H); minor diastereomer (partial data) 4.70 (dd, 1H, J = 2.4, 6.0 Hz), 1.82 (s, 3H), 0.77 (s, 3H), 1.14−1.05 (m, remaining H's).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*R*,2*R*)-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-dienes (16). Mixture of diastereomers (3.5:1); total yield 67% as a colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ major diastereomer 5.94 (ddd, 1H, J = 1.5, 6.3, 10.1 Hz), 5.19 (dd, 1H, J = 3.4, 9.5 Hz), 4.88 (d, 1H, J = 6.3 Hz), 3.60 (d, 1H, J = 1.9 Hz), 2.48−2.20 (m, 2H), 2.05−1.93 (m, 1H), 1.76−1.64 (m, 1H), 1.57−1.52 (m, 1H), 1.42−1.29 (m, 2H), 1.19−0.80 (m, 3H), 1.09, 0.98, 0.92, 0.87, 0.83 (5 s's, 3H each); minor diastereomer (partial data) 5.95 (m, 1H), 5.21 (dd, 1H, J = 3.3, 9.6 Hz), 4.87 (d, 1H, J = 6.3 Hz), 3.54 (d, 1H, J = 2.0 Hz), 1.09, 1.04, 0.99, 0.91, 0.86 (5s's, 3H each).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[(1*R*,2*R*)-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-dienes (17). Mixture of diastereomers (7.5:1): total yield 76% as a colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ major diastereomer 5.75 (ddq, 1H, J = 6.1, 0.7, 1.6 Hz), 4.77 (ddq, 1H, J = 6.1, 2.4, 0.5 Hz), 3.46 (d, 1H, J = 1.9 Hz), 2.54 (dddt, 1H, J = 17.8, 9.6, 2.5, 0.5 Hz), 2.35 (dd, 1H, J = 1.6, 17.8 Hz), 1.98 (dddd, 1H, J = 2.2, 5.8, 9.0, 12.5 Hz), 1.88 (qdd, 1H, J = 0.5, 1.6, 9.6 Hz), 1.82 (dq, 3H, 1.6, 0.5 Hz), 1.74−1.66 (m, 1H), 1.60−1.54 (m, 1H), 1.39−1.30 (m, 2H), 1.12−0.91 (m, 2H), 1.11, 1.09, 1.04, 0.98, 0.90 (5 s's, 3H each); minor diastereomer (partial data) 4.74 (ddq, 1H, J = 6.1, 2.5, 0.6 Hz), 3.52 (d, 1H, J = 1.9 Hz).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*S*,2*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-diene (18). Mixture of diastereomers (1:1). combined yield 50% as a colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ 5.97 (ddd,1H + 1H, J = 2.1, 6.0, 9.6 Hz), 5.26 (dd, 1H, J = 3.1, 9.6 Hz), 5.23 (dd, 1H, 3.4, 9.6 Hz), 4.72 (d, 1H, J = 6.0 Hz), 4.69 (d, 1H, J = 6.0 Hz), 4.09 (ddd, 1H, J = 1.8, 3.3, 9.3 Hz), 4.02 (ddd, 1H, J = 1.9, 3.4, 9.3 Hz), 2.47−1.99 (m, 4H + 4H), 1.73−1.50 (m, 2H + 2H), 1.34−1.14 (m, 2H + 2H), 1.13−0.94 (m, 2H + 2H), 0.91, 0.90, 0.89, 0.88, 0.86, 0.85 (6 × s's, 3H each), 0.77, 0.73 (2 × s's, 6H each).

(5*R* and 5*S*)-1-[[(1*R*,2*R*)-1,7,7-Trimethylbicyclo[2.2.1]-hept-2-yl]oxy]-4-methyl-5-(1-cyano-1-methylethyl)cyclohexa-1,3-dienes (20). Mixture of diastereomers (1:1.8): total yield 82% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87−5.81 (m, 1H + 1H), 4.69 (dd, 1H, J = 2.3, 5.9 Hz), 4.67 (major, dd, 1H, J = 2.3, 5.1 Hz), 3.73−3.65 (m, 1H + 1H), 2.78−2.61 (m, 1H + 1H), 2.28−2.15 (m, 2H + 2H), 1.91 (s, 3H + 3H), 1.75−1.48 (m, 4H + 4H), 1.26−1.21 (m, 1H + 1H), 1.10−0.99 (m, 2H + 2H), 1.34, 1.34, 1.33, 1.33, 0.97, 0.93, 0.90, 0.87, 0.81, 0.81 (10 s's, 3H each).

