Thermodynamic Control of Regioselectivity in the Addition of Carbanions to (Arene)tricarbonylchromium Complexes

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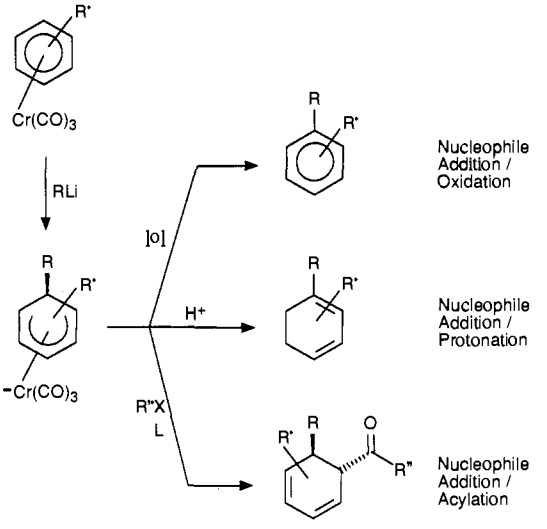
Abstract: The results of a study of the question of kinetic or thermodynamic control of the addition of carbon nucleophiles to (arene)$Cr(CO)_3$ complexes are presented. 2-Lithio-2-methylpropionitrile (**1**) is shown to add reversibly to (naphthalene)$Cr(CO)_3$ (**2**), (5,8-dimethoxynaphthalene)$Cr(CO)_3$ (**5**), (anisole)$Cr(CO)_3$ (**12**), and (*tert*-butylbenzene)$Cr(CO)_3$ (**15**). Definite evidence for equilibration via carbanion dissociation and readdition was obtained by crossover experiments with complexes **5** and **12** by using the labeled compounds **1**-d_6, **5**-d_6, and **12**-d_3 and product analysis by quantitative GLC and high-resolution MS. First-order kinetics were observed for the dissociation of **1** from the anionic cyclohexadienyl complexes, and the following rate constants were found in THF: complex **5** [C(2) adduct **6**], 2.8×10^{-4} s^{-1} (−40 °C); complex **12**, 1×10^{-6} s^{-1} (−30 °C); complex **15** (meta adduct), 5×10^{-4} s^{-1} (−30 °C). In reactions with complexes **2** and **5** equilibration of the initially formed mixtures of regioisomeric addition products led after oxidative decomplexation to single arene products (1-substituted, respectively 1,4,5-trisubstituted naphthalenes). With complex **15**, a 3:7 (meta:para) mixture was obtained at equilibrium, whereas in reactions of complex **12** with nucleophile **1** regioselectivity is invariant (meta addition) in passing from kinetic to thermodynamic control. Reversibility of nucleophilic additions to these four (arene)$Cr(CO)_3$ complexes is shown to be strongly linked to the nature of the cation (rate $Li^+ > K^+$) and the medium (rate in THF > THF/HMPA). With complex **5** rate differences of up to 4 orders of magnitude were observed. The activation parameters for the dissociation of **1** from **6** [addition product to C(2) in complex **5**] were determined in THF/HMPA (3:1): $\Delta H^{\ddagger} = 23.4 \pm 1.5$ kcal/mol, $\Delta S^{\ddagger} = 5 \pm 3$ cal/mol·K. The extension of the study to other carbon nucleophiles showed the nitrile-stabilized carbanions LiC(Me)(CN)(OCH(Me)OEt) (**22**), $LiCH_2CN$ (**20**), and $LiCMe_2CN$ (**1**), and the ester enolate $LiCH_2CO_2$-*t*-Bu (**21**) to add reversibly to **5**, whereas the sulfur-stabilized nucleophiles dithianelithium (**23**) and methyldithianelithium (**24**) as well as phenyllithium (**25**) showed no migratory aptitude in the temperature range −78 to 0 °C.

Reactive carbon nucleophiles add readily to (arene)$Cr(CO)_3$ complexes to yield anionic cyclohexadienyl intermediates (Scheme I). These in turn can be elaborated to give substituted arenes on oxidation (addition/oxidation sequence),[1-7] monosubstituted cyclohexadienes on treatment with acids (addition/protonation sequence),[2h-m,7b,c,8] or trans-disubstituted cyclohexadienes on reaction with carbon electrophiles (nucleophile addition/acylation sequence).[7c,9,10] The presence of a leaving group in the arene

Scheme I



allows the incorporation of the nucleophile without loss of the $Cr(CO)_3$ group (addition/elimination sequence).[11-14]

In this article we focus on the addition/oxidation sequence and report the results of our study on the reversibility of the addition

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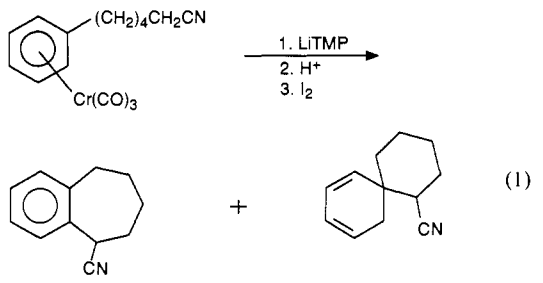
of carbon nucleophiles to a series of substituted arene complexes.

Substituted arenes when complexed to the $Cr(CO)_3$ fragment, often react with carbon nucleophiles highly regioselectively, and the addition/oxidation sequence has been developed into useful synthetic methodology. The question of kinetic versus thermodynamic control of the addition is pivotal to the interpretation of observed regioselectivity. A fair amount of extant quantitative data deals with this question in reactions of phosphorous and amine nucleophiles to more electrophilic, cationic, cyclic π-hydrocarbon complexes.[15] Quantitative results, however, are notably absent for reactions with carbanions—synthetically the most important class of nucleophiles, and for reactions of the neutral (arene)-$Cr(CO)_3$ complexes—by far the most widely used complexes in arene transformations via transition metals.

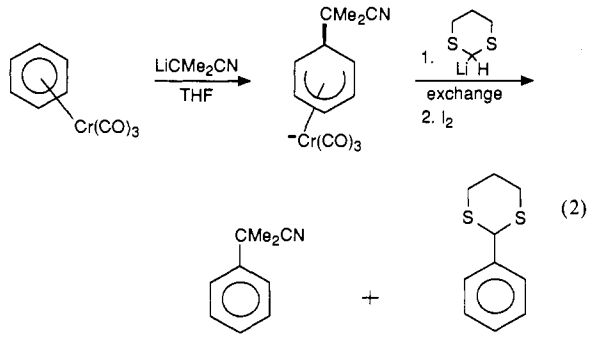
In early experiments with (chlorobenzene)$Cr(CO)_3$, Semmelhack et al. observed the kinetically formed meta addition products to undergo slow isomerization at 25 °C, a process that ultimately led to chloride displacement.[2f,10] Another more recent example of a reversible addition is the intramolecular alkylation shown in eq 1.[2e]



(1)

-70°	: 72	:	28
0° / 24h	: 3	:	97

This implies slow rearrangement processes that require long reaction times at temperatures of 0–50 °C. Typically, reactive stabilized carbanions (e.g., sulfur- or cyano-stabilized carbanions and ester enolates) add efficiently at temperatures between −78 and 0 °C. In those cases where this point was investigated, product distribution in the temperature range −78 to 25 °C was reported to be both time and temperature independent.[2d,h,n] Moreover, the crossover experiment shown in eq 2 indicated the exchange of carbanions in the addition product to be very slow.[2g]



(2)

exchange :	0°/0.5h	91	:	9
	24°/52h	43	:	57

Consequently, carbanion addition to (arene)$Cr(CO)_3$ complexes has been assumed to be under kinetic control under standard conditions (−78 to 0 °C), and regioselectivity in the product has been interpreted in terms of charge and/or orbital control.[2h,n,q,3-5,16,17]

In this paper we show that the situation is more complex. We provide definite evidence for the ready reversibility of the addition of 2-lithio-2-methylpropionitrile (**1**) to several (arene)$Cr(CO)_3$ complexes at temperatures well below 0 °C. Quantitative data give information on the rate and the mechanism of equilibration and on the factors that permit some reversibility control. Finally, we report on the migratory aptitude of other stabilized carbanions. Part of the work described here has been published in preliminary form.[7b,c,9b]

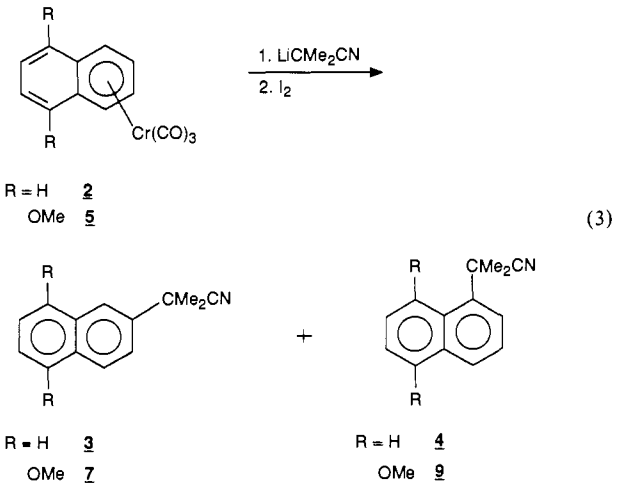
Table I. Product Distribution in the Addition/Oxidation Sequence with $LiCMe_2CN$ (**1**) and (Naphthalene)$Cr(CO)_3$ (**2**) or (1,4-Dimethoxynaphthalene)$Cr(CO)_3$ (**5**) (Equation 3)

entry	complex	medium	time, h/temp, °C[a]	product mix[b] 4 or 9	product mix[b] 3 or 7	combined yield,[b,c] %
1	**2**	THF	0.3/−65	81[d]	19[d]	79[d]
2	**2**	THF	0.5/0	>99	<1	96
3	**2**	THF/HMPA[e]	0.3/−65	42[d]	58[d]	88[d]
4	**5**	THF	0.1/−72	38	62	81
5	**5**	THF	1/−60	39	61	89
6	**5**	THF	1/−40	79	21	95
7	**5**	THF	1/0	>98[d]	<2[d]	78[d]
8	**5**	THF/HMPA[f]	0.5/−60	22	78	69
9	**5**	THF/HMPA[f]	1/−40	27	73	84
10	**5**	THF/HMPA[f]	2/0	47	53	76
11	**5**	THF/HMPA[f]	46/0	>98[d]	<2[d]	84[d]

[a] In all cases the anion and the complex were mixed at −78 °C. [b] All compounds were isolated and independently characterized. The product ratios are based on isolated material (unless otherwise noted). [c] The percentage yield refers to isolated (column chromatography) material after separation (unless otherwise indicated). [d] Ratio was determined by ^1H NMR integration and GLC; combined yields refer to mixtures of the α and β isomers. [e] Reaction medium was THF/HMPA (2.5:1). [f] Reaction medium was THF/HMPA (3:1).

Results and Discussion

1. Additions of 2-M-2-Methylpropionitrile (M = Li or K) to (a) (Naphthalene)$Cr(CO)_3$ (2). (Naphthalene)CrL_3 (L = CO, PF_3, PF_2OMe) complexes have been shown to react with a number of reactive nucleophiles to yield, after oxidation, the 1-substituted naphthalene **4** with high regioselectivity.[2h,7a] Surprisingly, when the reaction of complex **2** with $LiCMe_2CN$ (**1**) was carried out at low temperature rather than at the standard 0 °C used in the previous experiments, regioselectivity changed. With a reaction time of 15 min at −65 °C, followed by oxidative decomplexation, a mixture of 1- and 2-substituted naphthalenes (**4** and **3**) in the ratio of 4:1 was obtained in 79% yield. Changing the reaction medium to THF/HMPA (3:1) resulted in a product ratio of 3:2 (yield 88%) (Table I, entries 1–3).



(3)

This was unexpected as neither charge nor orbital considerations would predict addition to C(2) in **2**. Charge control in these reactions is linked to preferred eclipsed conformations adopted by the $Cr(CO)_3$ group relative to the aromatic ring.[3,16,17] It cannot account for the regioselectivity here, as the $Cr(CO)_3$ group in the symmetric complex **2** preferentially adopts a staggered confor-

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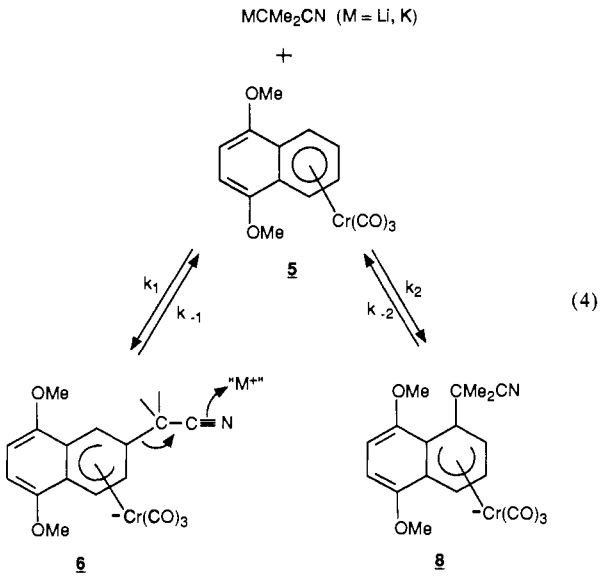
mation.[18] Frontier orbital considerations, based on the lowest unoccupied arene-centered molecular orbital, favor addition to C(1) in **2**.[2h,19] The importance of steric effects in the regioselectivity of additions of tertiary carbanions to substituted (arene)$Cr(CO)_3$ complexes is well documented,[2q] however, and we therefore favor an interpretation by which peri interactions contribute to regioselectivity at low temperatures. Peri interactions are larger in 1,4-disubstituted naphthalenes, and based on this fact as well as in view of the synthetic potential, (5,8-dimethoxynaphthalene)$Cr(CO)_3$ (**5**) was used in subsequent experiments in the naphthalene series.

