Mechanistic Studies on the Reaction of Fischer Carbene Complex with Alkynes: Does the Alkyne Insertion Intermediate Form Irreversibly?

Marcey L. Waters,[1] Mary E. Bos, and William D. Wulff*

Contribution from the Searle Chemistry Laboratory, Department of Chemistry, University of Chicago, Chicago, Illinois 60637

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Abstract: The regioselectivity of the formation of three different products from the reaction of 1-phenylpropyne with (methoxy)(2-methoxyl-1-phenyl)methylene pentacarbonyl chromium **12** was examined in detail. The phenol product is formed with a substantial regioselectivity which is temperature-dependent, but the indene products (obtained as two compounds: indene and indenone) are formed as a nearly equal mixture of regioisomers. The proportion of indene and phenol products is dependent on the concentration with greater amounts of phenol products being formed at higher concentrations. The total regioselectivity of all of the products is also a function of the concentration. This result could be due either to an equilibrium of the η^1,η^3-vinyl carbene intermediates in this reaction or to a change in mechanisms in the formation of the η^1,η^3-vinyl carbene intermediates from one involving a dissociative incorporation of the alkyne to one involving an associative incorporation of the alkyne. Kinetic studies reveal that at 45 °C and at 0.5 M (but not 0.0001 M) the reaction is bimolecular with a first-order dependence on both the carbene complex and the alkyne. However, at 90 °C the reaction is first-order in carbene complex and zero-order in alkyne over the concentration range of 0.05–0.005 M where the total regioselectivity changes from 2.5:1.0 to 1.5:1. This observation constitutes the first experimental evidence for the equilibration of regioisomeric vinyl carbene intermediates during the benzannulation reaction. This equilibration could occur as a result of a deinsertion of the alkyne or via a cyclopropene intermediate. Finally the generality of the unprecedented bimolecular reaction of complex **12** with 1-phenylpropyne at high concentrations was examined for the reaction methoxy(phenyl)methylene pentacarbonyl chromium **28** with diphenylacetylene and phenylacetylene at 0.5 M, and it was found that both reactions are first-order in carbene complex only.

The reaction of Fischer carbene complexes with alkynes to give substituted phenols is the most important reactions of this class of carbene complexes in organic synthesis.[2] The determination of the mechanism of this reaction thus will be important in synthetic planning, yet this is by no means the only driving force for the study of this mechanism. Since the reaction assembles three different components in a single step and since a large number of structurally different products can be formed in the reaction under only slightly modified conditions, the complexity of the reaction manifold is rivaled by few reactions. The obvious challenges presented in understanding this reaction have attracted both experimentalists and theorists. A summary of the current understanding of the reaction of α,β-unsaturated Fischer carbene complexes with alkynes is presented in Scheme 1.

The first and rate-limiting step of the reaction was long ago proposed by Dötz et al. on the basis of kinetic studies to be a

carbon monoxide dissociation from the starting carbene complex to give the 16 e$^-$ electron unsaturated species **3**.[3] Subsequent reaction with the alkyne was proposed to give the vinyl carbene complex intermediate **4**. Recently, this view has been called into question by a theoretical study by Sola and co-workers, which concluded that the first step is an insertion of the alkyne to give the pentacarbonyl species **2** and then a rate-limiting loss of CO to give the unsaturated vinyl carbene complex **4**.[4] However, this inconsistent with the kinetic studies of Dötz et al., which clearly demonstrated that the first step was CO loss and that the second step was dependent on the alkyne concentration.[3] The vinyl carbene or alkyne insertion product has been suggested to exist in a number of different forms. It was first suggested by us in 1987 that the alkyne insertion product **4** may exist as the 18 e$^-$ η^1,η^3-vinyl carbene complex **5**.[5] Subsequently, extended Hückel calculations by Hoffman and co-workers found that **4** and **5** are of comparable energy, and they also ruled out a metallacyclobutene intermediate as a precursor to **5**.[6] There have been two recent density functional calculations (DFT) performed, and the one by Hess and co-workers[7] found that **5** is more stable than **4**, whereas the one by Sola and co-workers

(1) ACS Organic Division Fellow 1995–1996 (John Wiley & Organic Reactions).

(2) For reviews on the synthetic applications of Fischer carbene complexes, see: (a) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (b) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Vol 12. (c) Hegedus, L. S. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Vol 12. (d) Doyle, M. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Vol 12. (e) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271.
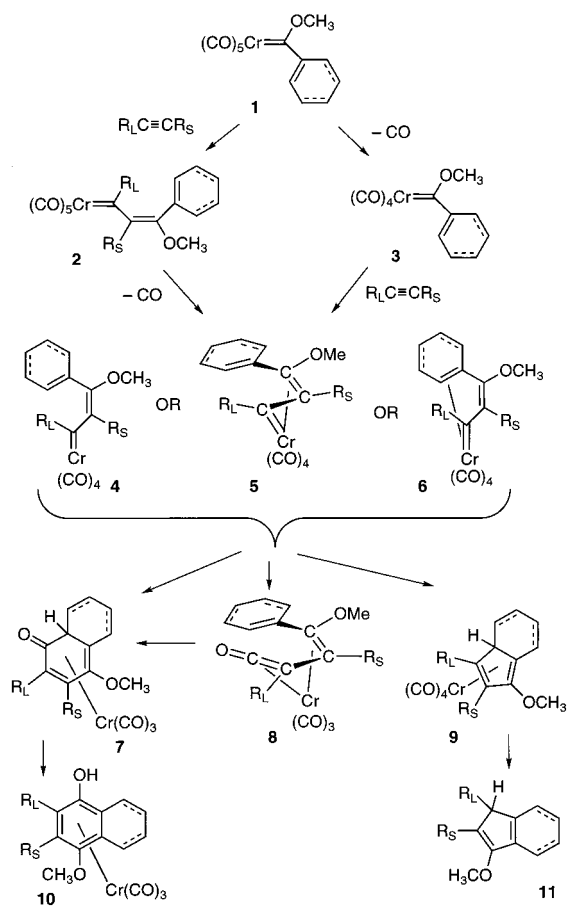
(3) Dötz, K. H.; Fischer, H.; Mühlemeier, J.; Märkl, R. *Chem. Ber.* **1982**, *115*, 1355.

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(5) Chan, K. S.; Peterson, G. A.; Brandvold, T. A.; Faron, K. L.; Challener, C. A.; Hyldahl, C.; Wulff, W. D. *J. Organomet. Chem.* **1987**, *334*, 9–56.
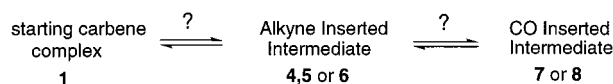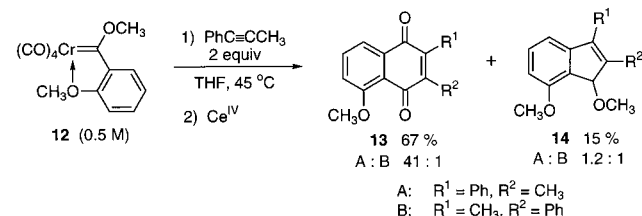
Scheme 1

found that **4** is more stable than **5**.[8] Barluenga[9] provided spectral evidence for the structure **6** involving coordination to the distal double bond, and the recent DFT calculation by Sola finds that **6** is more stable than either **4** or **5**.[8] The insertion of the CO was originally proposed by Dötz to occur to give the η^4-vinyl ketene complex **8** which upon electrocyclic ring closure and tautomerization gave the observed phenol complexes **10**.[10] The DFT studies reveal that this is the case for aryl complexes,[7] but for alkenyl carbene complexes there was no local minimum for the vinyl ketene complex but rather CO insertion and electrocyclic ring closure occurred in the same step.[7,8]

In terms of carbon–carbon bond formation, the two main events in the reaction are the alkyne insertion and the CO insertion. Information about the rates and reversibility of these processes have been hard to come by due to a rate-limiting CO dissociation followed by rapid conversion to product, which is consistent with the difficulty in detection of reaction intermediates.[11] The DFT study by Hess and co-workers suggests that both steps should be irreversible,[7] and the DFT study by Sola

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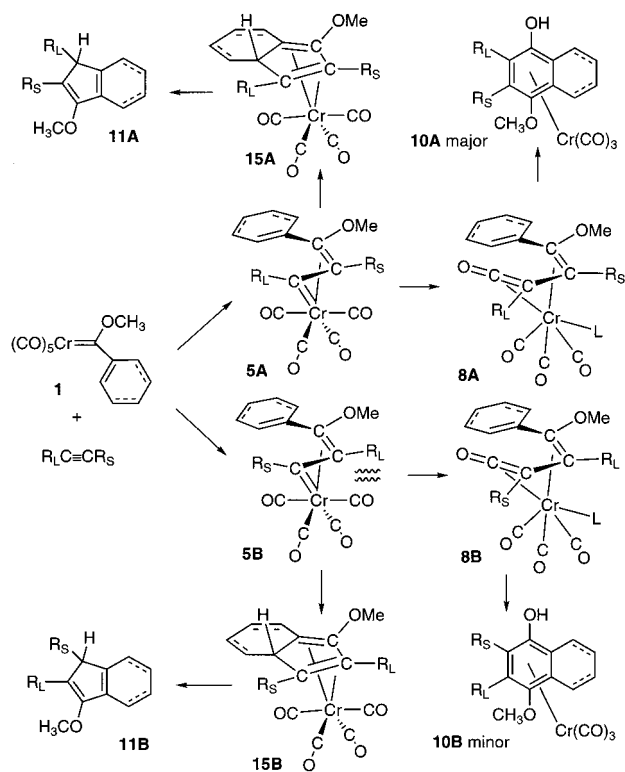(7) Gleichmann, M. M.; Dötz, K. H.; Hess, B. A. *J. Am. Chem. Soc.* **1996**, *118*, 10551.

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(9) Barluenga, J.; Aznar, F.; Martin, A.; Garcia-Granada, M. S.; Perez-Carreno, E. *J. Am. Chem. Soc.* **1994**, *116*, 11191.

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(11) (a) Foley, H. C.; Strubinger, L. M.; Targos, T. S.; Geoffroy, G. L. *J. Am. Chem. Soc.* **1983**, *105*, 3064. (b) Knorr, J. R.; Brown, T. L. *Organometallics* **1994**, *13*, 2178.