(6*R* and 6*S*)-6-(Cyanomethyl)-1-[[(1*R*,2*R*)-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl]oxy]-4-(trimethylsilyl)cyclohexa-1,3-dienes (25). Mixture of diastereomers (1.4:1): yield 66% as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.23 (dd, 1H, J = 1.2, 6.0 Hz), 5.07 (dd, 1H, J = 2.0, 6.0 Hz), 3.63 (d, 1H, J = 1.7 Hz), 2.69−2.61 (m, 1H), 2.60−2.52 (m, 1H), 2.44−2.33 (m, 2H), 2.19−2.10 (m, 1H), 1.90−1.80 (m, 1H), 1.74−1.63 (m, 1H), 1.55−1.49 (m, 1H), 1.47−1.37 (m, 1H), 1.19−1.15 (m, 1H), 1.07−0.99 (m, 1H), 1.11, 1.00, 0.85 (3 s's, 3H each), 0.08 (s, 9H); minor diastereomer (partial data) 6.21 (dd, 1H, J = 1.2, 6.0 Hz), 5.05 (dd, 1H, J = 2.0, 6.0 Hz), 3.68 (d, 1H, J = 1.7 Hz), 1.10, 1.06, 0.78 (3 s's, 3H each), 0.08 (s, 9H).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*R*,2*R*)-1,2,7,7-tetramethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-dienes (39). Mixture of diastereomers (1:1.8): total yield 89% as a colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ major diastereomer 6.00−5.94 (m, 1H), 5.21 (dd, 1H, J = 3.2, 9.6 Hz), 4.75 (d, 1H, J = 6.0 Hz), 2.60−2.46 (m, 1H), 2.35−2.15 (m, 2H), 1.66−1.52 (m, 2H), 1.28, 0.98, 0.96, 0.91, 0.85, 0.81 (6 s's, 3H each), 1.38−1.78 (m, remaining H's); minor diastereomer (partial data) 5.20 (m, 1H), 4.71 (d, 1H, J = 6.1 Hz), 1.20, 1.01, 0.99, 0.94, 0.87, 0.82 (6 s's, 3H each).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[(1*R*,2*R*)-1,2,7,7-tetramethylbicyclo[2.2.1]hept-2-yl]oxy]-

(22) Wakefield, B. J. *Organolithium Methods*; Academic Press London, 1988; p 189.