(b) (5,8-Dimethoxynaphthalene)$Cr(CO)_3$ (5). (5,8-Dimethoxynaphthalene)$Cr(CO)_3$ (**5**) is readily available in high yield via thermolysis of $Cr(CO)_6$ in the presence of the arene, and as has been noted previously, the $Cr(CO)_3$ group is incorporated highly regioselectively into the unsubstituted ring of 1,4-dimethoxynaphthalene.[20] The addition of nucleophile **1** to complex **5** at −72 °C, followed by oxidation, yielded the 1,4,6-trisubstituted naphthalene **7** predominantly (Table I, entry 4). The high yield of products in this reaction shows that the nucleophile adds efficiently at −72 °C. When the reaction time and/or temperature was increased, product distribution changed. The kinetically favored β addition product **6** rearranged to the thermodynamically more stable α addition product **8**, as shown by the formation of increasing proportions of the 1,4,5-trisubstituted naphthalene **9** after oxidation of the reaction mixture. The data are collected in Table I (entries 4–7).

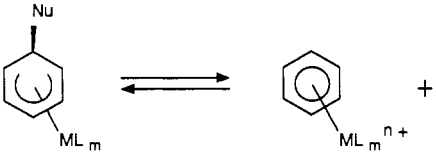
The addition of HMPA to the reaction mixture resulted in a drastic deceleration of the rate of rearrangement. Whereas rearrangement occurs readily at −40 °C in THF, it is very slow at 0 °C in THF/HMPA (Table I, entries 8–11). The reaction rates in the two reaction media were measured by GLC analysis of oxidized samples and are reported in Table III. The first-order kinetic plots, shown in Figure 1, for the rearrangement **6** → **8** are all linear within experimental error. In good approximation the observed rate constant k_{obsd} represents k_{-1}. This follows from the order of the rate constants of the reaction in eq 4, which is found



(4)

to be $k_1,k_2 \gg k_{-1} > k_{-2}$. Nucleophile **1** adds rapidly to complex **5** at −72 °C to give both **6** and **8**, while equilibration (k_{-1},k_{-2}) does not occur at an observable rate at temperatures below −60 °C. This asserts the first part of the above order: $k_1,k_2 \gg k_{-1},k_{-2}$. The order for $k_{-1} > k_{-2}$ is indicated by the complete conversion of **6** to **8**, by the different behavior of **6** and **8** in their reaction with (benzene)$Cr(CO)_3$ (these crossover experiments are described below), and by the direct determination of k_{-2} by a double-labeling experiment.

As the reaction rates in THF/HMPA (3:1) are much slower, rates were determined in this medium at 0, 10, and 20 °C to yield the activation parameters for the dissociation: $\Delta H^{\ddagger} = 23.4 \pm 1.5$ kcal/mol, $\Delta S^{\ddagger} = 5 \pm 3$ cal/mol·K. The addition of phosphines to cationic (arene)$Cr(CO)_3$ complexes is readily reversible (eq 5), and in a few cases the activation parameters for the dissociation



(5)

have been determined. The values of these analogous dissociations,

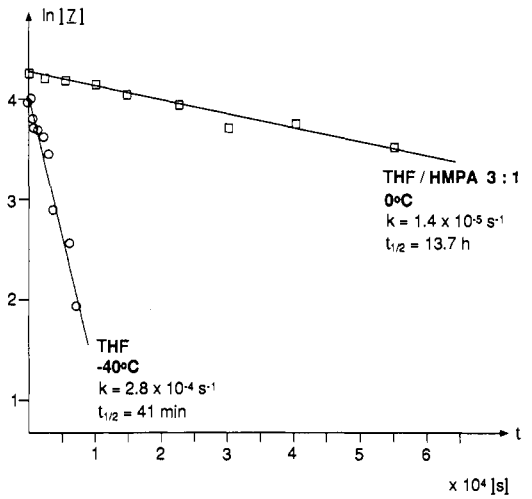


Figure 1. First-order kinetic plots for the rearrangement **6** → **8** in THF and THF/HMPA (3:1) (eq 4; Table III).

Table II. Activation Parameters for the Dissociation of the Nucleophile in the Reaction Shown in Equation 5

MLn	nucleophile	solvent	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/mol·K	ref
$Mn(CO)_3^+$	PBu_3	acetone	19.1	8	22
$Fe(C_6H_6)^{2+}$	PPh_3	CD_3CN	12.4	−1	23
$Ru(C_6H_6)^{2+}$	PPh_3	CD_3CN	12.2	0	23
$Os(C_6H_6)^{2+}$	PPh_3	CD_3CN	13.9	3	23

Table III. Kinetic Data of the Rearrangement **6** → **8** shown in Equation 4[a]

nucleophile	medium[b]	temp, °C	rates[a] $k_{obsd} \times 10^5$, s^{-1}
$LiCMe_2CN$	THF[c]	−40	28 ± 2
$LiCMe_2CN$	THF/HMPA (3:1)[d]	0	1.4 ± 0.1
$LiCMe_2CN$	THF/HMPA (3:1)[d]	10	9.3 ± 0.6
$LiCMe_2CN$	THF/HMPA (3:1)[d]	20	32.5 ± 2
$KCMe_2CN$	THF[e]	−20	2.4 ± 0.15
$KCMe_2CN$	THF[e]	−10	11.4 ± 0.7
$KCMe_2CN$	THF[e]	2	75 ± 5
$LiCMe_2CN$	THF + 3 equiv of TMEDA	−40	33 ± 2

[a] The experimental data indicate the rates to follow the order $k_1,k_2 \gg k_{-1} > k_{-2}$. First-order kinetics is observed for the rearrangement **6** → **8** with $k_{obsd} = k_{-1}$. Rate constants were calculated with a least-squares program. A minimum of five data points defined each straight-line plot. Correlation was between 0.992 and 0.999 for all plots. [b] Solutions of 0.04 M complex **5**. [c] Initial ratio of **6** and **8** was 3:1. [d] The initial ratio of **6** and **8** is 3:2. The activation parameters for the rearrangement **6** → **8** with M = Li are $\Delta H^{\ddagger} = 23.4 \pm 1.5$ kcal/mol, $\Delta S^{\ddagger} = 5 \pm 3$ cal/mol·K. [e] The initial ratio of **6** and **8** is 4:1. The activation parameters for the rearrangement **6** → **8** with M = K are $\Delta H^{\ddagger} = 21.2 \pm 1.5$ kcal/mol and $\Delta S^{\ddagger} = 4 \pm 2$ cal/mol·K.

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(19) The LUMO in (naphthalene)$Cr(CO)_3$ is arene centered. It is 83% character of the LUMO of naphthalene itself (personal communication from T. Albright, University of Houston).
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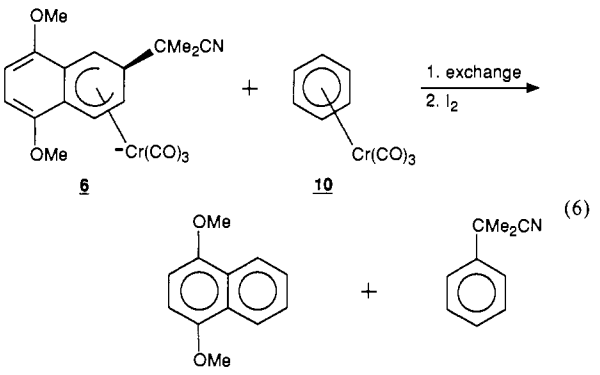
which involve less reactive nucleophiles but much more electrophilic metal complexes,[21] are listed in Table II for comparison.

At −40 °C, the half life of the rearrangement **6** → **8** in THF is 40 min. This is 5×10^4 times faster than the rate of the reaction in THF/HMPA (3:1) (extrapolated from the Arrhenius plot of the values listed in Table III).

This rate acceleration, when taken together with the dissociative mechanism of the rearrangement (see double crossover experiments below), indicates to us that the cation plays a key role in the carbon–carbon bond breaking step as shown in eq 4. This mechanistic interpretation of C–C bond breaking in intermediate **6** receives support from a recently published X-ray structure of an α-nitrile carbanion which shows lithium to be coordinated to the nitrogen atom rather than to the "carbanion" carbon.[24] HMPA modifies the polarity of the medium and, by coordination, the solvation and hence Lewis acidity of the cation. The nucleophile dissociation is very sensitive to these changes. In order to evaluate the role of the cation more directly, we extended the investigation to $KCMe_2CN$. If Lewis acidity of the cation is important in the carbanion dissociation step, potassium is expected to be far less efficient than lithium in this reaction. The data in Table III show this to be the case as the replacement of Li by K resulted in a ca. 500-fold rate decrease in the rearrangement. On the other hand, the addition of 3 equiv of tetramethylethylenediamine (TMEDA) to the reaction of $LiCMe_2CN$ in THF had, if any, a slightly accelerating effect on the rearrangement (Table III). As the chromium naphthalene bond is cleaved by Lewis bases,[25-28] large quantities of TMEDA cannot be used in this reaction.

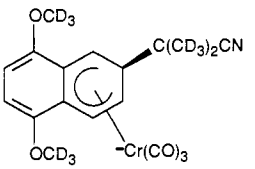
Crossover Experiments. The dissociative mechanism of the rearrangement is indicated by two crossover experiments. In a first experiment, shown in eq 6 and carried out in THF/HMPA



rate of exchange in THF / HMPA (3:1) at 0 °C : 2.1 ± 0.2 x 10^{-5} s^{-1}

(3:1), (benzene)Cr(CO)$_3$ was added at −78 °C to the mixture of **6** and **8**. After placing the reaction mixture at 0 °C, aliquots were removed at intervals, oxidized, and analyzed by GLC. The experiment established that the intermolecular migration of the carbon nucleophile **1** from the intermediate **6** to (benzene)Cr(CO)$_3$ (**10**) occurs under the same conditions as those of the rearrangement **6** → **8**. Moreover, the rate of migration (k_{obsd} = 2.1 × 10^{-5} s^{-1}) is of the same order as that of **6** → **8**. The concentration of intermediate **8**, which represents 24% of the initially formed mixture of the addition reaction, remained constant (±4%) throughout this reaction, hence carbanion transfer from **6** to **10** is preferred to the rearrangement **6** → **8**.[29] This is supported by a separate experiment in which nucleophile **1** was reacted first with the benzene complex **10** to give the cyclohexadienyl complex **11**. Complex **5** and HMPA were then added, and the reaction was stirred at 0 °C for 21 h before oxidation and product isolation. The mixture consisted of 2-phenyl-2-methylpropionitrile and 1,4-dimethoxynaphthalene. The trisubstituted naphthalenes **7** and **9** were notably absent.

While the above results make a dissociative mechanism very probable, a bimolecular reaction mechanism between **6** and **10** resulting in carbanion transfer[30] could not be ruled out at this point. In fact, (benzene)Cr(CO)$_3$ (**10**) could act as Lewis acid and induce carbon–carbon bond breaking in a way similar to that proposed above for Li. The slight rate increase observed for this crossover reaction to that of the reaction **6** → **8** could well show this to be a contributing factor. This could have been explored further by investigating the rate dependence on the amount of added complex **10**, but we chose instead to solve the question unambiguously via a double crossover experiment. In addition, these experiments were to yield information on the relative rates of the dissociation of anion **1** from the α and β intermediates **8** and **6**. Both the arene complex **5** and the nucleophile **1** were deuterium labeled. Solutions of the doubly labeled (arene and nucleophile) and unlabeled addition products were prepared separately and then mixed at −78 °C (the doubly labeled **6**-d_{12} is shown). GLC and MS analyses



6-d_{12}

(after oxidation) of samples taken before and after mixing showed the addition reaction to be complete and to contain the α and β addition products in the usual ratio. No label exchange had taken place on mixing at low temperature.

