Reactivity of (η^6-Arene)tricarbonylchromium Complexes toward Additions of Anions, Cations, and Radicals

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Abstract: A computational and experimental study of additions of electrophiles, nucleophiles, and radicals to tricarbonylchromium-complexed arenes is reported. Competition between addition to a complexed arene and addition to a noncomplexed arene was tested using 1,1-dideuterio-1-iodo-2-((phenyl)tricarbonylchromium)-2-phenylethane. Reactions under anionic and cationic conditions give exclusive formation of 1,1-dideuterio-1-((phenyl)tricarbonylchromium)-2-phenylethane arising from addition to the complexed arene. Radical conditions (SmI_2) afford two isomeric products, reflecting a 2:1 preference for radical addition to the noncomplexed arene. In contrast, intermolecular radical addition competition experiments employing ketyl radical addition to benzene and (benzene)tricarbonylchromium show that addition to the complexed aromatic ring is faster than attack on the noncomplexed species by a factor of at least 100 000. Density functional theory calculations using the B3LYP method, employing a LANL2DZ basis set for geometry optimizations and a DZVP2+ basis set for energy calculations, for all three reactive intermediates showed that tricarbonylchromium stabilizes **all three** types of intermediates. The computational results for anionic addition agree well with established chemistry and provide structural and energetic details as reference points for comparison with the other reactive intermediates. Intermolecular radical addition leads to exclusive reaction on the complexed arene ring as predicted by the computations. The intramolecular radical reaction involves initial addition to the complexed arene ring followed by an equilibrium leading to the observed product distribution due to a high-energy barrier for homolytic cleavage of an exo bond in the intermediate cyclohexadienyl radical complex. Mechanisms are explored for electrophilic addition to complexed arenes. The calculations strongly favor a pathway in which the cation initially adds to the metal center rather than to the arene ring.

Introduction

The chemistry of chromium tricarbonyl-complexed arenes[1] continues to fascinate researchers more than 40 years after the initial discovery of (benzene)tricarbonylchromium,[2] with applications in diastereoselective synthesis,[3] enantioselective synthesis,[4] chiral ligands,[5] and even total synthesis.[6] Complexation of an arene ring by tricarbonylchromium imparts dramatic changes to the reactivity of the arene moiety and is summarized by Figure 1. Most significant, considering the long history of aromaticity and aromatic chemistry, is that chromium complexation of aryl rings dramatically alters their electronic nature. While there is no reduction in the aromaticity,[7] there is a remarkable enhancement in reactivity of the arene ring toward direct anti nucleophilic addition due to the electron-withdrawing character of the tricarbonylchromium fragment. Nucleophilic additions by anions are extremely facile, the reactivity patterns

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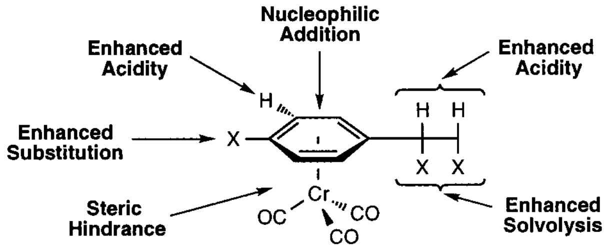

Figure 1. Effects of complexation of arenes by tricarbonylchromium.

are well defined, and the chemistry is widely utilized in synthesis.[1a,b,e] The paucity of reports on electrophilic and radical addition reactions stands in stark contrast to the extensive body of literature on nucleophilic additions.

Electrophilic reactions of arene complexes were examined soon after the discovery of these complexes and, given the rich chemistry of electrophilic additions to aromatic compounds, this was a natural course to pursue. However, only sporadic investigations have been reported since, and often with conflicting results. In their classic paper on nucleophilic substitution reactions of arene complexes, Nicholls and Whiting reported that arene complexes failed to undergo Friedel–Crafts acetylation and concluded that it was "unlikely that electrophilic substitution will prove useful synthetically in this field".[8] However, the first successful Friedel–Crafts acetylation reactions were reported the same year, but few details were provided.[9] A subsequent paper reported that the isomeric ratios obtained from the toluene complex (o:m:p = 39:15:46) were different from those of the free ligand (o:m:p = 9:2:89) and that the complexed arenes were less reactive.[10] Brown and coworkers examined the rate of acetylation of the benzene complex and found it to be more reactive than the free ligand.[11] They also suggested that electrophilic addition may involve dual attack at the ring and at the metal. In an interesting series of papers, Jackson and co-workers found that the isomer ratios in Friedel–Crafts acetylation reactions of arene complexes are different than those of the free arenes and that the ratios could be rationalized based upon preferred conformations of the tricarbonylchromium moiety.[12] Electrophilic addition occurred on carbons not eclipsed by metal carbonyl bonds. They also found that complexed arenes reacted much more slowly than the free arenes. Von Rosenberg and Pinder examined the acetylation reaction more carefully and definitively concluded that complexed benzene was less reactive than free benzene.[13] They went on to test interesting monocomplexed α,ω-diphenylalkane substrates and concluded that the tricarbonylchromium group deactivates attached arene rings toward electrophilic substitution to a small extent. Rosca and co-workers explored Friedel–Crafts acetylation reactions in the same systems as those of von Rosenberg and Pinder and found similar, though not identical, results and also cited the deactivating nature of the tricarbonylchromium moiety.[14] They proposed a mechanism wherein electrophilic addition on chromium was followed by rate determining transfer of the electrophile to the aryl ring. Like most previous researchers, low yields of acetylated product were obtained. There are no reports of Friedel–Crafts alkylation reactions of arene complexes. Electrophilic mercuration of complexed benzene has also been reported, but attempts on substituted analogues failed.[15] Electrophiles such as nitrosonium ion and benzenediazonium ion react at the metal of arene complexes, leading to ligand substitution or oxidation processes.[16] Arene complexes have been activated toward electrophilic addition through reduction to the anionic η^4 complex[17] or through nucleophilic catalysis of electrophilic desilylation.[18] There are several reports on protonation of (benzene)tricarbonylchromium.[14,19] Protonation occurs at the metal and exchange with ring protons occurs, but at a slower rate than that for free benzene.

The mechanistic question of the regioselectivity of initial electrophilic addition by a carbocation to the ring (exo or endo) or the metal in (arene)tricarbonylchromium complexes was addressed by Bly, though he was not looking at arene substitution reactions, but rather neighboring group participation by arenechromium complexes in solvolytic reactions.[20] In a complex series of papers, Bly examined solvolysis reactions of tricarbonylchromium-complexed substituted phenethyl and benzonorbornenyl methanesulfonates. Both d orbital (C–Cr bond) and σ–π-type (endo C–C bond) participation were evaluated based on reaction rates and stereochemistry, though most of the data could not differentiate between them. He eventually concluded that direct metal–carbon interactions were not likely to be involved and attributed differing rate effects to σ–π-type and ion–dipole interactions. Wells and Trahanovsky also tested the solvolysis of benzonorbornenyl complexes.[21] While their data

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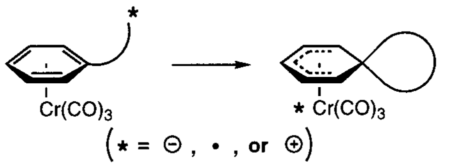
could not differentiate between d orbital and $\sigma-\pi$-type participation, they favored the former. We recently reexamined these benzonorbornenyl systems with density functional theory methods. Computations strongly favored chromium−carbon interactions in the cationic intermediates rather than $\sigma-\pi$-type interactions.[22] A recent solvolysis study on an adamantyl complex found no interaction of the chromium or the arene and a β-cation, though this system was sterically congested.[23] Surprisingly, only two systems have been explored in attempts to exploit electrophilic addition reactions for synthetic purposes. Jaouen examined intramolecular Friedel−Crafts acylation reactions of chiral-complexed β-phenylpropionic acid derivatives leading to diastereomeric indanone complexes and obtained modest levels of selectivity and low yields of products.[24] Uemura used this chemistry to prepare tetralone derivatives in good yields and excellent diastereoselectivity.[25]

Radical processes are even less tested than electrophilic reactions. Only five examples of radical addition have been reported and the mechanisms and scope of transformations are far from being delineated.[26] Schmalz discovered that ketyl and azaketyl radicals add intramolecularly to chromium arene complexes, but the mechanistic details of this new addition reaction were not explored. Significantly, the relative reactivity of arenes and arene complexes toward radical addition is not known.

Many theoretical calculations, initially employing Hückel molecular orbital theory and recently ab initio methods, on arene complexes have focused on bonding, structure, electron densities, and spectral properties,[27] but there have been a few computational studies on addition reactions to complexed arene rings. Brown used Hückel molecular orbital theory and found that nucleophilic addition should be enhanced, but the results for electrophilic and radical addition were ambiguous.[28] He concluded that the rates of the latter two reactions should not differ significantly between benzene and its complex. Albright and Carpenter used extended Hückel molecular orbital theory to examine nucleophilic and electrophilic, but not radical, addition reactions.[29] They mainly explored the regioselectivity of addition to alkyl-substituted complexes (Jackson experiments, vide supra) which, unlike complexes with electron-donating or -withdrawing substituents, is not well explained by resonance theory arguments.[30] Instead, the regioselectivity is controlled by the conformation of the $Cr(CO)_3$ unit, which in turn depends on the steric size of the alkyl substituent. Nucleophilic addition occurs preferentially at eclipsed arene carbons while electrophilic addition occurs at staggered arene carbons as a consequence of intermixing between π^* levels induced by the $Cr(CO)_3$ orbitals. They commented that a small electrophile like a proton should add directly to the metal. Weber and co-workers used semiempirical quantum chemical methods derived from extended Hückel molecular orbital theory to examine nucleophilic addition reactions to indole complexes and were able to reproduce experimental trends.[31] Recently, Koga and co-workers employed HF, B3LYP, and MP2 levels of theory to study molecular electrostatic potentials and electron density topographies of arene chromium complexes.[27a] Although they confirmed the results of Albright and Carpenter, they did not consider electrophilic addition to the metal and did not examine radical addition at all.

Given our long-term interest in metal-templated radical reactions,[27c,32] we initiated studies on the unexplored chemistry of radical additions to arene chromium complexes. Our primary focus was on radical chemistry, but we expanded the scope of these investigations to include anionic and cationic addition reactions (eq 1) since anionic reactions would provide calibration points against known benchmarks and cationic reactions would allow entry into the unexplored Friedel−Crafts alkylations of arene complexes. We report herein on (a) an intramolecular rearrangement test that uses a single compound to directly examine the relative reactivities of free and tricarbonylchromium-complexed phenyl rings toward addition of an alkyl anion, cation, and radical, (b) intermolecular radical addition competition experiments, and (c) density functional theory calculations on intra- and intermolecular addition of anions, cations, and radicals to chromium-complexed aryl rings. Coupling the experimental and theoretical results to provide a mechanistic framework, we find that a $Cr(CO)_3$ moiety can activate arene rings toward anion, cation, **and** radical addition reactions.



