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Alkyne Competition in the Benzannulation Reaction with Chromium Carbene Complexes

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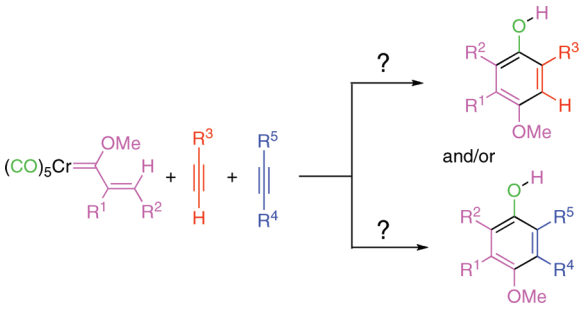


The benzannulation reaction of Fischer carbene complexes is investigated under conditions where the reaction of the carbene complex is occurring in the presence of two different alkynes. A series of competition experiments are examined where the effects of various structural factors are explored by pitting 10 different carbene complexes with 11 different alkynes. Terminal alkynes will react selectively over internal alkynes in all cases examined including both aryl and alkenyl complexes. Aryl carbene complexes with methoxy substituents do not give quite as high selectivity for terminal alkynes over internal alkynes (~95:5) as do isopropoxy substituents (> 99:1), whereas most alkenyl complexes give high selectivity with both substituents (> 99:1). Competition experiments between two different terminal alkynes or between two different internal alkynes did not result in anything more than very modest selectivities at best (~2:1). Excellent selectivities were realized between two different terminal acetylenes if one of the terminal acetylene was protected with a trimethylsilyl group. Finally, it was demonstrated that the high selectivities between terminal and internal alkynes can be utilized in the reaction with molecules that contain both types of alkyne functions.

Introduction

The reaction of chromium carbene complexes with alkynes is one of the most useful methods for the synthesis of phenols and quinones.[1] One aspect of the utility of this benzannulation reaction is the very high regioselectivity observed in the reaction with terminal alkynes.[2] For example, the reaction of the phenyl complex **1a** with phenylacetylene has been reported to give the phenol **2** in 87% yield with no detectable amount of the phenol **3**, which would be the result of the other regioisomeric outcome of this reaction (Scheme 1).[3] The selectivity was reported to be at least 179:1. Similarly, the reaction of the *o*-methoxy complex **4** with 1-pentyne has been reported to give the quinone **4** with a > 111:1 selectivity over the quinone **5**.[2a] In this case the crude reaction mixture was submitted to an oxidative workup since the isolation of the quinone **4** would be more representative of the true reaction yield than the air-sensitive phenol **6**. Unsymmetrical internal alkynes do not give benzannulated products with high levels of regioselectivity unless the steric difference between the two alkynes substituents is large.[2] This is illustrated by reactions of the complex **4** with the internal alkynes shown in Scheme 1.[2a,4] The regioselectivity is 2.9:1 with *n*-propyl methyl acetylene[2a] and increases to only 4.8:1 with isopropyl

(1) (a) Waters, M. L.; Wulff, W. D. *Org. React.* **2008**, *70*, 121–623. (b) Dötz, K. H.; Stendel, J., Jr. *Chem. Rev.* **2009**, *109*, 3227.

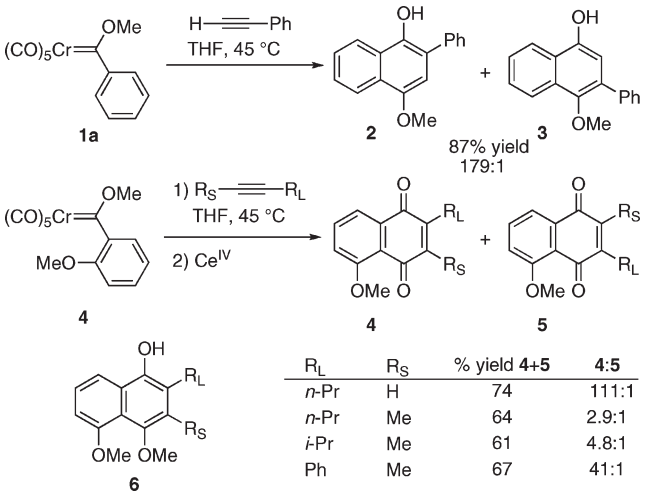
(2) (a) Wulff, W. D.; Tang, P.-C.; McCallum, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 7677. (b) Dötz, K. H.; Mühlemeier, J.; Schubert, U.; Orama, O. *J. Organomet. Chem.* **1983**, *247*, 187. (c) Wulff, W. D.; Chan, K.-S.; Tang, P.-C. *J. Org. Chem.* **1984**, *49*, 2293. (d) Yamashita, A.; Toy, A. *Tetrahedron Lett.* **1986**, *27*, 3471.