Migration of the nucleophile to the α-carbon (to give **8**) was then induced by letting the reaction mixture warm up to 0 °C (0.5 h). The products were analyzed by GLC and high-resolution MS. As expected, the rearrangement was complete under these conditions and oxidation of the reaction mixture yielded exclusively labeled and unlabeled **9** (GLC analysis). The intensity of the peaks of the fragments of mass 255, 261, and 267 in the high-resolution mass spectrum revealed a statistic 1:2:1 distribution of the label. This clearly demonstrates that the addition of carbanion **1** to complex **5** is reversible at both positions C(1) and C(2). Separate experiments, however, indicate that carbanion dissociation in intermediate **8** is slower than in **6**. In THF/HMPA (3:1), dissociation of **1** from **8** is completely suppressed at 0 °C, whereas carbanion dissociation from **6** occurs with a $t_{1/2}$ of ca. 14 h.[31] These qualitative observations are confirmed in the determination of the value of k_{-2} in eq 4 in THF by high-resolution MS analyses of samples removed periodically from a reaction mixture containing doubly labeled and unlabeled **8** exclusively. This was realized by letting **6** and **6**-d_{12} rearrange to **8** and **8**-d_{12} (0 °C, 0.5 h) before mixing the solutions at −78 °C. Analysis, assuming a first-order reversible reaction for the interchange of **8** and **8**-d_{12} to yield **8**, **8**-d_6, and **8**-d_{12}, yielded a straight-line plot for the rate expression $\ln (A_0 - A_\infty)/(A_t - A_\infty) = 2k_{obsd}t$. The rate constant

(21) The activation of a π-hydrocarbon by a complex fragment follows the order $Fe(C_6H_6)^{2+} > Mn(CO)_3^+ > Fecp^+ > Cr(CO)_3$. A numeric estimate in the above series is $2 \times 10^8/1 \times 10^3/1$/"very small" (ref 15).

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(27) (a) Kündig, E. P.; Timms, P. *J. Chem. Soc., Dalton Trans.* **1980**, 991. (b) Kündig, E. P.; Perret, C.; Spichiger, S.; Bernardinelli, G. *J. Organomet. Chem.* **1985**, *286*, 183.
(28) Howell, A. S. J.; Dixon, D. T.; Kola, J. C.; Ashford, N. F. *J. Organomet. Chem.* **1985**, *294*, C1.

(29) Separate experiments in which the migration **6** → **8** was carried out first followed by the addition of complex **10** showed that migration of $LiCMe_2CN$ from **8** to **10** does not occur under these conditions.

(30) Nucleophile "abstraction" by an added (arene)Cr(CO)$_3$ complex was proposed in ref 2g to account for carbanion interchange in (arene)Cr(CO)$_3$ complexes.

(31) GLC and high-resolution MS analysis of samples removed in the course of this reaction indicated the rate of intramolecular exchange to be approximately equal to the rate of intermolecular exchange.

Table IV. Kinetics of the Reversible Addition of 2-Lithio-2-methylpropionitrile (1) to (Anisole)Cr(CO)$_3$ (12) (Equation 7)[a]

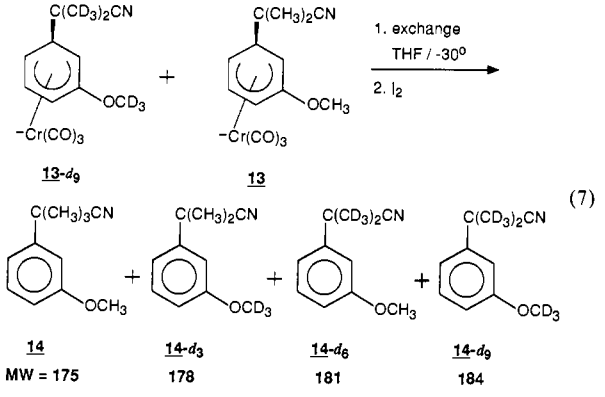
entry	time, s	m/z 175	178	181	184
1	0	48.9	4.6	0	46.6
2	900	44.3	7.4	4.4	43.9
3	3000	36.9	14.4	12.3	36.4
4	7200	30.6	21.0	19.8	28.6
5	14220	27.5	24.0	22.7	25.8
6	77460	25.7	25.1	24.5	24.7

[a] The increase in intensity of the monolabeled arenes of mass 178 and 181 and decrease of unlabeled (mass 175) and doubly labeled (mass 184) arenes follow first-order kinetics (reversible reaction). k_{av} is 1 ± 0.08 × 10^{-4} s^{-1}. Correlations of the first-order plots are 0.991–0.999.

k_{-2} (k_{obsd}) was determined to be (2.0 ± 0.2) × 10^{-5} s^{-1} at −30 °C. This is ~2 orders of magnitude smaller than k_{-1} at this temperature and establishes the relative order in rate constants $k_1, k_2 \gg k_{-1} > k_{-2}$ in eq 4.

In the section above we have described the methods used to obtain evidence as well as kinetic data for the reversible addition of $LiCMe_2CN$ to (5,8-dimethoxynaphthalene)Cr(CO)$_3$. The same techniques can be applied to the investigation of kinetic versus thermodynamic control of carbon nucleophile addition to other substituted arenes. This is shown below for (anisole)Cr(CO)$_3$ (**12**).

(c) (Anisole)Cr(CO)$_3$ (12). Semmelhack and co-workers have shown complex **12** to react with $LiCMe_2CN$ in THF to give, after oxidation, almost exclusively the meta addition product (meta: ortho = 97:3).[2d] Varying reaction time, temperature, and medium (THF or THF/HMPA) we found no significant change of regioselectivity (±2%) in the temperature range −78 to 0 °C. This poses three alternatives: (a) the addition is under kinetic control in the temperature range investigated, (b) equilibration is rapid even at −78 °C, and (c) equilibration takes place at an intermediate temperature but the transition from kinetic to thermodynamic control is not accompanied by a change in regioselectivity. Premises (a) and (c) are plausible, whereas the results with complex **5** in THF/HMPA make (b) unlikely. The right answer proved to be (c). This was determined via the experiment shown in eq 7. GLC analysis, after oxidation, of a sample taken shortly



(7)

after mixing the solutions of **13** and **13**-d_9 at −78 °C showed the reaction to be complete (96% yield, GLC). The high-resolution mass spectrum showed only a trace of a peak at m/z 178 (Table IV) assigned to **14**-d_3. On warming, carbanion exchange was found to take place. Rates for the exchange reaction were determined at −30 °C by following the exchange for 2 half-lives of the dissociation. Equilibrium concentrations were determined after 10 half-lives of the reaction. The data are listed in Table IV and the first-order plot of the growth of singly labeled **14**-d_3 is presented in Figure 2. The half-life for the dissociation of carbon nucleophile **1** from (anisole)Cr(CO)$_3$ at −30 °C in THF is 2 h.

(d) (*tert*-Butylbenzene)Cr(CO)$_3$ (15). Addition of nucleophile **1** to complex **15** (in THF/HMPA) was reported previously to yield approximately 1:1 mixtures of meta (**17**) to para (**19**) product.[29,32]

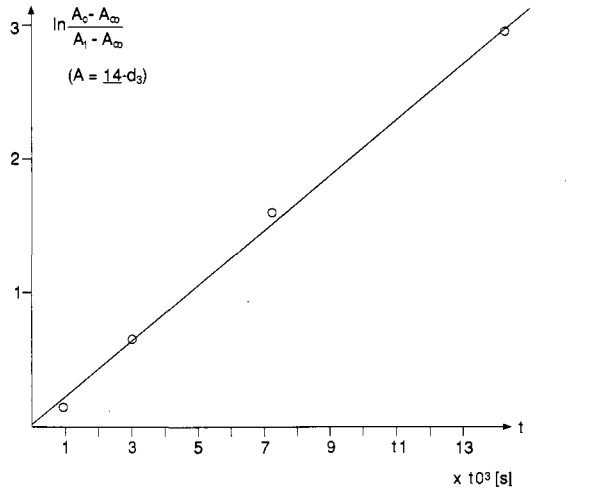


Figure 2. Crossover reaction with the doubly labeled and the unlabeled meta addition products of 2-lithio-2-methylpropionitrile to (anisole)Cr(CO)$_3$ (**12**). The kinetic plot shown is that for the growth of the singly labeled isomer **14**-d_3 (eq 7; Table IV) as determined by the intensity of the peak at m/z 178 in the high-resolution mass spectrum.

Table V. Regioselectivity in the Reaction of 2-Lithio-2-methylpropionitrile (**1**) with (*tert*-Butylbenzene)Cr(CO)$_3$ (**15**) in THF (Equation 8)

entry	temp, °C/ time, min	product mix ratio,[a] % 17	19	combined yield,[b] %
1[c]	−75/5	49	51	94
2[c]	−30/5	44	56	96
3[c]	−30/20	38	62	94
4[c]	−30/54	33	67	91
5[c]	−30/257	31	69	85

[a] Determined by GLC analysis. [b] GLC yield. In separate experiments **17** and **19** were isolated (yield 85%), separated by preparative GLC, and characterized by ^1H NMR. [c] Solution was 0.04 M; samples (entries 1–5), taken from the same stock solution after the time and temperature indicated, were oxidized (I_2) and analyzed by GLC to give the ratios of products **17** and **19** in columns 3 and 4.

In THF a very similar initial distribution of products was obtained when the addition/oxidation was carried out at −70 °C (1:1 mixture of **17** and **19**). The results listed in Table V demonstrate that, here again, equilibration occurs readily at −30 °C to afford the thermodynamic mixture 1:2.2 (**17**/**19**). First-order plots were again obtained for the reversible reaction between **16** and **18** assuming the rate law

$$\ln (A_0 - A_\infty)/(A(t) - A_\infty) = (k_{-1} + k_{-2})t$$

with

$$k_{-1} = (4.9 \pm 0.3) \times 10^{-4}\ s^{-1}$$

Interestingly, the rearrangement here occurs at the expense of the meta addition product **16** (eq 8, Table V). In THF, equilibrium is reached in approximately 2 h at −30 °C, whereas in THF/HMPA (3:1) it requires more than 2 days at 0 °C. Double crossover experiments have not been carried out on this system, but the qualitatively very similar (although quantitatively less striking) behavior of complex **15** compared to that of the naphthalene complex **5** described above makes a strong point for an analogous interpretation.

2. Migratory Aptitude of Other Stabilized Carbanions in Additions to (5,8-Dimethoxynaphthalene)Cr(CO)$_3$ (5). Of the range of carbon nucleophiles known to react with (arene)Cr(CO)$_3$ complexes[2] a few were selected (**20**–**25**) and probed for reversibility

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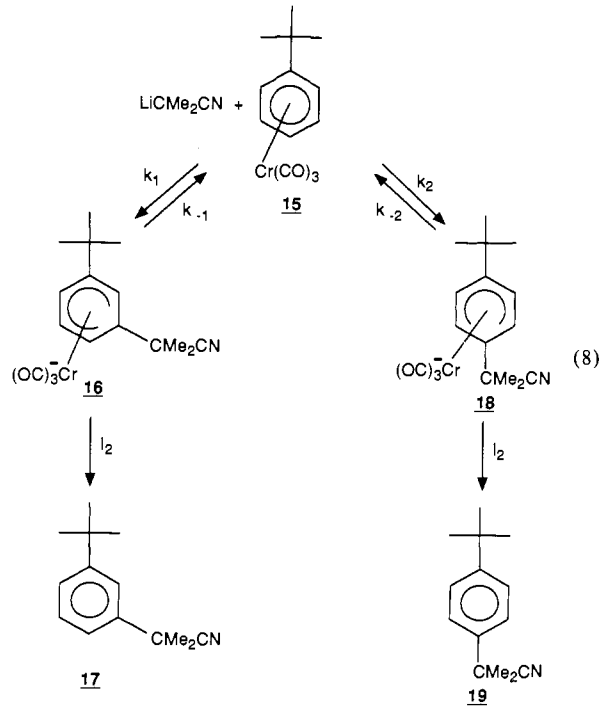


(8)

in their addition to complex **5**. Product distribution from reactions at low and higher temperatures and with or without HMPA are shown in Table VI.

These data confirm and extend the findings with $LiCMe_2CN$ (**1**) detailed in Table I. Steric effects are apparent at low temperature. The small nucleophiles 2-lithioacetonitrile (**20**) and the ester enolate **21** yield predominantly the α substitution product (entries 1–6) at low temperature, whereas under analogous conditions the sterically more demanding **1** and **22** give predominantly the β addition product (Table I, entries 4 and 8; Table VI, entry 7). Comparison of the data in Tables I and VI reveals that reversibility depends to a large degree on the nature of the carbanion. The cyanohydrin nucleophile LiC(Me)(CN)(OCH(Me)OEt) (**22**), the other nitrile-stabilized carbanions $LiCH_2CN$ (**20**) and $LiCMe_2CN$ (**1**), and the ester enolate $LiCH_2CO_2$-*t*-Bu (**21**) add reversibly. In all cases HMPA slows down the rearrangement. In the addition reactions of dithianelithium (**23**), methyldithianelithium (**24**), and phenyllithium (**25**) 1–3 molar equiv of HMPA was necessary. The sulfur-stabilized nucleophiles and phenyllithium (**25**) showed no migratory aptitude in the temperature range −78 to 0 °C even on prolonged reaction time. As **23** belongs to the group of nucleophiles that has found application in the nucleophile/acylation sequence involving (arene)$Cr(CO)_3$ complexes,[9] we interpret their addition to be under kinetic control; this point is discussed in the next section.