(Eq 1)

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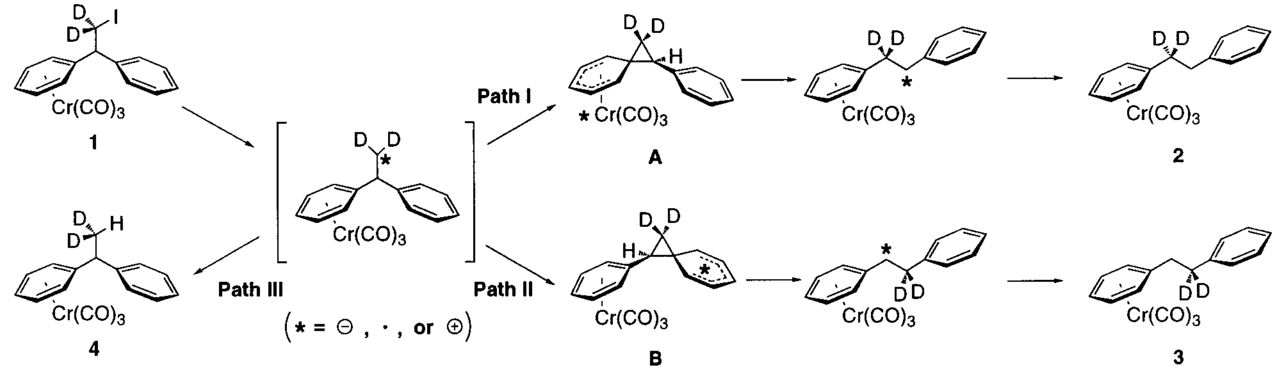
Scheme 1. Rearrangement of the Diphenylethyl System



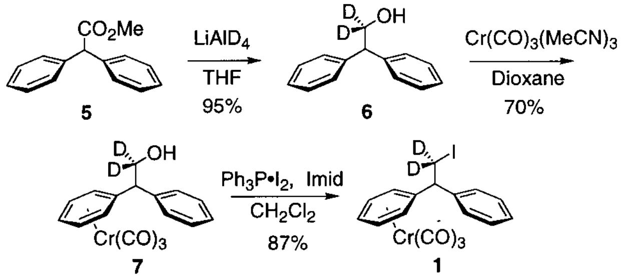
Results

Experimental Design and Competition Experiments. We sought a single substrate that could be used to study cationic, anionic, and radical additions to chromium-complexed arenes and to compare directly the relative reactivities of aryl rings and chromium tricarbonyl-complexed aryl rings. Diphenylethyl iodide proved to be an ideal candidate for our study due to the possibility of having one complexed and one noncomplexed arene in the same substrate. System **1** can give rise to two rearranged regioisomers, **2** and **3**, via an internal competition experiment between the two arenes (Scheme 1). This allows for facile determination of relative reactivities as well as providing a means of direct comparison among the three possible types of reactive intermediates. In path **I**, initial addition of the anion, cation, or radical occurs on the complexed phenyl ring anti to the chromium atom.[33] Cleavage of a cyclopropyl bond in the hexadienyl complex leads to a benzylic reactive intermediate. Reaction quenching with a proton, hydride, or hydrogen atom provides substituted diphenylethane **2**. Path **II** proceeds through ion or radical addition to the noncomplexed ring. Bond cleavage provides the reactive intermediate stabilized by the complexed phenyl ring which, upon quenching, yields complementary isomer **3**. In our experimental design, the relative amounts of **2** and **3** indicate which path is preferred for each of the reactive intermediates. Quenching the initial reactive intermediate without rearrangement yields reduction product **4** (path **III**).

This test system harks back to the classic work on the phenonium ions.[34] Cram demonstrated in 1949 that solvolysis of a β-substituted ethylbenzene leads to a Wagner–Meerwein rearrangement via the phenyl-bridged species, rather than the classical "open" carbonium ion (eq 2).[35] Since Cram's original proposal, numerous investigators have examined this system, concentrating on the nature of the intermediate ion.[36] Although a number of researchers became embroiled in a controversy over the existence of this species, the "phenonium ion" is now a well-accepted carbocation rearrangement intermediate.[37] Even though σ-bridged ethylenebenzenium ions have been subject to such intense investigation over the last five decades,[34] no clear study on the effects of $Cr(CO)_3$ complexation of the phenonium ion has been reported.

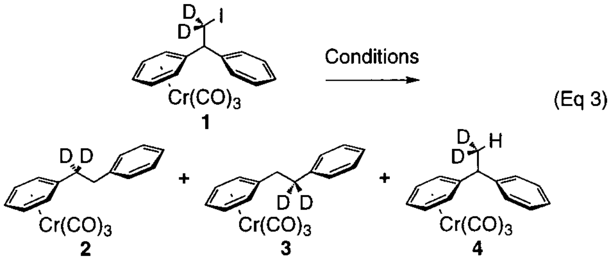
(Eq 2)

Scheme 2. Synthesis of Competition Substrate



Synthesis of the desired competition substrate **1** proved straightforward (Scheme 2). Reduction of methyl diphenylacetate with lithium aluminum deuteride provided deuterium-labeled alcohol **5**, which was then monocomplexed with $Cr(CO)_3(CH_3CN)_3$[38] in 70% yield. The complexed alcohol **7** was converted into iodide **1** in 87% yield by treatment with freshly recrystallized $PPh_3{\cdot}I_2$ and imidazole in CH_2Cl_2.

With the key substrate in hand, we then explored the anionic, cationic, and radical competition rearrangements. Upon treatment of iodide **1** with *tert*-butyllithium at −78 °C, allowing the reaction mixture to warm slowly to 25 °C, and quenching with dilute HCl, the anion was found to rearrange in 40% conversion to isomer **2** (eq 3). The remaining material was 1,1-dideuterio-2-((phenyl)tricarbonylchromium)-2-phenylethane (**4**), resulting from simple reduction of iodide **1**. When the complexed diphenylethyl iodide was treated under radical initiating



(Eq 3)

	2	:	3	% Rearrangement
t-BuLi, H_2O	> 99	:	< 1	40
SmI_2, HMPA, *t*-BuOH	33	:	67	11
$AgBF_4$, Et_3SiH	> 99	:	< 1	94

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[33] Endo addition or addition to the metal will be addressed later.

[34] Lancelot, C. J.; Cram, D. J.; Schleyer, P. v. R. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. 3, Chapter 27, pp 1347–1483 and references therein.

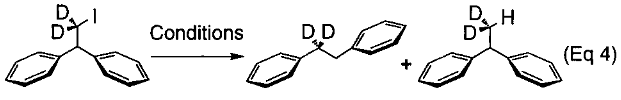
[35] (a) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3863–3870, 3871–3875, 3875–3883. (b) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2129–2137, 2137–2148, 2149–2151, 2152–2159, 2159–2165. (c) Cram, D. J. *J. Am. Chem. Soc.* **1964**, *86*, 3767–3772.

[36] (a) Fornarini, S.; Muraglia, V. *J. Am. Chem. Soc.* **1989**, *111*, 873–877. (b) Olah, G. A.; Porter, R. D. *J. Am. Chem. Soc.* **1971**, *93*, 6877–6887. (c) Olah, G. A.; Porter, R. D. *J. Am. Chem. Soc.* **1970**, *92*, 7627–7629.

conditions—SmI_2/HMPA[39] and *tert*-butyl alcohol in THF at room temperature—isomers **2** and **3** were formed in a ratio of 1:2 in an 11% conversion. The product ratio and conversion depended somewhat on the reaction conditions, but this result was typical. Again, the unrearranged material was reduced to **4**. Analogously, the cationic rearrangement, performed by reaction of the iodide with $AgBF_4$ at room temperature in the presence of Et_3SiH as a hydride trap, afforded **2** in 94% yield. Isomers **2** and **3** are readily differentiated by ^1H NMR as the noncomplexed benzylic methylene protons in **2** are observed as a singlet at 2.36 ppm and the protons benzylic to the chromium-complexed ring in **3** are seen as a singlet at 2.14 ppm.[40] Given the significant chemical shift difference, the detection limit was less than 1%.

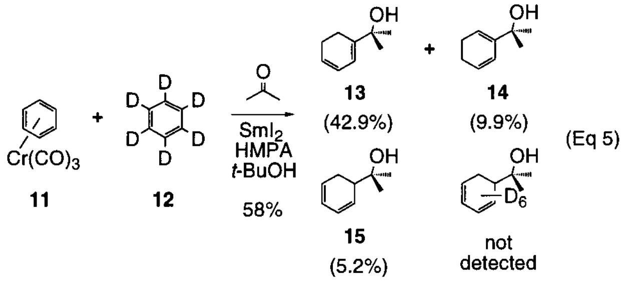
These initial results demonstrated that complexation by chromium dramatically activates the phenyl ring toward addition of both anions and cations, but that the $Cr(CO)_3$ entity has a slight deactivating character for radical addition to the arene ring in this system. While the results for the anion were expected, the results for the cation and radical were not. This led to further analysis of these systems.

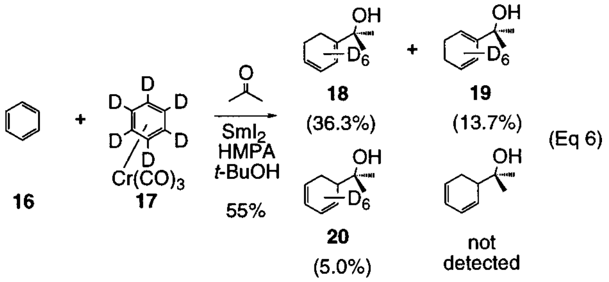
To verify that the product ratio reflected the ratio of cyclization pathways, a control was needed for each of the three cases, and the obvious standard to use was the noncomplexed system **8** (eq 4). When this symmetric diphenylethyl iodide was treated under the same anionic reaction conditions, no rearranged product was observed; only net reduction of the iodide to **10** was seen in 84% yield. This result is consistent with the work of Zimmerman and Zweig, who found that rearrangement in a similar system required refluxing conditions for several hours.[41,42] The radical reaction, also run under the same conditions employed for the complexed case, yielded only 12% rearrangement (**9**), the remaining mass recovery being the reduced product (**10**). The low rearrangement conversion for the radical reaction is consistent with the results of Slaugh,[43] who observed only 2−5% rearrangement of 2-phenylethyl radical at 170 °C. Upon treatment of **8** with $AgBF_4$ under the same conditions as before for a cationic rearrangement, only starting material was recovered. This result was surprising in light of the reactivity of the complexed substrate and thus was repeated several times. It suggests either enhancement of reactivity of the iodide by chromium complexation or direct participation in the cationic reaction by the chromium.



8	9		10
t-BuLi, H_2O	< 1	:	> 99
SmI_2, HMPA, *t*-BuOH	12	:	88
$AgBF_4$, Et_3SiH	---	:	---

Because of the low conversion to the rearranged product in the radical reaction of **1**, we sought to determine whether our system was providing an unintentional bias due to the constained angle of addition. Thus, to remove any bias, we tested intermolecular radical additions. Remarkably, reaction of acetone and samarium(II) iodide in the presence of 6 equiv of benzene-d_6 and 1 equiv of (benzene)tricarbonylchromium (**11**) yielded a 74:17:9 mixture of **13**:**14**:**15** in 58% yield.[44] No evidence of addition to the noncomplexed deuterium-labeled arene was obtained by mass spectrometric analysis! As a control reaction, the reverse sequence was carried out using 6 equiv of benzene and 1 equiv of (benzene-d_6)tricarbonylchromium (**17**) and similar results were found. Repetition of the reaction shown in eq 5, but using 100 equivalents of benzene-d_6, again resulted in no observed addition to the noncomplexed deuterium-labeled aromatic substrate with a detection limit of 0.1%.





Upon completion of the competition experiments, we turned to computational studies to examine in greater detail the electronic and structural effects controlling the direct addition of anions, cations, and radicals to complexed and noncomplexed arenes. In particular, we wished to answer two intriguing and nonintuitive questions. First, why is the intramolecular cation addition from **1** strongly favored on the chromium-complexed phenyl group, when the tricarbonylchromium moiety is generally thought of as an electron-withdrawing substituent comparable to a nitro group and nearly all reports on intermolecular electrophilic aromatic substitution reactions of arene complexes find them less reactive than the respective free arenes?[9−14] Second, given that complexation by tricarbonylchromium can activate phenyl rings toward addition of *both* anions and cations,

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(37) (a) Okuyama, T.; Ochiai, M. *J. Am. Chem. Soc.* **1997**, *119*, 4785−4786. (b) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 4578−4593. (c) Olah, G. A.; Head, N. J.; Rasul, G.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1995**, *117*, 875−882.