(3) Bao, J.; Wulff, W. D.; Fumo, M. J.; Grant, E. B.; Heller, D. P.; Whitcomb, M. C.; Yeung, S.-M. *J. Am. Chem. Soc.* **1996**, *118*, 2166.

(4) Waters, M. L.; Bos, M. E.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 6403.

DOI: 10.1021/jo100433k Published on Web 06/09/2010

SCHEME 1



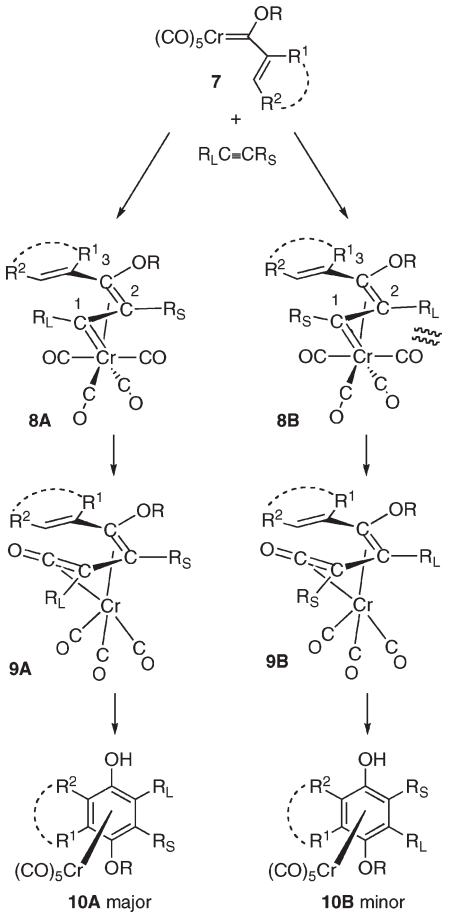
R_L	R_S	% yield **4+5**	**4:5**
n-Pr	H	74	111:1
n-Pr	Me	64	2.9:1
i-Pr	Me	61	4.8:1
Ph	Me	67	41:1

methyl acetylene,[2a] but with phenyl methyl acetylene[4] a 41:1 selectivity is observed. While the regioselectivity can be affected by sterics, the influence of electronics on the benzannulation reaction is not normally observed to any great extent.[5]

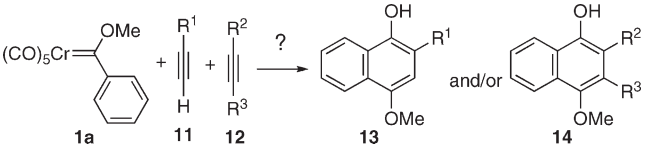
The source of the regioselectivity is thought to be related to the relative stability of the isomeric η^1,η^3-vinyl carbene complexed intermediates **8A** and **8B** (Scheme 2).[6a] According to the best understanding of the mechanism of the benzannulation at this time,[1,4,5a,6] these intermediates are generated by a rate-limiting loss of a carbon monoxide ligand from the pentacarbonyl carbene complex **7** and then reaction of the alkyne with the chromium−carbon double bond of the unsaturated intermediate. Calculations reveal that the substituent at the 2-position of these intermediates is much closer to a carbon monoxide ligand than a substituent at the 1-position. Thus as the steric differential between the substituents R_L and R_S increases, intermediate **8A** should be increasingly favored over **8B**. Subsequent to the formation of the η^1,η^3-vinyl carbene complexed intermediate **8** is the CO insertion to give the ketene complex **9** and then electrocyclic ring closure and tautomerization to give the phenol tricarbonyl complex **10**, which can be isolated but is normally oxidized to give either a phenol or quinone product.