Kinetic vs Thermodynamic Control of Carbon Nucleophile Addition. Regioselectivity in (arene)$Cr(CO)_3$ complexes was initially correlated to the size of the LUMO coefficients of the substituted arene.[2h] Subsequently, on the basis of ^{1}H NMR studies and EHMO calculations, the conclusion was advanced that regiochemistry is controlled not only by the substituent on the arene but also by the preferred conformation of the $Cr(CO)_3$ group and that arene carbons eclipsed by a Cr–CO bond are preferentially attacked by nucleophiles[16,17,31] (Chart I). A series of experimental studies corroborates these conclusions.[2o,3a,32] Recently, ^{1}H NMR coordination shifts of arene protons have been proposed as a predictive tool to determine the site of nucleophilic addition.[3b]

A more differentiated picture has emerged out of an elegant study by Semmelhack and co-workers demonstrating the interplay of charge and orbital control in the addition reaction.[2q] Orbital control is favored in cases of a good electrophile LUMO and nucleophile HOMO energy match and in the absence of a strong preference for an eclipsed conformation of the $Cr(CO)_3$ group.

All the above interpretations are based on the properties of the starting complex and are therefore limited to reactions that are

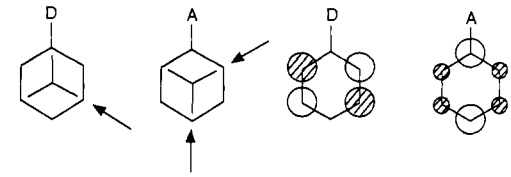
Chart I

KINETIC CONTROL :

Regioselectivity as a result of a balance of charge control and orbital control.

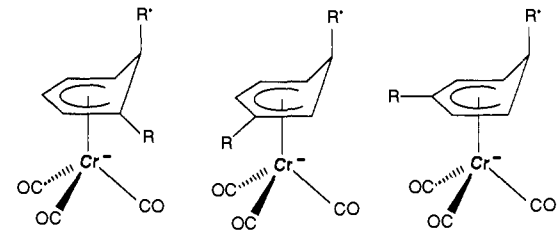
a) Charge control : charge induced by the prefered conformation adopted by the $Cr(CO)_3$ group

b) Frontier orbital control : lowest unoccupied arene centered MO

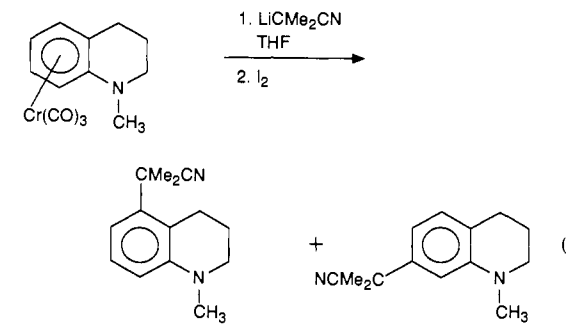


THERMODYNAMIC CONTROL :

Regioselectivity controlled by the relative thermodynamic stability of the intermediate cyclohexadienyl complex :



under kinetic control. As our study shows, this is not generally the case. 2-Lithio-2-methylpropionitrile (**1**), in particular, has been used extensively in mechanistic investigations of the addition/oxidation sequence with (arene)$Cr(CO)_3$ complexes.[2,3] Our results indicate that positional equilibration of the isobutyronitrile group is often complete when the reaction mixture is left to warm up to 0 °C for a short period before oxidation. Rates of "carbanion" dissociation of $LiCMe_2CN$ (**1**) vary considerably, however, at this temperature. The dissociation from the 2-position in intermediate **6** to regenerate (5,8-dimethoxynaphthalene)$Cr(CO)_3$ (**5**) occurs with a half-life of ca. 1 s at 0 °C, whereas the corresponding number in (anisole)$Cr(CO)_3$ (**11**) is approximately 3 min.[33] Evidence for very fast rearrangements was also reported by Ohlsson and Ullenius, who found migration of **1** in a tetrahydroquinoline complex to occur at temperatures as low as −70 °C (eq 9).[6]



(9)

-70° / 1 min :	35	:	64
-70° / 8.6 h :	2	:	97

Under equilibrium conditions, the relative stabilities of the cyclohexadienyl complexes alone determine the regioselectivity (Chart I). In (anisole)$Cr(CO)_3$ for example, it is immediately apparent that the OMe group will least destabilize the highest

(33) The values are extrapolated from the observed rates assuming a $\Delta H^{\ddagger}$ of 23.4 kcal/mol (see Table III) for the dissociation of **1**.

Table VI. Product Distribution in the Addition/Oxidation Sequence with Carbon Nucleophiles and (5,8-Dimethoxynaphthalene)$Cr(CO)_3$ (5)

entry	LiR	medium[a]	time, h/temp, °C	product yield,[b] %		combined yield
1	$LiCH_2CN$ (20)	THF	0.5/−65	>99 (27)	<1 (26)	39
2	$LiCH_2CN$ (20)	THF	0.5/−20	>99 (27)	<1 (26)	72
3	$LiCH_2CN$ (20)	THF/HMPA[c]	1/−50	75[d] (27)	25[d] (26)	34[d]
4	$LiCH_2CN$ (20)	THF/HMPA[e]	30/−20	>99 (27)	<1 (26)	72
5	$LiCH_2CO_2{}^tBu$ (21)	THF/HMPA[c]	1/−40	64 (29)	36 (28)	82
6	$LiCH_2CO_2{}^tBu$ (21)	THF/HMPA[c]	48/0	>99 (29)	<1 (28)	84
7	LiCMe(CN)(OR) (22)	THF	1/−55	31[d,f] (31)	69[d,f] (30)	54[d]
8	LiCMe(CN)(OR) (22)	THF	2/−10	>99[f] (31)	<1 (30)	70
9	$LiCHS(CH_2)_3S$ (23)	THF/HMPA[e]	24/−40	22[d] (33)	78[d] (32)	41
10	$LiCHS(CH_2)_3S$ (23)	THF/HMPA[e]	24/−40	18 (33)[d]	82[d] (32)	48
11	$LiCMeS(CH_2)_3S$ (24)	THF/HMPA[g]	1/0	<1 (35)	>99 (34)	61
12	$LiCMeS(CH_2)_3S$ (24)	THF/HMPA[g]	48/0	<1 (35)	>99 (34)	71
13	LiPh (25)	THF/HMPA[h]	20/−40	83[d] (37)	17[d] (36)	78
14	LiPh (25)	THF/HMPA[h]	20/0	84[d] (37)	16[d] (36)	78

[a] In all cases the anion and the complex were mixed at −78 °C. [b] Unless otherwise noted, the product ratios and yields refer to isolated material. The former were checked by GLC and NMR analysis of the crude mixture. The estimated detection level is 1% for the minor isomer. [c] The reaction medium was THF/HMPA (2.5:1). [d] The ratio was determined by ^1H NMR integration and GLC analysis; the combined yield refers to the mixture of the α and β isomers. Compounds **26**, **33**, and **36** were not isolated analytically pure. [e] The reaction medium was THF with 0.7 mL of HMPA. [f] The product is the acetyl derivative, obtained by hydrolysis of the cyanohydrin. [g] The reaction medium was THF/HMPA (2:1). [h] The reaction medium was THF with 0.35 mL of HMPA. [g] The reaction medium was THF/HMPA (3:1).

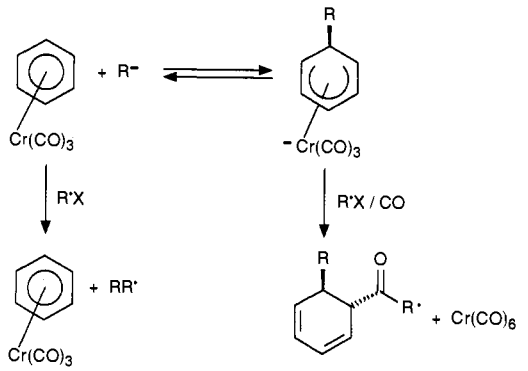
occupied cyclohexadienyl orbital when meta to the nucleophile.[34] As meta selectivity is also predicted under kinetic control based on the preferred conformation adopted by the $Cr(CO)_3$ group, a change of regioselectivity would not be expected in this case with the onset of equilibration. As we have seen, this is confirmed by experiment. Other cases, unfortunately, are less amenable to prediction. The equilibrium situation in (*tert*-butylbenzene)$Cr(CO)_3$ for example indicates an exceedingly small energy difference between the two regioisomers, and in this and analogous situations there is little hope for reliable predictions of regioselectivity on the basis of theoretical analysis.

Another factor that has to be considered in thermodynamically controlled additions is the effect of the substituent R on the conformation of the $Cr(CO)_3$ group in the anionic cyclohexadienyl intermediates. Barriers of rotation of the ML_3 fragment with respect to the cyclohexadienyl ligand are much higher than those found in arene complexes. Typical values are in the range of 9–13 kcal/mol.[35] In all reported compounds, the preferred conformation adopted is that depicted in Chart I, in which a metal ligand bond eclipses the sp^3 carbon and the meta carbons of the cyclohexadienyl ligand. In this conformation, a bulky substituent in the meta position is unfavorable as it will interact with the eclipsed carbonyl group. It is tempting to attribute the direction of the rearrangement (meta to para) observed in the reactions of (*tert*-butylbenzene)$Cr(CO)_3$ (eq 9, Table V) at least in part to this interaction.

Conclusion

Kinetic studies and double crossover experiments reveal that addition reactions of carbon nucleophiles to (arene)$Cr(CO)_3$ complexes can be readily reversible even at low temperature. It follows that interpretation of observed regioselectivity in the nucleophile addition/oxidation sequence with (arene)$Cr(CO)_3$ complexes must be based on a firmly established situation of either kinetic or thermodynamic control of the addition. While the transition from kinetic to thermodynamic control can lead to different regioselectivity [e.g., in (naphthalene)$Cr(CO)_3$, (5,8-dimethoxynaphthalene)$Cr(CO)_3$, (*tert*-butylbenzene)$Cr(CO)_3$, and (tetrahydroquinoline)$Cr(CO)_3$[6]], the example of (anisole)$Cr(CO)_3$ demonstrates that this is not always the case.

Scheme II



The present study shows that carbanion dissociation can be significantly suppressed by the choice of conditions. For the addition reaction to be under kinetic control, one or a combination of the following three requirements has to be met: temperatures below −50 °C, efficient solvation of the Lewis acidic cation (e.g., by HMPA), and very reactive carbanions. These findings form the basis for the control of the different pathways observed for the reaction of the anionic (cyclohexadienyl)$Cr(CO)_3$ complexes with carbon electrophiles which results either in the regeneration of the starting arene complex[2g] or in the alkylation at the metal center ultimately leading to trans disubstituted dihydroarenes[7c,9] (Scheme II).

Experimental Section

1. General, Starting Materials, and Solvents. All manipulations involving chromium complexes or carbon nucleophiles were carried out under an atmosphere of purified nitrogen or argon and using an inert gas/vacuum double manifold and standard Schlenk techniques.[36] Tetrahydrofuran, diethyl ether, and di-*n*-butyl ether were distilled from sodium–benzophenone ketyl immediately prior to use. Toluene was refluxed for 4 h over sodium before distillation. Pentane, hexane, 2-methylpropionitrile, and *trans*-decalin were distilled from CaH_2. Hexamethylphosphoramide (HMPA) and dimethyl sulfoxide (DMSO) were stirred with CaH_2 for 15 h at 60 °C before distillation under a reduced atmosphere (10 mmHg) of nitrogen. Benzene-d_6 was vacuum transferred after stirring with CaH_2. Acetonitrile (puriss, Fluka) was dried and distilled from CaH_2. Diisopropylamine and bis(trimethylsilyl)amine (Fluka) were distilled from KOH pellets. Methyl-d_3 iodide was obtained from Ciba-Geigy and vacuum transferred from P_2O_5 prior to use. 2-Propanol-d_8 (>99% d) was purchased from Ciba-Geigy and used as received. $Cr(CO)_6$ was obtained from the Pressure Chemical Co. or from

(34) This analysis has been made previously. It was raised as a possible explanation of regioselectivity in a situation of a late transition state in a kinetically controlled addition of a carbon nucleophile to an (arene)$Cr(CO)_3$ complex (footnote 21 in ref 2q). It should be noted, however, that mechanistic studies of P- and N-donor nucleophile addition to cationic arene complexes indicate the transition state to usually be an early one.[15]

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Strem Chemicals and used as received. Potassium hydride (~20% in oil) was obtained from Fluka. It was stored under nitrogen in a Mecaplex GB 80 stainless steel glovebox equipped with a dry-train. Immediately before use, the oil was removed by washing repeatedly with hexane and after weighing, the KH was suspended in THF. *n*-BuLi and PhLi (Fluka) were titrated before use according to the method of Gilman.[37]

Gas–liquid chromatography (GLC) analysis was carried out on a Perkin-Elmer 900 spectrometer with flame-ionization detector by using a 2 m × 6 mm glass column packed with Chromosorb W/OV 225 (10%). For quantitative GLC analysis, calibration curves for the pure products were established and *trans*-decalin was added as an internal standard. Analytical and preparative TLC were carried out with Merck silica gel 60 F_{254} plates. Column chromatography was carried out by the flash method described by Still.[38] ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM-360 spectrometer (^{1}H at 360 MHz, ^{2}H at 55.29 MHz, ^{13}C at 90.6 MHz) and a Varian XL-200 spectrometer (^{1}H at 200 MHz, ^{13}C at 50.3 MHz). Chemical shifts are given (ppm) relative to $SiMe_4$. IR spectra were recorded on a Perkin-Elmer 681 grating spectrometer or a Mattson Instruments Polaris Fourier transform spectrometer by using NaCl solution cells. Electron impact (70 eV) mass spectra were obtained on a Varian CH 4 or SM 1 spectrometer, relative intensities are given in parentheses. High-resolution mass spectra were measured on a VG analytical 7070E instrument (data system 11 250, resolution 7000). Melting points were determined on a Büchi 510 apparatus and are not corrected. Elemental analyses were performed by E. Thommen, Mikroanalytisches Labor, Universität Basel, H. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, Université de Genève, and E. Pascher, Mikroanalytisches Labor, Remagen.