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(40) The ^1H NMR spectrum of an authentic sample of (dibenzyl)-tricarbonylchromium (see Experimental Section in the Supporting Information) exhibits a triplet resonance at 2.37 and 2.15 ppm for the noncomplexed benzylic methylene protons in **2** and the complexed benzylic methylene protons in **3**, respectively. See also: Traylor, T. G.; Goldberg, M. J. *J. Am. Chem. Soc.* **1987**, *109*, 3968−3973.

(41) Zimmerman, H. E.; Zweig, A. *J. Am. Chem. Soc.* **1961**, *83*, 1196−1213.

(42) For reviews on anionic 1,2-aryl rearrangements, see: (a) Grovenstein, E., Jr. Aryl Migrations in Organometallic Compounds of the Alkali Metals. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1977; Vol. 16, pp 167−210. (b) Grovenstein, E., Jr. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 313−332.

(43) Slaugh, L. H. *J. Am. Chem. Soc.* **1959**, *81*, 2262−2266.

(44) The ratio of isomers is based on ^1H NMR analysis, while the yield is based on 15% recovered starting material **11**.

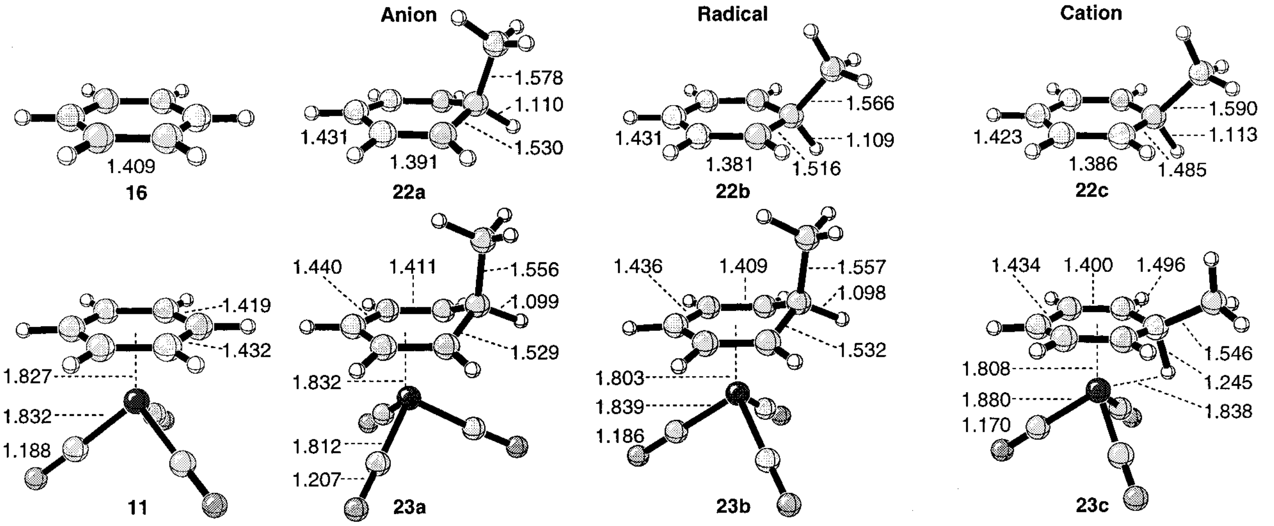
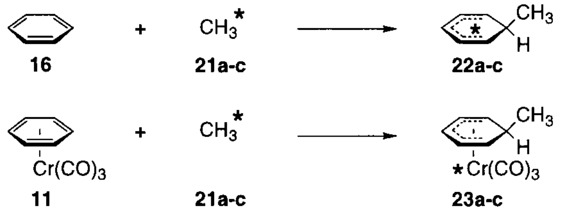


Figure 2. (U)B3LYP/LANL2DZ-optimized structures of starting materials and products of CH_3* addition reactions. Selected distances are in Å.

Table 1. Heats of Reaction for CH_3* Addition to Benzene and (Benzene)tricarbonylchromium[a]



	Noncomplexed ΔH	Chromium bound ΔH	ΔΔH
Anion (a)	-24.1 (-32.6)	-78.5 (-96.4)	-54.4 (-63.8)
Radical (b)	-10.9 (-9.2)	-19.9 (-17.4)	-9.0 (-8.2)
Cation (c)	-86.6 (-86.4)	-96.3 (-89.1)	-9.5 (-2.7)

[a] All values are in kcal/mol. Energies were calculated using the DZVP2+ basis set. Values in parentheses are from the LANL2DZ basis set which is a lower level of theory.

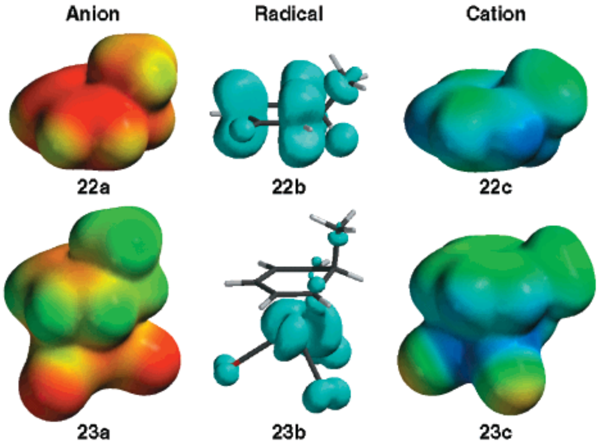


Figure 3. Electrostatic potential surfaces of free and $Cr(CO)_3$-complexed ions and constant spin density surfaces for free and $Cr(CO)_3$-complexed radicals formed from CH_3* addition reactions.

why is there no significant selectivity in the intramolecular radical addition tested, but there is in the intermolecular radical additions?

Computed Structures of Free and $Cr(CO)_3$-Complexed Arene Species

Intermolecular Additions. Additions of methyl anion, radical, and cation to the aromatic ring of benzene and of (benzene)tricarbonylchromium were investigated. Optimized structures of the starting materials and products were obtained using density functional theory calculations as discussed in the Methods Section in the Supporting Information (Figure 2). The Δ*H* for each reaction was calculated from the energies of these structures, and a comparison between reactions of free and chromium-complexed benzene provided the ΔΔ*H* due to complexation (Table 1). The large calculated exothermicity of the ionic reaction systems stems, in part, from the inherent reactivity of the bare gas-phase methyl ions.

Methyl anion addition to benzene, forming product **22a**, is exothermic by 24.1 kcal/mol. Anion addition to (benzene)tricarbonylchromium (**11**) yields compound **23a**. The electron-withdrawing nature of the chromium fragment results in a greatly enhanced reaction: 54.4 kcal/mol more favorable than the noncomplexed case. Delocalization of the negative charge onto the chromium center results in increased back-bonding from the metal to the CO ligands. This is reflected structurally in a 0.02 Å decrease in the Cr−C bond lengths and a 0.02 Å increase in the C−O bond lengths in **23a** in comparison to **11** (Figure 2). Delocalization of charge onto the chromium moiety is also apparent upon examination of the electrostatic potential surfaces shown in Figure 3. In the noncomplexed case, the bulk of the negative charge lies in the pentadienyl fragment. In the chromium complex, the six-membered ring is more positive, as negative charge has been transferred to the chromium fragment. This charge distribution is also reflected in the calculated Mulliken charges. In the anionic chromium complex **23a**, the sp^3 carbon of the six-membered ring is tipped up away from the metal. This inclination of the substituted carbon away from the metal compares closely with the X-ray crystal structure of the product of dithiane nucleophilic addition to (benzene)tricarbonylchromium as reported by Semmelhack and co-workers.[45,46] They report an inclination of 38.6° away from the

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[45] Semmelhack, M. F.; Hall, H. T., Jr.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535−3544.

[46] A more recent X-ray crystal structure of an anion adduct was reported and the structural features are similar, though slightly distorted due to heteroatom substitution, see: Fretzen, A.; Ripa, A.; Liu, R.; Bernardinelli, G.; Kündig, E. P. *Chem. Eur. J.* **1998**, *4*, 251−259.

plane defined by the pentadienyl fragment while complex **23a** shows an inclination of 38.3°. The distance between chromium and the plane defined by the pentadienyl fragment in complex **23a** is 1.832 Å. This is 0.09 Å longer than the comparable distance in Semmelhack's dithiane complex.

Methyl radical addition is less favorable than the methyl anion addition, though still exothermic in both the free and chromium-bound reactions. In this case, the complexed reaction, forming **23b**, is 9.0 kcal/mol more exothermic than the noncomplexed reaction, forming **22b**. The optimized structure of metal complex **23b** is qualitatively similar to that of anionic complex **23b**. The sp^3 carbon of the six-membered ring is inclined away from the metal, forming an angle of 33.4° with the pentadienyl plane. The chromium tricarbonyl fragment is rotated by 60° relative to **23a**, and the chromium is 1.803 Å from the pentadienyl plane. The spin-density surface in Figure 3 demonstrates the nearly complete transfer of radical character from the ring to the metal fragment.

Addition of methyl cation to benzene, forming **22c**, is the most exothermic reaction of this series (86.5 kcal/mol), reflecting the inherent reactivity of the methyl cation. Wheland intermediate **22c** was previously examined by Raos and co-workers using RHF calculations and a 6-31G* basis set.[47] These researchers found an optimal distance of 1.5588 Å for the bond between the methyl and the ring carbon, compared to our calculated distance of 1.590 Å. An X-ray crystal structure of a related Wheland intermediate was recently reported.[48] Chromium complexation increases the exothermicity of this reaction by 4.3 kcal/mol. In complex **23c**, lengthening of the $Cr-C_{(CO)}$ bonds by 0.05 Å and slight (0.002 Å) shortening of the C−O bonds indicates a decrease in back-bonding to the CO ligands as a result of the withdrawal of electron density from the chromium fragment. Again, the electrostatic potential surfaces in Figure 3 reflect the transfer of charge from the six-membered ring to the chromium tricarbonyl moiety. Cationic chromium complex **23c** also exhibits a very interesting agostic interaction of the metal center with the hydrogen on the sp^3 center. Unlike the previous two cases, this sp^3 carbon is inclined toward the metal center by 10.3°. This C−H bond is lengthened to 1.245 Å (compared to 1.099 Å in the anionic case) and the Cr−H distance is 1.838 Å. Known chromium−hydride bonds have measured lengths ranging from 1.42 to 2.014 Å,[49] and a Cr−H agostic interaction has been noted at a distance of 2.124 Å,[50] so the Cr−H distance in **23c** is well within this range. This agostic interaction is not observed in the anion and radical cases, as the ipso hydrogens of **23a** and **23b** are tilted away from the metal. Early studies on protonation of (arene)tricarbonylchromium complexes using NMR analysis suggested predominant metal protonation,[19,51] but agostic structures, and the resulting spectroscopic consequences, were not considered.[52,53]

Intramolecular Reactions. The next reactions to be considered computationally were the cyclizations of phenylethyl intermediates, forming spirocyclic products. Optimized geometries of the starting materials and products are shown in Figure 4. These structures more closely resemble our experimental system, and the reactions are considerably less exothermic than the methyl additions (even endothermic for the radical and anion cases) due to the strain of the spiro[5.2]octane skeleton. Cyclization of the noncomplexed phenylethyl anion **24a** to spirocycle **25a** is endothermic by 5.4 kcal/mol, but complexation by the electron-withdrawing chromium moiety makes this reaction favorable by 19.8 kcal/mol (Table 2). We were unable to find a fully optimized acyclic chromium-bound phenylethyl anion as cyclization to **27a** is too favorable; every starting geometry minimized to the cyclic structure. To calculate structure **26a**, the exocyclic $C_{ipso}-C_{\alpha}-C_{\beta}$ angle was constrained to 110° and the rest of the molecule was allowed to relax. The calculated structure for cyclized product **27a** is comparable to that of methyl anion addition, **23a**. In particular, the sp^3 carbon of the ring is tilted away from the metal center (36.6° relative to the pentadienyl plane). Examination of bond lengths and electrostatic potential surfaces again reflects polarization of charge toward the chromium tricarbonyl fragment (Figure 5).