Whereas the regioselectivity of the benzannulation reaction of unsymmetrical alkynes has been studied extensively, the chemoselectivity of a competition between two different alkynes has not been examined in any systematic fashion.[1,7]

SCHEME 2



SCHEME 3



Specifically, if the benzannulation of a carbene complex of the type **1a** was carried out in the presence of a terminal and an internal alkyne, which product would dominate, the phenol **13** derived from the terminal alkyne or the phenol **14** derived from the internal alkyne (Scheme 3)? From the regioselectivity known for this reaction, it might be suspected that the terminal alkyne would react faster, but this has never been put to the test in a controlled fashion. In the only study that gives some insight in the chemoselectivity of the benzannulation reaction for two different alkynes, Finn and coworkers found that added alkynes could affect the product distribution from intramolecular benzannulation reactions without the added alkynes being incorporated into any of the products.[9] This effect was termed the zenochemical effect. The goal of the present work is to carry out the first systematic

(5) (a) Waters, M. L.; Brandvold, T. A.; Isaacs, L.; Wulff, W. D. *Organometallics* **1998**, *17*, 4298. (b) Chamberlin, S.; Waters, M. L.; Wulff, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3113. (c) Dötz, K. H.; Szesni, N.; Nieger, M.; Nättinen, K. *J. Organomet. Chem.* **2003**, *671*, 58. (d) Davies, M. W.; Johnson, C. N.; Harrity, J. P. *J. Org. Chem.* **2001**, *66*, 3525. (e) Gordon, D. M.; Danishefsky, S. J.; Schulte, G. K. *J. Org. Chem.* **1992**, *57*, 7052.

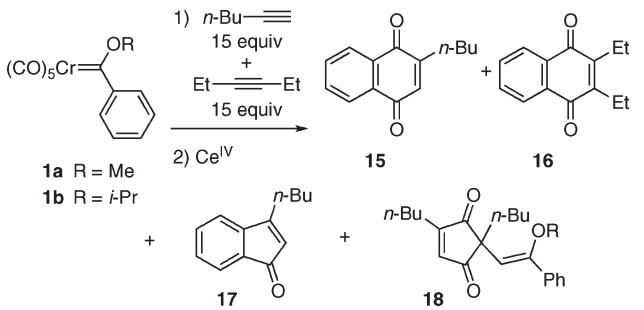
(6) (a) Hofmann, P.; Hämmerle, M.; Unfried, G. *Nouv. J. Chim.* **1991**, *15*, 769. (b) Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293. (c) Wulff, W. D.; Bax, B. M.; Brandvold, T. A.; Chang, K. S.; Gilbert, A. M.; Hsung, R. P. *Organometallics* **1994**, *13*, 102. (d) Gleichmann, M. M.; Dötz, K. H.; Hess, B. A. *J. Am. Chem. Soc.* **1996**, *118*, 10551. (e) Torrent, M.; Duran, M.; Sola, M. *J. Am. Chem. Soc.* **1999**, *121*, 1309. (f) Barluenga, J.; Aznar, F.; Gutierrez, I.; Martin, A.; Garcia-Granda, S.; Llorca-Baragano, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 1314. (g) 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. (h) Oscar, J.; Jimenez-Halla, C.; Sola, M. *Chem.—Eur. J.* **2009**, *15*, 12503.

(7) The 2-alkyne annulation involves the reaction of alkyl carbene complexes with diynes. The citations in ref 8 contain a few cases where this reaction has been investigated with unsymmetrical diynes.

(8) (a) Wulff, W. D.; Kaesler, R. W.; Peterson, G. A.; Tang, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1060. (b) Anderson, B. A.; Bao, J.; Brandvold, T. A.; Challener, C. A.; Wulff, W. D.; Xu, Y.-C.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *115*, 10671. (C) Mori, M.; Kuriyama, K.; Ochifugi, N.; Watanuki, S. *Chem. Lett.* **1995**, 615.

(9) Cross, M. F.; Finn, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 10921.

TABLE 1. Temperature and Solvent Effects on the Competition between 1-Hexyne and 3-Hexyne[a]



entry	carbene complex	temp (°C)	solvent	% yield **15**[b]	ratio **15**:**16**[c,d]
1	**1a**	80	benzene	84	93:7
2	**1a**	80	THF	42	94:6
3	**1a**	80	MeCN	41	98:2
4	**1a**	40	benzene	69	95:5
5	**1a**	40	THF	35	98:2
6	**1a**	40	MeCN	33	98:2
7	**1a**	40	hexane	64	96:4
8	**1b**	80	benzene	84	94:6
9	**1b**	80	THF	56	99:1
10	**1b**	80	MeCN	41	99:1
11	**1b**	40	benzene	74	>99:1
12	**1b**	40	THF	55	99:1
13	**1b**	40	MeCN	40	98:2
14	**1b**	40	hexane	79	>99:1

[a]All reactions were carried out with 0.3−0.5 mmol of **1** in 5 mL of solvent with 15 equiv of 1-hexyne and 15 equiv of 3-hexyne. Reaction time was 16 h at 80 °C and 22 h at 40 °C. [b]Isolated yield by silica gel chromatrography. [c]Determined by GC and GC−MS analysis of the crude reaction mixture. [d]Trace amounts of **17** and **18** were detected by GC−MS.