2. Synthesis of Complexes. (Benzene)Cr(CO)$_3$ (**10**), (anisole)Cr(CO)$_3$[39] (**12**), (anisole-d_3)Cr(CO)$_3$, and (*tert*-butylbenzene)Cr(CO)$_3$[40] (**15**) were prepared by using the method described by Mahaffy and Pauson.[41] (Naphthalene)Cr(CO)$_3$[42] (**2**) was prepared as described previously[7a] except for the addition of 10 mL of hexane to the reaction mixture.

[1-4a,8a-η-(5,8-OMe)$_2$C$_{10}$H$_6$]Cr(CO)$_3$ (5).[20] Cr(CO)$_6$ (4.4 g, 20 mmol), 1,4-dimethoxynaphthalene (7.52 g, 40 mmol), dibutyl ether (100 mL), hexane (10 mL), and THF (1 mL) were placed in a 250-mL flask fitted with a wide-bore condenser and a magnetic stirring bar and submitted to three freeze–pump–thaw cycles. The solution was refluxed in the dark for 70 h by means of a 160 °C oil bath. The deep red solution was cooled to 20 °C, diluted with hexane, and placed on dry ice overnight. Decantation of the now pale solution left a red solid which was taken up in hot toluene (80 mL). Filtration over Celite and cooling to −20 °C yielded a single isomer of (5,8-dimethoxynaphthalene)Cr(CO)$_3$[20] as orange-red crystals (5.92 g, 91%) which were washed with hexane in order to free them from traces of dimethoxynaphthalene and vacuum dried: mp 191–193 °C dec (lit.[20] mp 160 °C dec); IR (hexane) 1986 (vs), 1917 (vs) cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.55 (s, 2 H, $H^{6,7}$), 6.47 (m, 2 H, $H^{1,4}$), 5.49 (m, 2 H, $H^{2,3}$), 3.96 (6 H, OMe); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 231.9 (CO), 148.5 ($C^{5,8}$), 103.6 ($C^{6,7}$), 98.5 ($C^{4a,8a}$), 91.6 ($C^{2,3}$), 85.7 ($C^{1,4}$), 56.0 (OMe). Anal. Calcd ($C_{15}H_{12}CrO_5$): C, 55.56; H, 3.73. Found: C, 55.62; H, 3.63.

[1-4a,8a-η-(5,8-OMe-d_3)$_2$C$_{10}$H$_6$]Cr(CO)$_3$ (5-d_6) was prepared analogously from 1,4-dimethoxy-d_6-naphthalene obtained in 43% yield by methylation of 1,4-dihydroxynaphthalene with sodium hydride/methyl-d_3 iodide in THF according to published procedures.[43]

(1,4-OMe-d_3)$_2$C$_{10}$H$_6$: mp 85–86 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.25–8.15 (m, 2 H, $H^{5,8}$), 7.55–7.45 (m, 2 H, $H^{6,7}$), 6.70 (s, 2 H, $H^{2,3}$); ^{2}H NMR (55.29 MHz, $CHCl_3$) δ 3.84 (OCD_3); IR ($CHCl_3$) 3010 (w), 2060 (w), 1610 (w), 1600 (m), 1460 (s), 1425 (w), 1390 (m), 1285 (s), 1245 (m), 1160 (w), 1116 (s), 1081 (w), 1025 (w), 966 (w), 808 (w), 700 (w) cm^{-1}; MS, *m/z* 194 (69), 176 (100), 148 (20), 130 (12), 102 (10), 94 (5), 76 (7); high-resolution MS ($C_{12}H_6{}^2H_6O_2$) calcd 194.1208, found 194.1216.

[1-4a,8a-η-(5,8-OMe-d_3)$_2$C$_{10}$H$_6$]Cr(CO)$_3$ (5-d_6): ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.54 (s, 2 H, $H^{6,7}$), 6.47 (m, 2 H, $H^{1,4}$), 5.49 (m, 2 H, $H^{2,3}$); ^{2}H NMR (55.29 MHz, $CHCl_3$) δ 3.98 (OCD_3); IR ($CHCl_3$) 2930 (w), 2100 (w), 1970 (vs), 1895 (vs), 1620 (w), 1445 (w), 1369 (w), 1288 (m), 1112 (m), 670 (m) cm^{-1}; MS, *m/z* 330 (10), 274 (10), 246 (58), 228 (18), 194 (15), 176 (23), 52 (100); high-resolution MS ($C_{15}H_6{}^2H_6CrO_5$) calcd 330.0460, found 330.0479.

The same alkylation procedure was used to prepare anisole-d_3 ($C_6H_5OCD_3$) from phenol/sodium hydride/methyl-d_3 iodide in 53% yield.

(η^6-C$_6$H$_5$OMe-d_3)Cr(CO)$_3$ (12-d_3): ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.65 (t, 2 H, $H^{3,5}$), 4.30 (d, 2 H, $H^{2,6}$), 3.95 (d, 1 H, H^4); IR (hexane) 1980 (s), 1910 (s), 1530 (w), 1450 (w), 1380 (w), 1215 (w) cm^{-1}; MS, *m/z* 247 (30), 214 (5), 191 (20), 163 (35), 145 (20), 111 (26), 52 (100); high-resolution MS ($C_{10}H_5{}^2H_3CrO_4$) calcd 247.0013, found, 247.0037.

3. Preparation of Carbon Nucleophiles. Freshly prepared solutions of the carbon nucleophiles were used in all experiments. The nucleophiles were generated as follows:

LiC(CH$_3$)$_2$CN (1). A solution of lithium diisopropylamide was prepared by dropwise addition via syringe of *n*-BuLi (0.94 mL of a 1.6 M solution in hexane, 1.5 mmol) to diisopropylamine (0.210 mL, 1.5 mmol) in THF (15 mL) at −50 °C. After 0.3 h at 0 °C, the solution was cooled to −78 °C and 2-methylpropionitrile (0.135 mL, 1.5 mmol) was added dropwise. After being stirred for 0.3 h at 0 °C, this reagent solution was used in the addition reactions described below. The same procedure was used in the preparation of solutions of **LiC(CD$_3$)$_2$CN (1-d_6)**, **LiCH$_2$CN (20)**, **LiCH$_2$COO-*t*-Bu (21)**, and **LiC(CH$_3$)(CN)(OCH(CH$_3$)OCH$_2$CH$_3$) (22)**.[44]

DC(CD$_3$)$_2$CN. 2-Propanol-d_8 was converted to its tosylate and crystallized at −20 °C from ether/hexane (yield 90%). 2-Methylpropionitrile-d_7 was obtained via the procedure described by Simchen and Kobler.[45] The tosylate-d_7 (11.27 g, 51 mmol), $Et_4N^+CN^-$ (8.76 g, 56 mmol) and DMSO (50 mL) were placed into a two-neck flask equipped with a magnetic stirring bar and a condenser and heated at 60 °C for 14 h. The low-boiling materials were vacuum transferred and subsequently distilled at atmospheric pressure. The fraction distilling between 95 and 100 °C was collected, dried over CaH_2, and redistilled to yield 2-methylpropionitrile-d_7 (2.48 g, 64%): isotopic purity >99% (by ^{1}H NMR); bp 100 °C; ^{2}H NMR ($CHCl_3$) δ 2.81 (s, 1 D), 1.44 (s, 6 D); IR ($CHCl_3$) 3025 (s), 2240 (s), 2150 (w), 2120 (w), 2080 (w), 1230 (m), 1160 (w), 1155 (w), 1060 (s) cm^{-1}; MS, *m/z* 76 (4), 74 (95), 58 (40), 56 (14), 54 (18), 52 (10), 48 (78), 46 (100); high-resolution MS ($C_4{}^2H_7N$) calcd 76.1011, found 76.1024.

KC(CH$_3$)$_2$CN. HN(SiMe$_3$)$_2$ (0.270 mL, 1.3 mmol) was added dropwise via syringe to a stirred suspension of KH (0.055 g, 1.4 mmol) in THF (6 mL) at −78 °C. After being stirred for 1 h at 20 °C, the mixture was cooled to −78 °C and 2-methylpropionitrile (0.117 mL, 1.3 mmol) was added. The temperature was maintained at −78 °C and stirring was continued for 0.3 h.

LiCHS(CH$_2$)$_3$S (23) and **LiC(CH$_3$)S(CH$_2$)$_3$S (24)** were prepared following the procedure of Corey and Seebach.[46]

4. General Procedure for Nucleophile Addition/Oxidation Reactions with (Arene)Cr(CO)$_3$ Complexes. A 1-mmol aliquot of the (arene)Cr(CO)$_3$ complex was added in one portion either as a solid, via a solid addition tube, or as a −78 °C solution in THF, via a Teflon transfer tube, to the −78 °C solution of the carbon nucleophile (1–1.1 mmol). When required, *trans*-decalin (GLC standard), HMPA, or TMEDA was then added dropwise while the temperature of the solution was maintained at −78 °C. After the complex and cosolvent (HMPA) had dissolved, which required warming to −60 °C in some cases, stirring was continued for the time and at the temperature indicated before recooling to −78 °C. A cold solution (−78 °C) of 5–6 mmol of I_2 in 10 mL of THF was then added rapidly via transfer tube. After a few minutes, the cooling bath was removed and the reaction allowed to warm up to 20 °C and left at that temperature for ca. 4 h. The mixture was concentrated in vacuo and the crude product taken up in ether (40 mL) and washed sequentially with aqueous $NaHSO_3$ solution (10%, 10 mL), 1 N HCl (10 mL; three portions when cosolvents were used), aqueous $NaHCO_3$ solution (saturated, 10 mL), water (2 × 10 mL), and aqueous NaCl solution (saturated, 10 mL). The organic phase was dried over $MgSO_4$, and ether was removed in a rotavapor to give the crude product.

5. Addition of LiCMe$_2$CN (1) to (Naphthalene)Cr(CO)$_3$ (2). Formation and Characterization of 3 and 4. In THF, 0.25 h, −65 °C: The general procedure was followed (0.5-mmol scale) by adding a 78 °C solution of the complex [prepared by dissolving 134 mg (0.51 mmol) of (naphthalene)Cr(CO)$_3$ (**2**) in 4 mL of cold (<−30 °C) THF][47] to $LiCMe_2CN$ (0.56 mmol) in 6 mL of THF at −78 °C. The homogeneous reaction mixture was stirred at −65 °C for 15 min followed by oxidation. Workup gave 195 mg of an oil which GLC analysis indicated to consist of a 4:1 mixture of **4** and **3** (79% yield). This ratio was confirmed by ^{1}H NMR. Pure **3** and **4** were obtained by preparative TLC [eluent

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hexane/ether 1:1, R_f = 0.33 (4) and 0.44 (3)]. IR and ^{1}H NMR spectra were identical with those of the compounds prepared via double methylation of 1-naphthylacetonitrile and 2-naphthylacetonitrile (see below).

In THF/HMPA (3:1), 0.25 h, −65 °C: Under identical conditions as above except for the addition of HMPA [medium THF/HMPA (3:1)] to the reaction mixture, a 79% isolated yield (GLC yield, 88%) of a mixture of **3** and **4** was obtained. The ratio of **3** and **4** was determined by GLC and ^{1}H NMR to be 2:3.

Synthesis of 3 and 4 via Double Methylation of 2-Naphthylacetonitrile and 1-Naphthylacetonitrile. 3 and **4** were synthesized in 93 and 83% yield by the addition (at −78 °C) of methyl iodide (2.5 equiv) to the reaction mixture obtained from LDA (2.2 equiv) and the naphthylacetonitriles (1 equiv) in THF/HMPA (5:1).