Radical cyclization was endothermic in both the noncomplexed and complexed cases, by 11.8 and 10.9 kcal/mol, respectively. The cyclization of phenylethyl radical **24b** to spirocycle **25b** was previously examined at the HF/STO-3G[54,55] and UMP2/6-31G*[56] levels. In the cyclic structure, previous researchers report distances of 1.525,[54] 1.521,[55] and 1.526 Å[56] for the newly formed carbon−carbon bond. Our fully minimized structure has a distance of 1.572 Å for this bond. The calculated structures in the complexed case resemble those for anionic cyclization. The tilt of the substituted carbon away from the metal in **27b** is less pronounced (Figure 5), though, at 24.2° relative to the pentadienyl fragment plane. In both acyclic and cyclic radical structures, the chromium tricarbonyl fragment is rotated 60° relative to anion **27a**. Although both cyclizations are endothermic, the calculated energetic preference for radical cyclization onto the complexed aryl ring is at odds with the experimental results.

To further elucidate details of the radical cyclizations, transition states were computed (Figure 6). Phenylethyl radical **24b** cyclizes to spirocycle **25b** via transition state **29** wherein the partially formed bond is 1.809 Å. Previous calculations on this transition state predicted the partially formed bond to be 1.847 Å[54] and 1.804 Å.[55] Transition state **29** is 16.3 kcal/mol higher in energy than phenylethyl radical **24b** (Figure 7). Chromium-bound phenylethyl radical **26b** cyclizes to complexed spirocycle **27b** via transition state **30** where the partially formed bond is 1.834 Å long. This transition state is 16.1 kcal/mol higher in energy than compound **26b**. A second transition state, **31**, was also found, in which the partially formed bond is endo to the chromium tricarbonyl moiety. This was much higher in energy, 21.6 kcal/mol higher than compound **26b**. Transition

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[49] (a) Petersen, J. L.; Brown, R. K.; Williams, J. M. *Inorg. Chem.* **1981**, *20*, 158−165. (b) Girolami, G. S.; Salt, J. E.; Wilkinson, G.; Thornton-Pett, M.; Hursthouse, M. B. *J. Am. Chem. Soc.* **1983**, *105*, 5954−5956. (c) Heintz, R. A.; Haggerty, B. S.; Wan, H.; Rheingold, A. L.; Theopold, K. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1077−1079. (d) Jagirdar, B. R.; Palmer, R.; Klabunde, K. J.; Radonovich, L. J. *Inorg. Chem.* **1995**, *34*, 278−283.

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[51] For reviews on protonation of metal centers versus ligand sites, see: (a) Henderson, R. A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 946−967. (b) Kristjánsdóttir, S. S.; Norton, J. R. In *Transition Metal Hydrides*; Dedien, A., Ed.; VCH: Weinheim, 1992; pp 309−359.

[52] Brookhart, M.; Green, M. L. H. *J. Organomet. Chem.* **1983**, *250*, 395−408.

[53] For reports on protonation at the metal of electron-rich (η^6-arene)-molybdenum−(phosphine)$_3$ complexes, see: (a) Kowalski, A. S.; Ashby, M. T. *J. Am. Chem. Soc.* **1995**, *117*, 12639−12640. (b) Ashby, M. T.; Asirvatham, V. S.; Kowalski, A. S.; Khan, M. A. *Organometallics* **1999**, *18*, 5004−5016. (c) Asirvathan, V. S.; Gruhn, N. E.; Lichtenberger, D. L.; Ashby, M. T. *Organometallics* **2000**, *19*, 2215−2227.

[54] Yamabe, S. *Chem. Lett.* **1989**, 1523−1526.

[55] Leardini, R.; Nanni, D.; Pedulli, G. F.; Tundo, A.; Zanardi, G.; Foresti, E.; Palmieri, P. *J. Am. Chem. Soc.* **1989**, *111*, 7723−7732.

[56] Smith, W. B. *J. Phys. Org. Chem.* **1995**, *8*, 171−7732.

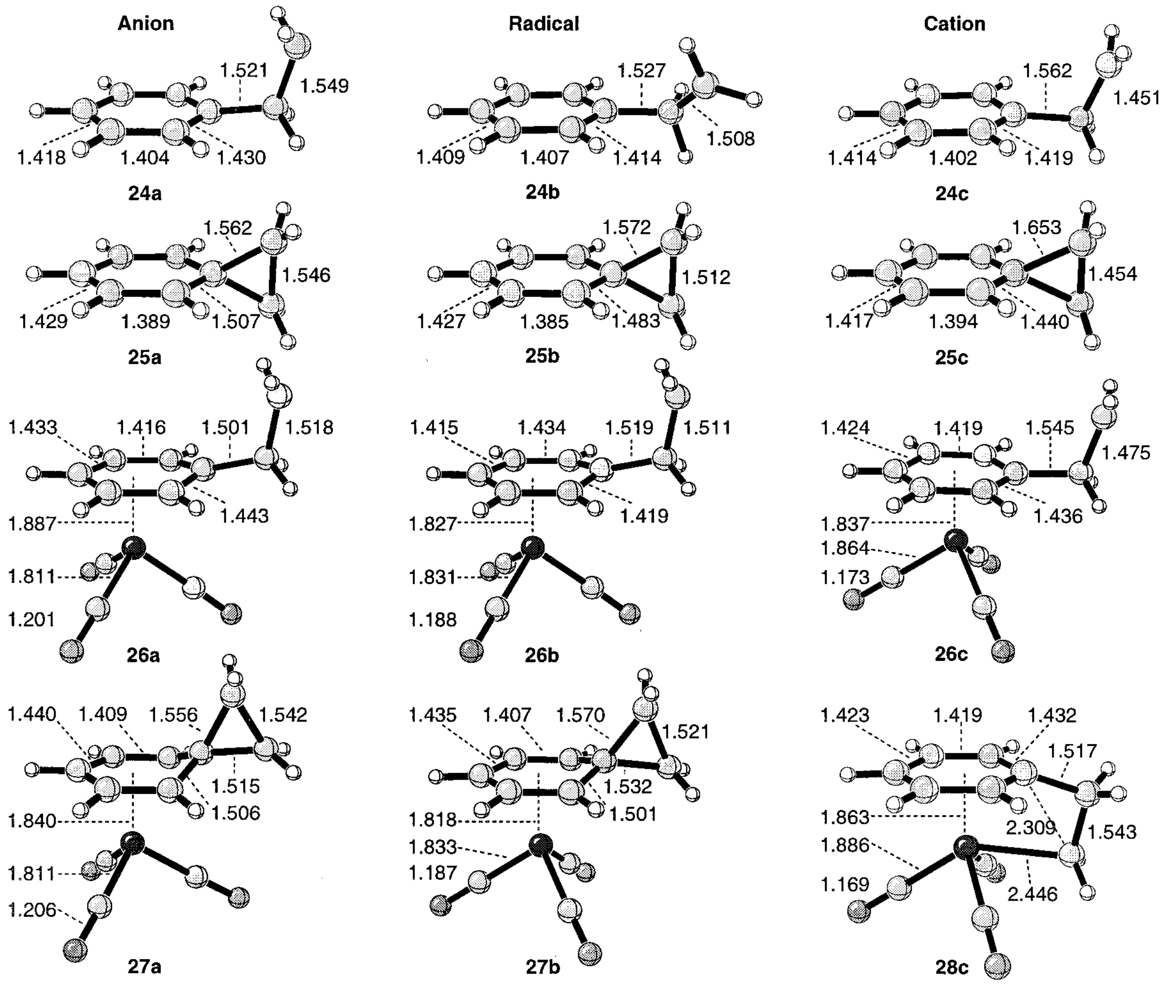
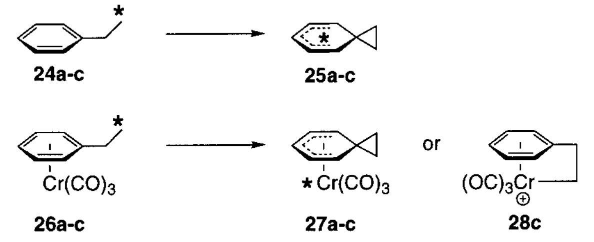


Figure 4. (U)B3LYP/LANL2DZ-optimized structures of starting materials and products for phenylethyl cyclizations. Selected distances are in Å.

Table 2. Heats of Reaction for Phenylethyl Cyclizations[a]



	Noncomplexed ΔH	Chromium bound ΔH	$\Delta\Delta H$
Anion (a)	+5.4 (+7.3)	-19.8 (-21.2)	-25.3 (-28.5)
Radical (b)	+11.8 (+17.0)	+10.9 (+14.3)	-0.9 (-2.7)
Cation (c) (optimized)	-26.9 (-23.7)	-32.3 (-29.1)	-5.4 (-5.5)
Cation (c) (constrained)	-26.9 (-23.7)	-20.7 (-17.8)	+6.2 (+5.9)

[a] All values are in kcal/mol. Energies were calculated using the DZVP2+ basis set. Values in parentheses are from the LANL2DZ basis set. Structure **28c** is the optimized cation geometry.

state **31** does not connect intermediate **27b** to primary radical **26b**; instead it is the transition state connecting **27b** to primary radical **32**, a rotamer of **26b**, that is 2.2 kcal/mol higher in energy (Figure 7). This corresponds to the ring-opening step in our radical rearrangement reaction and has important consequences in interpreting our competition results (vide infra).

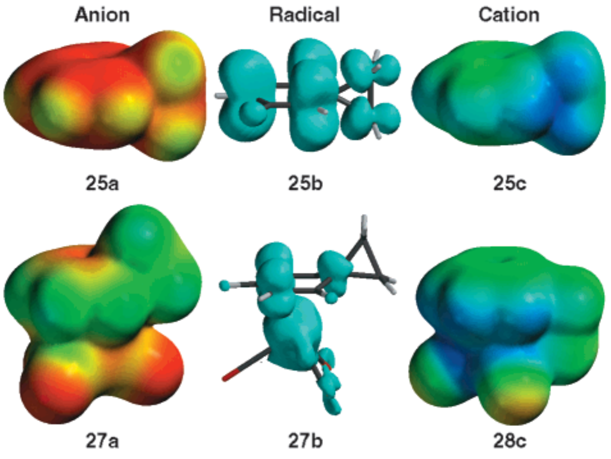


Figure 5. Electrostatic potential surfaces of free and $Cr(CO)_3$-complexed ions and constant spin density surfaces for free and $Cr(CO)_3$-complexed radicals formed from phenylethyl cyclizations.