Scheme 2

Scheme 3

and co-workers suggests the alkyne insertion should be irreversible but this information on the CO insertion step was not provided.[8] Energy barriers to reactions are underestimated by pure density functional calculations, but the relative energy of the barriers should be more reliable. In previous work we had experimentally determined that, in the reaction of a 2- furyl carbene complex with 1-pentyne, at least one of these steps must be irreversible (Scheme 2).[12] This work was initiated in an effort to determine whether both of the steps are irreversible or, if not, which of the steps is reversible.

Background

The genesis of the present study was the observation that the quinone and indene products from the reaction of complex **12** with 1-phenylpropyne were formed with different levels of regioselectivity (Scheme 3). In this reaction, an oxidative workup with cerium (IV) ammonium nitrate is used to remove the metal from the product which concurrently oxidizes the naphthol to the naphthoquinone. The naphthol chromium tricarbonyl products are air sensitive, and thus, precise determination of the yield by isolation is usually difficult. The o-methoxyl group was used as a method to preserve the regiochemical information in the naphthol product. The quinone **13** was isolated in 67% yield and obtained as a 41:1 mixture of regioisomers with the major isomer having the phenyl group of the alkyne incorporated adjacent to the CO derived carbonyl (R_L in **10**, Scheme 1). The indene was isolated in 15% yield as a 1.2:1 mixture of isomers in which the major isomer corresponds to the major isomer of the quinone. It was quite surprising to find that the regiochemistry of the two products would be different despite the fact that the regiochemistry of indene formation has never been carefully examined for alkoxy chromium complexes.[13–16] From the mechanism proposed for the formation of these two products (Scheme 4), it seemed reasonable that both products would be formed with the same level of regioselectivity and perhaps this is why an investigation of the regioselectivty of indene formation has never been carried out.

The branch point between indene and phenol products is most often proposed to be the alkyne insertion intermediate which is drawn as the η^1,η^3-vinyl carbene complex **5** in Scheme 4.[15,17]

(12) McCallum, J. S.; Kunng, F.-A.; Gilbertson, S. R.; Wulff, W. D. *Organometallics* **1988**, *7*, 2346.

(13) The reaction of an aryl complex with 1-pentyne has been reported to give a 3.3:1 mixture of indene isomers.[14]

(14) Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293.

(15) Indene formation with 1-phenylpropyne has been reported to give a single regioisomer with an amino carbene complex: Yamashita, A. *Tetrahedron Lett.* **1986**, *27*, 5915.

(16) Indene formation with 1-phenylpropyne has been reported to give a single regioisomer with a tungsten complex.[11a]
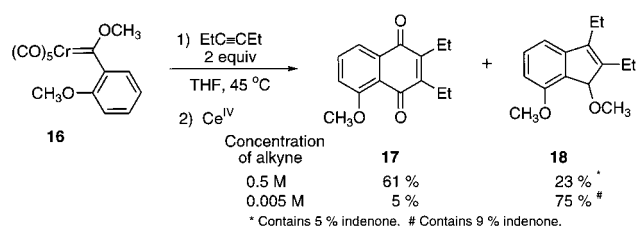
Scheme 4

Scheme 5

For reasons of brevity, alternative schemes with structures **4** and **6** will not be presented but are of course possible. Cyclization of **5** produces the isoindene **15** which upon 1,5-hydrogen shift and loss of the metal gives the indene product which is different in molecular weight from the naphthol product by the 28 mass units of a carbon monoxide molecule. In addition to the direct cyclization of **5** shown here, it is also possible that the formation of **15** occurs in a two-step process involving a chromacyclohexadiene intermediate.[17]

The regioselectivity difference for the indene and quinone products from the reaction of complex **12** was unexpected and has not been previously studied. The regiochemistry of naphthol formation is known[18] to be mainly a function of the steric difference between the two substituents on the alkyne, although electronic effects can be significant in certain cases.[19] One explanation for the direction of the regioselectivity of naphthol formation that has been put forth involves the η^1,η^3-vinyl carbene-complexed intermediate **5**. From a calculated structure of **5**, it was found that the C-2 substituent is about 1 Å closer to it's nearest CO ligand than is the C-1 substituent.[6a] The largest substituent on the alkyne (R_L) thus can be more easily accommodated at the C-1 position in **5A** than the C-2 position in **5B**. This results in a preference for the intermediate **5A** over **5B** and in a preference for the formation of the isomer **10A**. The unexpected regioselectivity in the formation of the indenes **11A** and **11B** (Scheme 3) could be accounted for by a difference in rate for the CO insertion and the electrocyclic ring closure

that is not the same for the major isomer **5A** as it is for the minor isomer **5B** (Scheme 4). One possibility for this is that the rate for CO insertion is the same for each intermediate while the rate for cyclization is slower for **5A** than it is for **5B** due to the more severe close contacts experienced by the large substituent (R_L = phenyl) in **5A** than for the small substituent (R_S = methyl) in **5B**. The fact that **11B** is not a predominate product could be due to a greater proportion of **5A** relative to **5B** in solution.

Further complicating the mechanistic picture is our previous observation that the ratio of indene and naphthol products can be controlled by variations in the concentration of the alkyne.[14] This is illustrated by the example in Scheme 5, where the reaction of the carbene complex **16** with 3-hexyne can give either quinone **17** or indene **18** as the major product by simply changing the concentration. This effect was found to be dependent on the concentration of the alkyne and not on the concentration of the carbene complex. This effect was termed the allochemical effect and was intended to mean a reaction for which the product distribution is affected by a process that involves the interaction of a molecule of one of the substrates with a chemical intermediate of the reaction that has already had a molecule of that substrate covalently incorporated and that this interaction leads to a change in the distribution of products all of which have the first, but not the second, molecule of substrate covalently incorporated.

All of this suggested to us that regioselectivity could be used as a label to determine if the η^1,η^3-vinyl carbene-complexed intermediate is formed reversibly or not. If the regioisomeric vinyl carbene intermediates **5A** and **5B** are formed irreversibly, then the total regiochemistry of the reaction would be fixed. Variation of the concentration to produce different amounts of indene and naphthol products would result in an invariant ratio of the A isomers to the B isomers. On the other hand, if **5A** and **5B** are formed reversibly or can otherwise equilibrate, then the total regiochemistry of the reaction, calculated from the amounts of the major and minor isomers of the indene and naphthol products, could change as the ratio of the indene and naphthol products changes. The ability to conclude that an observation of a change in concentration leading-to-different ratios of indene and naphthol products and thus to a change in total regiochemistry means that the vinyl carbene-complexed intermediates are formed reversibly or are otherwise in equilibrium requires that there is no change in mechanism as the concentration is changed. For example, the bimolecular reaction of **1** with alkyne to give **2** may occur with a different regiochemistry than the reaction of the alkyne with the intermediate **3** generated from **1** by a rate-limiting loss of CO. Thus kinetic studies will be required over the concentration ranges examined to determine if a change in mechanism occurs. The previous kinetic study that has been performed on this reaction indicates that the reaction is first-order in carbene complex and zero-order in alkyne; however, this study was only done at one concentration.[3]

(17) Casey, C. P. In *Reactive Intermediates*; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1981; Vol. 2, p 155.

(18) (a) Wulff, W. D.; Tang, P. C.; McCallum, J. *J. Am. Chem. Soc.* **1981**, *103*, 7677. (b) Dötz, K. H.; Mühlemeier, J.; Schubert, U.; Orama, O. *J. Organomet. Chem.* **1983**, *247*, 187. (c) Yamashita, A.; Toy, A. *Tetrahedron Lett.* **1986**, *27*, 3471.

(19) (a) Chamberlin, S.; Waters, M. L.; Wulff, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3113. (b) Brandvold, T. A.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1991**, *113*, 5459. (c) Brandvold, T. A.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 1645.

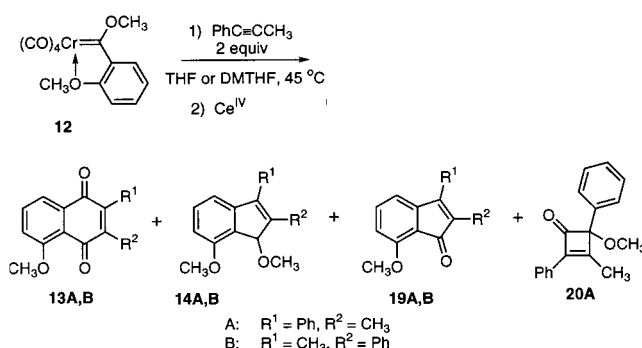**Table 1.** Regioselectivity of the Reaction of Complex 12 with 1-Phenylpropyne[a]

entry	run	temp (°C)	[12] (M)	[alkyne] (M)	PPh₃ (equiv)	% yield 13	(A/B)[b]	% yield 14	(A/B)[c]	% yield 19	(A/B)[c]	% yield 20A[c]	Σ % yield	Σ A/B[d]
1	1	45	0.5	1.0		73	≥35:1.0	11	1.0:1.0	~3[e]	1.0:1.0	~7[e]	~94	9.4:1.0
2	2	45	0.5	1.0		67	41:1.0	15	1.2:1.0	0		7	89	9.6:1.0
3	1	45	0.005	0.01		25	≥48:1.0	43	1.1:1.0	9	1.5:1.0	0	77	2.1:1.0
4	2	45	0.005	0.01		21	49:1.0	62	1.0:1.0	13	1.0:1.3	0	96	1.5:1.0
5	1	45	0.5	1.0	2	29	≥27:1.0	24	1.0:1.5	4	1.6:1.0	15	72	3.3:1.0
6	1	45	0.005	0.01	2	13	≥35:1.0	67	1.2:1.0	6	1.2:1.0	2	88	1.7:1.0
7	1	90	0.05	0.1		35.5	18.6:1.0	56.7	1.3:1.0	3.9	1.0:1.1		96.1	2.4:1.0
8	2	90	0.05	0.1		32.7	17.6:1.0	62.0	1.3:1.0	1.8	1.0:1.0		96.5	2.3:1.0
9	1	90	0.05	0.01		4.6	17.2:1.0[f]	76.1	1.4:1.0	9.0	1.0:1.2[f]		89.7	1.4:1.0
10	2	90	0.005	0.01		5.3	19.9:1.0[f]	71.7	1.4:1.0	9.4	1.0:1.0[f]		86.4	1.5:1.0
11	1	90	0.05	0.1	2	16.6	15.8:1.0[e]	68.5	1.3:1.0	2.4	1.0:1.1[e]		87.5	1.7:1.0
12	1	90	0.005	0.01	2	7.9	18.7:1.0[e]	81.2	1.3:1.0	4.9	1.0:1.6[e]		94.0	1.4:1.0

[a] Unless otherwise specified, all yields are for isolated products by column chromatography on silica gel. The solvent at 45 °C is THF and at 90 °C it is 2,5-dimethyltetrahydrofuran (DMTHF). [b] Ratio determined by GC (average of 3 determinations). [c] Ratio determined by ¹H NMR. [d] Ratio of the sum of the yields of the A isomers of products **13**, **14**, **19**, and **20** to that of the sum of the B isomers. For those entries where the ratio of **13A** to **13B** was determined as a minimum, the minimum value is used to calculate the yields of **13A** and **13B**. [e] The product could only be isolated in 80−90% purity from these reactions. [f] Yields determined by ¹H NMR integration using Ph₃CH as an internal standard.