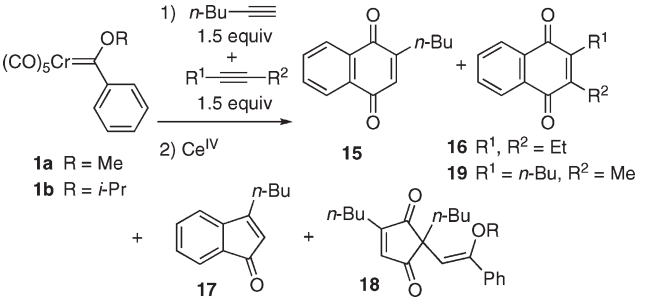
study of the competition between two different alkynes in the intermolecular benzannulation of chromium carbene complexes.

Results

It was deemed important to begin the competition under conditions where the concentration of each alkyne would not significantly change even if one of the alkynes were to react in complete preference. Thus, the first experiments were carried out with the carbene complex **1a** and 15 equiv of 1-hexyne and 15 equiv of 3-hexyne, and the results are presented in Table 1. The crude reaction mixtures were oxidized by ceric ammonium nitrate, and the ratio of the quinones **15** and **16** were determined by GC−MS analysis of the crude reaction mixture with the aid of authentic samples of each quinone. Small and varying amounts of the indenone **17** and cyclopentendione **18** were detected by GC−MS but were not quantified. In all cases the major product was the quinone **15** resulting from selective reaction with the terminal alkyne with selectivities ranging from a minimum of 93:7 up to >99:1. In each case the yield of quinone **15** was determined by isolation after purification by silica gel chromatography. The chemoselectivity was examined as a function of the temperature (40 or 80 °C), the solvent, and the size of the alkyl group in the alkoxy group of the carbene complex (methyl or isopropyl). The benzannulations of isopropoxy complexes generally give higher yields than methoxy complexes.[10] Several trends are

(10) Liptak, V. P.; Wulff, W. D. *Tetrahedron* **2000**, *56*, 10229.

TABLE 2. Competition Reactions with 1.5 Equiv of Alkynes[a]



entry	carbene complex	R^1	R^2	% yield **15**[b]	ratio **15**:**16** or **19**[c,d]
1	**1a**	Et	Et	78	96:4
2	**1b**	Et	Et	75	>99:1
3	**1a**	*n*-Bu	Me	70	97:3
4	**1b**	*n*-Bu	Me	85	>99:1

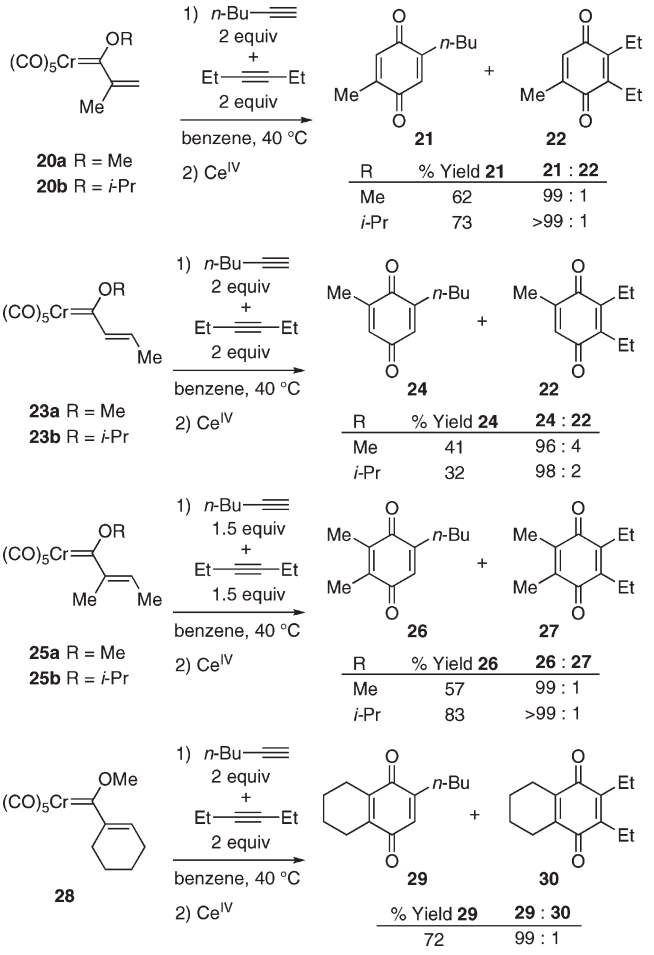
[a]All reactions were carried out with 0.3 mmol of **1** in 5 mL of benzene with 1.5 equiv of 1 -hexyne and 1.5 equiv of 3-hexyne or 2-heptyne. Reaction time was 22 h at 40 °C. [b]Isolated yield by silica gel chromatrography. [c]Determined by GC and GC−MS analysis of the crude reaction mixture. [d]Small amounts of **17** and **18** were detected by GC−MS.

