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The Tricarbonylchromium Template for Stereocontrol in Radical Reactions of Arenes

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Chromium tricarbonyl complexed aryl aldeyhydes and ketones underwent Sm(II)-promoted radical lactone formation in the presence of α,β-unsaturated esters to produce diastereomerically pure lactones in good yields. The completely diastereoselective lactone formation involves capture of the benzylic ketyl radical by the ester anti to the chromium tricarbonyl moiety. The relative stereochemistry of the lactone and chromium tricarbonyl moieties was proven by X-ray crystallography and supports the proposed mechanism. Enantiopure chromium tricarbonyl complexed arenes afforded single enantiomers when subjected to Sm(II)-promoted radical lactone formation condiditions. The enantio- and diastereomerically pure chromium tricarbonyl complexed lactones were subsequently treated with $BF_3{\cdot}OEt_2$ to generate a mixture of diastereomers via Lewis acid promoted chromium tricabonyl directed cationic rearrangement. The diastereomers were separated and individually decomplexed with I_2 to afford both of the corresponding chromium-free enantiomerically pure lactones starting from a single enantiomerically pure chromium tricarbonyl complex.

Introduction

Radical reactions have found tremendous utility in organic synthesis, but control of stereochemistry in these processes remains a formidable challenge.[1] Diastereoselectivity, and ultimately enantioselectivity in radical reactions, can result from substrates containing proximal chirality,[2] substrates containing chiral auxiliaries,[3] use of tethers,[4] and prochiral substrates reacting with chiral radical traps.[5] Intriguing results have even been achieved in enantioselective radical reactions using chiral reagents which are not covalently bonded to the substrate or product.[2g,6] While there are reports of excellent stereoselectivity, many approaches have performed modestly and none of the processes achieve complete stereocontrol in a general sense. In contrast, transition metal-templated ionic reactions are exceptional in their oftentimes formation of single isomeric products.[7] However, there are only a few reports on the use of organometallic substrates for stereoselective radical reactions.[8] Early work in this lab on the use of transition metal complexes in radical reactions demonstrated that transition metal complexes are effective in controlling the stereochemistry of radical reactions and that certain transition metal-centered radicals enjoyed enhanced stabilities and thus imparted special reactivity.[8b,c] The chromium tricarbonyl moiety, in particular, is a useful metal template for numerous anionic and cationic reactions of arene substrates since the chromium tricarbonyl moiety exerts a large steric and electronic influence, which generally directs reactants exclusively anti to the arene face bound

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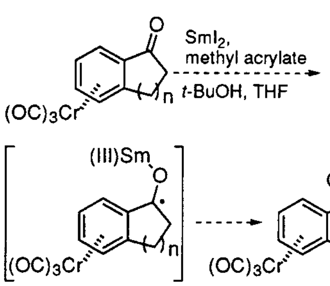
to chromium.[9] Considering the efficacy of the chromium tricarbonyl moiety to control reaction stereochemistry, we initiated studies on stereoselective radical reactions of arene complexes.[10,11] Herein, we report on intermolecular radical coupling reactions of chromium complexed arenes which result in diastereomerically and enantiomerically pure products and the application to selective synthesis of either enantiomer of lactones from single enantiomeric arene complexes.

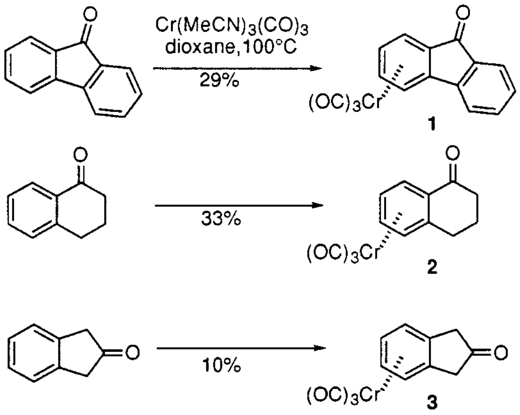
Results

Reaction Design. We modeled our current studies on the radical coupling reactions developed by Fukuzawa[12] which utilize samarium diiodide[13] to reductively generate ketyl radicals which are captured with α,β-unsaturated esters affording spirocyclic lactones. It was reasoned that chromium-complexed aryl ketones would also undergo similar chemistry and that the sterically imposing $Cr(CO)_3$ moiety would influence the diastereoselectivity (Scheme 1). If enantiopure arenechromium complexes were subjected to samarium-mediated lactonizations, then diastereomerically and enantiomerically pure reaction products should be formed. In addition, by taking advantage of the tricarbonylchromium's ability to template cationic reactions at benzylic positions, it should be possible to synthesize both enantiomers of a spirocyclic lactone starting from the same starting spirocyclic lactone complex. These hypotheses were tested and found to be true.

Scheme 1



Scheme 2



Preparation of Substrates. The methods for substrate preparation fell into two categories: direct complexation of the substrate precursor and complexation of a substrate derivative followed by subsequent steps to unveil the reactive functionality. Complexation of 9-fluorenone using $Cr(CH_3CN)_3(CO)_3$[14,15] gave the racemic chromium complex **1** in 29% yield as a purple solid, and none of the doubly complexed species was detected (Scheme 2). The complexation yield was low due to the electron-withdrawing ketone functionality.[16] Since the two aryl rings are differentiated by the $Cr(CO)_3$ moiety, two sets of aryl protons are observed in the ^1H NMR spectrum with the arene protons on the chromium-complexed arene shifted upfield to between 4.0 and 6.0 ppm. As is typical for arene complexes, the chromium-complexed carbons resonate between 80 and 110 ppm in the ^{13}C NMR spectrum. Similarly, complexation of 1-tetralone using $Cr(CH_3CN)_3(CO)_3$ gave the chromium complex (*rac*)-**2** in 33% yield as a red oil. Again, the electron-withdrawing effect of the aryl carbonyl hampered the reaction. Complexation by $Cr(CO)_3$ differentiates the enantiotopic arene faces and consequently all the aliphatic protons are diastereotopic. Complexation of

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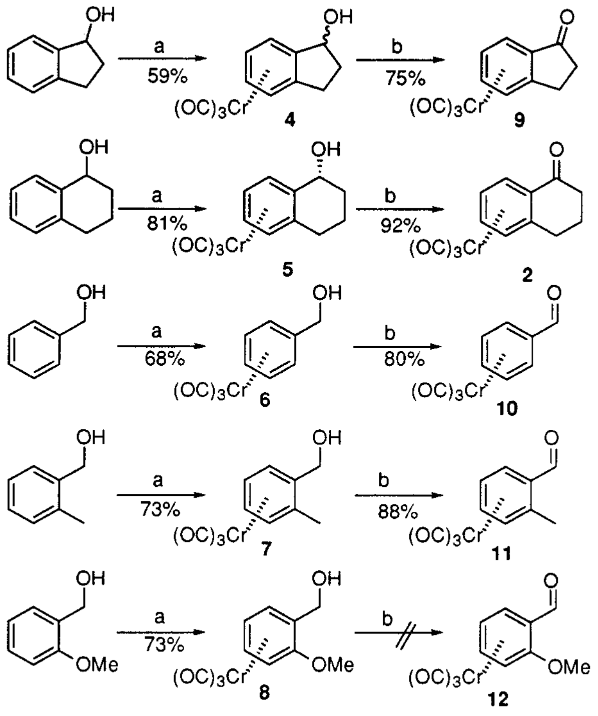
Scheme 3



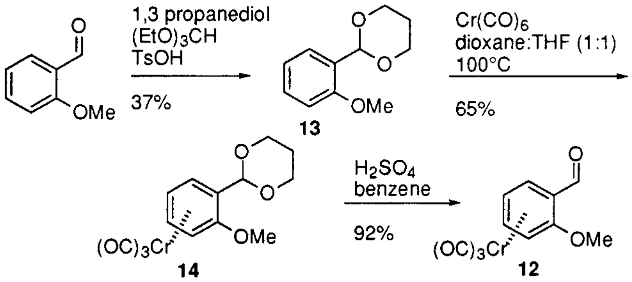
a) $Cr(CH_3CN)_3(CO)_3$, dioxane,100°C b) DMSO, Ac_2O

2-indanone afforded (η^6-2-indanone)tricarbonylchromium (**3**) in only 10% yield as an unstable oil.[17] This one-step procedure suffers from poor yields due to the unstable nature of the starting material and the somewhat electron poor nature of the aromatic ring. A longer, but more efficient, synthesis of this molecule is described in the literature.[17] Interestingly, the *J* value for the geminal coupling of the aliphatic protons is 21 Hz!