Unexpectedly, no fully optimized structure could be found for a chromium-bound cation with a spirocyclic geometry analogous to **27a** and **27b**. Instead, the primary cation adds to the chromium atom, forming chromacyclic structure **28c**. Formation of a Cr−C bond is indicated by pyramidalization of this carbon and a Cr−C distance of 2.446 Å. This is longer than known strain-free chromium−alkyl bonds, which have been measured from 2.054 to 2.206 Å.[57] The $C_{ipso}-C_\alpha$ bond exocyclic to the arene ring is inclined toward the metal by 19.2° from the arene plane to facilitate direct interaction of the β carbon with

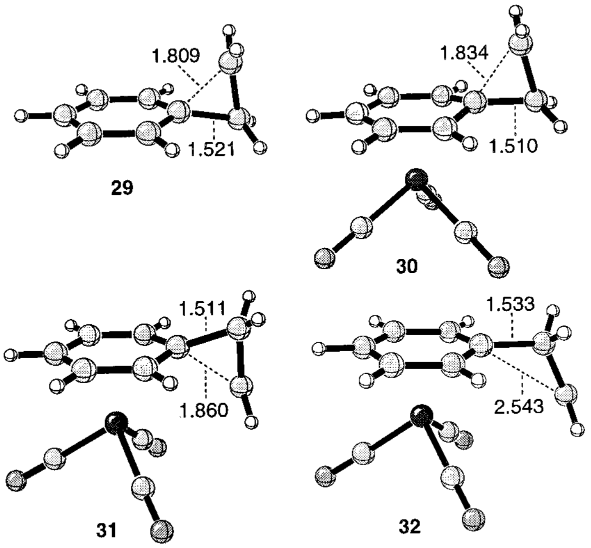


Figure 6. UB3LYP/LANL2DZ-optimized geometries of transition states and product for radical rearrangements. Selected distances are in Å.

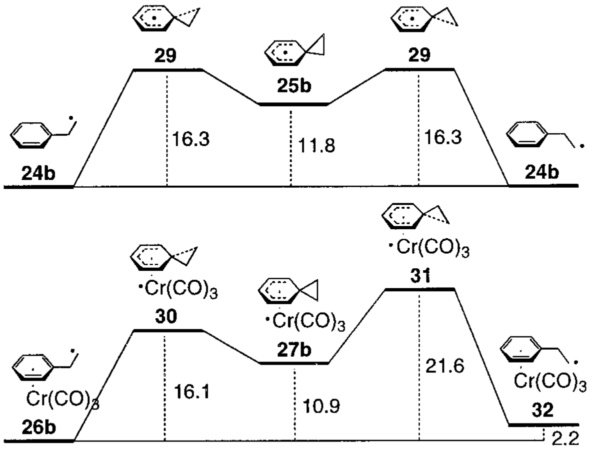
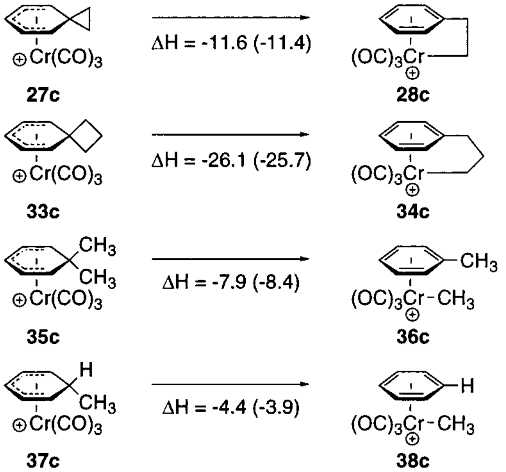


Figure 7. Radical reaction profiles (all energies in kcal/mol).

the chromium. Bond lengths within the six-membered ring of **28c** indicate that it is best viewed as a normal delocalized aromatic system (in contrast to **27a** and **27b** which have longer bonds to the sp^3 carbon). In both the free and metal-bound phenylethyl cations (**24c** and **26c**), the exocyclic $C_{ipso}-C_{\alpha}-C_{\beta}$ angle was constrained to 110°. We were unable to fully optimize minima for primary cations, which instead prefer to cyclize. Cyclization to chromacycle **28c** from acyclic cation **26c** is exothermic by 32.3 kcal/mol and is more favorable than cyclization of noncomplexed cation **24c** to **25c** by 5.4 kcal/mol. The parent phenonium cation (**25c**) has been studied computationally by several researchers and continues to be explored using different methods and levels of theory.[58] Sieber and Schleyer reviewed prior literature reports on **25c** and also reported an MP2/6-31G* optimization.[59] The distance between the two methylene units is 1.426 Å; our computed structure has a distance of 1.454 Å. They further report a distance of 1.625 Å between each of the methylenes and the arene ring, compared to a distance of 1.653 Å in our structure. For comparison with the cyclic anionic and radical cases, a spirocyclic chromium-bound cation (**27c**) was obtained by constraining the interior angles of the three-membered ring and allowing the rest of the molecule to relax. This structure was 11.6 kcal/mol less favorable than fully optimized chromacycle **28c**. Cyclization to this structure would still be exothermic by 20.7 kcal/mol, but would be 6.2 kcal/mol less favorable than cyclization in the noncomplexed case. This result is important with regard to the debate on the mechanism of electrophilic additions to the arene complexes (vide infra).

Scheme 3. Heats of Reaction for Rearrangements of Cationic Complexes[a]



[a] All values are in kcal/mol. Energies were calculated using the DZVP2+ basis set. Values in parentheses are from the LANL2DZ basis set.

The preference of the cation to exist as chromacycle **28c** led us to question whether this was a general phenomenon for carbocations interacting with chromium arene complexes. Therefore, a series of comparisons was made as shown in Scheme 3. For all cases except complex **27c** (vide supra), fully optimized minima were found for both starting material and product. In each case, shifting a carbon from the hexadienyl ring to the chromium center is strongly favored. These carbon migrations convert formally 16-electron complexes to more stable closed shell 18-electron complexes. The agostic interaction in **23c** discussed above also demonstrates the preference of the electron-deficient metal to interact with another ligand as an additional formal source of two electrons, though the absence of a complete hydrogen shift may reflect bond energies.

The first suggestion that chromium can interact with remote cations (γ position) came from calculations on cations **33c** and **34c**. Closure of the primary cation onto the arene ring forming spirocycle **33c** and onto the chromium atom forming chromacycle **34c** are both exothermic, but **34c** is more favorable by 26.1 kcal/mol. Structure **34c**, like **28c** and the known benzylic cation complex,[27c,d,60] has closed shell electron configurations at both chromium and the reactive carbon. The calculated chromium$-CH_2$ bond length of **34c** is 2.365 Å, which is close to known chromium$-$alkyl bond lengths which range from 2.054 to 2.206 Å.[57]

To compare the relative energetics of chromacycles with pseudo four- or five-membered rings, the constitutional isomers **39c** and **40c** were examined (eq 7). Isomer **40c**, with the less

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[57] (a) Fryzuk, M. D.; Leznoff, D. B.; Rettig, S. J. *Organometallics* **1997**, *16*, 5116−5119. (b) Heintz, R. A.; Leelasubcharoen, S.; Liable-Sands, L. M.; Rheingold, A. L.; Theopold, K. H. *Organometallics* **1998**, *17*, 5477−5485. (c) Fryzuk, M. D.; Leznoff, D. B.; Rettig, S. J.; Young, V. G., Jr. *J. Chem. Soc., Dalton Trans.* **1999**, 147−154.

[58] del Rio, E.; Menendez, M. I.; Lopez, R.; Sordo, T. L. *J. Phys. Chem. A* **2000**, *104*, 5568−5571.

[59] Sieber, S.; Schleyer, P. v. R.; Gauss, J. *J. Am. Chem. Soc.* **1993**, *115*, 6987−6988.

[60] Jaouen, G.; Top, S.; McGlinchey, M. J. *J. Organomet. Chem.* **1980**, *195*, C5−C8 and references therein.

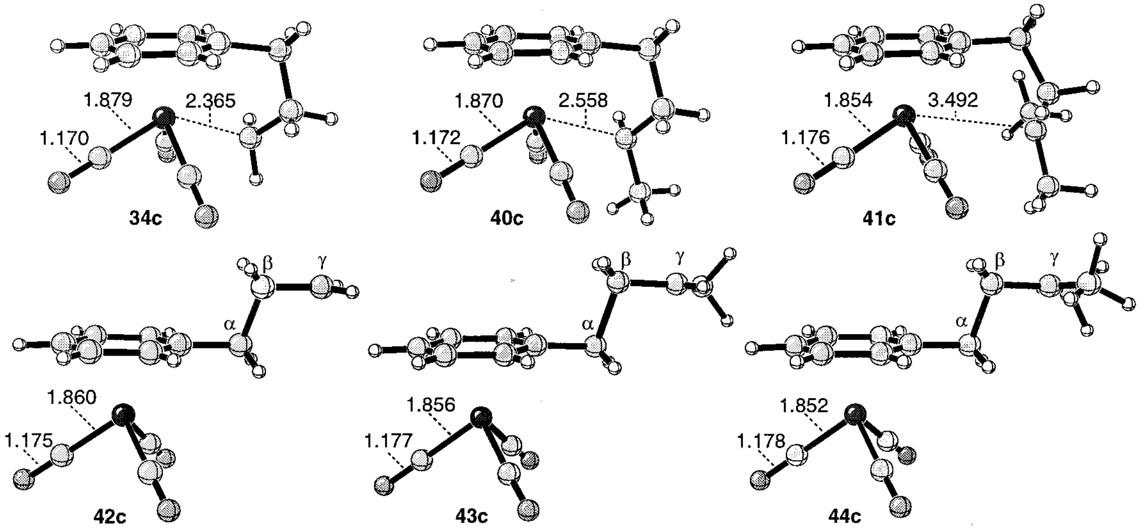
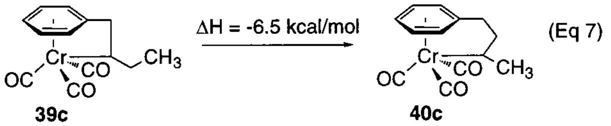


Figure 8. Cation substitution pattern (distances in Å).



39c **40c**

strainedpseudo five-membered ring size, is lower in energy by 6.5 kcal/mol. This energy difference is intuitively assigned to the ring strain and several geometric parameters confirm this. The $C_{ipso}-C_\alpha-C_\beta$ angle about the methylene connecting the arene ring to the cationic carbon in **39c** is 99.9°, compared to an angle of 108.2° for the benzylic methylene in **40c**. In addition to the greater Baeyer (angle) strain, **39c** also has greater Pitzer (eclipsing) strain. While complex **40c** has substituents in a staggered conformation, the substituents in **39c** are close to eclipsed. Most importantly, the ethyl group in **39c** eclipses one of the CO ligands of the $Cr(CO)_3$ unit. These geometric features lead to a Cr−C distance of 2.791 Å in **39c**, which shortens to 2.558 Å in **40c**. From Benson's strain corrections for cycloalkanes,[61] the energy difference of 6.5 kcal/mol between **39c** and **40c** is closer to the 6.3 kcal/mol difference between cyclopentane and cyclohexane than it is to the 19.9 kcal/mol difference between cyclobutane and cyclopentane. From the perspective of ring strain, the chromium phenyl fragment is roughly equivalent to three methylene groups. Overall, calculations suggest that interaction of chromium with remote γ cations is not only a favorable process, but more favorable than interaction with a β postion.

To explain prior experimental results and guide future studies, we desired a clearer understanding of the effect of alkyl substitution on chromium stabilization of the acyclic positive charge. Compound **34c** has chromium bonded to a primary carbon, while **40c** involves a secondary carbon, so fully optimized structure **41c** was calculated in which a tertiary carbon coordinates to the metal (Figure 8). Acyclic cations without chromium−carbon bonds were calculated by fixing dihedral angles about the $C_{ipso}-C_\alpha$ and $C_\alpha-C_\beta$ bonds. In the case of primary cation **42c**, it was also necessary to constrain the $C_\alpha-C_\beta$ bond length and the two $C_\beta-H$ bond lengths to prevent cationic rearrangement upon optimization.