2-(1′-Naphthyl)-2-methylpropionitrile (4):[48,49] ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.56 (d, J = 9 Hz, 1 H), 7.84–7.96 (m, 2 H), 7.44–7.68 (m, 4 H), 1.96 (s, 6 H); IR ($CHCl_3$) 3055 (m), 2990 (m), 2940 (m), 2880 (w), 2238 (m), 1600 (m), 1511 (m), 1459 (m), 1400 (m), 1392 (m), 1370 (m), 1347 (w), 1241 (m), 1200 (m), 800 (s), 778 (s) cm^{-1}; MS, m/z 195 (94), 180 (100), 153 (70), 128 (13), 86 (25), 84 (38), 49 (57); high-resolution MS ($C_{14}H_{13}N$) calcd 195.1048, found, 195.1053. Anal. Calcd ($C_{14}H_{13}N$): C, 86.12; H, 6.71; N, 7.17. Found: C, 85.86; H, 6.74; N, 7.11.

2-(2′-Naphthyl)-2-methylpropionitrile (3):[49] mp 23 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.95 (d, 1 H, $^4J_{meta}$ = 1 Hz), 7.86–7.91 (m, 3 H), 7.49–7.60 (m, 3 H), 1.78 (s, 6 H); IR ($CHCl_3$) 3060 (m), 2985 (s), 2935 (m), 2875 (w), 2240 (m), 1633 (w), 1600 (m), 1507 (s), 1459 (s), 1370 (m), 1274 (m), 1200 (m), 1133 (m), 1089 (w), 1021 (w), 959 (m), 952 (m), 859 (s), 815 (s); MS, m/z 195 (48), 180 (100), 170 (38), 153 (27), 149 (27), 141 (35), 77 (45); high-resolution MS ($C_{14}H_{13}N$) calcd 195.1048, found 195.1052. Anal. Calcd ($C_{14}H_{13}N$): C, 86.12; H, 6.71; N, 7.17. Found: C, 86.00; H, 6.76; N, 7.17.

6. Nucleophile Addition/Oxidation Reactions with (5,8-Dimethoxynaphthalene)Cr(CO)$_3$ (5). (a) Addition of LiCMe$_2$CN to Complex 5. Formation and Characterization of 7 and 9. In THF, 1 h, 0 °C: Following the general procedure, 480 mg (1.48 mmol) of (5,8-dimethoxynaphthalene)Cr(CO)$_3$ (**5**) was added as a solid to a solution of $LiCMe_2CN$ (1.50 mmol) in 10 mL of THF at −78 °C. The reaction mixture was stirred for 1 h at 0 °C before recooling and oxidation. GLC analysis of the crude solid showed two products in the ratio of 99:1. Crystallization of this material from toluene/hexane yielded 263 mg (70%) of colorless crystals of **9**. Chromatography of the mother liquor yielded another 20 mg (5%) of **9** together with a trace of **7**.

2-(5′,8′-Dimethoxynaphth-1′-yl)-2-methylpropionitrile (9): mp 132–133 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.31 (d, 1 H, $^3J_{ortho}$ = 8 Hz, H$^{4'}$), 7.58 (d, 1 H, $^3J_{ortho}$ = 8 Hz, H$^{2'}$), 7.42 (t, 1 H, $^3J_{ortho}$ = 8 Hz, H$^{3'}$), 6.79–6.92 ([AB] q, J = 8 Hz, 2 H, H$^{6',7'}$), 3.98 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 1.94 (s, 6 H, $C(CH_3)_2CN$); IR ($CHCl_3$) 3015 (w), 2965 (w), 2945 (w), 2845 (w), 2235 (w), 1650 (m), 1610 (m), 1464 (s), 1411 (s), 1378 (m), 1367 (m), 1270 (s), 1238 (s), 1118 (m), 1070 (m), 1032 (m) cm^{-1}; MS, m/z 255 (100), 240 (83), 225 (8), 212 (15), 199 (11), 183 (28), 171 (10), 155 (14), 139 (8), 127 (13), 115 (13). Anal. Calcd ($C_{16}H_{17}NO_2$): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.31; H, 6.74; N, 5.51.

In THF, 1 h, −40 °C: The reaction was carried out exactly as before except for the reaction temperature which was −40 °C. Recooling, oxidation, and workup yielded 420 mg of an oil. TLC (eluent toluene/ether 11:1) indicated two products with R_f = 0.45 (**7**) and 0.28 (**9**). Column chromatography on silica gel (eluent toluene/ether 15:1) furnished first 75 mg (20%) of 2-(5′,8′-dimethoxynaphth-2′-yl)-2-methylpropionitrile (**7**) followed by 287 mg (76%) of **9**.

2-(5′,8′-Dimethoxynaphth-2′-yl)-2-methylpropionitrile (7): mp 62.5–64.5 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.31 (d, 1 H, $^4J_{meta}$ = 2 Hz, H$^{1'}$), 8.25 (d, 1 H, $^3J_{ortho}$ = 8.8 Hz, H$^{4'}$), 7.62 (dd, 1 H, $^3J_{ortho}$ = 8.8 Hz, $^4J_{meta}$ = 2 Hz, H$^{3'}$), 6.71–6.78 ([AB] m, 2 H, H$^{6',7'}$), 3.99 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 1.83 (s, 6 H, $C(CH_3)_2CN$); IR ($CHCl_3$) 3005 (m), 2995 (m), 2942 (m), 2842 (m), 2240 (w), 1635 (w), 1605 (s), 1465 (s), 1374 (m), 1365 (m), 1280 (s), 1118 (s), 1092 (s) cm^{-1}; MS, m/z 255 (65), 240 (100), 225 (13), 210 (14), 197 (7), 182 (9), 127 (10), 57 (12). Anal. Calcd ($C_{16}H_{17}NO_2$): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.29; H, 6.78; N, 5.50.

In THF, 1 h, −60 °C: Proceeding as above except for the addition of the complex as a −78 °C solution in THF (12 mL) and stirring the reaction at −60 °C for 1 h before recooling and oxidation yielded after workup and separation 205 mg (54%) of **7** and 132 mg (35%) of **9**.

In THF, 0.1 h, −72 °C: Analogously, oxidation after 6 min of reaction time at −72 °C gave 189 mg (50%) of **7** and 116 mg (31%) of **9**.

In THF/HMPA (2.5:1), 46 h, 0 °C: Under identical conditions as above except for the addition of the complex as a solid followed by the addition of 4 mL of HMPA (medium THF/HMPA 2.5:1) (see general procedure) and a reaction time of 2 days at 0 °C yielded after chromatography 317 mg (84%) of **9**.

From analogous experiments on the same scale and in the same medium [THF/HMPA (2.5:1)] but varying time and temperature, compounds **7** and **9** were isolated as follows. **0 °C/2 h**: 151 mg (40%) of **7** and 135 mg (36%) of **9**. **−40 °C/1 h**: 230 mg (61%) of **7** and 86 mg (23%) of **9**. **−60 °C/0.5 h** (complex **5** added as THF solution): 204 mg (54%) of **7** and 58 mg (15%) of **9**.

(b) Addition of LiCH$_2$CN (20) to Complex 5. Formation and Characterization of 26 and 27. Following the general procedure, 500 mg (1.54 mmol) of the chromium complex **5** was added as a solid to a solution of $LiCH_2CN$ (1.55 mmol in 15 mL of THF and 0.7 mL of HMPA). The reaction was left stirring at −20 °C for 30 h before recooling and oxidation. Workup followed by chromatography on silica [eluent hexane/toluene (1:1), toluene, toluene/ether (8:1)] yielded 246 mg (72%) of **27** as a crystalline material.

(5,8-Dimethoxynaphth-1-yl)acetonitrile (27): mp (ether) 88–89 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.28 (dd, 1 H, $^3J_{ortho}$ = 8 Hz, $^4J_{meta}$ = 2 Hz, H^4), 7.42 (m, 2 H, H^{2,3}) (Dcpl at 8.28 gives an AB quartet at 7.42), 6.75–6.82 ([AB] q, 2 H, J = 9 Hz, H^{6,7}), 4.38 (s, 2 H, CH_2CN), 3.99 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3); IR (CH_2Cl_2) 3010 (w), 2960 (m), 2940 (m), 2840 (m), 2250 (w), 1625 (s), 1600 (s), 1465 (s), 1415 (s), 1405 (s), 1388 (s), 1235 (s), 1203 (m), 1170 (m), 1145 (s), 1115 (s), 1075 (s), 1040 (s), 975 (s), 810 (s) cm^{-1}; MS, m/z 227 (69), 212 (100), 185 (48), 170 (53), 141 (18), 115 (45), 114 (37), 77 (37), 63 (21), 52 (23); high-resolution MS ($C_{16}H_{17}NO_2$) calcd 227.0946, found 227.0940.

Analogously, except for the solvent, which was THF/HMPA (2.5:1), and the reaction conditions (addition at −78 °C, stirring at −50 °C for 1 h before recooling and oxidation) the reaction yielded after column chromatography (silica, toluene, toluene/ether, 9:1) a 3:1 mixture (by ^{1}H NMR) of **27** and **26** in 34% yield.

(5,8-Dimethoxynaphth-2-yl)acetonitrile (26): ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.23 (d, 1 H, $^3J_{ortho}$ = 9 Hz, H^4), 8.19 (br s, 1 H, H^1), 7.44 (dd, $^3J_{ortho}$ = 9 Hz, $^4J_{meta}$ = 1 Hz, H^3), 6.74 ([AB] q, 2 H, J = 8 Hz, H^{6,7}), 3.97 (s, 6 H, 2 OCH_3), 3.93 (s, 2 H, CH_2CN).

GLC analysis of the products of separate reactions in THF at −65 °C (0.5 h) and −20 °C (0.5 h) showed only one addition product, **27** (GLC yield: at −65 °C 40%; at −20 °C 72%).

(c) Addition of LiCH$_2$CO$_2$-*t*-Bu (21) to Complex 5. Formation and Characterization of 28 and 29. As detailed in the general procedure, 480 mg (1.48 mmol) of the chromium complex **5** was added as a solid to a solution of 1.5 mmol of $LiCH_2CO_2$-*t*-Bu in 10 mL of THF, followed by 5 mL of HMPA. After 15 min at −70 °C, the temperature was raised to −5 °C for 30 min before cooling and oxidation. Workup yielded a mixture of **28** (TLC: toluene/ether 8:1; R_f = 0.49) and **29** (R_f = 0.37) in the ratio 1:2 in 89% yield. Separation by chromatography on silica (eluent toluene/ether, 12:1) yielded the pure compounds as crystalline materials: 120 mg (27%) of **28** and 256 mg (57%) of **29**.

In a separate experiment under identical conditions except for the reaction time and temperature, which was 49 h at 0 °C, **29** was the only product obtained after chromatography (377 mg, 84% yield).

(5,8-Dimethoxynaphth-2-yl)acetic acid *tert*-butyl ester (28): mp (hexane) 56–57 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.18 (d, 1 H, $^3J_{ortho}$ = 9 Hz, H^4), 8.10 (d, 1 H, $^4J_{meta}$ = 1.8 Hz, H^1), 7.46 (dd, 1 H, $^3J_{ortho}$ = 9 Hz, $^4J_{meta}$ = 1.8 Hz, H^3), 6.65–6.73 ([AB] q, 2 H, J = 8 Hz, H^{6,7}), 3.95 (s, 6 H, 2 OCH_3), 3.70 (s, 2 H, CH_2), 1.41 (s, 9 H, *t*-Bu); IR ($CHCl_3$) 3010 (m), 2980 (s), 2935 (m), 2875 (m), 1720 (s), 1604 (m), 1463 (s), 1370 (s), 1275 (s), 1245 (m), 1150 (s), 1115 (vs), 1100 (s), 910 (vs) cm^{-1}; MS, m/z 302 (43), 246 (93), 231 (12), 201 (41), 171 (47), 145 (17), 115 (23), 85 (67), 83 (100), 56 (73); high-resolution MS ($C_{18}H_{22}O_4$) calcd 302.1518, found 302.1526.

(5,8-Dimethoxynaphth-1-yl)acetic acid *tert*-butyl ester (29): mp (hexane) 73–74 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.21 (dd, 1 H, $^3J_{ortho}$ = 8.5 Hz, $^4J_{meta}$ = 1.5 Hz, H^4), 7.41 (dd, 1 H, $^3J_{ortho}$ = 7, 8.5 Hz, H^3), 7.24 (br d, 1 H, $^3J_{ortho}$ = 7 Hz, H^2), 6.68–6.75 ([AB] q, 2 H, J = 8 Hz, H^{6,7}), 4.12 (s, 2 H, CH_2), 3.94 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 1.40 (s, 9 H, *t*-Bu); IR ($CHCl_3$) 3010 (m), 2980 (m), 2940 (m), 2840 (w), 1725 (s), 1625 (m), 1600 (s), 1463 (s), 1410 (s), 1390 (s), 1370 (s), 1270 (s), 1240 (vs), 1163 (vs), 1115 (m), 1075 (s), 1045 (s), 980 (w), 845 (w), 806 (w) cm^{-1}; MS, m/z 227 (100), 212 (96), 185 (32), 171 (26), 140 (12), 115 (21), 113 (13); high-resolution MS ($C_{18}H_{22}O_4$) calcd 302.1518, found 302.1513.