The alternate synthetic strategy for chromium arene complexes containing benzylic carbonyl groups required for complexation of a protected carbonyl derivative. Syntheses of (η^6-1-indanone)tricarbonylchromium and (η^6-1-tetralone)tricarbonylchromium began with complexation of 1-indanol and 1-tetralol, respectively. Due to the existing stereogenic center in these two compounds, diastereomeric mixtures are possible upon chromium complexation. Reaction of freshly crystallized 1-indanol with $Cr(CH_3CN)_3(CO)_3$ afforded the endo-product in 81% with only a trace amount of the exo-alcohol. For large scale complexations of 1-tetralol, it was more convenient to use $Cr(CO)_6$ as the complexing reagent which afforded the endo-alcohol in 84% yield. Due to the electronic effects of the $Cr(CO)_3$ moiety, the tertiary benzylic proton is shifted approximately 1 ppm upfield in the ^1H NMR spectrum.

The chromium complexes of 1-indanol and 1-tetralol were oxidized using a procedure[18] that requires excess Ac_2O in DMSO solvent to afford the corresponding red colored ketones (*rac*)-**9** and (*rac*)-**2** in 75% and 92% yields, respectively (Scheme 3). This oxidation method proved superior to MnO_2-mediated oxidation which gave products in only about 30% yields[19] Due to the increased acidity of the benzylic protons in the complexes, the acetate anion formed in the reaction is basic enough to effect the key deprotonation in the alcohol oxidation. Due to formation of acetic acid; however, this reaction must be run under rigorous exclusion of air and shielding from light due to the ease of oxidation of chromium arene complexes under these conditions. Both endo and exo complexes undergo oxidation equally well. The ^1H NMR spectrum for chromium-complexed indanone displays an exquisite ddd coupling pattern for each of the aliphatic protons. This synthesis of (*rac*)-**2** proceeds in 76% overall yield over two steps, which is more than double the yield of direct complexation.

Scheme 4



The two step strategy proved to be particularly advantageous for the synthesis of chromium complexed aryl aldehydes. Complexation of benzyl alcohol, 2-methylbenzyl alcohol and 2-methoxybenzyl alcohol proceeded smoothly to give the chromium complexes (*rac*)-**6**−**8** in high yields (Scheme 3). Subsequent oxidation of benzylic alcohols (*rac*)-**6** and (*rac*)-**7** using the DMSO/Ac_2O protocol generated chromium complexed aldehydes (*rac*)-**10** and (*rac*)-**11** in 80% and 88% yields, respectively. A surprising result was that the analogous oxidation of (*rac*)-**8** failed! The adjacent methoxy group may have reacted with the activated intermediate. Thus, a different route was employed. Acetalization of *o*-anisaldehyde using 1,3-propanediol, triethyl orthoformate, and catalytic *p*-toluenesulfonic acid followed by complexation using $Cr(CO)_6$ in THF:dioxane (1:1) provided chromium arene complex (*rac*)-**14** in 65% yield which was hydrolyzed using 60% H_2SO_4 to give the chromium complex of *o*-anisaldehyde (*rac*)-**12** in 92% yield (Scheme 4).

The synthetic strategy for optically pure (η^6-1-tetralone)tricarbonylchromium ((*S*)-**2**) was complexation of enantiopure 1,2,3,4-tetrahydro-1-naphthol followed by oxidation to the ketone. Racemic 1,2,3,4-tetrahydro-1-naphthol was resolved with Lipase Amano PS-30 and vinyl acetate in *t*-BuOMe (Scheme 5).[20] The recovered alcohol **15** was determined to have an ee of 78% using Mosher's acid method for ee determination,[21] and the optical rotation indicated that it was the *S* enantiomer.[20,22] The resultant acetate (*R*)-**16** was cleaved using MeOH and K_2CO_3 to give *R*-(−)-1-tetralol in 95% yield. Analysis using Mosher's acid revealed the presence of only a single diastereomer. The enantiopure tetralol was then complexed using $Cr(CH_3CN)_3(CO)_3$ to yield the endo-alcohol (*S*,*R*)-**17** whose rotation matched the reported value of −21°.[19] Oxidation to the ketone was performed using the DMSO/Ac_2O protocol to give enantiopure *S*-(+)-

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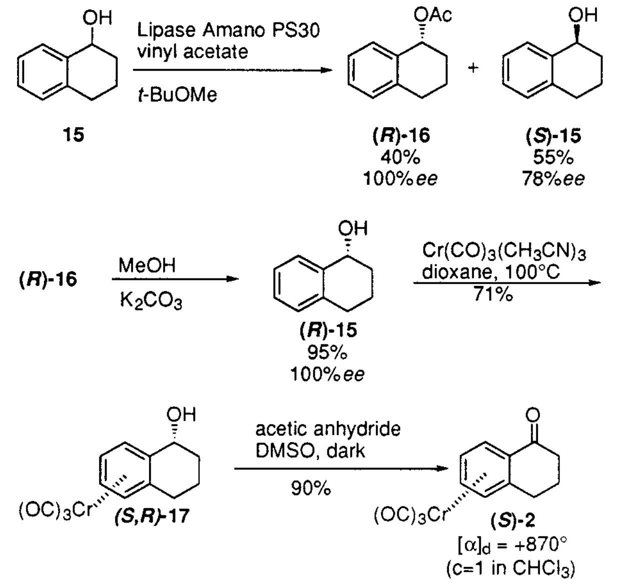
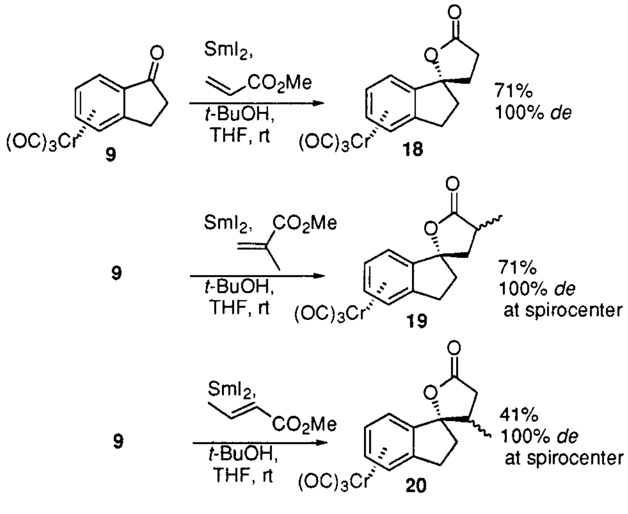
Scheme 5



Scheme 6



(η^6-1-tetralone)tricarbonylchromium ((*S*)-**2**). The optical rotations of enantiopure chromium complexes, especially the aryl carbonyls, can be very large. The rotation of resolved 1,2,3,4-tetrahydro-1-naphthol is 32°, and the rotation of the resolved chromium-bound 1,2,3,4-tetrahydro-1-naphthol is 21°, but the rotation of the complexed ketone is 870°.