Several geometric features point to relatively strong chromium−carbon interactions in the primary and secondary systems, but a weak chromium−carbon interaction in tertiary compound **41c**. First, the Cr−C distance is 2.365 Å in primary cation **34c** and 2.558 Å in secondary cation **40c**, but a much longer 3.492 Å in tertiary cation **41c**. Second, as the chromium donates more electron density to the carbocation, back-bonding to the CO ligands should diminish, and the distance from the metal to the CO's should increase. Indeed, while the average trans $Cr-C_{CO}$ distance is 1.856 Å in the acyclic complexes, the distances are 1.879, 1.870, and 1.854 Å in **34c**, **40c**, and **41c**, respectively. Third, the extent of Cr−C interaction is evidenced by the pyramidalization of the coordinated carbon. For a simple chromium−carbon bond with a sp^3 hybridized carbon, the sum of the bond angles to the organic substitutents should be 328.5° ($3 \times 109.5°$) while the sum of such bond angles would be 360.0° for a noninteracting sp^2 hybridized carbocation. The values for **34c**, **40c**, and **41c** are 335.0°, 340.1°, and 356.2°, respectively. Finally, the conclusions based upon geometric considerations are supported by the energies of cyclization from the acyclic cations. Cyclization of **42c** to **34c** and **43c** to **40c** is highly exothermic at 36.6 and 19.8 kcal/mol, respectively, while tertiary cation **44c** is only 3.7 kcal/mol less stable than **41c**.

Despite evidence for Cr−C interactions in cationic complexes, we found that direct interaction of the carbon with the chromium center is not favored in the anionic and radical cases (Table 3).[62] We were unable to find optimized minima for anions or radicals with geometries represented as **28a**, **28b**, **38a**, and **38b**. Instead, geometry optimizations of such species always led to cleavage of the chromium−carbon bond. Single point energies were calculated for these anions and radicals by using the geometries of **28c** and **38c** and were found to be significantly higher in energy (up to 99 kcal/mol) than the energies of **27a**, **27b**, **37a**, and **37b**.

The parent chromacyclic cation **28c** cannot undergo further rearrangement, as ring opening would lead to a primary carbocation. To understand the experimentally observed cationic rearrangment of **1** to **2**, we computed the structure of **45**, the chromacyclic intermediate that is actually formed under the experimental conditions (Figure 9). Appending a phenyl ring

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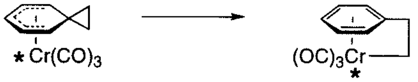
[61] Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; Haugen, G. R.; O'Neal, H. E.; Rodgers, A. S.; Shaw, R.; Walsh, R. *Chem. Rev.* **1969**, *69*, 279−324.

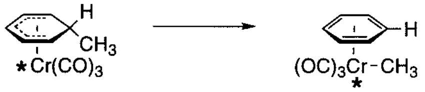
[62] Recently, researchers have invoked radical addition to the chromium atom of bis(benzene)chromium, but this system does not appear to be comparable with (benzene)tricarbonylchromium systems. Samuel, E.; Caurant, D.; Gourier, D.; Elschenbroich, C.; Agbaria, K. *J. Am. Chem. Soc.* **1998**, *120*, 8088−8092.

Table 3. Heats of Reaction for Rearrangements[a]



27a-c **28a-c**

	ΔH
Anion (a)	+68.2 (+105.2)
Radical (b)	+11.0 (+31.6)
Cation (c)	-11.6 (-11.4)



37a-c **38a-c**

	ΔH
Anion (a)	+99.1 (+123.3)
Radical (b)	+38.0 (+46.9)
Cation (c)	-4.4 (-3.9)

[a] All values are in kcal/mol. Energies were calculated using the DZVP2+ basis set. Values in parentheses are from the LANL2DZ basis set.

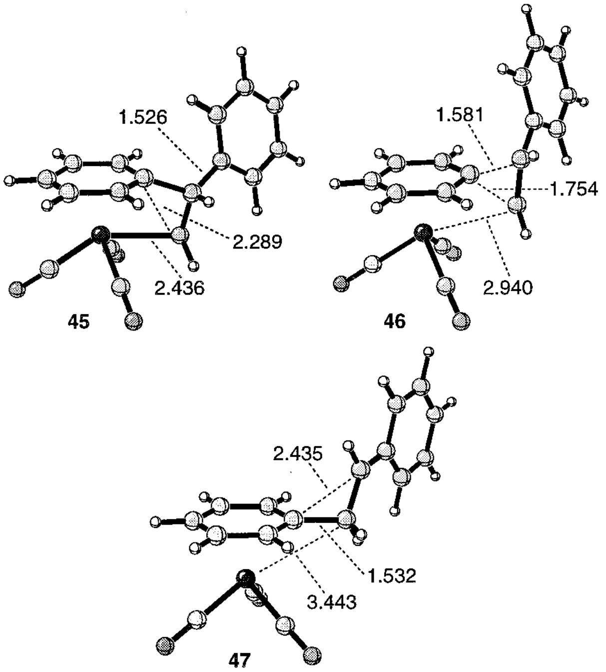


Figure 9. B3LYP/LANL2DZ-optimized geometries of stationary points in the cationic rearrangement mechanism. Selected distances are in Å.

does not greatly perturb the structure of **28c**. For instance, the chromium−methylene bond distance in intermediate **45** is 2.436 Å, compared to a distance of 2.446 Å in parent chromacycle **28c**. We further found transition state **46** leading smoothly to benzylic cation **47**, which can be quenched to afford observed product **2**. Animation of this transition state demonstrates that it is a concerted shift of the two-carbon bridge, with a slight rotation of the phenyl ring to bring it into conjugation with the forming carbocation. This transition state is 7.0 kcal/mol higher in energy than chromacyclic intermediate **45** and the overall reaction is exothermic by 3.7 kcal/mol. Thus, a cationic intermediate equivalent to **A** in Scheme 1 was not found in the computed reaction path, and related structure **46** was actually calculated to be a transition state, not an intermediate.

Discussion

Anion. The selectivity of the anionic rearrangement via addition to the complexed ring is expected from a simple electronics argument based on the known chemistry of chromium−arene complexes.[1] The fact that the rearrangement proceeds exclusively through addition to the complexed ring is further verified by the control reaction, where we only observe net reduction of the starting iodide and no addition into the free arene. Anion addition to simple phenyl rings is known to require elevated temperatures and prolonged reaction times.[41,42]

Our computational study of anionic addition neatly fits in with the current and reported experimental data, in particular the X-ray crystal structure of an anion adduct reported by Semmelhack,[45] but adds information on the energy changes. As a general rule, the intramolecular reactions studied are less favorable than the intermolecular reactions due to the introduction of strain in the cyclopropyl rings. In the anionic phenylethyl cyclization, chromium complexation makes the difference between an endothermic reaction and an exothermic reaction. This has implications for the competitive cyclization depicted in Scheme 1. We should expect the exothermic anionic cyclization to form intermediate **A** instead of the endothermic cyclization to form **B**, and indeed, this is what we observe experimentally. Overall, the calculations on anionic addition provide a baseline for evaluating the methodology and for comparison with the cation and radical results. Further, it is the necessary prelude to the next level of analysis of predicting the regiochemistry of addition to unsymmetrical arene complexes.[63]

Radical. Interestingly, we detected no enhancement for addition of radicals into the complexed arene in our intramolecular competition experiment. This is initially surprising given that chromium complexation activates aryl rings toward other additions. Further, Schmalz and co-workers demonstrated that radical addition to metal-bound arenes can in fact occur in a facially specific manner.[26] However, they never examined a substrate where the intermediate is given a choice between radical addition to a free or chromium-complexed aryl ring. In contrast to the intramolecular competition, the intermolecular competition experiment yielded complete selectivity for radical addition to the complexed arene ring. In fact, the experiment employing a 100-fold excess of benzene-d_6 found a $>99.9:<0.1$ ratio of nondeuterated and hexadeuterated products. Ignoring a possible secondary kinetic isotope effect, that translates into a greater than 100 000:1 ratio of relative reactivities for complexed and noncomplexed benzene. These seemingly disparate results are actually nicely explained by mechanistic rationale developed from the computational results.

The computational results for radical cyclization were initially troubling. Formations of both **25b** and **27b** are endothermic, so as neither radical cyclization in Scheme 1 is favorable, the radical reaction is expected to be fairly unproductive. Indeed, the radical reaction gives a low conversion to rearranged products. The problem is that the calculated energies of the radical spirocyclic intermediates do not explain the observed experimental product ratios. In the intramolecular radical competition experiments we observe varying ratios of roughly 1 to 1 up to a maximum of 1 to 4 for products **2** and **3**, respectively. The best ratio would correspond to a 0.8 kcal/mol preference for addition to the noncomplexed arene, which is in contrast to our computed preference of cyclization to complexed

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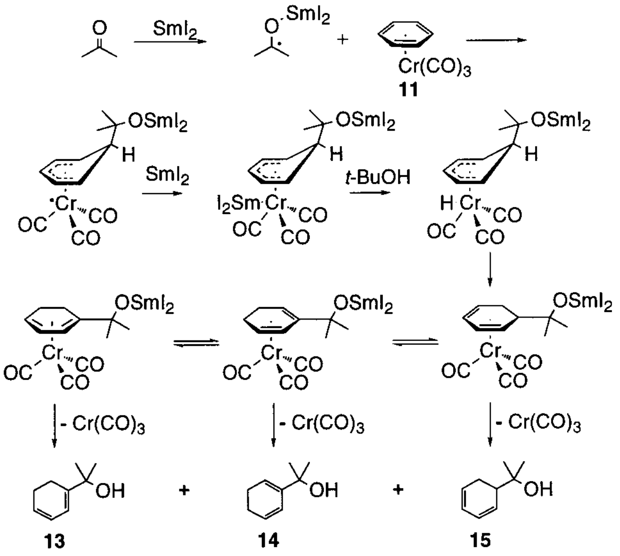
(63) Semmelhack, M. F. Nucleophilic Addition to Arene−Metal Complexes. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, England, 1991; Vol. 4, pp 517−549.

intermediate **27b** by 0.9 kcal/mol. This discrepancy demands that we consider the transition states for cyclization rather than simply the intermediates (Figure 6). An examination of reaction energy profiles for the two radical cyclizations tells the story (Figure 7). Cyclization of phenylethyl radical **24b** to intermediate **25b** proceeds with a barrier of 16.3 kcal/mol via transition state **29**. Since the two faces of the six-membered ring are equivalent, ring opening to form the phenylethyl radical proceeds via an identical transition state. In the chromium-bound arene, though, the two faces of the six-membered ring are different. Cyclization of complexed phenylethyl radical **26b** to intermediate **27b** is expected and calculated to occur with radical approach anti to the chromium tricarbonyl moiety with a barrier of 16.1 kcal/mol. In the experimental system, rearrangement products would have to come from cleavage of the endo bond of the three-membered ring, via transition state **31**. This step for intermediate **27b** in the phenethyl model has a barrier of 21.6 kcal/mol relative to the starting material, making this the rate-limiting step for the overall reaction. Therefore, while formation of complexed intermediate **27b** is somewhat preferred relative to **25b**, it is noncomplexed intermediate **25b** that has a lower energy pathway leading to rearranged product. To further refine the reaction profile, the fact that the experimental system is substituted with a phenyl ring must be taken into account. We estimate that the phenyl substituent should decrease the barrier for ring opening via complexed transition state **31** by 4.6 kcal/mol.[64] Such a correction would make the highest point along the metal-bound pathway higher than the highest point along the noncomplexed pathway by <1 kcal/mol, correlating well with our experimental observations. Thus, while radical addition to the complexed arene ring is favored kinetically, the observed product ratio resulted from an equilibration process.