In our previous studies on the mechanism of the allochemical effect, we provided evidence that the point at which the alkyne affected the product distribution was after the first alkyne inserted and after the η^1,η^3-vinyl carbene-complexed intermediate **5** was formed. Specifically, it was proposed that the higher proportion of quinone product at higher concentration was due to an interaction of the alkyne with the unsaturated form of the alkyne insertion product (**4**), which results in an increase in the rate of CO insertion relative to the rate of cyclization to a five-membered ring. This is supported in the present work by kinetic studies (vide infra) which show that a significant allochemical effect can be seen under conditions in which the order of the reaction in alkyne does not change. Moreover, the kinetic studies to be described in this work reveal that there is no change in mechanism under conditions where it was found that the total regiochemistry of the reaction does change.

Results

The distribution between phenol and indene products is known to be a function of both concentration and temperature where lower concentration and higher temperatures favors indene formation.[5,14] Thus the regioselectivity of product formation from the reaction of complex **12** with 1-phenylpropyne was examined as a function of concentration at 45 and 90 °C, and the results are presented in Table 1. The chelated complex **12** was used rather than the nonchelated complex **16** to simplify the analysis. Either could be used since both complexes give the same distribution between phenol and indene products[14] due to the fact that complex **16** undergoes conversion to **12** during the course of the reaction. The assignments of the regiochemistry of the isomers of **13**, **14**, **19**, and **20** are described in the Experimental Section. The cyclobutenone is not formed at 90 °C, and this is presumably because it undergoes a thermal electrocyclic ring opening and subsequent cyclization to give the quinone **13**. Cyclobutenone **20** is formed as a single regioisomer, whereas the indene **14** and the indenone **19** are formed as nearly 1:1 mixtures of isomers. The regioselectivity of the formation of quinone **13** drops off with temperature from a 41:1 mixture of isomers at 45 °C to an 18:1 mixture of isomers at 90 °C. This is the first time that the effect of temperature on the regioselectivity of the reaction of carbene complex with alkynes has ever been reported. If it is assumed that the rates of CO insertion in **5A** and **5B** are the same, then this temperature effect suggests a decrease in the proportion of **5A** relative to **5B** at elevated temperature.


The total regioselectivity (Σ A/B) of the reaction is expressed as the ratio of the number of moles of the A isomers of all the products to the number of moles of the B isomers. The regioselectivity for each product was not affected by concentration. The distribution between phenol and indene products was quite sensitive to concentration, but at the same time, the total mass balance of the reaction is uniformly high. Thus, as expected from the data in Schemes 3 and 5, the total regiochemistry of the reaction is a function of the concentration. The change in total regiochemistry is much greater at 45 °C than it is at 90 °C, and this is simply because there is not as great a change in the amount of quinone formed at the higher temperature.[14] The error in the measurement of the total regiochemistry mainly results from the loss of material in determining the isolated yields. In most instances of duplicate runs, the yields were found not to vary by more than ±3%. The one exception is entry 3 in Table 1, and in this instance the mass balance of the indene product was low and the total regiochemistry increased from 1.5:1.0 to 2.1:1.0. The indene can be lost if oxidation in the workup does not completely remove the metal, in which case chromium tricarbonyl complexes may not necessarily coelute with the indenes and also may decompose during elution. It was decided not too repeat this reaction since, on the basis of the other entries, if all of the indene had been isolated it would most likely have been nearly a 1:1 ratio of regioisomers and the total regiochemistry would have dropped from 2.1:1.0. More importantly, it was decided not to repeat this reaction since, as will be described below, there is a change in mechanism between the reactions at 0.5 and 0.005 M at 45 °C, thus allowing alternate explanations for this effect. As discussed above, to conclude that the vinyl carbene-complexed intermediates **5A** and **5B** are formed irreversibly and/or are in equilibration, one must show that there is not a change in mechanism as the concentration is
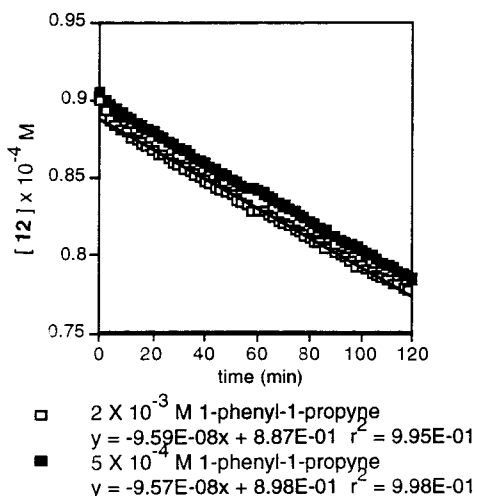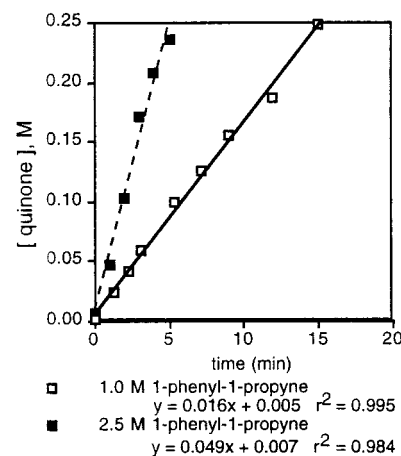
Figure 1. Initial rate plot: 9×10^{-5} M **12** and 2×10^{-3} or 5×10^{-3} M 1-phenylpropyne at 45 ± 0.5 °C.
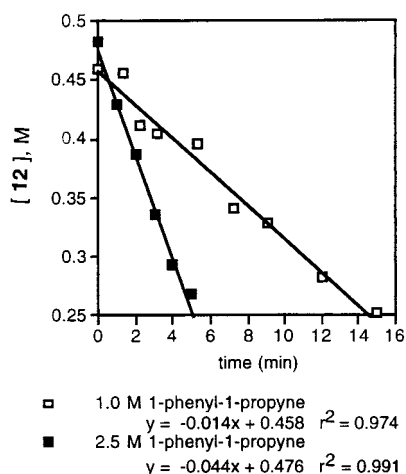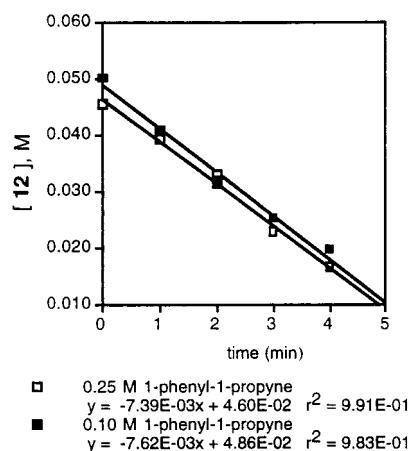
Figure 2. Initial rate plot: 0.5 M **12** and 1.0 or 2.5 M 1-phenylpropyne at 45 ± 0.5 °C.

Figure 3. Initial rate plot of quinone formation: 0.5 M **12** and 1.0 or 2.5 M 1-phenylpropyne at 45 ± 0.5 °C.

Figure 4. Initial rate plot: 0.05 M **12** and 0.25 or 0.1 M 1-phenyl-propyne at 89.5 ± 0.5 °C.

changed. As will be shown below, this was found to be the case for the reactions at 90 °C.

To probe for a change in mechanism, we first determined the order of the reaction of complex **12** with 1-phenylpropyne at 45 °C at both 0.5 and 0.00009 M in complex **12**. Initial rates were measured to avoid complications of multiple product formation. The low concentration regime was measured by UV/vis spectroscopy, but due to the large extinction coefficient of the carbene complex, at high concentration the rates were measured by quenching aliquots of the reaction and analyzing them by GC. As shown in Figure 1, at 9.0×10^{-5} M carbene complex **12** the reaction rate was measured with 0.002 and 0.0005 M alkyne. The rate of reaction was unaffected by a change in alkyne concentration. The reaction rate was also measured at 4.5×10^{-5} M **12**, and the rate was slower by a factor of 2 than at 9.0×10^{-5} M. Thus, the reaction is first-order in carbene complex and zero-order in alkyne, just as Fischer and Dötz observed for the reaction of the phenyl carbene complex **28** with diphenylacetylene.[3] At 0.5 M in carbene complex **12**, the reaction rate was again measured at two different alkyne concentrations: 1.0 and 2.5 M alkyne. To our surprise, *at 0.5 M in carbene complex there is a first-order dependence in alkyne* (Figure 2). Figure 3 shows the corresponding effect of alkyne concentration on the formation of quinone. The unimolecular rate constant at 9×10^{-5} M **12** is

1.8×10^{-5} s^{-1}, whereas the rate constant for the bimolecular reaction at 0.50 M and 45 °C is approximately 6×10^{-4} M^{-1} s^{-1}.

Although the benzannulation reaction is occurring by two different mechanisms at high and low concentrations of **12** at 45 °C, this change in mechanism is not necessarily the source of the change in regioselectivity. To determine if there is a connection between the these two factors, one must analyze the regioselectivity at concentrations where only one mechanism is operating. An increase in the temperature of the reaction should entropically favor a unimolecular reaction, and thus, the kinetics at 89.5 °C were examined. This is indeed what was observed: at 89.5 °C and 0.1 M **12** in dimethyl THF (DMTHF) both mechanisms are occurring as was ascertained from kinetic data taken at 0.1 M in **12** and 0.2 and 0.6 M in phenylpropyne (data not shown). However, when the concentration of carbene complex is dropped to 0.05 M at 90 °C, the reaction is unimolecular (Figure 4), as it is at 0.005 M (Figure 5). The observed rate constant is 2.5×10^{-3} s^{-1} at 89.5 °C (Table 2). Although the magnitude of the effect is significantly smaller than that at 45 °C, the same trend is seen: the regioselectivity is dependent on concentration. At 0.05 M carbene complex, the total regioselectivity is 2.4:1, but at 0.005 M carbene complex, the selectivity drops to 1.5:1. Therefore, the change in mechanism observed at 45 °C cannot account for the concentration dependence of the regioselectivity. To verify that changing solvents did not affect the product distributions, we ran the
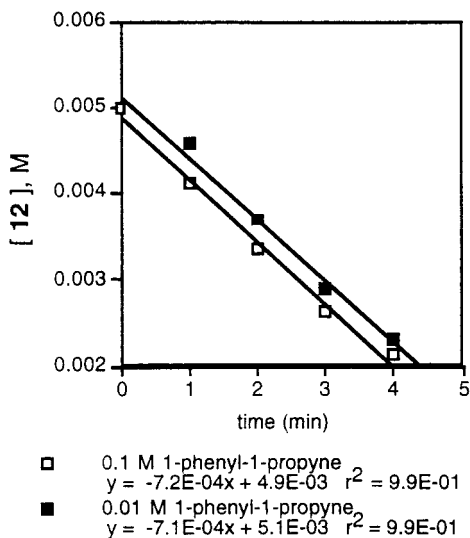
Figure 5. Initial rate plot: 0.005 M **12** and 0.1 or 0.01 M 1-phenyl-propyne at 89.5 ± 0.5 °C.