Preparation of enantiopure (η^6-*o*-anisaldehyde)tricarbonylchromium, (*S*)-**12**, was achieved by a chromatographic separation of diastereomeric hydrazone derivatives following a literature procedure.[23]

Samarium(II)-Promoted Radical Lactone Formation. With the chromium tricarbonyl complexed aldehydes and ketones in hand, the templated analogue of Fukuzawa's radical coupling chemistry was examined. Reaction of chromium-complexed indanone (*rac*)-**9** with 2.5 equiv of samarium(II) iodide[12] and 5 equiv of methyl acrylate in the presence of *tert*-butyl alcohol afforded the spirocyclic lactone (*rac*)-**18** as a single diastereomer (Scheme 6). The assignment of the relative stereochemistry was initially assumed based upon a trapping mechanism wherein the ester approaches the intermediate ketyl radical anti to the chromium. Unfortunately, this could not be proven spectroscopically, so the configuration of the lactone relative to the metal was established by X-ray crystallography (vide infra). Addition of HMPA, which can increase the reducing potential of SmI_2,[25] did not noticeably affect the yield of the reaction. Small traces of reduced product were sometimes isolated;[26] otherwise, the reaction is very clean, unlike reactions of non-chromium-complexed substrates.[26] Without the acrylate trap present, the ketyls dimerized to give a mixture of meso and *dl* diols, which has been reported previously.[8o,27] The spirocyclic lactone (*rac*)-**18** is surprisingly polar and is not soluble in many nonpolar solvents such as benzene, dioxane, or ether and is only sparingly soluble in chloroform and methylene chloride. Because of this insolubility, deuterated nitromethane or acetone were used as NMR solvents.

Methyl methacrylate and methyl crotonate were relatively efficient radical traps, though substitution at the β-position of the ester decreased the product yield somewhat (Scheme 6). The stereochemistry at the methyl substituent in products (*rac*)-**19** and (*rac*)-**20** was not controlled and led to isomeric mixtures of approximately 2:1 and 3:2, respectively. However, the diastereoselectivity at the benzylic position was not compromised as only single isomers were detected. Several other traps were tested in explorations of the scope of these radical couplings. Phenyl vinyl sulfone did not capture the ketyl radical, presumably because SmI_2 effectively reduces sulfones to sulfoxides.[13b] Acrylonitrile and dehydroalanine were also incompatible with the reaction conditions and did not generate radical trapped products. Not surprisingly, methyl cinnamate did not capture the radical due to steric hindrance at the β-position of the ester. Somewhat surprising was the failure of (β-styrenyl)methoxymethylenepentacarbonylchromium to capture the benzylic radical. Despite the large phenyl group, it is known that chromium carbene complexes are excellent radical scavengers and usually only 1 equiv of the carbene is needed as compared to 5–15 equiv of methyl acrylate.[8b,c] The carbene most likely underwent reduction with Sm(II) as the carbene complex was consumed during the reaction.

The tetralone chromium complex (*rac*)-**2** was similar in reactivity to the chromium-complexed indanone, and again the diastereoselectivity was 100% (Scheme 7). The stereochemistry of (*rac*)-**21** where the lactone moiety is syn to the metal was determined by X-ray crystallography.[28] The fluorenone complex (*rac*)-**1** was slightly less effective under the standard conditions as the intermediate doubly benzylic radical enjoys a conjugated stability that lowers its reactivity. Remarkably, the steric influence of the chromium tricarbonyl moiety extends to aryl β-ketones. Reaction of chromium-complexed 2-indanone **3** with methyl acrylate under the standard

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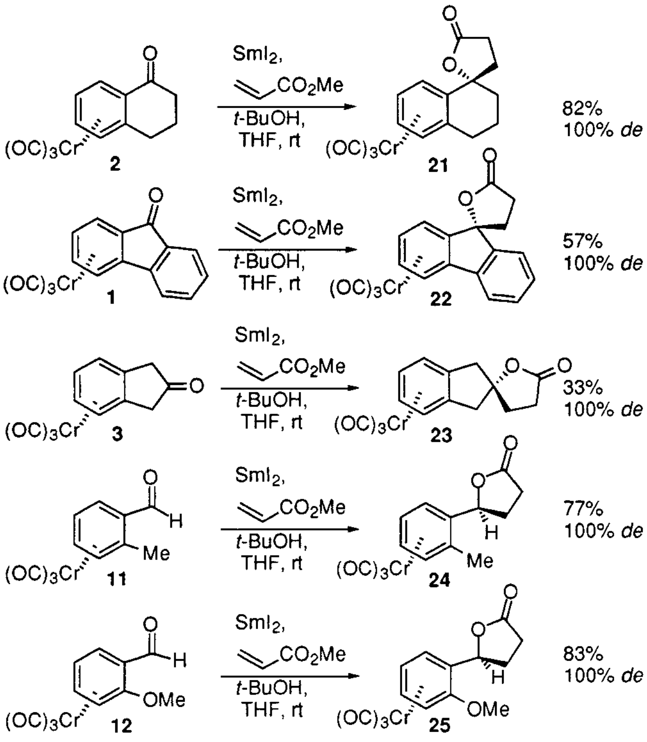
[25] (a) Otsubo, K.; Kawamura, K.; Inanaga, J.; Tamaguchi, M. *Chem. Lett.* **1987**, *7*, 1487–1490. (b) Shabangi, M.; Flowers, R. A. *Tetrahedron Lett.* **1997**, *38*, 1137–1140.

[26] The amount of reduced ketone (alcohol) varies. Noncomplexed arenes undergo aldol and Michael side reactions as well as reduction to the alcohol.

[27] Taniguchi, N.; Uemura, M. *Tetrahedron Lett.* **1998**, *54*, 12775–12788.

[28] See Supporting Information.

Scheme 7

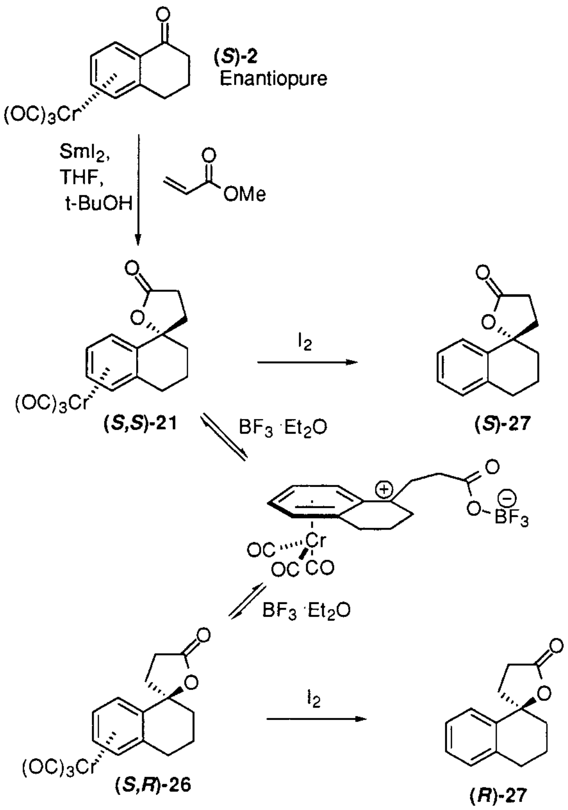


reaction conditions gave the spirocyclic lactone **23** again as a single diastereomer. The modest yield is attributed to the instability of the starting ketone complex.[29]

Even ortho-substituted aldehydes serve as partners for stereoselective radical reactions as reactions of complexes (*rac*)-**11** and (*rac*)-**12** gave lactones (*rac*)-**24** and (*rac*)-**25** as single isomers (Scheme 7).[30] The selectivity seen with these substrates arises from reaction of the preferred conformation (drawn) in analogy to anion addition reactions.[31] Aldehyde substrates (*rac*)-**11** and (*rac*)-**12** were somewhat sensitive to the reaction conditions and required a slower addition into the SmI_2 solution for efficient couplings.

Having achieved radical coupling reactions with 100% diastereoselectivity, we explored enantioselective synthesis next. Reaction of enantiopure ketone (*S*)-**2** with samarium diiodide, methyl acrylate, and *t*-BuOH in THF yielded endo-lactone complex (*S*,*S*)-**21** in 81% yield in 100% de and 100% ee (Scheme 8). Compound (*S*,*S*)-**21** has an optical rotation of +280°. Assignment of the relative stereochemistry of (*S*,*S*)-**21** was based on the X-ray crystal structure of racemic **21**.[28] Oxidative decomplexation with iodine afforded enantiopure lactone (*S*)-**27**. It was assumed that the iodine promoted decomplexation would not epimerize the lactone.