These results have important consequences for the synthetic design of radical addition reactions to chromium-complexed arenes. Since loss of an endo radical substituent via a pathway similar to transition state **31** is disfavored, then radical ipso substitutions of chromium arene complexes should not be high-yielding reactions. Instead, a different mechanistic pathway should be pursued to take advantage of the **favored** radical addition to a chromium-complexed aryl ring (**27b** vs **25b**). For example, electron transfer to intermediate **27b** would lead to stable 18-electron anionic hexadienylchromium complex **27a**. Thus, following radical addition steps with anionic chemistry should allow one to observe net favorable radical addition reactions to chromium-complexed aryl rings. Indeed, the few radical addition reactions of arenechromium complexes reported by Schmalz[26] fortunately take advantage of this exact pathway. With this mechanistic rationale, it should be possible to design other radical transformations of arenechromium complexes.

Indeed, the intermolecular radical competition results fit perfectly within this mechanistic framework. Reduction of acetone with SmI_2 generates a ketyl radical that adds to the benzene complex anti to the chromium forming a 17-electron hexadienyl complex (Scheme 4). Next capture by a second SmI_2 generates a stable 18-electron hexadienyl complex. Subsequent protonation at the metal center and reductive elimination isomerization yields the final products. These latter steps are in direct analogy to the known arene complex chemistry of nucleophilic addition followed by protonation as first reported by Semmelhack[65] and mechanistically elucidated by Kündig.[66] While ketyl–olefin coupling reactions represent one of the most widely studied SmI_2-promoted radical processes,[39c,67] ketyl–arene coupling reactions are rare.[68] Use of arene chromium complexes can now dramatically broaden the scope of these coupling reactions. The reactivity enhancement by a factor of 100 000 due to complexation with $Cr(CO)_3$ will allow access to many otherwise unfavorable reactions and will allow facile discrimination between aryl groups within the same substrate.

Scheme 4. Proposed Mechanism for Intermolecular Radical Addition



The calculated and observed selectivity for radical addition to complexed arenes is readily understood from a molecular orbital analysis. The SOMO of nucleophilic radicals such as ketyl radicals will interact with the arene LUMO. Since complexation by a tricarbonylchromium moiety lowers the arene LUMO energy, complexed arenes are more reactive than free arenes toward radical addition. This picture is in agreement with the few reported SmI_2-promoted ketone–arene coupling reactions where intermolecular[68b,e] and even intramolecular[68d] reactions require electron-withdrawing substituents on the arene ring.

Studies are in progress exploring the range of radical additions to complexed arenes and regioselectivity for substituted arenes. As with anionic addition reactions, computational studies based on the results reported herein will prove useful for explaining and predicting the regiochemical outcome of the radical reactions.

Cation. The high selectivity found in the cationic rearrangement case comes as a surprise because the opposite regioisomer would be expected electronically since the $Cr(CO)_3$ moiety is electron withdrawing. Indeed, reports on electrophilic aromatic substitution reactions have found arene tricarbonylchromium

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[64] This correction comes from calculating the difference in activation energies between the ring opening of cyclopropylcarbinyl radical and 2-phenylcyclopropylcarbinyl radical. The rate of each of these reactions has been measured, and the ΔE_a can be computed using the Arrenhius equation. See: (a) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1473–1482. (b) Newcomb, M.; Johnson, C. C.; Manek, M. B.; Varick, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 10915–10921.

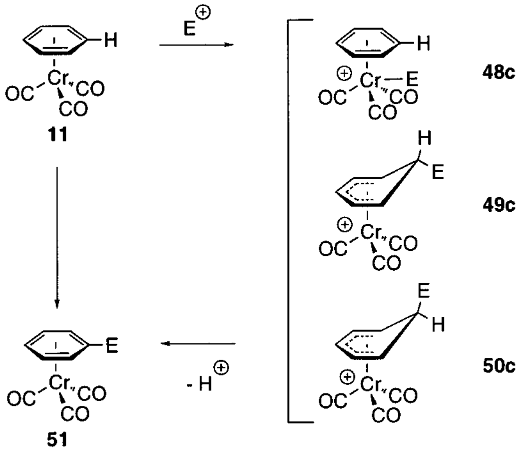
[65] (a) Semmelhack, M. F.; Hall, H. T. *J. Am. Chem. Soc.* **1974**, *96*, 7092–7094. (b) Semmelhack, M. F.; Hall, H. T.; Yoshifuji, M. *J. Am. Chem. Soc.* **1976**, *98*, 6387–6389. (c) Semmelhack, M. F.; Cark, G. R.; Garcia, J. L.; Harrison, J. J.; Thebtaranonth, Y.; Wulff, W. *Tetrahedron* **1981**, *37*, 3957–3065.

[66] Kündig, E. P.; Amurrio, D.; Bernardinelli, G.; Chowdhury, R. *Organometallics* **1993**, *12*, 4275–4277.

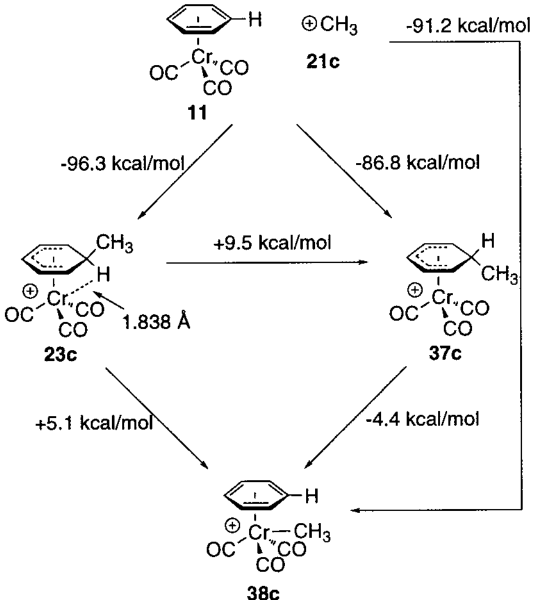
[67] Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338.

[68] (a) Williams, D. B. G.; Blann, K.; Holzapfel, C. W. *J. Org. Chem.* **2000**, *65*, 2834–2836. (b) Shiue, J.-S.; Lin, M.-H.; Fang, J.-M. *J. Org. Chem.* **1997**, *62*, 4643–4649. (c) Maury, O.; Villiers, C.; Ephritikhine, M. *Tetrahedron Lett.* **1997**, *37*, 6591–6594. (d) Kise, N.; Suzumoto, T.; Shono, T. *J. Org. Chem.* **1994**, *59*, 1407–1413. (e) Shiue, J.-S.; Lin, C.-C.; Fang, J.-M. *Tetrahedron Lett.* **1993**, *34*, 335–338.

Scheme 5. Three Modes of Electrophilic Addition to Arene Complexes



Scheme 6. Energetics of Methyl Cation Addition to (Benzene)tricarbonylchromium[a]



[a] All values are in kcal/mol. Energies were calculated using the DZVP2+ basis set.

complexes to be less reactive than the respective free arenes.[8−10,12−16] Here our calculations point to an important alternate mechanistic pathway.

There are three possible modes of electrophilic addition to arene complexes: addition to the metal atom, endo addition to the arene ring, and exo addition to the arene ring (Scheme 5). Previous researchers have considered these pathways, but never together in a systematic treatment examining all three. Net electrophilic aromatic substitution arises from proton loss from the ring adducts while the metal-bound electrophile (e.g., **48c**) would first have to rearrange to the endo adduct (**49c**).

In the specific case where the electrophile is a methyl cation, addition in all three modes is calculated to be exothermic, but endo addition is less favored by >9 kcal/mol (Scheme 6). Surprisingly, the exo adduct is most favorable of the three due to an agostic interaction with the endo proton. In the absence of the agostic interaction, as in the geminal dimethyl cation **35C**, the metal-bound electrophile, **36C**, is strongly favored. Similarly, with methylene groups as the substitutents (**27c** and **33c** vs **28c** and **34c**), the metal-coordinated cation is again highly favored. There are important chemical consequences of these computational predictions. First, all three modes are feasible, so the specific pathway will likely depend on the substituents. Second, there are stereochemical implications (vide infra).

Thirty years ago, Bly and co-workers considered an intermediate such as **28c** in their study of the solvolyses of methanesulfonates β to chromium-complexed arenes.[20] Upon further kinetic studies, they rejected direct chromium involvement with the cation (as in **28c**), reasoning that it did not explain all of their rate data. Instead, they argued that the rate enhancement by chromium was due to an electrostatic effect, with the partially negative end of the arene-to-chromium dipole stabilizing the forming positive charge as solvolysis proceeds.[20f] The current computational results favoring direct carbon−chromium interaction call for a reconsideration of their conclusion. Chromium-complexed phenonium **27c** is a 16-electron metal complex, while chromacycle **28c** is a more favorable 18-electron species. Formation of the chromium-complexed phenonium structure also involves breaking the aromatic π system,[69] an energetic price that does not have to be paid in the formation of **28c**.

In addition, consideration of the frontier molecular orbitals of the fragments involved also points toward the formation of the chromacycle. Figure 10 depicts the combinations of the HOMO of a chromium tricarbonyl fragment with the LUMO's of the phenonium ion (**25c**) and phenylethyl cation (**24c**) to form the complexed phenonium (**27c**) and chromacycle species (**28c**), respectively. A cursory examination of the LUMO of the phenylethyl cation, which can be considered as largely a p orbital on the primary cation, shows that this orbital has a greater spatial overlap with the chromium fragment HOMO than does the phenonium LUMO. Shifting the two ethyl carbons down toward the metal increases this overlap still further. The calculated energy of the phenylethyl cation LUMO is lower than the energy of the phenonium LUMO. This leads to a more favorable energetic matching between this LUMO and the chromium fragment HOMO. Both of these effects lead to a greater stabilization of the HOMO of the chromacycle relative to the complexed phenonium, favoring the chromacyclic structure.

The chromacycle-type intermediate provides a clear mechanistic understanding for an intriguing stereochemical experiment reported by Bly and co-workers.[20a] Solvolysis of L-*threo*-3-[(phenyl)tricarbonylchromium]-2-butyl methanesulfonate occurred with net retention of stereochemistry. Invoking participation by chromium, anchimeric assistance to the ionization would generate a chromacyclic intermediate with inversion of the carbon stereochemistry. Subsequent nucleophilic displacement of chromium with inversion at the carbon would lead to net retention of stereochemistry. Although Bly considered such a mechanism, he was unable to differentiate it from an arene participation pathway. The large calculated energy difference between the two pathways strongly argues for the chromium participation pathway.

The rearrangements examined in Scheme 3 demonstrate that this direct interaction of cations with the metal center can be preferred.[22,70] In all cases this can be rationalized by the preference for transition metals to form 18-electron complexes. In the cyclic cases, shifting the carbon to the metal center also involves release of ring strain, increasing the exothermicity of these rearrangements. Direct interaction of the chromium with distant cations, as in the formation of **34c**, suggests that chromium complexation of arenes could influence solvolysis

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[69] $Cr(CO)_3$ complexation does not reduce the aromaticity of benzene, see: ref 27b.

[70] Merlic, C. A.; Miller, M. M. *Organometallics* **2001**, *20*, 373−375.