observed from the data in Table 1. First, higher chemical yields are observed in less polar or less coordinating solvents such as benzene or hexane which more than offset the slightly higher selectivities observed in THF and acetonitrile. Second, a clear trend is seen across both the solvent and the nature of the carbene complex that lower temperatures lead to higher selectivity. Thus, for each carbene complex the optimal conditions involve performing the reaction in benzene at 40 °C, which gives a 95:5 selectivity for the methoxy complex **1a** (entry 4) and a >99:1 selectivity for the isopropoxy complex **1b** (entry 11).

Although the chemoselectivity between the terminal alkyne 1-hexyne and the internal alkyne 3-hexyne is complete (complex **1b**) or nearly complete (complex **1a**), the fact that 15 equiv of both alkynes was used is not synthetically practical (Table 1). Thus, this competition was repeated with only 1.5 equiv of each alkyne, and the results are shown in Table 2. Remarkably, the selectivities with both carbene complexes in benzene at 40 °C are essentially the same whether 15 equiv or 1.5 equiv of the alkynes is used. A competition was also performed between 1-hexyne and the internal alkyne *n*-butyl methyl acetylene (2-heptyne), and in this case the selectivity with the methoxy carbene complex **1a** is about the same (97:3) as it is with diethyl acetylene (96:4). The isopropoxy complex **1b** is completely selective for 1-hexyne over both internal alkynes, showing no detectable amount of the quinone **16** or **19** in the reactions with 3-hexyne or 2-heptyne, respectively.

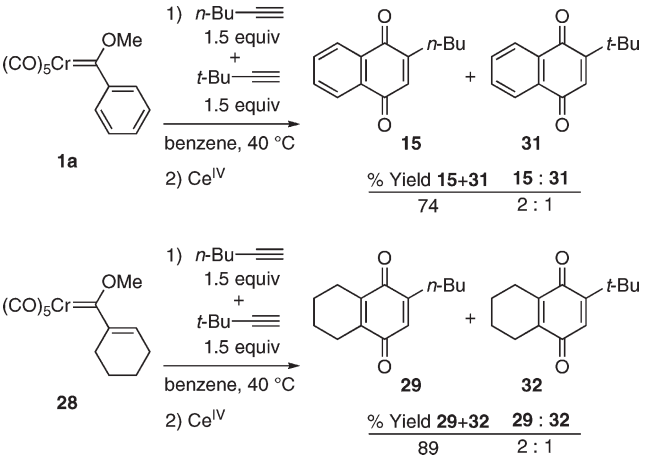
Like aryl complexes, the benzannulation of alkenyl carbene complexes with alkynes is also a very important reaction in the synthesis of phenols and quinones.[1] Therefore, a series of alkenyl complexes shown in Scheme 4 were examined for their ability to undergo chemoselective reactions with terminal alkynes in the presence of internal alkynes. The seven different complexes were subjected to a 1:1 mixture of 1-hexyne and 3-hexyne (1.5−2 equiv of each) in benzene at 40 °C under an argon atmosphere. Upon oxidative workup, the crude reaction mixture was analyzed by GC and/or GC−MS to determine the ratio of products from each alkyne, and then subsequently the major product was isolated in pure form by silica gel chromatography. In each case, the analysis of the