Scheme 8



Novel access to the diastereomer of (*S*,*S*)-**21** (endo-lactone), and hence the enantiomer of (*S*)-**27**, was achieved via a Lewis acid-mediated cationic rearrangement (Scheme 8). Treatment of endo-lactone complex (*S*,*S*)-**21** with 0.5 equiv of $BF_3 \cdot Et_2O$ in 1,2-dichloroethane for 1 min resulted in rearrangement to an 8:1 ratio of isomers (*S*,*R*)-**26** and (*S*,*S*)-**21**, respectively. After separation, the optical rotation for the exo complex (*S*,*R*)-**26** was +286°, while complex (*S*,*S*)-**21** had a rotation of +280°. Other Lewis acids such as $ZnCl_2$ and silyl and alkyl triflates were also effective in promoting this rearrangement. Use of 1 equiv of $BF_3 \cdot Et_2O$ for 5 min gave an equilibrium mixture of the exo and endo isomers with, surprisingly, only a slight preference (1.3:1) for the exo-isomer (*S*,*R*)-**26**. This result is surprising in light of the fact that the carboxylate must attack the benzylic cation syn to the metal to regenerate the endo-lactone. When pure exo-isomer was treated with $BF_3 \cdot Et_2O$, formation of the endo-isomer (*S*,*S*)-**21** was observed, providing evidence that the reaction is indeed an equilibrium. Regardless, the diastereomers were readily separable (ΔR_f of 0.2 on silica gel), and oxidative decomplexation of (*S*,*R*)-**26** afforded enantiopure lactone (*R*)-**27** whose optical rotation was nearly equal in magnitude, but opposite in sign to (*S*)-**27**. Therefore, by coupling radical chemistry with the ionic rearrangement, *both* enantiomers of the lactone were derived from a *single* enantiomer of ketone **2**.

This methodology was also applied to the synthesis of enantiopure lactones from enantiopure aryl aldehydes. Reaction of enantiopure (*S*)-**12** under the standard radical lactonization conditions afforded (*S*,*R*)-**25** in 83% yield in 100% de and 100% ee. The ee is assumed not to have changed during the course of the reaction as this would require decomplexation followed by recomplexation on the opposite enantiotopic face of the ketone. The optical rotation of (*S*,*R*)-**25** is +164°. The relative stereochemistry was assigned based on analogy to the known nucleophilic addition of methyl Grignard onto (*o*-anisaldehyde)tricarbonylchromium[31] and is in agreement with results reported by Uemura.[31] As in the racemic series, none of the other diastereomer was detected. Facile decomplexation of (*S*,*R*)-**25** using I_2 in chloroform afforded enantiomerically pure (*R*)-**29** (Scheme 9). It was

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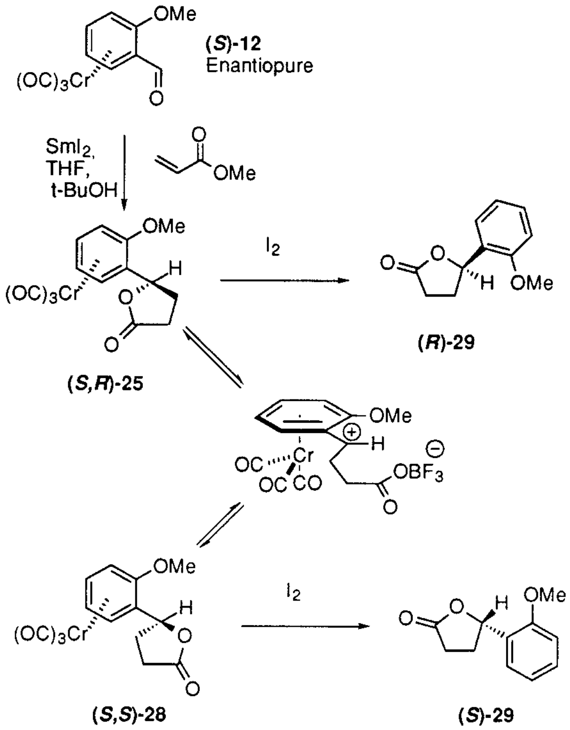
(29) Jackson, W.; Mitchell, T. *J. Chem. Soc. (B)* **1969**, 1228−1230.

(30) Taniguchi, N.; Uemura, M. *Tetrahedron Lett.* **1997**, *38*, 7199−7202.

(31) Davies, S. G.; Goodfellow, C. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 393−407.

Scheme 9



assumed that the I_2 decomplexation would not epimerize the lactone.

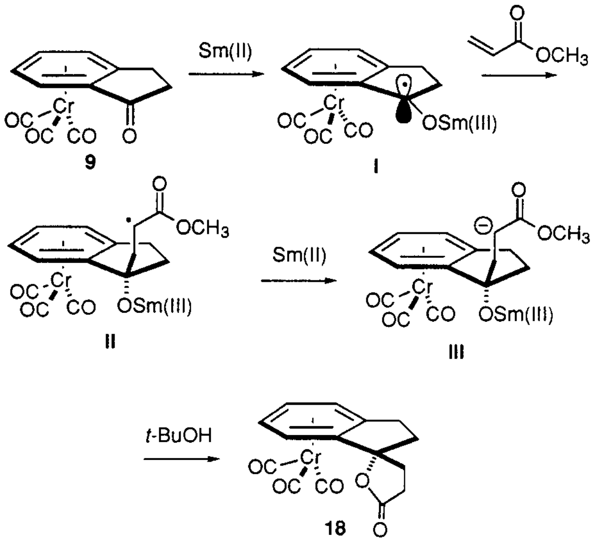
We then achieved the synthesis of the diastereomer of (*S*,*R*)-**25**, and hence the enantiomer of (*R*)-**29**, using the same Lewis acid-promoted rearrangement as described earlier. Treatment of (*S*,*R*)-**25** with 0.5 equiv of $BF_3{\cdot}Et_2O$ led to a mixture of diastereomers (*S*,*S*)-**28** and (*S*,*R*)-**25** in a ratio of approximately 1:1 (Scheme 9). Treatment of (*S*,*S*)-**28** with $BF_3{\cdot}Et_2O$ generated (*S*,*R*)-**25**, signifying that the inversion is an equilibrium process. Again, it is puzzling that the selectivity does not favor exclusive formation of (*S*,*S*)-**28**. These lactones also exhibit the same differences in polarity as their cyclic counterparts and are thus easily separable via column chromatography. The optical rotation of (*S*,*S*)-**28** is +71°. Oxidative decomplexation of (*S*,*S*)-**28** by exposure to light in chloroform afforded (*S*)-**29** whose optical rotation was equal in magnitude and opposite in sign to (*R*)-**29**.

Discussion

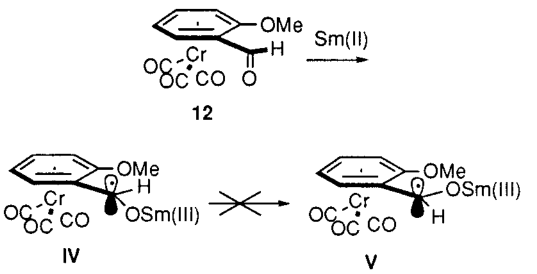
Sm(II)-Mediated Couplings. Samarium(II)-mediated coupling of chromium arene complexes with α,*β*-unsaturated esters proceeded quickly and cleanly to provide products that were diastereomerically pure at the benzylic position. Ketones coupled well at room temperature; however, aldehyde complexes were more sensisitve to the reaction conditions. A notable feature of the chromium-complexed lactones is their unusual polarity. The lactones are all yellow crystalline compounds which are insoluble in nonpolar solvents and only sparingly soluble in $CHCl_3$ and THF.

A significant challenge was assignment of the relative stereochemistry of the lactone products which lack a convenient spectroscopic handle to relate the lactone and arene stereochemistries. Mechanistically, the coupling reaction is presumed to begin with reduction of the aryl ketone with samarium(II) iodide to afford the ketyl-radical **I** (Scheme 10).[12] Subsequent trapping of the radical with an unsaturated ester affords the ester-stabilized radical **II**. Another e^- transfer by samarium(II) to the ester-stabilized radical gives the anionic compound **III**, which is quenched by *t*-BuOH and subsequently cyclizes to give a lactone. The high diastereoselectivity observed is attributed to the sterically demanding $Cr(CO)_3$ moiety which efficiently shields the α-face from radical capture. The relative stereochemistry of each product was initially assigned based upon this model of ester trapping from the face opposite the chromium tricarbonyl moiety. Subsequent X-ray crystallographic analysis[28] confirmed the proposed stereochemistry of lactone (*rac*)-**21**, and the other products were assigned by analogy.