(d) Addition of LiC(Me)(CN)(OCH(Me)OEt) (22) to Complex 5. Formation and Characterization of 30 and 31. As detailed in the general procedure, 320 mg (1 mmol) of complex **5** was added in one portion to a solution of 1.1 mmol of **22**[44] in 24 mL of THF. The reaction mixture

(48) (a) Buu-Hoi, N. P.; Cagniant, P. *Compt. Rend.* **1944**, *219*, 455. (b) Julia, M.; Baillargē, M. *Bull. Soc. Chim.* **1957**, 928. (c) Brenner, S.; Bovete, M. *Tetrahedron* **1975**, *31*, 153.

(49) Clark, G. R. Ph.D. Thesis, Cornell University, 1978.

was stirred for 1 h at −55 °C followed by recooling to −78 °C, oxidation, and workup as described. The crude product in ether (40 mL) was stirred for 3.5 h at 25 °C with 20 mL of aqueous H_2SO_4 (10%). The mixture was then neutralized with solid $NaHCO_3$ and the ether layer separated and stirred overnight with 20 mL of aqueous NaOH (10%). The organic phase was washed with aqueous NH_4Cl solution (saturated) and water and dried over $MgSO_4$. Solvent removal yielded 240 mg (54%) of an oil, which ^{1}H NMR showed to contain **30** and **31** in the ratio of 7:3. The two isomers were separated by column chromatography (silica, eluent hexane/ether, 1:1).

A parallel experiment with a longer reaction time (2 h) and at a higher temperature (−10 °C) yielded the α addition product **31** exclusively (70% yield).

6-Acetyl-1,4-dimethoxynaphthalene (30):[50] mp 112 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.84 (d, 1 H, $^4J_{meta}$ = 2 Hz, H^5), 8.27 (d, 1 H, $^3J_{ortho}$ = 9 Hz, H^8), 8.07 (dd, 1 H, $^3J_{ortho}$ = 9 Hz, $^4J_{meta}$ = 2 Hz, H^7), 6.75–6.87 ([AB] q, 2 H, J = 8 Hz, $H^{2,3}$), 4.00 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 2.74 (s, 3 H, CH_3); IR ($CHCl_3$) 3010 (w), 2960 (w), 2940 (w), 2840 (w), 1680 (s), 1630 (m), 1605 (m), 1465 (m), 1368 (s), 1240 (s), 1228 (s), 1110 (s), 1090 (m), 810 (m) cm^{-1}; MS, m/z 230 (68), 215 (100), 200 (2), 187 (14), 172 (9), 157 (11), 144 (3), 129 (8), 115 (11), 101 (15), 75 (13), 63 (8), 57 (4), 51 (4); high-resolution MS ($C_{14}H_{14}O_3$) calcd 230.0943, found 230.0955.

5-Acetyl-1,4-dimethoxynaphthalene (31): ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.28 (d, 1 H, $^3J_{ortho}$ = 8 Hz, H^8), 7.50 (t, 1 H, $^3J_{ortho}$ = 8 Hz, H^7), 7.28 (d, 1 H, $^3J_{ortho}$ = 8 Hz, H^6), 6.76–6.84 ([AB] m, 2 H, $H^{2,3}$), 3.98 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 2.52 (s, 3 H, CH_3); IR ($CHCl_3$) 3005 (w), 2960 (m), 2940 (m), 2860 (w), 2840 (w), 1697 (s), 1640 (m), 1588 (m), 1465 (s), 1410 (m), 1380 (m), 1355 (m), 1255 (vs), 1158 (w), 1110 (m), 1060 (w), 1025 (w), 965 (w), 805 (w) cm^{-1}; MS, m/z 230 (32), 215 (33), 200 (16), 185 (14), 165 (10), 151 (12), 137 (15), 125 (26), 111 (43), 87 (60), 83 (58), 69 (71), 57 (100); high-resolution MS ($C_{14}H_{14}O_3$) calcd 230.0943, found 230.0932.

(e) Addition of $\overline{LiCHS(CH_2)_3S}$ (23) to Complex 5. Formation and Characterization of 32 and 33. A solution of 1,3-dithiane (266 mg, 2.2 mmol) in 20 mL of THF was deprotonated with *n*-BuLi (1.24 mL of a 1.79 M solution in hexane) over a period of 1 h at −78 °C.[46] HMPA (0.7 mL, 4 mmol) and 20 mL of a −50 °C solution of 500 mg (1.5 mmol) of complex **5** in THF were then added. After the reaction mixture was brought to −40 °C, half of the solution was transferred via cannula and placed at 0 °C. After 24 h both solutions were oxidized in the usual manner. The solid crude products were chromatographed on silica (eluent hexane, hexane/diisopropyl ether 10:1) to give mixtures of **32** and **33** in the ratio of 78:22 (−40 °C) and 82:18 (0 °C). Yields were 41% (−40 °C) and 48% (0 °C).

2-(1′,4′-Dimethoxynaphth-6′-yl)-1,3-dithiane (32): ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.32 (d, 1 H, $^4J_{meta}$ = 2 Hz, $H^{5'}$), 8.18 (d, 1 H, $^3J_{ortho}$ = 9 Hz, $H^{8'}$), 7.60 (dd, 1 H, $^3J_{ortho}$ = 9 Hz, $^4J_{meta}$ = 2 Hz, $H^{7'}$), 6.69 (s, 2 H, $H^{2',3'}$), 5.35 (s, 1 H, H^2), 3.93 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.04–3.15 (m, 2 H, $H^{4,6}$), 2.88–2.98 (m, 2 H, $H^{4,6}$), 2.14–2.22 (m, 1 H, H^5), 1.90–2.04 (m, 1 H, H^5); IR ($CHCl_3$) 2980 (m), 2940 (m), 2900 (m), 2840 (w), 1610 (m), 1470 (s), 1370 (m), 1270 (s), 1100 (s), 930 (s), 880 (s), 765 (s); MS, m/z 306 (55), 275 (34), 231 (50), 217 (38), 201 (100), 185 (60), 171 (32), 170 (32), 114 (47); high-resolution MS ($C_{16}H_{18}O_2S_2$) calcd 306.0748, found 306.0733.

2-(1′,4′-Dimethoxynaphth-5′-yl)-1,3-dithiane (33): ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.26 (dd, 1 H, $^3J_{ortho}$ = 8.5 Hz, $^4J_{meta}$ = 1.5 Hz, $H^{8'}$), 7.94 (dd, 1 H, $^3J_{ortho}$ = 7 Hz, $^4J_{meta}$ = 1.5 Hz, $H^{6'}$), 7.47 (dd, 1 H, $^3J_{ortho}$ = 7 Hz, $^3J_{ortho}$ = 8.5 Hz, $H^{7'}$), 6.99 (s, 1 H, H^2), 6.72–6.84 ([AB] q, 2 H, J = 8.5 Hz, $H^{2',3'}$), 3.97 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.03–3.19 (m, 2 H, $H^{4,6}$), 2.88–3.00 (m, 2 H, $H^{4,6}$), 2.12–2.23 (m, 1 H, H^5), 1.88–2.04 (m, 1 H, H^5); IR ($CHCl_3$) 3010 (w), 2970 (m), 2940 (m), 2840 (w), 1600 (m), 1460 (s), 1415 (m), 1370 (m), 1270 (s), 1230 (m), 1100 (m), 755 (m); MS, m/z 306 (63), 232 (100), 217 (88), 201 (47), 173 (24).

(f) Addition of $\overline{LiCMeS(CH_2)_3S}$ (24) to Complex 5. Formation and Characterization of 34. A solution of 2-methyl-1,3-dithiane (221 mg, 1.65 mmol) in 10 mL of THF was deprotonated with *n*-BuLi (0.964 mL of a 1.68 M solution in hexane) over a period of 2 h at −25 °C.[46] To this solution at −78 °C was added 500 mg (1.5 mmol) of complex **5** as a solid followed by 5 mL of HMPA (dropwise). The reaction was then left stirring at 0 °C for 1 h before iodine addition, workup as described above, and chromatography over silica (toluene/hexane 1:1) to give 290 mg (60%) of a single product shown to be **34**.

In a separate experiment, the reaction mixture was stirred for 44 h at 0 °C before oxidation to yield 340 mg (71%) of **34**.

2-Methyl-2-(1′,4′-dimethoxynaphth-6′-yl)-1,3-dithiane (34): mp 130–131 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.77 (d, 1 H, $^4J_{meta}$ = 2 Hz, $H^{5'}$), 8.12 (d, 1 H, $^3J_{ortho}$ = 9 Hz, $H^{8'}$), 8.09 (dd, 1 H, $^3J_{ortho}$ = 9 Hz, $^4J_{meta}$ = 2 Hz, $H^{7'}$), 6.73 (s, 2 H, $H^{2',3'}$), 3.99 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 2.74–2.81 (m, 4 H, $H^{4,6}$), 1.91–1.99 (m, 2 H, H^5), 1.87 (s, 3 H, CH_3); IR (CH_2Cl_2) 3010 (w), 2960 (m), 2940 (m), 2910 (m), 2840 (m), 1643 (m), 1600 (s), 1465 (s), 1360 (s), 1245 (s), 1105 (vs), 1093 (s), 808 (s) cm^{-1}; MS, m/z 320 (38), 246 (100), 231 (65), 213 (10), 201 (31), 59 (38): Anal Calcd ($C_{17}H_{20}O_2S_2$): C, 63.71; H, 6.29; S, 20.01. Found: C, 63.75; H, 6.32; S, 19.84.

(g) Addition of PhLi (25) to Complex 5. Formation and Characterization of 36 and 37. To a cold (−78 °C) solution of 324 mg (1 mmol) of complex **5** in 20 mL of THF and 0.35 mL (2 mmol) of HMPA was added 1.04 mmol of PhLi (0.500 mL of a 2.08 M solution in cyclohexane/ether). The reaction mixture was brought to −40 °C. Half of the solution was transferred via cannula and placed at 0 °C. After 20 h the brown reaction mixtures were oxidized in the usual manner. Workup as described in the general procedure followed by column chromatography (silica, hexane, hexane/diisopropyl ether 10:1) yielded identical mixtures of **36** and **37** (ratio 1:5) in 78% yield.

1,4-Dimethoxy-6-phenylnaphthalene (36): ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.43 (dd, 1 H, $^4J_{meta}$ = 2 Hz, $^5J_{para}$ = 0.6 Hz, H^5), 8.27 (dd, 1 H, $^3J_{ortho}$ = 8.5 Hz, $^5J_{para}$ = 0.6 Hz, H^8), 7.73–7.82 (m, 3 H, $H^{7,phenyl}$), 7.35–7.55 (m, 3 H, H^{phenyl}), 6.76 ([AB] m, 2 H, $H^{2,3}$), 3.99 (s, 6 H, OCH_3); IR ($CHCl_3$) 3010 (w), 2960 (m), 2940 (m), 2840 (w), 1600 (m), 1463 (s), 1422 (m), 1363 (m), 1270 (s), 1236 (s), 1103 (vs), 1088 (m), 807 (m) cm^{-1}; MS, m/z 264 (100), 249 (95), 234 (15), 206 (15), 178 (13), 152 (12), 132 (10), 102 (7).

1,4-Dimethoxy-5-phenylnaphthalene (37): mp 89–90 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.29 (dd, 1 H, $^3J_{ortho}$ = 8.5 Hz, $^4J_{meta}$ = 1.5 Hz, H^8), 7.49 (dd, 1 H, $^3J_{ortho}$ = 8.5 Hz, $^3J_{ortho}$ = 6.5 Hz, H^7), 7.32 (s, 5 H, H^{phenyl}), 7.27–7.36 (m, 1 H, H^6), 6.68–6.80 ([AB] q, 2 H, J = 8.5 Hz, $H^{2,3}$), 3.99 (s, 3 H, OCH_3), 3.39 (s, 3 H, OCH_3); IR ($CHCl_3$) 2960 (m), 2925 (s), 2855 (m), 1619 (w), 1593 (w), 1463 (s), 1407 (m), 1258 (vs), 1111 (w), 1093 (m), 1055 (w), 1011 (w), 967 (w), 822 (w), 807 (w), 768 (m), 704 (m) cm^{-1}; MS, m/z 264 (100), 249 (47), 233 (35), 218 (78), 205 (32), 189 (38), 176 (17), 152 (21), 116 (44), 95 (32), 76 (41); high-resolution MS ($C_{18}H_{16}O_2$) calcd 264.1150, found 264.1147.