Table 2. Rates of Reaction of Complex 12 at 90 °C

| [**12**] (M)	[alkyne] (M)	k_{obs} (s^{-1})	initial rate (M s^{-1})
0.05	0.25	$2.5 \pm 0.2 \times 10^{-3}$	$1.2 \pm 0.1 \times 10^{-4}$
0.05	0.10	$2.5 \pm 0.2 \times 10^{-3}$	$1.3 \pm 0.1 \times 10^{-4}$
0.005	0.10	$2.4 \pm 0.2 \times 10^{-3}$	$1.2 \pm 0.1 \times 10^{-5}$
0.005	0.01	$2.4 \pm 0.2 \times 10^{-3}$	$1.2 \pm 0.1 \times 10^{-5}$

[a] Rates were measured by GC analysis at 89.5 ± 0.5 °C in 2,5-dimethyltetrahydrofuran with hexadecane as internal standard.

reaction at 45 °C in DMTHF. The same product distribution was obtained as in THF.
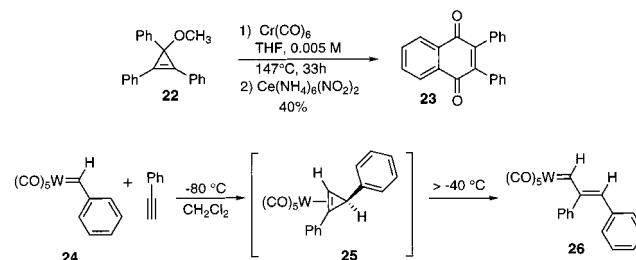
Mechanism for the Interconversion of 5A and 5B. The data above are not consistent with the irreversible formation of the alkyne inserted intermediate **5** as probed through the ratio of **5A** and **5B**, the two regioisomers of **5**. Under conditions where the reaction is first-order in carbene complex and zero-order in alkyne, the two isomers of **5** must have some mechanism for interconversion to explain the variation in total regiochemistry of the reaction with alkyne. One possibility is that alkyne insertion is reversible and that **5A** and **5B** undergo deinsertion to the alkyne and the unsaturated carbene complex **3** (the possibility of isomerization via an alkyne complex of **3** cannot be distinguished in the present study). Another possibility is that the isomerizations of **5A** and **5B** occur via the cyclopropene complex **21** which would maintain a covalent bond between the two carbon fragments at all times.

If the isomerization involved the cyclopropene, the concentration effect could be accounted for by the following. The cyclopropene metal complex is coordinatively unsaturated, so the equilibration may only occur when a ligand (such as the alkyne) can coordinate and stabilize this intermediate (Scheme 6). Thus, at higher alkyne concentrations the equilibration occurs and the product distribution reflects the competition between CO insertion and non-CO insertion, but at low concentration, equilibrium is not reached and the product distribution reflects the kinetic ratio of **5A** and **5B**. Ligand-induced isomerization was investigated by adding two equivalents of PPh₃ to the reaction (Table 1, entries 6 and 7 and entries 12 and 13). If this mechanism were responsible for the observed regioselectivities, then adding phosphines should give results similar to those at 0.5 M, where the alkyne concentration is high. However, added phosphine resulted in low total regioselectivity, just as at low concentration. Thus, this mechanism (Scheme 6) cannot account for the observed concentration dependence of the regioselec-
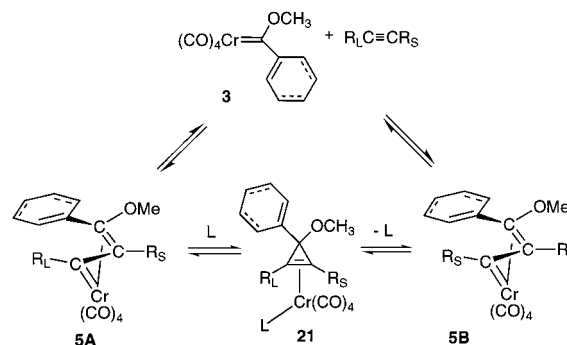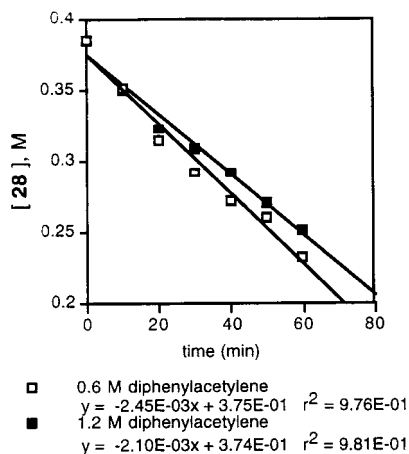
Scheme 6

Scheme 7

tivity. However, the cyclopropene intermediate could provide a mechanism for the isomerization of **5A** and **5B** while the concentration dependence is a function of the allochemical effect.[14]

Support for the intermediacy of a cyclopropene in these reactions comes from the fact that Semmelhack has shown that in the presence of M(CO)₆ cyclopropenes will open up to give typical benzannulation products, such as naphthols and indenes.[20] For example, he found that, when 3-methoxy-1,2,3-triphenylcyclopropene **22** was heated to 100−145 °C in the presence of one equivalent of Cr(CO)₆, a 40% yield of the quinone **14** was obtained which is the same product seen from the reaction of carbene complex **28** and diphenylacetylene (Scheme 7). Another case which implicates the intermediacy of a cyclopropene complex is the reaction of the unstabilized tungsten carbene complex **24** with phenylacetylene (Scheme 7).[21] H. Fischer found that, at −80 °C, an intermediate was observable and that, upon warming to −40 °C, this intermediate transformed into a new carbene complex **26**. This intermediate was characterized as the cyclopropene metal complex **25** by IR, ¹H NMR, and ¹³C NMR and by the ¹H NMR of the deuterated intermediate formed from phenylacetylene-*d*. This reaction occurs without the loss of CO, which has been shown to be the rate-limiting step in the benzannulation reaction[3] but which has recently been called into question by recent theroetical studies.[4] In either case, this complex is highly reactive, which may make direct mechanistic comparisons between these two systems a bit precarious. This is confirmed by the fact that complex **25** opens up stereoselectively to the regioisomer **26** that is less favored in the η^1,η^3-vinylcarbene intermediate **5**. Whether the equilibration occurs via the cyclopropene complex **21** cannot be determined at this time. Nonetheless, this does not affect the conclusion from the above data that the regioisomeric vinyl carbene-complexed intermediates **5A** and **5B** must be undergoing isomerization faster than CO insertion.

(20) (a) Semmelhack, M. F.; Ho, S.; Steigerwald, M.; Lee, M. C. *J. Am. Chem. Soc.* **1987**, *109*, 4397. (b) Semmelhack, M. F.; Ho, S.; Cohen, D.; Steigerwald, M.; Lee, M. C.; Lee, G.; Gilbert, A. M.; Wulff, W. D.; Ball, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 7108.

(21) Fischer, H.; Hofmann, J.; Mauz, E. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 998.
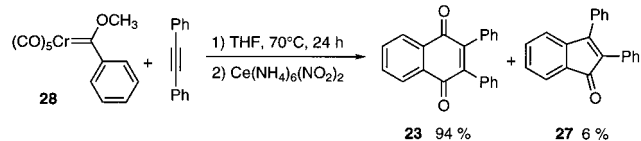
Figure 6. Initial rate plot: 0.4 M **28** and 0.6 or 1.2 M diphenylacetylene at 45.0 ± 0.5 °C.
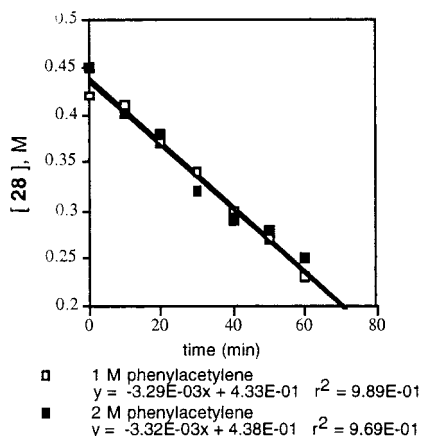
Figure 7. Initial rate plot: 0.45 M **28** and 1.0 or 2.0 M phenylacetylene at 45.0 ± 0.5 °C.

Scheme 8

Generality of the Bimolecular Mechanism. The unprecedented bimolecular mechanism observed for the reaction of *o*-methoxyphenyl chromium carbene complex **12** with 1-phenyl-1-propyne impelled us to investigate whether this was a general phenomenon. Although Fischer and Dötz had investigated the kinetics of phenylmethoxy chromium carbene complex **28** with various substituted diphenylacetylenes, all of their studies were done at 5×10^{-3} M carbene complex.[3] The most typical concentrations for running a benzannulation reaction are at 0.1–0.5 M carbene complex, significantly more concentrated than Fischer's kinetic studies. Thus, we reinvestigated the reactions of **28** with diphenylacetylene (Figure 6) and with phenyl acetylene (Figure 7), at 0.4–0.5 M carbene complex and 0.6–2.0 M alkyne at 45 °C. The product analysis was performed at 70 °C as indicated in Scheme 8, but the kinetics were performed at 45 °C to compare with the previous kinetics studies at lower concentrations.[3] We found that, under these typical reaction conditions, the rates of both reactions are independent of alkyne concentration. This is not surprising, given the first-order rate constants for the reaction of **12** versus **28**. Fischer and Dötz reported a rate constant of 2.55×10^{-4} s^{-1} for the reaction of **28** with diphenylacetylene at 45.4 °C. The first-order rate

constant for the reaction of **12** is an order of magnitude smaller at the same temperature in the unimolecular regime ($k_{\text{obs}}(\mathbf{12}) = 1.8 \times 10^{-5}$ s^{-1}). If the rate constants for the bimolecular reactions of **12** and **28** are of similar magnitude, then more extreme conditions would be required to make the bimolecular pathway of **28** competitive with the unimolecular pathway. For example, if one assumes that the bimolecular rate constant for **28** would be equal to the one measured for complex **12**, then in order for the bimolecular mechanism to be 100 times faster than the unimolecular reaction, the alkyne concentration must be on the order of 40 M. Thus, it is not surprising that no bimolecular reaction was observed for complex **28**. The reason for the slower unimolecular reaction for complex **12** versus complex **28** is thought to be due to the intramolecularity of the chelation of the methoxyl group and not to a chromium–methoxyl bond that is stronger than a chromium–carbon monoxide bond.