cyclohexa-1,3-dienes (40). Mixture of diastereomers (1:9.5): yield 81% as a colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ 5.81 (dq, 1H, J = 6.1, 0.6 Hz), 4.68 (dd, 1H, J = 2.6, 6.1 Hz), 2.62 (ddd, 1H, J = 3.0, 4.5, 13.4 Hz), 2.49 (dddt, 1H, J = 0.7, 2.5, 9.3, 17.6 Hz), 2.20 (dd, 1H, J = 1.5, 17.6 Hz), 1.81 (dd, 3H, J = 0.6, 1.5 Hz), 1.75 (ddd, 0.7, 1.5, 9.4 Hz), 1.64−1.52 (m, 2H), 1.38−1.23 (m, 3H), 1.22, 1.15, 1.12, 1.10, 0.96, 0.83 (6 s's, 3H each); minor diastereomer (partial data) 5.79 (m, 1H), 4.57 (dd, 1H, J = 2.5, 6.1 Hz), 2.11 (dd, 1H, J = 1.4, 17.4 Hz), 1.84 (dd, 3H, 0.5, 1.5 Hz), 1.23, 1.09, 1.08, 1.06, 0.93, 0.82 (6 s's, 3H each).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[(1*R*,2*S*)-2-phenyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-dienes (41). Mixture of diastereomers (4:1): total yield 95% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer 7.55−7.95 (m, 5H, Ph), 5.58 (ddd, 1H, J = 1.8, 6.2, 9.6 Hz), 4.98 (dd, 1H, J = 3.6, 9.6 Hz), 4.22 (d, 1H, J = 6.2 Hz), 2.53−1.51 (m, 7H), 1.18, 0.98, 0.91, 0.86, 0.85 (5 s's, remaining H's); minor diastereomer (partial data) 5.63 (ddd, 1H, J = 1.9, 6.2, 9.6 Hz), 4.99 (dd, 1H, J = 9.6 Hz), 4.27 (d, 1H, J = 6.2 Hz).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[(1*R*,2*S*)-2-phenyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]oxy]cyclohexa-1,3-dienes (42). Mixture of diastereomers (24:1): total yield 63% as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ major diastereomer 7.39−7.19 (m, 5H), 5.57 (ddq, 1H, J = 0.5, 6.2, 1.5 Hz), 3.96 (dd, 1H, J = 6.2, 2.6 Hz), 2.68 (ddd, 1H, J = 2.6, 9.8, 17.9 Hz), 2.38 (ddd, 1H, J = 3.2, 4.4, 14.3 Hz), 2.35 (dd, J = 1.2, 17.9 Hz), 2.27 (dd, 1H, J = 1.2, 9.8 Hz), 2.13 (d, 1H, J = 14.3 Hz), 1.80 (d, 3H, J = 1.5 Hz), 1.70 (m, 1H), 1.26−1.08 (m, 3H), 1.27, 1.26, 1.05, 0.94, 0.89 (5 s's, 3H each), 0.79 (ddd, 1H, J = 4.0, 9.3, 13.5 Hz); minor (partial data) 4.01 (dd, J = 2.6, 6.2 Hz).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[(1*R*,2*R*)-1,2,3,3-tetramethylbicyclo[2.2.1]hept-2-yl]oxy]-cyclohexa-1,3-dienes (43). Mixture of diastereomers (1:1): total yield 91% as a colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ 5.76−5.70 (m, 1H + 1H), 4.72 (dd, 1H, J = 2.4, 6.2 Hz), 4.67 (dd, 1H, J = 2.3, 6.1 Hz), 2.62−2.12 (m, 4H + 4H), 1.83 (s, 3H), 1.81 (s, 3H), 1.94−1.72 (m, 2H + 2H), 1.50−1.21 (m, 3H + 3H), 1.20 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H), 1.05 (s, 9H), 1.00 (s, 3H), 0.96 (s, 3H), 0.87 (s, 3H), 0.84 (s, 3H), 1.13−0.91 (m, remaining H).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-1-[[spiro-2,3′-[1,3]dioxolan]-[(1*R*,2*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl]oxy]cyclohexa-1,3-dienes (49). Mixture of diastereomers (1:7.6): yield 86% as a colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ major diastereomer 5.96 (ddd, 1H, J = 2.1, 6.1, 9.5 Hz), 5.24 (dd, 1H, J = 3.7, 9.5 Hz), 5.04 (dd, 1H, J = 6.1 Hz), 3.90 (s, 1H), 3.50−3.25 (m, 4H), 2.49−2.33 (m, 2H), 2.26−2.19 (m, 1H), 1.40, 0.93, 0.91, 0.86, 0.77 (5 s's, 3H each), 1.56−1.12 (m, remaining protons); minor diastereomer (partial data) 5.09 (d, 1H, J = 6.1 Hz), 3.86 (s, 1H).

(5*R* and 5*S*)-5-(1-Cyano-1-methylethyl)-4-methyl-1-[[spiro-2,3′-[1,3]dioxolan]-[(1*R*,2*S*)-1,7,7-trimethylbicyclo-[2.2.1]heptan-2-yl]oxy]cyclohexa-1,3-dienes (50). Mixture of diastereomers (1:17): total yield 65% as white crystals; ^{1}H NMR (300 MHz, C_6D_6) δ major diastereomer 5.79 (dqd, 1H, J = 0.5, 1.6, 6.1 Hz), 4.93 (dd, 1H, J = 2.4, 6.1 Hz), 3.80 (s, 1H), 3.55−3.20 (m, 4H), 2.56 (ddd, 1H, J = 2.4, 9.5, 17.6 Hz), 2.31 (dd, 1H, J = 1.0, 17.6 Hz), 1.87 (ddd, 1H, J = 1.0, 9.5, 0.5 Hz), 1.88 (d, 3H, J = 1.6 Hz), 1.54−1.51 (m, 1H), 1.48−1.42 (m, 2H), 1.26−1.17 (m, 1H), 1.06−0.93 (m, 1H), 1.38, 1.16, 1.11, 0.90, 0.76 (5 s's, 3H each); minor diastereomer (partial data) 4.86 (dd, 1H, J = 2.2, 6.0 Hz), 4.11 (s, 1H).

(5*R* and 5*S*)-1-[[(1*R*,2*R*,3*S*)-3-Benzhydryl-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]oxy]-4-methyl-5-(1-cyanoethyl-1-methyl)cyclohexa-1,3-dienes (55). Mixture of diastereomers from complex **54**: yield 76% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer (partial data) 7.45−6.96 (m, 10H), 5.59 (dq, 1H, J = 6.2, 1.7 Hz), 4.59 (dd, 1H, J = 6.2, 2.5 Hz), 4.34 (d, 1H, J = 12.9 Hz), 4.18 (d, 1H, J = 8.2 Hz), 2.74 (dd, 1H, J = 12.9, 8.2 Hz), 2.0−0.7 (m, remaining protons); minor diastereomer (partial data) 4.66 (dd, 1H, J = 6.4, 2.3 Hz).