7. Kinetics of the Rearrangement of 6 to 8. Kinetic experiments were carried out with 0.04 M solutions of mixtures of **6** and **8** prepared at −70 °C from 1.5 mmol of complex **5** as described above. A sample was removed and oxidized to establish the yield and initial distribution of the products. The stock solution was then placed in a bath held constant (±0.5 °C) at the required temperature. The temperature was measured by a thermometer immersed in the reaction mixture. At intervals, samples (3 mL) were removed and transferred rapidly via a precooled cannula to a −78 °C solution of I_2 in THF. After 4–6 h at room temperature, the products were extracted as described above and the ether solutions were analyzed by GLC using *trans*-decalin as internal standard. Typically, the reactions were monitored to greater than 2 half-lives and five to nine samples were taken in each experiment. This procedure was used in the four sets of kinetic experiments shown in Table III. All kinetic plots displayed good to excellent linearity with correlation coefficients of 0.992 to 0.999. Initial yields of **6** and **8** were in the range 77–99%. Quantitative GLC analysis with the OV 225 column was carried out with a temperature program. With an initial oven temperature of 100 °C (1 min) and a final temperature of 265 °C (gradient, 24 °C/min) and a flow rate of 40 mL/min (carrier gas N_2) retention times were as follows: *trans*-decalin, 3 min; 1,4-dimethoxynaphthalene, 7.5 min; 7, 21 min; 9, 22 min.

8. Crossover Experiments with (5,8-Dimethoxynaphthalene)Cr(CO)$_3$ (5). (a) Addition of (Benzene)Cr(CO)$_3$ (10) to Intermediates 6 and 8. A 0.06 M solution of **6** and **8** in THF/HMPA (3:1) was prepared in the usual manner with 1 mmol of complex **5**. *trans*-Decalin was added as GLC standard, and the solution was left overnight at −60 °C. GLC analysis of a sample removed at this point showed **6** and **8** to be present in the ratio 76:24 (GLC yield 92%); 214 mg (1 mmol) of (benzene)Cr(CO)$_3$ (**10**) was then added at −78 °C as a solid in one portion. After dissolution of the solid (5 min), the mixture was placed in an ice/water bath. Over a 30-h period, seven samples (3 mL each) were removed, oxidized, worked up as described above, and analyzed quantitatively by GLC. First-order kinetics were observed and linear plots were obtained for the decrease in **6** and the increase in 2-phenyl-2-methylpropionitrile.[2g] The concentration of **8** remained constant (±4%) over the entire period.

Proceeding as above except for stirring the reaction at 0 °C for 70 min prior to recooling to −78 °C and adding complex **10** and HMPA afforded **9** exclusively in 92% yield (GLC).

In a separate experiment, 0.5 mmol of each of the complexes **5** and **10** was added simultaneously at −78 °C to 1.05 mmol of the nucleophile **1** in THF/HMPA (3:1). After 1 h at −60 °C, the reaction was worked

(50) Rama Rao, A. V.; Deshpande, V. H.; Laxma Reddy, N. *Tetrahedron Lett.* **1982**, *23*, 4373.

up as usual and analyzed by GLC. A 96% yield (GLC) of a mixture consisting of **7** (15%), **9** (29%), and 2-phenyl-2-methylpropionitrile (52%) was obtained.

(b) Addition of Complex 5 to a Solution of the Cyclohexadienyl Complex 11. **5** (324 mg, 1 mmol) and HMPA (6 mL) were added at −70 °C to a solution of the cyclohexadienyl complex **11**,[28] prepared by addition of 214 mg (1 mmol) of complex **10** to 1.05 mmol of nucleophile **1** in 18 mL of THF. After the addition of **5**, the mixture was stirred at 0 °C for 21 h before oxidation and workup as usual. GC analysis showed exclusively 2-phenyl-2-methylpropionitrile and 1,4-dimethoxynaphthalene.

(c) Double Crossover Experiments with 6 and 6-d_{12}. Double crossover experiments were realized with 0.08 M solutions of **6**-d_{12} and **8**-d_{12} (hereafter called A), which were prepared from deuterium-labeled complex **5**-d_6 and nucleophile **1**-d_6, and corresponding solutions of unlabeled **6** and **8** (hereafter called B). Before and after mixing solutions A and B samples were removed at −70 °C, which served to establish the yield (GLC) and the initial distribution of the products (high-resolution MS).

In THF, 0 °C. Initial composition of A: **6**-d_{12}, 66%; **8**-d_{12}, 31%. Initial composition of B: **6**, 63%; **8**, 35%. Equal volumes of A and B were mixed at −70 °C. The reaction flask was placed in an ice/water bath for 35 min before recooling the solution, oxidation, and workup as described above. GLC analysis showed, besides 3% dimethoxynaphthalene (**5** and **5**-d_6), exclusively **2-(5′,8′-dimethoxynaphth-1′-yl)-2-methylpropionitrile** (9, 9-d_6, 9-d_{12}): 97% yield (GC); MS, m/z 267 (22), 261 (50), 255 (27). Estimated accuracy of relative intensities, 10%.

In THF/HMPA (3:1), 0 °C. Initial composition of A: **6**-d_{12}, 75%; **8**-d_{12}, 22%. Initial composition of B: **6**, 73%; **8**, 21%. (HMPA was added dropwise to the solutions of the nucleophiles **1** and **1**-d_6 prior to the addition of the complexes **5** and **5**-d_6.) After mixing equal volumes (10 mL) of A and B at −70 °C, the temperature of the solution was brought to 0 °C. GLC and high-resolution MS analysis of a sample indicated the mixture at this point to contain **6**, **8**, **6**-d_{12}, and **8**-d_{12} in the ratio 41:12:37:10 (The deviations from an exact 1:1 mixture of unlabeled and doubly labeled compounds can be traced back to the slightly different yield and composition of the solutions A and B as well as to small differences in volumes mixed). Over a period of 55 h, five samples were removed, oxidized, and worked up as usual. Product yields determined by quantitative GLC analysis for all samples were in the range 90–94%. Analysis by high-resolution MS of the last sample (after 5 days at 0 °C), which by GLC contained exclusively 9 (9, 9-d_6, 9-d_{12}) (84%), yielded relative intensities for 9, 9-d_6 and 9-d_{12} (obsd. mass 255.1422, 261.1719, 267.2021) of 34:36:30. Calculated final relative intensities assuming only **6** and **6**-d_{12} to undergo reaction are 32.5:39:28.5.

In THF, 0 °C. Determination of k_{-2} in Equation 4. The solutions A and B, prepared in the usual manner, were stirred at 0 °C for 30 min. At −78 °C the solution, now containing only **8**-d_{12} and **8**, respectively, were mixed and brought to −30 °C. Over a period of 6.5 h, seven samples were removed and analyzed by GLC and high-resolution MS. Straight-line plots (correlations, 0.991 and 0.992) were observed for the decrease of **8** (m/z 255.1280) and increase of **8**-d_6 (m/z 261.1681) assuming the rate expression $\ln (A_0 - A_\infty)/(A_t - A_\infty) = 2k_{obsd}t$. Rate constants obtained for the two plots were 2.01 and 2.03 × 10^{-5} s^{-1} at −30 °C.

9. Nucleophile Addition/Oxidation Reactions with (Anisole)Cr(CO)$_3$ 12. (a) Regioselectivity: The general procedure was followed by adding 244 mg (1 mmol) of complex **12** to the −78 °C solution of the nucleophile **1** to give the addition product **13**. The homogeneous reaction mixture was stirred at −60 °C for 10 min and then oxidized. GLC analysis of the crude mixture indicated a single addition product. Workup gave an 86% yield of **14**. Analogous experiments on the same scale but varying time and temperature gave the following yields of **14**: 63% (THF/HMPA 3:1, 0 °C, 18 h); 83% (THF, −60 °C, 10 min); 72% (THF, 0 °C, 2.5 h). GLC analysis of the crude product showed in all cases 1–2% of a second product, tentatively identified by its NMR spectrum as the ortho addition product.

2-(3′-Methoxyphenyl)-2-methylpropionitrile (14): ^{1}H NMR (200 MHz, C_6D_6) δ 7.28 (dt, 1 H, $^3J_{ortho}$ = 8 Hz, $^5J_{para}$ = 0.5 Hz, H$^{5'}$), 7.03 (ddd, $^3J_{ortho}$ = 8 Hz, $^4J_{meta}$ = 2 Hz, $^4J_{meta}$ = 1 Hz, H$^{4'}$), 6.98 (dt, 1 H, $^4J_{meta}$ = 2 Hz, $^5J_{para}$ = 0.5 Hz, H$^{2'}$), 6.82 (ddd, $^3J_{ortho}$ = 8 Hz, $^4J_{meta}$ = 2 Hz, $^4J_{meta}$ = 1 Hz, H$^{6'}$), 3.80 (s, 3 H, OCH_3), 1.69 (s, 6 H, C-$(CH_3)_2$CN); IR ($CHCl_3$) 3015 (m), 2985 (m), 2937 (w), 2835 (w), 2232 (w), 1601 (s), 1585 (s), 1485 (s), 1461 (m), 1433 (m), 1293 (s), 1263 (vs), 1048 (s), 700 (s) cm^{-1}; MS, m/z 175 (54), 160 (100), 133 (23), 108 (12), 77 (12); high-resolution MS ($C_{11}H_{13}NO$) calcd 175.0997, found 175.0997.

(b) Double Crossover Experiment with 13 and 13-d_9. Kinetics of LiCMe$_2$CN Exchange. Two 0.012 M solutions of **13** and **13**-d_9 in THF were prepared separately. GLC analysis of samples removed and oxidized showed 97% addition for **13** and 95% addition for **13**-d_9. The solutions (2 × 12 mL) were mixed at −78 °C, and the flask was placed in a thermostated bath at −30 °C. Fractions were transferred via a precooled cannula and oxidized as described in section 7. GLC and high-resolution MS analysis of the samples gave the results listed in Table IV.

The rates for the decrease in the cyclohexadienyl complexes **13** and **13**-d_9 and increase in **13**-d_3 and **13**-d_6 were calculated from the values from samples 1–5. A typical plot is shown in Figure 2.

10. Nucleophile Addition/Oxidation Reactions with (*tert*-Butylbenzene)Cr(CO)$_3$ (15). Following the general procedure, 270 mg (1 mmol) of (*tert*-butylbenzene)Cr(CO)$_3$ was added to 1.1 mmol of LiCMe$_2$CN in 12 mL of THF. After 50 min at −70 °C, the mixture was oxidized. GLC and ^{1}H NMR analysis showed the crude product (0.195 g) to consist of a 1:1 mixture of two isomers of the 2-methyl-2-propionitrile addition product. They were separated by preparative GLC and identified as **17** and **19**.

2-(3′-*tert*-Butylphenyl)-2-methylpropionitrile (17):[32] ^{1}H NMR (360 MHz, CD_2Cl_2) δ 7.52 (dt, 1 H, $^4J_{meta}$ = 1.8 Hz, $^5J_{para}$ = 0.6 Hz, H$^{2'}$), 7.38 (dt, 1 H, $^3J_{ortho}$ = 7.5 Hz, $^4J_{meta}$ = 1.8 Hz, H$^{4' \text{ or } 6'}$), 7.33 (dt, 1 H, $^3J_{ortho}$ = 7.5 Hz, $^5J_{para}$ = 0.6 Hz, H$^{2'}$), 7.29 (dt, 1 H, $^3J_{ortho}$ = 7.5 Hz, $^4J_{meta}$ = 1.8 Hz, H$^{4' \text{ or } 6'}$), 1.73 (s, 6 H, C$(CH_3)_2$CN), 1.35 (s, 9 H, C$(CH_3)_3$); IR ($CHCl_3$) 3020 (m), 2980 (s), 2910 (w), 2860 (w), 2250 (w), 1600 (m), 1490 (m), 1460 (m), 1370 (m), 1240 (m), 800 (w), 710 (s) cm^{-1}; MS, m/z 201 (6), 186 (100), 159 (12), 115 (10), 91 (17); high-resolution MS ($C_{14}H_{19}N$) calcd 201.1517, found 201.1507.

2-(4′-*tert*-Butylphenyl)-2-methylpropionitrile (19):[32] ^{1}H NMR (360 MHz, CD_2Cl_2) δ 7.40–7.46 ([AB] m, 4 H, H$^{2',3',5',6'}$), 1.71 (s, 6 H, C$(CH_3)_2$CN), 1.32 (s, 9 H, C$(CH_3)_3$); IR ($CHCl_3$) 3030 (m), 2980 (s), 2910 (m), 2880 (m), 2240 (w), 1520 (m), 1460 (m), 1410 (w), 1370 (m), 1275 (w), 1130 (m), 1020 (w), 840 (s) cm^{-1}; MS, m/z 201 (8), 186 (100), 158 (10), 91 (13); high-resolution MS ($C_{14}H_{19}N$) calcd 201.1517, found 201.1515.

In a separate experiment aliquots were removed at −30 °C (see Table V). GLC analysis of six samples taken over a period of 1 h was used to determine the rates of dissociation of **1** from **16** and **18**.

In THF/HMPA (3:1) **17** and **19** were obtained in the proportions 48:52 after 2 h at −55 °C and 32:68 after 66 h at 0 °C (77% yield).

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