Conclusion

The data presented in this work provides the first evidence that isomers of the alkyne insertion intermediate in the reaction of Fischer carbene complexes with alkynes are in equilibrium. It was found that the total regiochemistry of the indene and phenol products is a function of concentration. Since it was found that this occurs over a concentration range in which the reaction is zero-order in alkyne, this means that the ratio of regioisomers of the alkyne insertion product **5A** and **5B** cannot be affected by the alkyne. Thus the change in regiochemistry must be a consequence of the interconversion of **5A** and **5B** and a change in the distrbution between indene and phenol products that is affected by the alkyne in a second step. The data are consistent with the formation of the alkyne insertion product **5** by a process that is first-order in carbene complex and zero-order in alkyne with a rate-limiting formation of an open coordination site on the metal. This could involve the intermediacy of **3** as originally proposed by Dötz (or an alkyne coordination complex of **3**).[3] However, at this point the data cannot distinguish whether the isomerization of the regioisomers of the alkyne insertion intermediate occurs by a deinsertion or the intermediacy of a cyclopropene complex. The present work also provides the first example of a bimolecular reaction of a heteroatom-stablized carbene complex with an alkyne in the absence of CO pressure, thus supporting Sola's recent results.[4] The fact that the isomers of the alkyne insertion intermediate do equilibrate rapidly with respect to subsequent CO insertion may play a role in the determination of the stereochemistry[22] and product distributions[2] from the benzannulation reaction.

Experimental Section

General Procedure for the Reaction of Carbene Complex 12 with 1-Phenyl-1-propyne at 45 °C. Carbene complex **12**[23] (160 mg, 0.51 mmol), 0.13 mL of 1-phenylpropyne (1.02 mmol), and THF (0.89 mL to give 0.5 M **12** or 98.2 mL to give 0.005 M **12**) were combined in a flame-dried flask with a threaded Teflon stopcock and a sidearm under argon. In some cases, 2 equiv of triphenylphosphine was added. The flask was sealed, the sidearm was placed under vacuum, and the solution was frozen in liquid nitrogen. It was then opened to vacuum for 1–2 min, resealed, and warmed to room temperature. This degassing process was repeated three times. The solution was then placed under argon and warmed to 45 °C. The reaction was heated for 12–24 h, then cooled to room temperature and transferred to a round-bottom flask. The

(22) (a) Hsung, R. P.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1994,** *116,* 6449. (b) Hsung, R. P.; Wulff, W. D.; Challener, C. A. *Synthesis* **1996,** 773. (c) Hsung, R. P.; Quinn, J. F.; Weisenberg, B. A.; Wulff, W. D.; Yap, G. P. A.; Rheingold, A. L. *J. Chem. Soc., Chem. Commun.* **1997,** 615.

solvent was removed, and the crude product was dissolved in about 40 mL of ether. The product was oxidized with 5 mL of 0.5 M CAN. The solution was transferred to a separatory funnel, and the organic layer was washed twice with water and once with brine. The organic layer was dried over MgSO$_4$ and filtered through Celite, and the solvent was removed under reduced pressure. A crude ^{1}H NMR was taken prior to purification. In some cases, one tenth of the crude reaction mixture was separated and analyzed by GC. The products were then isolated from the remaining nine tenths by column chromatography on silica gel using a 10:1:1 mixture of hexane/methylene chloride/ether to give the indenes **14** and the indenones **19** in separate fractions, and then upon further elution with a 4:1:1 solvent mixture, the quinones **13**.

The ratios of regioisomers for the indenes and indenones were determined by ^{1}H NMR on the crude reaction mixtures. The ratios of regioisomers of the quinones were determined by GC analysis on a Varian 3600 GC on the quinones obtained from the chromatography column or by GC analysis of the crude reaction mixture. GC analysis was performed on a 30 m, 0.32 mm i.d. Alltech SE−54 column with a split injector under the following conditions: injector temp, 300 °C; detector temp, 300 °C; head pressure, 12 psig; initial column temp, 150 °C (2 min); final column temp, 300 °C; ramp rate, 20 °C/min; and hold time, 5 min for analysis of reactions at 0.05 M. For GC analysis of the crude reaction mixtures, the following conditions were used: T = 210 °C, hold 25 min; R_T of quinone A = 19.6 min; and R_T for quinone B = 18.4 min. Reported ratios are from the average of 6 runs.

The quinones obtained from this reaction were highly enriched in isomer **13A**, and as result, a pure sample of quinone **13A** could be obtained by crystallization from chloroform/hexanes. The assignment of the quinone **13A** as the major isomer of this reaction is based on the regioselectivity that has previously been established for the reactions of carbene complexes with alkynes.[18] The spectral data for the minor isomer **13B** of the quinone product were obtained on a sample that was prepared by an independent synthesis described below. The spectral data for the indenes **14** and the indenones **19** were taken on mixtures of the two regioisomers in each case.

General Procedure for the Reaction of Carbene Complex 12 with 1-Phenyl-1-propyne at 90 °C. The carbene complex **12**[23] (100 mg, 0.32 mmol) was dissolved in 6.3 mL (to give 0.05 M **12**) of dimethyltetrahydrofuran (DMTHF) or 63.74 mL of DMTHF (to give 0.005 M **12**), in a flame-dried single-necked flask equipped with a threaded Teflon high vacuum stopcock. In some cases, 2 equiv of triphenylphosphine was added. After 1-phenyl-1-propyne was added (2 equiv, 0.08 mL, 0.64 mmol) and the flask was sealed with the threaded stopcock at 25 °C, the mixture was cooled to −78 °C and the flask was opened to vacuum for 30 s. The flask was then resealed and allowed to warm to room temperature. This was repeated three times (the reaction mixture was not frozen in liquid nitrogen due the expansion of DMTHF upon freezing, which tends to break the flask). After being warmed to room temperature the third time, the flask was filled with argon, sealed, and placed in a 90 °C oil bath for 2−4 h (0.05 M **12**) or 6−12 h (0.005 M **12**). The DMTHF was then removed, and the remaining yellow-orange mixture was dissolved in approximately 20 mL of ether. Oxidation of the crude products was performed by the addition of 5 mL 0.5 M cerium ammonium nitrate in water and stirring for 30 min (0.05 M) or 10−15 min (0.005 M). The mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was washed twice with ether. The combined organic layers were washed once with water and once with brine. The solution was dried over magnesium sulfate, filtered, and concentrated. After taking a crude ^{1}H NMR spectrum, the products were eluted from a silica gel column with a 10:1:1 mixture of hexane/ether/methylene chloride to give the indenes **14** and the indenones **19** in separate fractions and then, upon further elution with a 4:1:1 solvent mixture, the quinones **13**. For the 0.005 M reaction, one tenth of the crude reaction mixture was set aside for GC analysis. The yields for indenones and quinones in the 0.005 M reactions were determined by ^{1}H NMR integration using triphenylmethane as an internal standard.

(23) (a) Dötz, K. H.; Sturms, W.; Popall, M.; Riede, J. *J. Organomet. Chem.* **1984**, *277*, 267. (b) Wulff, W. D.; Tang, P.-C.; Chan, K.-S.; McCallum, J. S.; Yang, D. C.; Gilbertson, S. R. *Tetrahedron* **1985**, *41*, 5813.

The ratios of regioisomers for the indenes and indenones were determined by ^{1}H NMR on the crude reaction mixtures. The ratios of regioisomers of the quinones were determined by GC analysis on a Varian 3600 GC on the quinones obtained from the chromatography column for the reactions at 0.05 M, and by GC analysis of the crude reaction mixture for the reactions at 0.005 M. GC analysis was performed on a 30 m, 0.32 mm i.d. Alltech SE−54 column with a split injector under the following conditions: injector temp, 300 °C; detector temp, 300 °C; head pressure, 12 psig; initial column temp, 150 °C (2 min); final column temp, 300 °C; ramp rate, 20 °C/min; hold time, 5 min for analysis of reactions at 0.05 M. The retention time for **13A** was 9.5 min and for **13B** was 9.3 min. For GC analysis of the crude reaction mixtures at 0.005 M, the following conditions were used: T_i = 200 °C, hold 5 min; T_f = 250 °C, rate 5 °C/min, hold 1 min; R_T of quinone A = 14.6 min; and R_T for quinone B = 14.2 min. Reported ratios are from the average of 6 runs.

Quinone 13A. R_f = 0.27 (4:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl$_3$) δ 2.06 (s, 3H), 4.03 (s, 3H), 7.20 (d, 2H, J = 8 Hz), 7.29 (d, 1H, J = 8 Hz), 7.4−7.45 (M, 3H), 7.66 (t, 1H, J = 8.3 Hz), 7.73 (d, 1H, J = 8 Hz); ^{13}C NMR (CDCl$_3$) δ 14.83, 56.41, 117.30, 119.21, 127.85, 128.06, 128.29, 129.30, 133.51, 134.31, 134.61, 144.05, 145.92, 159.25, 184.22, 184.97; IR (thin film) 2924w, 1657s, 1587s, 1471m, 1437m, 1375s, 1331m, 1267s, 1061m, 964m, 705m cm^{-1}; mass spectrum m/z (% rel intensity) 278 M$^+$ (100), 263 (30), 261 (12), 249 (10), 235 (12), 189 (10), 115 (11), 104 (11), 76 (28). Anal. calcd for C$_{18}$H$_{14}$O$_3$: C, 77.68; H, 5.07. Found: C, 76.73; H, 5.18. Bright yellow solid, mp 155−7 °C.