Scheme 10



Scheme 11



The selective formation of diastereomerically pure lactones from aryl aldehydes must be addressed (Scheme 11). As mentioned earlier, the selectivity observed in the radical reactions of the cyclic ketones is governed by the sterically demanding tricarbonylchromium moiety which directs the alkylation to the *β*-face. Because the ketone complexes are planar, there is only one conformation of the benzylic radical. The preferred conformation of the radical generated from the aryl aldehydes, however, is determined by the ortho substituent. An initial thought was that, in the case of the *o*-anisaldehyde, the ortho methoxy group would chelate the Sm(III) alkoxide, forming a six-membered samarium chelate and thereby leading to lactone (*S*,*R*)-**25** as a result. Based on the X-ray structure of lactone (*rac*)-**25**,[30] this mechanism was not considered to be accurate. Instead, the mechanism of capture for the radicals derived from the aryl aldehydes is the same as the mechanism proposed for cyclic ketones and suggests that the samarium−adduct conformer **V** is

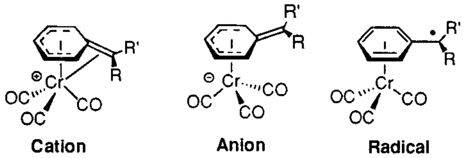


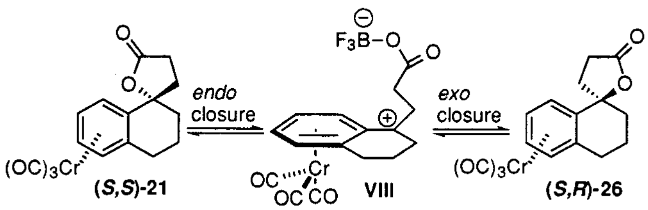
Figure 1.

destabilized due to the steric interactions of the ortho substituent whether the ortho substituent can chelate the samarium. This conformational arguement where the favored conformation of the aldehyde substituent dictates the reaction stereochemistry is the same as for nucleophilic addition to ortho-substituted aldehydes.[31] The rotational barrier of the ring$-CH_2$ bond in the parent benzyl radical chromium complex was recently calculated to be 12.3 kcal/mol.[8s] The barrier for a substituted system would be higher, disfavoring rapid interconversion between **IV** and **V**. Indeed, a recent paper by Schmalz reported "memory of chirality" in a reaction involving a complexed benzyl radical intermediate where there was greater than 95% retention of chirality and his substrate lacked an ortho substituent.[8v]

A major mechanistic question remaining is whether the chromium moiety exerts a stabilizing or destabilizing effect on the benzylic radical. Because the radical is in conjugation with the arene, and in light of the fact that chromium complexation strongly stabilizes *both* benzylic anions and benzylic cations through electronic interactions and structural changes (Figure 1),[9,32] the expectation was that the interaction would be stabilizing. In contrast, there is one report that chromium complexation destabilizes benzylic radicals.[11b] However, on the basis of experimental and theoretical results reported from this lab,[32] there is not significant added stabilization or destabilization of the benzylic radical by the tricarbonyl chromium moiety (Figure 1). As with other aryl substituted radicals,[33] there is little electronic effect of an aryl substituent on radical stability. Therefore, the stereoselectivities reported herein are governed solely by the steric effects about the chromium.

Inversion and Decomplexation. By utilizing the steric and electronic effects of chromium, it was possible to synthesize both enantiomeric lactones starting from the same enantiomeric ketone. Starting from the lactone, ionization of the carboxylate with BF_3 generates the zwitterionic complex then the carboxylate recloses from either face of the arene affording the endo and exo complexes. This is one of the few known examples of endo nucleophilic addition in an arene complex (Scheme 12).[34] For both the spirocyclic and monocyclic lactones, the process appears to be in equilibrium since isomeric mixtures could be formed starting from either endo or exo isomers. One puzzling result is the fact that the ratio of products changed based on the amount of BF_3 used. At substoichiometric quantities and short reaction times, the ratio of exo to endo lactone is approximately 8:1. Upon addition of a full equivalent of BF_3 and longer reaction times, the ratio changes to 1:1. The monocyclic lactones are less discriminating, and the ratio of the two diastereomers is approximately 1:1 even using substoichiometric quantities of BF_3. These results are especially unusual in light of the fact that chromium's control of benzylic cation capture with nucleophiles generally proceeds with high diastereoselectivities.[9] It was observed that the rate of ionization of the exo-lactone was faster than the rate of ionization of the endo-lactone due to the anti relationship of the exo-carboxylate to the metal which makes it more stereoelectronically reactive. However, this does not provide an adequate explanation for the rearrangement selectivities observed, so further experimentation will be required to solve this issue.

Scheme 12



Conclusion

In summary, use of a chromium tricarbonyl moiety as a metal template for radical reactions of aryl aldehydes and ketones provides for complete control of diastereoselectivity and enantioselectivity. The selectivity is attributed to the steric demand of the chromium tricarbonyl group which effectively shields one face of the arene from reaction. Diastereoselectivity occurs not only at the α position of a variety of aryl ketones, but also at the β position. Coupling this radical chemistry with anionic and cationic chemistry, chromium tricarbonyl serves as a unique stereochemical control element on arene substrates for diastereoselective and enantioselective synthesis.

Experimental Section

General. All reactions were carried out in flame-dried glassware in an inert atmosphere of Ar unless stated otherwise. Reaction solvents were distilled from the indicated drying agents: tetrahydrofuran (Na, benzophenone), diethyl ether (Na, benzophenone), dioxane (Na, benzophenone), and 1,2-dichloroethane (CaH_2). All reagents were purifed before use according to literature procedures.[35] Diiodomethane was distilled under reduced pressure over $CaCl_2$ in the dark and stored in a desiccator in the dark over copper turnings. Samarium metal was purchased from Aldrich and was kept in a drybox under N_2 atmosphere. Solvents for extractions and chromatography were not distilled. Flash column chromatography was performed by the method of Still[36] using 32−63 μm silica gel (ICN). ^1H NMR spectra was recorded at either 360, 400, or 500 MHz and ^{13}C NMR spectra was recorded at either 100 or 125 MHz using using $CDCl_3$ (δ 7.26 ppm for ^1H, d 77.0 ppm for ^{13}C), C_3D_6O (δ 2.05 ppm for ^1H, δ 29.92 and δ 206.68 ppm for ^{13}C), C_6D_6 (δ 7.16 ppm for ^1H, δ 128.39 ppm for ^{13}C) and CD_3NO_2 (δ 4.33 ppm for ^1H, δ 62.8 ppm for ^{13}C) as solvents and reference standards unless stated otherwise. Chemical shifts are given in ppm (δ); multiplicites are indicted by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broadened). Coupling constants, *J*, are reported in hertz.

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(32) Merlic, C. A.; Walsh, J. C.; Tantillo, D. J.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 3596−3606.

(33) Newcomb, M.; Choi, S. Y.; Toy, P. H. *Can. J. Chem.* **1999**, *77*, 1123−1135.

(34) (a) Schmalz, H. G.; Jope, H. *Tetrahedron* **1998**, *54*, 3457−3464. (b) Pigge, F. C.; Fang, S. Y.; Rath, N. P. *J. Organomet. Chem.* **1998**, *559*, 131−140. (c) Pearson, A. J.; Gontcharov, A. V. *J. Org. Chem.* **1998**, *63*, 152−162.

(35) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: Oxford, 1980.

(36) Still, C. W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

Infrared spectra (IR) were recorded on a Nicolet 510P spectrometer and signals are reported in cm^{-1}. High-resolution electron impact (EI) mass spectra were obtained with an ionization voltage of 70 eV. Data are reported in the form of *m*/*z* (intensity relative to base peak = 100). Analytical TLC was performed on Machery Nagel silica plates with UV 254 nm indicator. Visualization was accomplished with UV light and/or I$_2$.