1-Methoxy-4-methyl-6-(1-cyano-1-methylethyl)cyclohexa-1,3-diene (56, R* = R = Me) was isolated by TLC from the product mixture of addition of $LiCMe_2CN$ to (methoxytoluene)chromium tricarbonyl at −5 °C: yield 33% as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52 (ddq, 1H, J = 6.1, 3.0, 1.7 Hz), 5.11 (d, 1H, J = 6.1 Hz), 3.57 (s, 3H), 2.69 (dd, 1H, J = 18.5, 10.0 Hz), 2.37−2.28 (m, 2H), 1.77 (t, 3H, J = 1.7 Hz), 1.36 (s, 3H), 1.32 (s, 3H).

5-(1-Cyano-1-methylethyl)-4-methyl-2-cyclohexen-1-one (26). The cyclohexadienol ethers **11**−**14**, **16**, or **18** (0.05 mmol) and 2 mL of a 1:1 volume MeOH−HCl (5 M aqueous) mixture were sealed in a glass ampule and heated at 100 °C for 20 h. The resulting solution was diluted with water and extracted with ether. The product was isolated by TLC or flash chromatography on silica gel (hexanes−EtOAc as eluent). Yields of **26** from different batches of dienol ethers ranged from 75 to 87%.

5-(1-Cyano-1-methylethyl)-4-methyl-3-cyclohexen-1-one (28). Cyclohexadienol ether **17** (0.1 mmol) was treated with 1 mL of 1:1 volume mixture of THF and 5% aqueous HCl at room temperature overnight. Cyclohexenone **28** and the corresponding alcohol were separated by column chromatography (silica gel, hexanes−ethyl acetate 4:1as eluent): yield of **28** 46%; R_f 0.35 (3:1 hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (ddq, J = 2.8, 4.6, 1.6 Hz, 1H), 2.94 (ddq, J = 23.3, 2.8, 2.6 Hz, 1H), 2.87 (ddq, J = 23.3, 4.7, 1.6 Hz, 1H), 2.73 (dd, J = 14.7, 1.3 Hz, 1H), 2.64 (d (broad lines), J = 7.0 Hz, 1H), 2.58 (dd, J = 14.7, 7.0 Hz, 1H), 2.04 (dt, J = 2.6, 1.6 Hz, 3H), 1.40 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 134.0, 124.8, 124.4, 48.2, 41.5, 39.5, 36.5, 25.5, 25.0, 24.7.

(1*R*, 5*R*)- and (1*S*, 5*S*)-5-(1-Cyano-1-methylethyl)-2-cyclohexen-1-ol (29). The enone **26** (0.05 mmol) and an equimolar amount of $CeCl_3 \cdot 7H_2O$ were dissolved in 2 mL of methanol, and the resulting solution was cooled to 0 °C. Sodium borohydride (6 mg) was added, and the reaction mixture was stirred at room temperature for 30 min, after which it was quenched with 1 mL of 1 N aqueous HCl. The product was extracted with chloroform. The organic layer was washed with saturated $NaHCO_3$ solution and water and then dried with Na_2SO_4. Evaporation of the solvents in vacuum gave 95% of fairly pure **29**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddt, 1H, J = 10.0 Hz, 4,8, 1.0 Hz), 5.72 (d, 1H, J = 10.0 Hz), 4.34 (m, 1H), 2.28 (m, 1H), 2.19 (m, 1H), 1.98 (m, 1H), 1.73 (dddd, 1H, J = 2.3, 5.2, 11.1, 13.1 Hz), 1.38 (s, 3H), 1.35 (s, 3H), 1.33 (m, 1H).

Synthesis of Mosher's ester 30 was performed according to the known procedure.[12] A mixture of alcohol **29** (0.05 mmol), 30 mg of (+)-*S*-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA-Cl), 10 drops of dry pyridine, and 10 drops of CCl_4 was stirred at room temperature for 2 days. After that ca. 1 mL of water was added. The resulting solution was extracted with ether. The extract was washed thoroughly with 1 N HCl, water and a saturated solution of $NaHCO_3$ and dried with Na_2SO_4. The solvent was evaporated in vacuum. The resulting mixture of diastereomeric esters was used directly for NMR analysis (see discussion in text).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds (38 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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