Quinone 13B. R_f = 0.27 (4:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl$_3$) δ 2.03 (s, 3H), 3.96 (s, 3H), 7.19 (d, 2H, J = 7.4 Hz), 7.27 (d, 1H, J = 8.5 Hz), 7.36−7.42 (m, 3H), 7.65 (t, 1H, J = 8.1 Hz), 7.78 (d, 1H, J = 7.6 Hz); ^{13}C NMR (CDCl$_3$) δ 14.27, 56.36, 117.66, 118.93, 119.94, 127.90, 128.22, 129.35, 133.94, 134.34, 134.54, 141.66, 147.74, 129.59, 183.58, 186.08; IR (CHCl$_3$) 1658s, 1588s cm^{-1}; mass spectrum m/z (% rel intensity) 278 M$^+$ (100), 263 (30), 249 (12), 235 (14), 219 (13), 134 (23), 115 (18), 104 (23), 76 (60). Anal. calcd for C$_{18}$H$_{14}$O$_3$: C, 77.68; H, 5.07. Found: C, 77.05; H, 4.95. Yellow solid, mp 195−7 °C.

Indene 14A. R_f = 0.23 (10:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl$_3$, data from a 1.3:1 mixture of **14A/14B**) δ 2.03 (s, 3H), 3.14 (s, 3H), 3.94 (s, 3H), 5.14 (s, 1H), 6.75 (d, 1H, J = 8.3 Hz), 6.77 (d, 1H, J = 7.4 Hz), 7.21−7.53 (m, 6H, overlap with **14B**); ^{13}C NMR (CDCl$_3$, data from a mixture of **14A/14B**; peaks assigned by taking spectra of two samples with different isomer ratios) δ 12.07, 52.05, 55.53, 83.72, 108.64, 112.81, 126.58, 127.36, 128.35, 128.87, 130.13, 134.52, 139.42, 140.83, 146.81, 156.28; IR (CHCl$_3$, for mixture) 2931w, 1601m, 1586m, 1478s, 1439w, 1272m, 1259s, 1088m, 700m cm^{-1}; GC mass spectrum (R_T = 14.12 min for **14A**) m/z (% rel intensity) 266 M$^+$ (100), 251 (66), 235 (24), 223 (16), 189 (19), 178 (6), 165 (10), 115 (10). High-resolution mass spectrum (on mixture): calcd for C$_{18}$H$_{18}$O$_2$ m/z 266.1307, measd m/z 266.1293. Anal. calcd for C$_{18}$H$_{18}$O$_2$: C, 81.17; H, 6.81. Found (for mixture): C, 81.53; H, 7.18. White crystalline solid.

Indene 14B. R_f = 0.23 (10:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl$_3$, data from a 1.4:1 mixture of **14A/14B**) δ 2.27 (d, 3H, J = 1.3 Hz), 2.96 (s, 3H), 3.95 (s, 3H), 5.67 (d, 1H, J = 1.5 Hz), 6.81 (d, 1H, J = 8.2 Hz), 6.93 (d, 1H, J = 7.4 Hz), 7.21−7.53 (m, 6H, overlap with **14A**); ^{13}C NMR (CDCl$_3$, data from samples with different isomer ratios) δ 12.00, 51.49, 55.58, 82.16, 109.43, 112.26, 126.45, 126.90, 128.30, 128.74, 130.42, 135.25, 136.14, 140.89, 147.55, 156.04; IR (CHCl$_3$, for mixture) 2931w, 1601m, 1586m, 1478s, 1439w, 1272m, 1259, 1088m, 700m cm^{-1}; GC mass spectrum (R_T = 12.38 min for **14B**) m/z (% rel intensity) 266 M$^+$ (100), 251 (86), 235 (26), 223 (14), 189 (17), 178 (7), 165 (10), 115 (9). High-resolution mass spectrum (on mixture): calcd for C$_{18}$H$_{18}$O$_2$ m/z 266.1307, measd m/z 266.1293. Anal. calcd for C$_{18}$H$_{18}$O$_2$: C, 81.17; H, 6.81. Found (for mixture): C, 81.53; H, 7.18. White crystalline solid.

Indenone 19A. R_f = 0.15 (10:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl$_3$, data from a mixture of **19A/19B**) δ 1.90 (s, 3H), 3.96 (s, 3H, overlaps with methoxy peak of **19B**), 6.66 (d, 1H, J = 7.1 Hz), 6.78 (d, 1H, J = 8.6 Hz), 7.26 (t, 1H, J = 7.1 Hz), 7.38−7.49 (m,

5H, overlaps with aromatic peaks of **19B**); ^{13}C NMR (CDCl₃, data from a mixture of **19A/19B**; peaks assigned by comparison of spectra of samples with two different isomer ratios) δ 8.61, 56.01, 113.50, 113.98, 128.17, 128.57, 128.82, 131.48, 132.90, 135.21, 148.10, 152.21, 156.41, 196.17, 1 C not located; IR (thin film, mixture) 1703s, 1596m, 1475m, 1282m, 1261m, 1602w, 699m cm⁻¹; GC mass spectrum (R_T = 14.49 min for **19A**) *m/z* (% rel intensity) 250 M⁺ (100), 235 (31), 221 (45), 207 (19), 189 (24), 179 (10), 165 (10), 152 (8), 125 (5), 115 (11), 95 (6), 89 (7), 76 (9), 63 (5). Yellow oil.

Indenone 19B. R_f = 0.15 (10:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl₃, data from a mixture of **19A/19B**) δ 2.28 (s, 3H), 3.96 (s, 3H, overlaps with methoxy peak of **19A**), 6.79 (d, 1H, *J* = 7 Hz), 6.84 (d, 1H, *J* = 8.4 Hz), 7.29−7.41 (m, 6H, overlaps with aromatic peaks of **19A**); ^{13}C NMR (CDCl₃, data from a mixture of **19A/19B**; peaks assigned by comparison of spectra of samples with two different isomer ratios) δ 12.45, 56.01, 112.75, 114.33, 127.50, 128.12, 129.67, 131.28, 133.42, 135.58, 148.33, 151.32, 156.09, 194.48, 1 C not located; IR (thin film, mixture) 1703s, 1596m, 1475m, 1282m, 1261m, 1602w, 699m cm⁻¹; GC mass spectrum (R_T = 17.22 min for **19B**) *m/z* (% rel intensity) 250 M⁺ (100), 235 (25), 221 (34), 207 (15), 191 (20), 178 (17), 165 (8), 152 (7), 125 (7), 115 (12), 95 (5), 89 (6), 76 (8), 63 (5). Yellow oil.

Cyclobutenone 20. R_f = 0.20 (10:1:1 hexane/ether/methylene chloride); ^{1}H NMR (CDCl₃) δ 2.34 (s, 3H), 3.47 (s, 3H), 3.72 (s, 3H), 6.87 (d, 1H, *j* = 8.1 Hz), 7.00 (t, 1H, *J* = 7.4 Hz), 7.27−7.43 (m, 4H), 7.63 (d, 1H, *J* = 7.0 Hz), 7.57 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (CDCl₃) δ 13.80, 53.41, 55.60, 98.28, 111.61, 120.76, 124.52, 127.46, 128.58, 128.61, 128.97, 129.48, 129.61, 148.24, 157.00, 172.39, 190.56; IR (thin film) 2936m, 1759 vs (n_CO), 1640m, 1596m, 1490s, 1462m, 1253m, 1088s, 758m, 695m cm⁻¹; mass spectrum *m/z* (% relative intensity) 294 M⁺ (41), 279 (40), 251 (42), 235 (25), 135 (100), 115 (26), 105 (20), 77 (47). Calculated for C₁₉H₁₈O₃ *m/z* 294.1256. Found *m/z* 294.1206. White solid, mp 85−6 °C.

Assignment of Major and Minor Isomers of the Reaction Products. (A) Quinones 13. The assignment of the regioselectivity of the major quinone obtained from the reaction of complex **12** with 1-phenyl-1-propyne was made on the basis of the regioselectivity that is known for quinone formation from this reaction.[18] A sample of the minor isomer **13B** was obtained from the reaction of the methoxy *m*-methoxyphenyl chromium carbene complex **31** with 1-phenyl-1-propyne and used to obtain spectral data and GC retention times for **13B**.
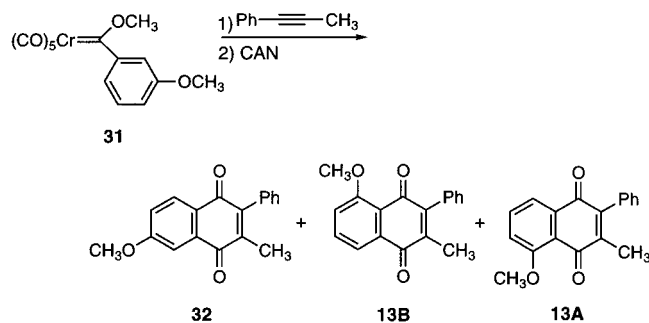

A deoxygenated solution of 694 mg of methoxy *m*-methoxyphenyl chromium carbene complex **31** and 510 μL of 1-phenyl-1-propyne (4.06 mmol) in 4 mL of THF (0.5 M) was heated at 45 °C for 23 h. Oxidative workup with CAN followed by chromatography on silica gel with a 10:1:1 to 4:1:1 mixture hexane/ether/methylene chloride gave two yellow bands which were collected, concentrated, and crystallized from chloroform/hexanes. No attempt to take second crops was made, although substantial material remained. Recovered were the quinone **32** (182 mg, 0.65 mmol, 32%) and quinone **13** (82 mg, 0.29 mmol, 14%), which was found to be a 14:1 mixture of **13B** to **13A**. The regioselectivity for the formation of quinone **32** was not determined.