***endo*-(Spiro[dihydro-2(3*H*)-furanone-5−1′(2′*H*)(3′*H*)-η^6-indane]) tricarbonylchromium ((*rac*)-18).** A solution of (η^6-1-indanone)tricarbonylchromium (50.0 mg, 0.20 mmol), *t*-BuOH (30 μL, 0.40 mmol), methyl acrylate (90 μL, 1.0 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (0.50 mmol) solution in THF (10 mL). After 5 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using 2:1 hexane:EtOAc followed by EtOAc as the eluent on silica gel to afford 42.6 mg (71%) of a yellow solid.

^{1}H NMR (500 MHz, C$_3$D$_6$O) δ: 2.22 (1H, d, *J* = 9.0 Hz), 2.36 (1H, d, *J* = 9.9 Hz), 2.45 (1H, br s), 2.56 (1H, br s), 2.73 (1H, d, *J* = 6.7 Hz), 2.76−2.81 (2H, m), 3.01 (1H, d, *J* = 6.0 Hz), 5.47 (1H, br s), 5.62 (1H, br s), 5.74 (1H, br s), 5.92 (1H, br s).

^{13}C NMR (100 MHz, C$_6$D$_6$) δ: 27.17, 28.77, 33.70, 35.87, 86.77, 88.02, 88.89, 90.13, 93.69, 112.61, 112.70, 174.46, 232.63.

IR (KBr): 2957, 1950, 1865, 1770, 1450, 1163, 663 cm^{-1}.

MS (70 eV): 324 (M$^+$, 65), 240 (80), 224 (100), 198 (50).

HRMS (EI): calcd for C$_{15}$H$_{12}$ CrO$_5$: 324.0089; found: 324.0088.

3-Methyl-*endo*-(spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)-(3′*H*)-η^6-indane])tricarbonylchromium ((*rac*)-19). A solution of (η^6-1-indanone)tricarbonylchromium (50.0 mg, 0.20 mmol), *t*-BuOH (30 μL, 0.40 mmol), methyl methacrylate (107 μL, 1.0 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (0.50 mmol) solution in THF (10 mL). After 5 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc and absorbed onto Celite. The residue was purified by chromatography using 2:1 hexane: EtOAc followed by EtOAc as the eluent on silica gel to afford 48.0 mg (71%) of a yellow solid as an approximate 2:1 mixture of epimers α to the ester.

^{1}H NMR (400 MHz, CD$_3$NO$_2$) (2:1 mixture) δ: 1.25 (2H, d, *J* = 7.0 Hz), 1.29 (1H, d, *J* = 7.2 Hz), 2.01 (1H, t, *J* = 12.5 Hz), 2.08−2.22 (1H, m), 2.41−2.46 (1H, m), 2.66−2.72 (1H, m), 2.81−2.84 (1H, m), 2.94−3.00 (2H, m), 5.38−5.43 (1H, m), 5.53 (1H, d, *J* = 6.5 Hz), 5.66−5.73 (1.3H, m), 5.81 (0.6H, d, *J* = 6.5 Hz).

^{13}C NMR (100 MHz, CD$_3$NO$_2$) (2:1 mixture) δ: 16.52, 17.77, 30.20, 30.33, 37.79, 38.18, 38.42, 41.15, 44.79, 44.97, 91.66, 91.82, 91.98, 92.23, 92.30, 93.03, 93.19, 93.44, 98.77, 116.91, 118.29, 118.85, 181.65, 182.15, 236.37, 236.45 (2 carbons unresolved).

IR (KBr) (mixture): 2361, 2343, 1950, 1871, 1772, 1450, 1161 cm^{-1}.

MS (70 eV) (mixture): 338 (M$^+$, 65), 254 (100), 182 (50).

HRMS (EI) (mixture): calcd for C$_{16}$H$_{14}$ CrO$_5$: 338.0246; found: 338.0246.

4-Methyl-*endo*-(spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)-(3′*H*)-η^6-indane])tricarbonylchromium ((*rac*)-20). A solution (η^6-1-indanone)tricarbonylchromium (50.0 mg, 0.20 mmol), *t*-BuOH (30 μL, 0.40 mmol), methyl crotonate (107 μL, 1.0 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (0.44 mmol) solution in THF (10 mL). After 5 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using 2:1 hexane:EtOAc followed by EtOAc as the eluent on silica gel to afford 28.0 mg (55%) of a yellow solid as an approximate 3:2 mixture of epimers β to the ester.

^{1}H NMR (400 MHz, CD$_3$NO$_2$) δ: 1.25 (1.8H, d, *J* = 7.0 Hz), 1.29 (1.2H, d, *J* = 7.2 Hz), 2.05−2.08 (0.7H, m), 2.19−2.24 (1H, m), 2.42−2.45 (1.3H, m), 2.67−2.72 (1H, m), 2.82−2.84 (1H, m), 2.90−3.10 (2H, m), 5.41−5.43 (1H, m), 5.53 (1H, d, *J* = 6.5 Hz), 5.66−5.68 (1.4H, m), 5.81 (0.6H, d, *J* = 6.5 Hz) (both isomers).

^{13}C NMR (125 MHz, C$_6$D$_6$) δ: 14.24, 27.03, 34.91, 35.18, 41.74, 87.22, 87.83, 88.81, 89.01, 94.02, 112.48, 113.54, 177.09, 236.70 (major isomer only).

IR (KBr) (mixture): 1959, 1871, 1772, 1450, 1161 cm^{-1}.

MS (70 eV) (mixture): 338 (M$^+$, 65), 254 (100), 182 (30), 128 (35).

HRMS (EI) (mixture): calcd for C$_{16}$H$_{14}$ CrO$_5$: 338.0246; found: 338.0241.

***endo*-(Spiro[dihydro-2(3*H*)-furanone-5, 1′(2′*H*)(3′*H*)-(4′*H*)-η^6-naphthalene])tricarbonylchromium ((*rac*)-21).** A solution of (η^6-1-tetralone)tricarbonylchromium (250 mg, 0.89 mmol), *t*-BuOH (130 μL, 1.78 mmol), methyl acrylate (381 μL, 1.0 mmol), and THF (20 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (2.22 mmol) solution in THF (50 mL). After 5 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using 2:1 hexane: EtOAc followed by EtOAc as the eluent on silica gel to afford 241 mg (82%) of a yellow solid.

Crystals suitable for X-ray analysis were prepared in the following manner. The lactone complex (50 mg) was dissolved in oxygen-free THF (4 mL), and oxygen-free Et$_2$O (4 mL) was then added. Crystals formed and a suitable crystal was chosen for X-ray analysis.

^{1}H NMR (500 MHz, C$_3$D$_6$O) δ: 2.04−2.07 (3H, m), 2.37−2.41 (1H, m), 2.58−2.60 (1H, m), 2.76−2.81 (5H, m), 5.44−5.56 (2H, m), 5.77 (1H, d, *J* = 6.2 Hz), 5.84 (1H, d, *J* = 6.6 Hz).

^{13}C NMR (125 MHz, CD$_3$NO$_2$) δ: 19.67, 28.05, 29.71, 34.78, 36.60, 84.90, 91.78, 93.11, 93.15, 97.29, 114.15, 114.70, 177.92, 235.21.

IR (KBr): 2957, 1961, 1884, 1855, 1770, 1238, 1163 cm^{-1}.

MS (70 eV): 338 (M$^+$, 30), 254 (35), 202 (40), 147 (100), 129 (40).

HRMS (EI): calcd for C$_{16}$H$_{14}$ CrO$_5$: 338.0246; found: 338.0241.

***endo*-(Spiro[dihydro-2(3*H*)-furanone-5-9′-(9*H*)-η^6-fluorene])tricarbonylchromium ((*rac*)-22).** A solution of (η^6-fluorenone)tricarbonylchromium (126.4 mg, 0.40 mmol), *t*-BuOH (59 μL, 0.8 mmol), methyl acrylate (172 μL, 2.0 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (0.90 mmol) solution in THF (10 mL). After 10 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc and absorbed onto Celite. The residue was purified by chromatography using 1:1 hexane:Et$_2$O followed by EtOAc as the eluent on silica gel to afford 85 mg (57%) of a yellow-orange solid.