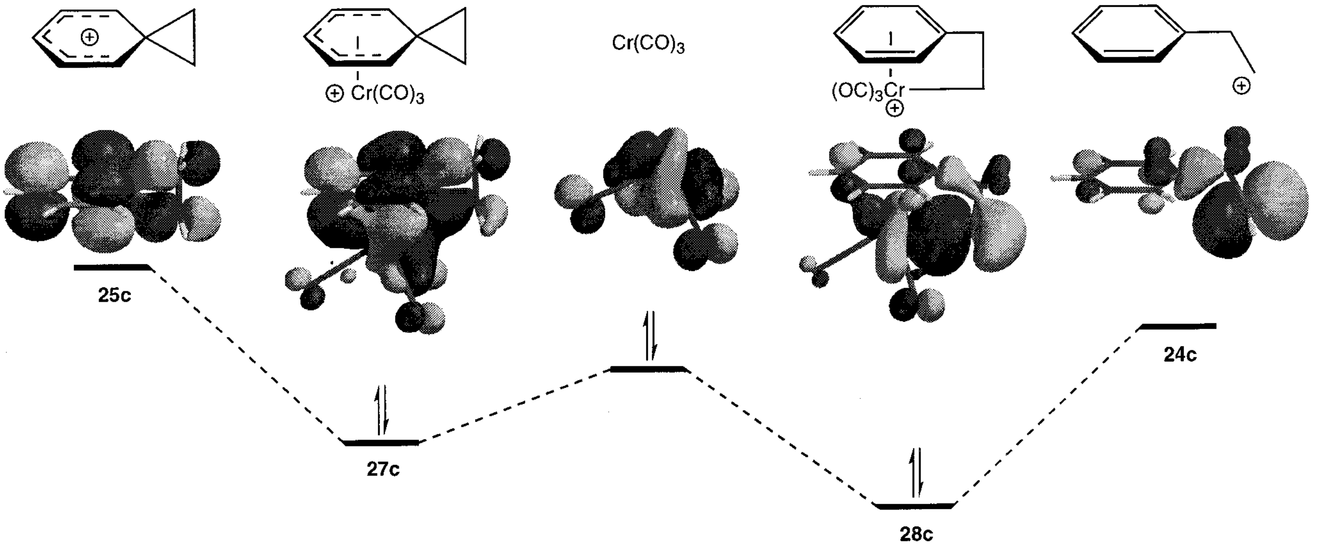
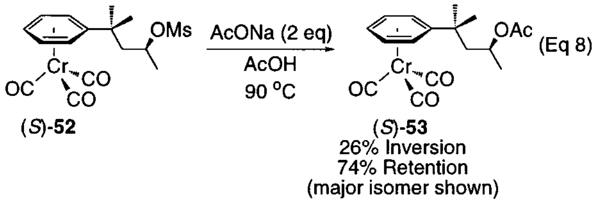
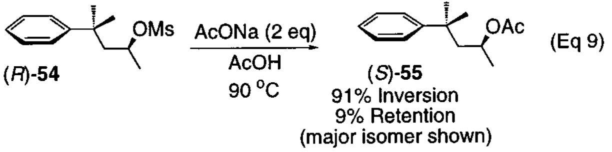


Figure 10. Frontier orbital interactions showing overlap between the HOMO of $Cr(CO)_3$ and the LUMOs of cations **25c** and **24c** to form chromium complexes **27c** and **28c**, respectively.

reactions beyond the presently known α- and β-positions,[1b,23,71] to the γ-position and perhaps beyond. Indeed, the computational comparison between pseudo four-membered ring **39c** and pseudo five-membered ring **40c** indicates that the larger ring is actually favored (eq 7). We recently reported experimental evidence of such a phenomenon (eqs 8 and 9).[70] Solvolysis of (*S*)-**52** with 2 equivs of sodium acetate in acetic acid at 90 °C gave acetate (*S*)-**53** (eq 8) and analysis[72] showed that substitution occurred with 74% *net retention of configuration*, employing the *gem*-dialkyl effect[73] to enhance the chromium participation. In contrast to the noncomplexed control reaction (eq 9), we propose that the 74% of substitution with retention in (*S*)-**52** occurs by ionization with inversion using neighboring group participation from chromium followed by displacement of chromium by the nucleophile, also with inversion. Thus, chromium *does* participate in the substitution reactions at remote centers. Calculations also point to a limit to metal–cation interactions in the case of tertiary carbons. Tertiary carbocations are not expected to interact strongly with chromium atoms and this is supported by the experimental work of Fry and coworkers.[23] The comparisons in Table 3 demonstrate that anions and radicals do not interact directly with the metal center. Again, this can be explained in terms of the 18-electron rule. Direct anion or radical addition to the metal would lead to a 20- or 19-electron species, respectively.





Friedel–Crafts *acylations* most likely proceed via exo addition. All the examples reported would benefit from an agostic interaction with the endo proton in the complexed Meisenheimer intermediate and none would suffer from ring strain. Then the observed reduced reactivity of complexed arenes would be a manifestation of electron withdrawal by the tricarbonylchromium moiety. This mechanistic rationale is analogous to ferrocene chemistry wherein small electrophiles add to iron, but acylation occurs anti to iron.[74]

The computational and experimental results for cationic and radical reactions call for revisions to our initial scheme for competitive cyclization (Scheme 1 vs Scheme 7). It is apparent that the anionic rearrangement proceeds along pathway **I**, starting with nucleophilic addition to the complexed arene. Radical rearrangement is slightly more complex. Initial radical addition via pathway **I** addition is calculated to be favored. However, the highly disfavored endo homolytic bond cleavage in the test substrate suggests a reversible addition leading to equilibration via pathway **II** to intermediate **B** that undergoes homolytic bond cleavage more readily, leading ultimately to favored product **3**. Finally, the cation proceeds through an intriguing mechanism, pathway **IV**. Initial cyclization is not to either arene ring, but to the metal center through a d orbital interaction, forming chromacyclic intermediate **C**. This intermediate rearranges via transition state **D** leading to product **2** upon hydride quenching. This metal-assisted pathway leading to rearranged product is also supported by our control reaction using 1,1-dideuterio-1-iodo-2,2-diphenylethane where we see a complete recovery of the starting iodide under the same reaction conditions, consistent with the idea that the cation rearrangement proceeds via neighboring group participation with formation of the metallacycle. We also computationally examined a pathway leading from chromacycle **C** toward product **3** via a 1,2-phenyl shift in the chromacycle,[75] but found it to be significantly higher in energy.

As noted for radicals, the results from the cationic processes have important implications for synthetic applications. First, the

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[71] Hegedus, L. S. *Transition Metals in Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, CA, 1994; Chapter 10, pp 307–333.

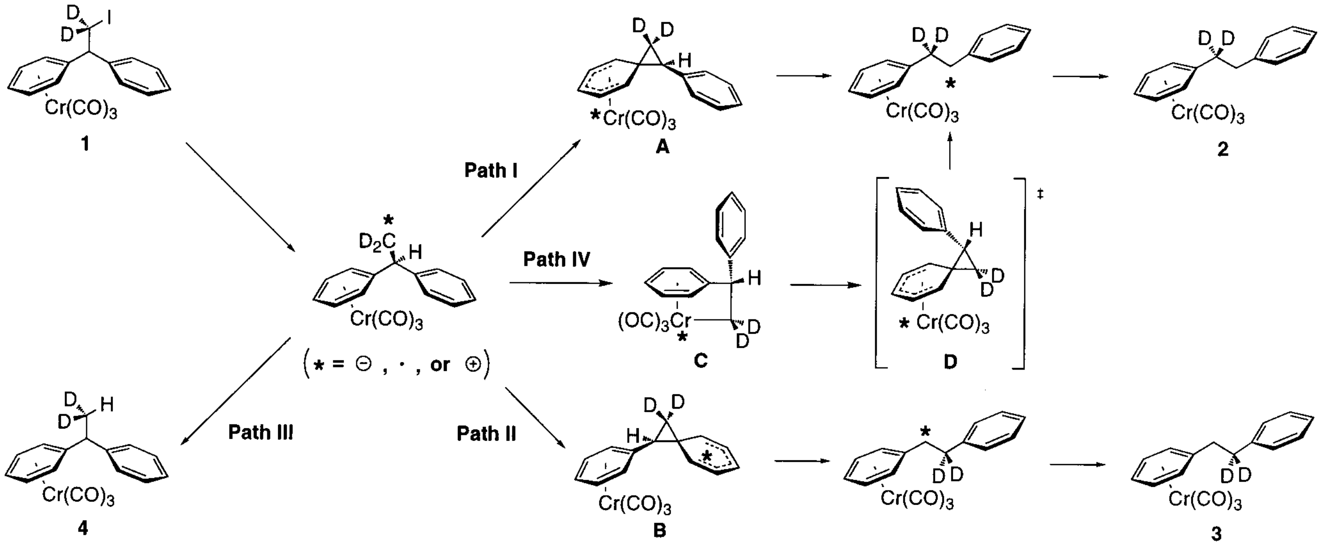
[72] The alcohol resulting from decomplexation and hydrolysis was analyzed by ^{19}F NMR of the Mosher's ester.

[73] (a) Jung, M. E. *Synlett* **1999**, 843–846. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224–232.

[74] Cunningham, A. F., Jr. *Organometallics* **1994**, *13*, 2480–2485.

[75] Transition state **56**. Included in the Supporting Information.

Scheme 7. Rearrangements of Chromium-Complexed 2,2-Diphenylethyl Anion, Cation, and Radical



direct carbon−chromium interactions illustrated in Scheme 3 suggest that there might be a general reaction rate enhancement (anchimeric assistance) for appropriately placed leaving groups beyond these reported for the benzylic[1f] and homobenzylic[20,23] positions. Second, there should be stereochemical consequences for neighboring group participation by chromium. Indeed, substitution with retention is well-known at the benzylic position[1f] and a few examples at the homobenzylic position have been reported.[20] However, this stereochemical control might extend to the third carbon out from the aryl ring[70] and the results from eqs 8 and 9 provide the first evidence for this.[70] Finally, there might be new manifolds of chemical reactivity to exploit, such as Friedel−Crafts alkylations,[76] based on electrophilic addition to the chromium atom.

Conclusions

In conclusion, we examined computationally and experimentally the reactivity of tricarbonylchromium-complexed aryl rings toward direct addition of reactive intermediates and found that chromium complexation can enhance the addition of anions, cations, **and** radicals to arene rings. Anion addition proceeds via a chromium-complexed analogue of the Meisenheimer intermediate and calculations provide structural details, charge distributions, and energy changes for the reaction. As expected, charge is localized on the chromium atom and addition is more favorable than in the noncomplexed arene by more than 30 kcal/mol. Likewise, complexation enhances direct addition of radicals to arene rings by about 8 kcal/mol, depending on the system, creating 17-electron intermediates structurally similar to anionic addition. Subsequent, homolytic cleavage of a bond endo to the metal is highly unfavorable due to large structural changes required. Instead, reduction of the intermediate radical complex resulting from radical addition results in a net favorable reaction. An intermolecular radical competition reaction designed on this premise found (benzene)tricarbonylchromium to be more reactive than benzene by a factor of more than 100 000:1, in strong agreement with the calculated energy differences. Finally, complexation leads to three mechanistic pathways for addition of electrophiles to arenes. Electrophilic addition to the ring endo relative to the metal is calculated to be significantly less favorable than addition exo to the ring or directly to the metal. Instead, electrophilic aromatic substitution in arene complexes is expected to occur via initial exo addition of the electrophile to the arene ring or initial addition to the metal followed by endo transfer to the arene ring. In an intramolecular experiment employing a primary carbon electrophile, the latter mechanism predominated in contrast with known intermolecular reactions with acylium ions. Calculations predict strong carbon−chromium bonding for primary and secondary, but not tertiary, cations and predict interactions with electrophilic sites at the γ position. Efforts to exploit the synthetic potential of radical and carbocation additions to arene complexes are currently underway in our laboratories.[70]

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Supporting Information Available: Full experimental procedures and spectral characterization for compounds reported in the text and computational methods and structural data for compounds **11** through **47** and **56** computed at the B3LYP/LANL2DZ level (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[76] Conversion of **1** to **2** is but one example.