(B) Indenes 14. The initial assignment of the regiochemistry of the indene products was made on the basis of the coupling constant (1.4 Hz) between the methyl group and the allylic hydrogen in the minor isomer which is due to long-range coupling that would be consistent

with **14B** but not **14A**. Thus, the assignment was confirmed by the following experiment in which a mixture of the indenes **14A** and **14b** was hydrogenated to the corresponding indanes. In a nitrogen-flushed Teflon sealed flask was placed 64 mg of 5% Pd−C (0.03 mm Pd, Kodak), 10 mL of absolute ethanol, and a 1.4:1 mixture of indenes **14A/14B** (79.2 mg, 0.30 mmol) in 2 mL of additional ethanol. The black slurry was stirred under an atmosphere of hydrogen overnight. The catalyst was filtered off onto Celite with methanol, and the solvent was removed. Preparative chromatography (500 μm plate, 10:1:1 hexane/ether/methylene chloride) gave 44.7 mg of a 1.4:1 mixture of indanyl ethers **33A** and **33B** in 56% combined yield. The ^{1}H NMR experiments summarized below allowed for the unambiguous assignment of the major isomer as 1,7-dimethoxy-2-methyl-3-phenyl-2-indane **33A**. The following spectral data were collected on the mixture of isomers: R_f = 0.40 (10:1:1 hexane/ether/methylene chloride); ^{13}C NMR (CDCl₃, partial data for mixture); **33A**, δ 12.10, 43.35, 54.75, 55.64, 58.84, 83.78, 106.65, 118.65, 126.36, 130.50, 131.12, 143.08, 157.17; **33B**, δ 20.00, 44.29, 54.25, - -, 58.13, 83.28, 108.74, 117.15, 126.40, 130.05, 132.45, 139.88, 150.44. Mass spectrum *m/z* (% rel intensity) 268 M⁺ (65), 237 (100), 221 (18), 191 (8); calcd for C₁₈H₂₀O₂, *m/z* 268.1463, found *m/z* 268.1456. White solid.

The ^{1}H NMR spectral data was collected on the 1.4:1 mixture of **33A/33B** in d₆-benzene and is summarized below. Specific assignments are given where possible below each isomer, and combined assignments are made following the individual assignments. Irradiation of the multiplet at 2.54 ppm (H_b) of the major isomer **33A** collapsed the three other multiplets into singlets. Conversely, irradiation of the multiplet corresponding to H_b in the minor isomer **33B** only affected two of the three remaining multiplets. This pattern can only be obtained for the given assignments: **33A**, H_a δ = 0.92 (d, 3H, *J* = 7.3 Hz), H_b δ = 2.54 (m, 1H), H_e δ = 3.33 (s, 3H), H_f δ = 3.47 (s, 3H), H_c δ = 4.05 (d, 1H, *J* = 8.5 Hz), H_d δ = 4.73 (d, 1H, *J* = 6.2 Hz); **33B**, H_a δ = 1.3 (d, 3H, *J* = 7.2 Hz), H_b δ = 3.14 (m, 1H), H_c δ = 3.26 (d, 1H, *J* = 5.6 Hz), H_d δ = 3.29 (s, 3H), H_e δ = 3.47 (s, 3H), H_f δ = 4.98 (d, 1H, *J* = 5.2 Hz); aryl protons, δ = 6.42 (t, 1H, *J* = 8.4 Hz), 6.72 (d, 1H, isomer A, *J* = 7.5 Hz), 6.82 (d, 1H, isomer B, *J* = 7.4 Hz), 6.96−7.24 (m, 12H), 7.50 (d, 1H, isomer B, *J* = 7.6 Hz).

33A   **33B**
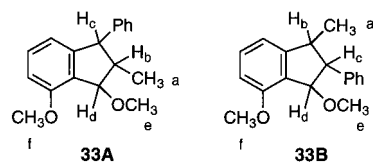
(C) Indenones 19. The regioisomers of the indenones were assigned by chemical correlation with the indenes **14**. A 2:1 mixture of indenes **14A** and **14B** (44.8 mg, 0.17 mmol) was dissolved in 1 mL of methylene chloride under argon. Upon addition of 0.05 mL of water and 43.4 mg of DDQ (0.19 mmol), the solution immediately turned dark blue−green. The solution was stirred at room temperature for 14 h. The final solution was a yellow−brown slurry. The solution was filtered through Celite and washed three times with saturated aqueous sodium bicarbonate. The aqueous layer was extracted twice with methylene chloride. The combined organic layers were washed with brine, dried over magnesium sulfate, and filtered. After removal of solvent, an 82% (34.7 mg; 0.14 mmol) yield of indenones was obtained as a 2:1 mixture of **19A** and **19B**. The major isomer **19A** obtained from this reaction was found by ^{1}H NMR to be identical with the minor indenone isomer obtained from the reaction of complex **12** with 1-phenyl-1-propyne: ^{1}H NMR spectrum (CDCl₃, for major isomer in a 2:1 mixture of **19A** and **19B**) δ 1.90 (s, 3H), 3.96 (s, 3H, overlaps with methoxy peak of **19B**), 6.66 (d, 1H, *J* = 7.1 Hz), 6.78 (d, 1H, *J* = 8.6 Hz), 7.26 (t, 1H, *J* = 7.1 Hz), 7.38−7.49 (m, 5H, overlaps with aromatic peaks of **19B**). The indenes **14A** and **14B** could also be oxidized to the indenones **19A** and **19B** with ceric ammonium nitrate although the reaction was slow at room temperature with complete conversion requiring several days and the yield was not determined.

(D) Cyclobutenone 20. Cyclobutenone **20** was obtained as a single diastereomer which was assigned as **20A** by chemical correlation. A sample of **20** was dissolved in benzene under nitrogen and heated

overnight in a pressure flask at 110 °C. After solvent removal and CAN oxidation, an NMR spectrum of the crude residue showed a single quinone product corresponding to the major quinone **13A** isolated from the benzannulation reaction.

Measurement of the Extinction Coefficient for 12. A 5.03×10^{-3}M stock solution of **12**[23]was made by dissolving 15.8 mg (0.05 mmol) of **12** in THF to a final volume of 10 mL in a volumetric flask. Three samples were made from this stock solution by diluting 0.2 mL of the stock solution to a final volume of 10 mL, resulting in a 1.0×10^{-4} M solution. The absorbance at 445.8 nm was measured for each sample three times, and the background absorbance was subtracted for each. The average absorbance was used to determine the extinction coefficient e from Beer's law: $A = elc$, where $A_{avg} = 1.15$, $l = 1$ cm, and $c = 10^{-4}$ M. Thus, $e \sim 11\,400$ M^{-1} cm^{-1}.

Kinetic Measurements of the Reaction of 12 with 1-Phenylpropyne at 9.8×10^{-5} M 12, 45 °C. (A) At 9.8×10^{-5} M 12 and 2×10^{-3} M 1-Phenylpropyne. A stock solution of **12**[23]was made by dissolving 15.6 mg (0.05 mmol) of **12** in THF to a final volume of 10 mL in a volumetric flask, giving a 4.97×10^{-3} M solution. A 0.99×10^{-4} M solution of **12** was prepared by diluting 0.2 mL of the 4.97×10^{-3} M solution to a final volume of 10 mL in a volumetric flask. A 0.304 M stock solution of 1-phenylpropyne was prepared by diluting 0.038 mL (0.304 mmol) of the alkyne in THF to a final volume of 1 mL in a volumetric flask.

In a quartz cuvette (1 cm path length) modified with a high vacuum Teflon stopper and a sidearm was added 3 mL of the 9.9×10^{-5} M solution of **12**. The solution was deoxygenated by cooling to −78 °C, opening to vacuum for a period of 1 min, sealing the flask, and warming to room temperature. This cycle was repeated three times. The flask was then filled with argon, and 0.02 mL of the 0.304 M solution of 1-phenylpropyne was added to the sidearm. The solution was placed in the cuvette holder in the spectrophotometer, which was connected to a recirculating bath set at 44.6 °C, and monitored with a thermocouple thermometer. The solution temperature was allowed to equilibrate for 5 min prior to mixing the alkyne in the sidearm with the carbene complex solution. Upon mixing, the reaction concentrations were 9.8×10^{-5} M **12** and 2.0×10^{-3} M 1-phenylpropyne. The scanning parameters were as follows: $l_{max} = 445.8$ nm; $T = 44.6$ °C; range = 600−350 nm; speed = 300 nm/min; interval = 2 min; and scans = 60. In all cases the background spectrum was subtracted. Rate = 1.7×10^{-9} M s^{-1}; $k_{obs} = 1.8 \times 10^{-5}$ s^{-1}.

(B) At 1.0×10^{-4} M 12 and 5.0×10^{-3} M 1-Phenylpropyne. Compound **12** (15.8 mg, 0.05 mmol) was dissolved in THF to a final volume of 10 mL to give a 5.03×10^{-3} M stock solution. A 0.30 M stock solution of 1-phenylpropyne was prepared by diluting 0.188 mL of 1-phenylpropyne with THF to a final volume of 5 mL. The reaction sample was made by combining 0.06 mL of the stock solution of **12** with 2.89 mL of THF in a cuvette fitted with a high vacuum threaded Teflon stopper and a sidearm. The solution was deoxygenated in the same manner as above. After being filled with argon, 0.05 mL of the stock solution of 1-phenylpropyne was put in the sidearm. After allowing the temperature of the cuvette to equilibrate to 44.6 °C (as above), we mixed the solutions and collected the UV spectra at 2 min intervals. The reaction concentrations were 1.0×10^{-4} M **12** and 5.0×10^{-3} M 1-phenylpropyne. The same parameters as above were used to collect the spectra. Rate = 1.6×10^{-9} M s^{-1}; $k_{obs} = 1.9 \times 10^{-5}$ s^{-1}.

(C) At 5×10^{-5} M 12 and 1×10^{-3} M 1-Phenylpropyne. Compound **12** (15.8 mg, 0.05 mmol) was dissolved in THF to a final volume of 10 mL to give a 5.03×10^{-3} M stock solution. A 0.15 M stock solution of 1-phenylpropyne was prepared by diluting 0.094 mL of 1-phenylpropyne with THF to a final volume of 5 mL. The reaction sample was made by combining 0.03 mL of the stock solution of **12** with 2.95 mL of THF in a cuvette fitted with a high vacuum threaded Teflon stopper and a sidearm. The solution was deoxygenated in the same manner as above. After being filled with argon, 0.02 mL of the stock solution of 1-phenylpropyne was put in the sidearm. After allowing the temperature of the cuvette to equilibrate to 44.6 °C (as above), we mixed the solutions and collected the UV spectra at 2 min intervals. The reaction concentrations were 5.0×10^{-5} M **12** and

1.0×10^{-3} M 1-phenylpropyne. The same parameters as above were used to collect the spectra. Rate = 7.7×10^{-10} M s^{-1}; $k_{obs} = 1.9 \times 10^{-5}$ s^{-1}.