^{1}H NMR (400 MHz, CD$_3$NO$_2$) δ: 2.7 (2H, t, *J* = 8.4 Hz), 3.08 (2H, t, *J* = 7.6 Hz), 5.46 (1H, t, *J* = 6.1 Hz), 5.85 (1H, t, *J* = 6.3 Hz), 6.12 (1H, d, *J* = 6.4 Hz), 6.17 (1H, d, *J* = 6.4 Hz), 7.46−7.54 (2H, m), 7.6 (1H, d, *J* = 7.2 Hz), 7.7 (1H, d, *J* = 7.2 Hz).

^{13}C NMR (125 MHz, CD$_3$NO$_2$) δ: 29.10, 34.37, 83.32, 87.90, 88.96, 88.99, 93.33, 109.16, 112.00, 120.65, 123.16, 129.73, 129.96, 136.56, 144.80, 175.29, 231.97.

IR (KBr): 1961, 1871, 1774, 1170, 1047 cm^{-1}.

MS (70 eV): 372 (M$^+$, 50), 288 (65), 236 (75), 181 (100), 165 (50).

HRMS (EI): calcd for C$_{19}$H$_{12}$ CrO$_5$: 372.0089; Found: 372.0090.

***endo*-(Spiro[dihydro-2(3*H*)-furanone-5-2′(1′*H*)(3′*H*)-η^6-indane])tricarbonylchromium ((*rac*)-23).** A solution of (η^6-2-indanone)tricarbonylchromium (70.0 mg, 0.26 mmol), *t*-BuOH (38 μL, 0.52 mmol), methyl acrylate (117 μL, 1.3 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI$_2$ (0.65 mmol) solution in THF (10 mL). After 10 min, the reaction was quenched with sat. K$_2$CO$_3$ (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using a gradient elution of

9:1 hexane:EtOAc, 4:1 hexane:EtOAc, followed by EtOAc as the eluent on silica gel to afford 27.0 mg (33%) of a yellow solid.

^{1}H NMR (400 MHz, CD_3NO_2) δ: 2.44 (2H, t, $J = 8.0$ Hz), 2.60 (2H, t, $J = 8.0$ Hz), 3.1 (2H, d, $J = 17.2$ Hz), 3.25 (2H, d, $J = 17.2$ Hz), 5.47 (2H, dd, $J = 4.8$, 2.7 Hz), 5.66 (2H, dd, $J = 4.7$, 2.8 Hz).

^{13}C NMR (100 MHz, CD_3NO_2) δ: 30.06, 33.99, 45.46, 91.99, 92.33, 94.38, 112.79, 178.13, 235.59.

IR (KBr): 2957, 1944, 1867, 1759, 1415, 1178, 667 cm^{-1}.

MS (70 eV): 324 (M$^+$, 30), 240 (100), 222 (45), 194 (35).

HRMS (EI): calcd for $C_{15}H_{12}$ CrO_5: 324.0090; found: 324.0096.

[5-(η^6-2′-Methylphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium ((*rac*)-24). A solution of (η^6-*o*-tolylaldehyde)tricarbonylchromium (50.0 mg, 0.20 mmol), *t*-BuOH (30 μL, 0.40 mmol), methyl acrylate (90 μL, 1.0 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI_2 (0.50 mmol) solution in THF (10 mL). After 5 min, the reaction was quenched with sat. K_2CO_3 (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using 4:1 hexane:EtOAc followed by 1:1 hexane:EtOAc as the eluent on silica gel to afford 48 mg (77%) of a yellow solid.

^{1}H NMR (360 MHz, $CDCl_3$) δ: 0.91 (1H, m), 1.49 (3H, s), 1.87 (3H, m), 4.30 (1H, d, $J = 6.1$ Hz), 4.45 (1H, t, $J = 6.2$ Hz), 4.54 (2H, m), 5.07 (1H, d, $J = 6.2$ Hz).

^{13}C NMR (100 MHz, C_6D_6) δ: 17.49, 27.96, 29.49, 75.97, 88.88, 89.43, 92.52, 93.10, 104.23, 108.06, 174.15, 232.79.

IR (KBr): 1958, 1867, 1778, 1458, 1217, 1143, 1039, 662, 630 cm^{-1}.

MS (70 eV): 312 (M$^+$, 45), 256 (75), 228 (60), 186 (100), 172 (75), 91 (60).

HRMS (EI): calcd for $C_{14}H_{12}CrO_5$: 312.0090; found: 312.0097.

[5-(η^6-2′-Methoxyphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium ((*rac*)-25). A solution of (η^6-*o*-anisaldehyde)tricarbonylchromium (15.0 mg, 0.055 mmol), *t*-BuOH (8 μL, 0.11 mmol), methyl acrylate (24 μL, 0.28 mmol), and THF (7 mL) was purged with argon for 20 min and then cannulated into a SmI_2 (0.14 mmol) solution in THF (5 mL). After 5 min, the reaction was quenched with sat. K_2CO_3 (1 mL). The reaction was filtered through a pad of silica gel, washed with EtOAc, and absorbed onto Celite. The residue was purified by chromatography using 1:4 hexane:EtOAc followed by 1:1 hexane:EtOAc as the eluent on silica gel to afford 15 mg (83%) of a yellow solid. This compound was also recrystallized from $CDCl_3$ and Et_2O.

^{1}H NMR (360 MHz, $CDCl_3$) δ: 2.13 (1H, m), 2.67 (3H, m), 3.78 (3H, s), 4.91 (1H, t, $J = 6.1$ Hz), 5.07 (1H, d, $J = 6.9$ Hz), 5.46 (1H, t, $J = 7.5$ Hz), 5.52 (1H, t, $J = 7.3$ Hz), 5.71 (1H, d, $J = 6.2$ Hz).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.52, 29.75, 55.90, 73.20, 82.91, 84.27, 91.91, 93.41, 97.52, 104.27, 175.90, 232.02.

IR ($CDCl_3$): 1959, 1869, 1774, 1468, 1267, 669, 630 cm^{-1}.

MS (70 eV): 328 (M$^+$, 75), 267 (40), 192 (80), 162 (100), 135 (95), 113 (70).

HRMS (EI): calcd for $C_{14}H_{12}CrO_6$: 328.0039; found: 328.0044.

(*S*,*S*)-(+)-*endo*-(Spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium ((*S*,*S*)-21). Lactonization of enantiopure (*S*)-(+)-(η^6-1-tetralone)tricarbonylchromium was carried out using the same procedure used for the racemic substrate. The optical rotation of (*S*,*S*)-(+)-*endo*-(spiro[dihydro-2(3*H*)-furanone-5-1′(2′H)(3′H)(4′H)-η^6-naphthalene])-tricarbonylchromium is +280 ($c = 1$ in THF).

(*S*,*R*)-(+)-*exo*-(Spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium ((*S*,*R*)-26). A solution of (*S*,*S*)-(+)-*endo*-(spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium ((*S*,*S*)-**21**) (35 mg, 0.1 mmol) and 1,2-dichloroethane (1 mL) was degassed via argon purge for 20 min. BF_3−etherate (6.5 μL, 0.05 mmol) was added as a single portion. After 1 min, H_2O (100 μL) was added, and the reaction was filtered through silica gel, washed with EtOAc, and absorbed onto Celite. The product was purified by chromatography using 2:1 hexane:EtOAc as the eluent followed by EtOAc on silica gel to afford 23 mg (66%) of a yellow solid. Starting material was also recovered, 3 mg (9%). The optical rotation of (*S*,*R*)-(+)-*exo*-(spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium is +286 ($c = 1$ in THF).

^{1}H NMR (500 MHz, CD_3NO_2) δ: 1.80−1.96 (4H, m), 2.50−2.56 (1H, m), 2.59−2.61 (1H, m), 2.70−2.85 (4H, m), 5.36 (1H, d, $J = 6.2$ Hz), 5.42 (1H, t, $J = 6.6$ Hz), 5.81 (1H, t, $J = 6.4$ Hz), 5.97 (1H, d, $J = 6.6$ Hz).