Kinetic Measurements of the Reaction of 12 with 1-Phenylpropyne at 0.5 M 12, 45 °C. (A) At 1.0 M 1-Phenylpropyne. Carbene complex **12**[23] (333.7 mg, 1.06 mmol) and triphenylmethane (259.3 mg, 1.06 mmol) were dissolved in THF to a final volume of 2 mL in a volumetric flask, giving a stock solution of 0.53 M **12** and 0.53 M triphenylmethane. To a 25 mL three-neck flask fitted with two glass stoppers and a vacuum adapter with a stopcock was added 1 mL of the stock solution. After the flask was sealed, the solution was frozen, evacuated under high vacuum, and warmed to room temperature again. This process was repeated three times to deoxygenate the solution. The flask was then filled with argon and placed in a 44.4 ± 0.3 °C oil bath monitored with a thermocouple thermometer. Once the temperature had equilibrated, 0.133 mL of 1-phenylpropyne was added, and 0.05 mL aliquots of the reaction were taken at 1 min intervals for the first 4 min, followed by 2−3 min intervals for the next 10 min. The reaction was followed for a total of 3 h. The initial reaction concentrations were 0.47 M **12** and 0.94 M 1-phenylpropyne.

The progress of the reaction was monitored by the disappearance of the carbene complex **12** which in turn was monitored by the disappearance of the corresponding ester, methyl 2-methoxy benzoate, from the crude reaction mixture obtained upon oxidative workup. The aliquots were quenched with 0.5 M CAN in methanol and diluted with 0.2 mL of ether. The progress of the reaction was followed by GC, using a 0.32 mm i.d. SE- (DB-5 equivalent) capillary column with a programmable on-column injector. GC conditions were as follows: head pressure = 7 psi; pressure = 15.2; velocity = 21.7; detector, 300 °C; injector, $T_1 = 80$ °C, $T_2 = 250$ °C, ramp rate = 150 °C/min, hold 10 min; column, $T_1 = 90$ °C, hold 1 min; $T_2 = 200$ °C, ramp rate = 50 °C/min; and $T_3 = 250$ °C, ramp rate = 20 °C/min, hold 12 min. The retention time for the ester (methyl 2-methoxy benzoate) was 4.7 min, and that for triphenylmethane was 7.9 min. The retention times for the quinones were 14.8 and 15.3 min. The response factor for the ester relative to triphenylmethane was $R_f = 0.38$. The response factor for the quinones relative to triphenylmethane was $R_f = 0.62$.

(B) At 2.5 M 1-Phenylpropyne. Carbene complex **12** (428.8 mg, 1.37 mmol) and triphenylmethane (333.2 mg, 1.37 mmol) were dissolved in THF to a final volume of 2 mL in a volumetric flask, giving a stock solution of 0.68 M **12** and 0.68 M triphenylmethane. Using the same setup as above, 0.69 mL of the stock solution was transferred to the reaction vessel. The solution was degassed and heated to 44.6 °C. Once the solution was equilibrated, 0.31 mL of 1-phenylpropyne (2.48 mmol) was added and aliquots of the reaction were taken every minute for the first 12 minutes, and then every 3 min for another 8 min. The reaction was followed for a total of 3 h. The reaction concentrations were 0.47 M **12**, 0.47 M triphenylmethane, and 2.48 M 1-phenylpropyne. The reaction progress was followed by GC as above. The temperature was 44.6 ± 0.2 °C.

Kinetic Measurements of the Reaction of 12 with 1-phenylpropyne at 90 °C. (A) At 0.05 M 12. Carbene complex **12**[23] (62.8 mg, 0.20 mmol) and hexadecane (29 mL, 0.099 mmol) were dissolved in dimethyltetrahydrofuran (DMTHF) to a total volume of 2 mL in a volumetric flask, giving a stock solution of 0.1 M **12** and 0.05 M hexadecane. A sample of (0.75 mL) of the stock solution was transferred to a flame-dried two-necked 10 mL Wheaton flask with screw caps containing Teflon-lined septa under argon. The solution was diluted with enough DMTHF so that the final volume after addition of 1-phenyl-1-propyne was 1.5 mL. The solution was deoxygenated by the freeze−pump−thaw method (3 cycles) and then placed in a preheated (89.7 °C ± 0.7 °C) oil bath. After two minutes, 1-phenyl-1-propyne was added (19−47 mL), giving a final concentration of 0.05 M **12**, 0.025 M hexadecane, and 0.1−0.25 M 1-phenyl-1-propyne.

The progress of the reaction was monitored by the disappearance of the carbene complex **12** which in turn was monitored by the disappearance of the corresponding ester, methyl 2-methoxy benzoate, from the crude reaction mixture obtained upon oxidative workup with hexadecane as the internal standard. Aliquots (0.05 mL) were taken every 1−10 min and quenched in 0.1 mL of 0.5 M cerium ammonium nitrate (CAN) in methanol. After oxidation for approximately 5 min,

each aliquot was diluted with 0.25 mL of ether and 0.2 mL of water. The layers were allowed to separate, and the bottom layer was removed with a pipet before GC analysis. GC analysis was performed on a Varian 3600 with a 30 m Alltech SE−54 0.53 mm i.d. megabore column and with an on-column injector. The following conditions were used: injector temp, 250 °C; detector temp, 300 °C; head pressure, 3 psig; initial column temp, 150 °C (2 min); final column temp, 250 °C; ramp rate, 10 °C/min; and hold time, 13 min. The retention time for the ester (methyl 2-methoxy benzoate) was 6.41 min, and that for hexadecane was 9.5 min. The response factor for the ester relative to hexadecane was $R_f = 0.65$.

(B) At 0.005 M 12. The same concentration of the stock solution was used as for the 0.05 M reactions. The reaction solution was made by diluting 0.075 mL of the stock solution with DMTHF so that the final volume after addition of the 1-phenyl-1-propyne was 1.5 mL. The solution was deoxygenated by the freeze−pump−thaw method (6 cycles) and then placed in an (89.5 ± 0.7 °C) oil bath. After two minutes, 1-phenyl-1-propyne was added (9−19 mL) to give a final concentration of 0.005 M **12**, 0.0025 M hexadecane, and 0.0479−0.1 M 1-phenyl-1-propyne.

Aliquots (0.05 mL) were taken every 1−10 min and were quenched in 0.05 mL of 0.5 M CAN in methanol. The preparation of aliquots for GC analysis was the same as for the 0.05 M reactions. GC analysis of the aliquots was performed under the following conditions: injector temp, 250 °C; detector temp, 300 °C; head pressure, 3 psig; initial column temp, 100 °C (8 min); final column temp, 230 °C; ramp rate, 20 °C/min; and hold time, 10 min. The retention time was 14.23 min for the ester (methyl 2-methoxy benzoate) and was 16.53 min for hexadecane. The lengthy hold time was necessary due to the large size of the solvent peak at these concentrations.

Kinetic Measurements of Phenyl Methoxy Chromium Carbene Complex 28 with Diphenylacetylene. (A) Stock Solutions. A stock solution of carbene complex **28** was made by combining 416.1 mg of CC (1.33 mmol) and 0.303 mL of dodecane (1.33 mmol) with THF in a 2 mL volumetric flask to give a 0.667 M solution of both CC and dodecane. A separate stock solution of diphenylacetylene was made by combining 534.8 mg of alkyne (3.00 mmol) with THF to a total volume of 1 mL in a volumetric flask, resulting in a 3.00 M solution of alkyne.

(B) At 1.2 M Diphenylacetylene and 0.4 M Complex 28. In a flame-dried three-necked 25 mL flask with two glass stoppers and one glass stopcock under argon were combined 0.6 mL of the carbene complex stock solution and 0.4 mL of the alkyne stock solution, giving a final concentration of 0.40 M **28**, 0.40 M dodecane, and 1.2 M alkyne. The solution was deoxygenated by the freeze−pump−thaw method (3 cycles), and the glass stopcock was then replaced with a septum. The flask was then placed in a preheated (44.2 ± 0.6 °C) oil bath. The progress of the reaction was monitored as described below.

(C) At 0.6 M Diphenylacetylene and 0.4 M Complex 28. With the same setup as above, 0.4 mL of the carbene complex stock solution, 0.2 mL of the alkyne stock solution, and 0.2 mL of THF were combined, deoxygenated as above, and placed in a preheated (44.5 ± 0.5 °C) oil bath. The progress of the reaction was monitored as described below.

Kinetic Measurements. The progress of the reaction was monitored by the disappearance of the carbene complex which in turned was monitored by the disappearance of the corresponding ester, methyl benzoate, from the crude reaction mixture obtained upon oxidative workup with dodecane as the internal standard. Aliquots (0.025 mL) were taken every 10 min for the first hour and then every 30 min for two more hours. The aliquots were quenched in 0.05 mL of 0.5 M cerium ammonium nitrate (CAN) in methanol. After oxidation for approximately 5 min, each aliquot was diluted with 0.5 mL of ethyl acetate and 1 mL of water. The layers were allowed to separate, and the bottom layer was removed with a pipet before GC analysis.

GC analysis was performed on a Varian 3600 with a 30 m Alltech SE−54 0.53 mm i.d. megabore column and with an on-column injector. The following conditions were used: injector temp, 250 °C; detector temp, 300 °C; head pressure, 3 psig; $T_1 = 80$ °C (2 min); $T_2 = 120$ °C; ramp rate, 10 °C/min; $T_3 = 300$ °C; ramp rate, 50 °C/min; and hold time, 6.4 min. The retention time for the ester (methyl benzoate) is $R_T = 5.72$ min. The retention time for dodecane (internal standard) is $R_T = 4.95$ min. The response factor of methyl benzoate relative to dodecane is $R_f = 0.55$.

Kinetic Measurements of Phenyl Methoxy Chromium Carbene Complex 28 with Phenylacetylene. A stock solution of carbene complex was made by combining 400 mg of **28** (1.28 mmol) and 0.291 mL of dodecane (1.28 mmol) with THF in a 2 mL volumetric flask to give a 0.641 M solution of both **28** and dodecane.

(A) At 0.5 M Complex 28 and 2.0 M Phenylacetylene. With the same setup as for diphenylacetylene, 0.78 mL of the stock solution of carbene complex was combined with 0.22 mL of phenylacetylene (2.00 mmol) for a final volume of 1 mL. The solution was degassed with three freeze−pump−thaw cycles and placed in a preheated oil bath at 44.4 ± 0.4 °C.

(B) At 0.5 M Complex 28 and 1.0 M Phenylacetylene. With the same setup as for diphenylacetylene, 0.78 mL of the stock solution of carbene complex was combined with 0.11 mL of phenylacetylene (1.00 mmol) and 0.11 mL of THF for a final volume of 1 mL. The solution was degassed with three freeze−pump−thaw cycles and placed in a preheated oil bath at 44.5 ± 0.5 °C. The progress of the reaction was monitored by the disappearance of the carbene complex just as for the reaction with diphenylacetylene. The same GC conditions were also used.

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