^{13}C NMR (125 MHz, CD_3NO_2) δ: 19.62, 29.66, 30.09, 35.46, 37.10, 85.41, 90.91, 92.29, 97.28, 98.75, 110.85, 115.74, 177.78, 235.05.

IR (KBr): 2957, 1986, 1856, 1773, 1160, 669 cm^{-1}.

MS (70 eV): 338 (M$^+$, 100), 254 (70), 212 (30), 147 (60), 129 (40).

HRMS (EI): calcd for $C_{16}H_{14}$ CrO_5: 338.0246; found: 338.0244.

(*R*)-(+)-Spiro(dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)-(4′*H*))-η^6-naphthalene ((*R*)-27). (*S*,*R*)-(+)-*exo*-(Spiro[dihydro-2(3*H*)-furanone-5,1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium (*S*,*R*)-**26** (43 mg, 0.13 mmol) was dissolved in THF (5 mL) and an excess amount of I_2 (125 mg, 0.49 mmol) was added, and the solution was stirred for 2 h. The reaction was then poured onto sat. Na_2SO_3, extracted into Et_2O, and dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was purified by chromatography using 1:1 Et_2O:hexane as the eluent on silica gel to afford 25 mg (97%) of lactone (*R*)-**27** as a yellow oil with a rotation of +4.35 ($c = 2.3$ in $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.86−1.91 (1H, m), 2.07−2.10 (2H, m), 2.16−2.18 (1H, m), 2.44 (2H, t, $J = 8.2$ Hz), 2.81 (2H, t, $J = 8.7$ Hz), 2.83−2.89 (2H, m), 7.14−7.17 (1H, m), 7.25−7.29 (2H, m), 7.36−7.40 (1H, m).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.89, 28.85, 28.97, 35.11, 36.01, 85.93, 125.89, 126.47, 127.94, 128.86, 136.85, 138.25, 176.73.

IR (KBr): 3021, 2951, 1769, 1449, 1217, 757 cm^{-1}.

MS (70 eV): 202 (M$^+$, 50), 147 (100), 129 (35).

HRMS (EI): calcd for $C_{13}H_{14}O_2$: 202.0994; found: 202.0991.

(*S*)-(−)-Spiro(dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)-(4′*H*))-η^6-naphthalene ((*S*)-27). (*S*,*S*)-(+)-*endo*-(Spiro[dihydro-2(3*H*)-furanone-5-1′(2′*H*)(3′*H*)(4′*H*)-η^6-naphthalene])tricarbonylchromium ((*S*,*S*)-**21**) (63 mg, 0.19 mmol) was dissolved in THF (5 mL), an excess amount of I_2 (250 mg, 1.0 mmol) was added, and the solution was stirred for 1 h. The reaction was then poured onto sat. Na_2SO_3, extracted into Et_2O, and dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was purified by chromatography using 1:1 Et_2O:hexane as the eluent on silica gel to afford 23 mg (61%) of lactone (*S*)-**27** as a yellow oil with a rotation of −4.27 ($c = 2.3$ in $CHCl_3$). Spectral data matched that of (*R*)-**27**.

(*S*,*R*)-(+)-[5-(η^6-2′-Methoxyphenyl)dihydro-2(3*H*)-furanone)] tricarbonylchromium ((*S*,*R*)-25). Lactonization of the enantiopure (η^6-*o*-anisaldehyde)tricarbonylchromium was carried out using the same procedure used for the racemic substrate. The optical rotation of (*S*,*R*)-(+)-[5-(η^6-2′-methoxyphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium is +164 ($c = 0.33$ in $CDCl_3$).

(*S*,*S*)-[5-(2′-η^6-Methoxyphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium ((*S*,*S*)-28). A solution of (*S*,*R*)-[5-(η^6-2′-methoxyphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium ((*S*,*R*)-**25**) (56 mg, 0.17 mmol) and dichloromethane (1 mL) was degassed via an argon purge for 20 min. BF_3−etherate (11 μL, 0.09 mmol) was added as a single portion. After 1 min, H_2O (100 μL) was added, and the reaction was filtered through silica gel, washed with EtOAc, and absorbed onto Celite. The product was purified by chromatography using 2:1 hexane:EtOAc as the eluent followed by EtOAc on silica gel to afford 19 mg (34%) of a yellow solid with an optical rotation of +71 ($c = 0.33$ in THF). Starting material was also recovered, 21 mg (38%). This compound was also recrystallized from $CDCl_3$ and hexane.

^{1}H NMR (360 MHz, $CDCl_3$) δ: 2.62 (1H, m), 2.71 (3H, m), 3.78 (3H, s), 4.87 (1H, t, $J = 6.2$ Hz), 5.03 (1H, d, $J = 6.8$ Hz), 5.56 (1H, t, $J = 6.9$ Hz), 5.65 (1H, t, $J = 6.1$ Hz), 5.71 (1H, d, $J = 6.3$ Hz).

^{13}C NMR (90 MHz, $CDCl_3$) δ: 28.99, 30.87, 56.03, 72.39, 74.62, 83.48, 94.78, 95.01, 97.05, 141.48, 176.01, 232.27.

IR ($CDCl_3$): 3135, 1971, 1896, 1794, 1643, 1469, 1383, 1095, 650, 623 cm^{-1}.

MS (70 eV): 328 (M^+, 60), 244 (100), 202 (75), 172 (70), 157 (30).

HRMS (EI): calcd for $C_{14}H_{12}CrO_6$: 328.0039; found: 328.0033.

(*R*)-(+)-5-(2′-Methoxyphenyl)dihydro-2(3*H*)-furanone ((*R*)-29). A solution of (*S*,*R*)-(+)-[5-(η^6-2′-methoxyphenyl)-dihydro-2(3*H*)-furanone)]tricarbonylchromium ((*S*,*R*)-**25**) (17 mg, 0.051 mmol) in $CDCl_3$ (2 mL) was exposed to light and air overnight. The clear, colorless solution was filtered through a pad of SiO_2 (Et_2O wash) to afford 8 mg (80%) of a clear, colorless oil that had a rotation of +71 ($c = 0.25$ in MeOH). The compound was purified via chromatography using 1:4 Et_2O:hexane then 1:1 Et_2O:hexane as the eluent on silica gel.

^1H NMR (500 MHz, $CDCl_3$) δ: 2.09−2.16 (1H, m), 2.61 (2H, t, $J = 7.0$ Hz), 2.69−2.74 (1H, m), 3.85 (3H, s), 5.77 (1H, t, $J = 7.0$), 6.90 (1H, d, $J = 8.2$), 6.98 (1H, t, $J = 7.5$), 7.31−7.35 (2H, m).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.59, 29.31, 55.37, 77.89, 110.51, 120.67, 125.63, 128.06, 129.28, 156.04, 177.60.

IR ($CDCl_3$): 3156, 1794, 1603, 1468, 1383, 1095, 989 cm^{-1}.

MS (70 eV): 192 (M^+, 100), 147 (50), 137 (95), 107 (35).

HRMS (EI): calcd for $C_{11}H_{12}O_3$: 192.0786; found: 192.0791.

(*S*)-(−)-5-(2′-Methoxyphenyl)dihydro-2(3*H*)-furanone ((*S*)-29). A solution of (*S*,*S*)-(+)-[5-(η^6-2′-methoxyphenyl)dihydro-2(3*H*)-furanone)]tricarbonylchromium (*S*,*S*)-**28** (17 mg, 0.051 mmol) in $CDCl_3$ (2 mL) was exposed to light and air overnight. The clear, colorless solution was filtered through a pad of SiO_2 (Et_2O wash) to afford 8 mg (80%) of a clear, colorless oil that had a rotation of −70 ($c = 0.25$ in MeOH). The compound was purified via chromatography using 1:4 Et_2O:hexane then 1:1 Et_2O:hexane as the eluent on silica gel.

Spectral data matched that of (*R*)-**29**.

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Supporting Information Available: Experimental procedures and spectral data for compounds **1**−**5**, **7**, **9**, **11**−**17**; an X-ray crystallographic report for **21**; and copies of ^1H and ^{13}C NMR spectra for compounds **18**−**29** described in the Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

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