SCHEME 4



product ratio was aided by an authentic sample of the minor product (**22**, **27**, or **30**), which was prepared independently by the reaction of the appropriate carbene complex and 3-hexyne. The results reveal that the methoxy alkenyl complexes give a higher chemoselectivity that the methoxy phenyl complex **1a**. In each case the competition results in a 99:1 selectivity in favor of the reaction with the terminal alkyne with the exception of the *trans*-propenyl complex **23a** where a 96:4 ratio is observed. As with the reactions of the aryl complex **1a**, analysis of the crude reaction mixtures from the reactions with the alkenyl complexes shown in Scheme 4 by GC−MS reveals the presence of trace amounts of products analogous to **17** and **18**. Interestingly, the reaction of the carbene complex **20a** gave only a single regioisomer of quinone **21**. The quinone **24** would have been formed in this reaction if the regiochemistry of the incorporation of 1-hexyne had been reversed, i.e., formed via intermediate **8B** in Scheme 2. We had previously investigated the regioselectivity of complexes **20a** and **23a** with 1-pentyne in THF and found that the complex **23a** is completely regioselective (> 99:1), whereas complex **20a** only gives a 93:7 selectivity.[2c] In the present study on the competition of complex **20a** with 1-hexyne and 3-hexyne, we observed only the quinone **21** and the regioisomeric quinone **24** could not be detected (< 1:99). Given the small difference between 1-pentyne and 1-hexyne, this leads to the conclusion that the complex **20a** is much more regioselective with terminal alkynes in benzene than in THF.

SCHEME 5



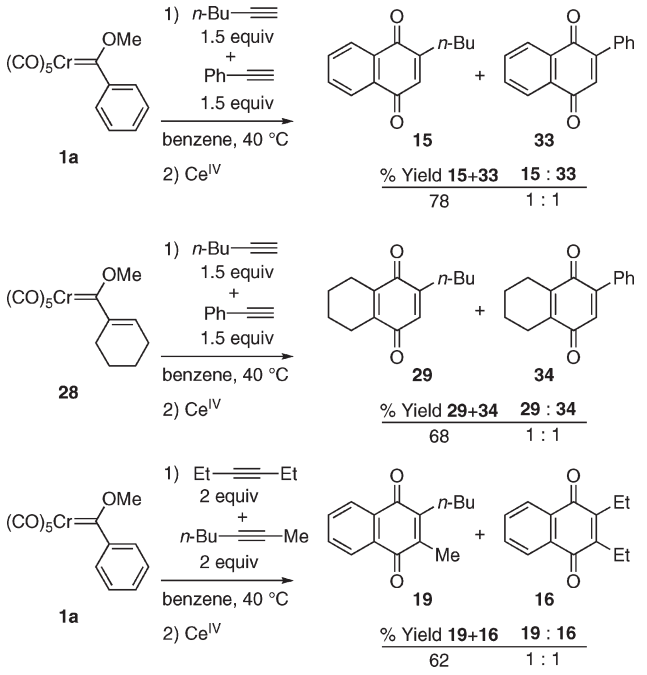
Next it was decided to determine if the very high selectivity of the benzannulation reaction for terminal alkynes over internal alkynes could be translated into selectivity between two different terminal alkynes. To maximize the difference in reactivity, the two terminal alkynes were chosen such that the steric difference between the substituents on each alkyne was large. Thus, the reaction of the methoxy phenyl complex **1a** was carried out with a 1: 1 mixture of *tert*-butyl acetylene and *n*-butyl acetylene (1.5 equiv of each), and after oxidative workup, both quinones **15** and **31** were isolated in a 2:1 ratio in a total of 74% yield (Scheme 5). The same selectivity was observed for the alkenyl complex **28**. These results suggest that it will not be possible to chemoselectively react a chromium carbene complex with a terminal alkyne in the presence of a second terminal alkyne.

While the difference in the rates of reaction of a terminal acetylene bearing a primary alkyl group and a terminal acetylene bearing a tertiary alkyl group are small but real (Scheme 5), the differences between the rates of an acetylene bearing a primary alkyl group and an acetylene bearing a phenyl group are nonexistent (Scheme 6). This was revealed in the competition of between *n*-butyl acetylene (1-hexyne) and phenyl acetylene which was found to give a 1:1 mixture of quinones **15** and **33** from the phenyl complex **1a** and also a 1:1 mixture of quinones **29** and **34** from complex **28**. An experiment was also conducted to test the chemoselectivity between two different internal alkynes. The phenyl complex **1a** was reacted with 1.5 equiv each of 3-hexyne and 2-heptyne and to give a 1:1 mixture of the quinones **19** and **16**. The results in Schemes 5 and 6 taken together indicate that it will not be possible to chemoselectively differentiate between two different terminal alkynes or two different internal alkynes in the benzannulation reaction.

In lieu of a direct discrimination between two different terminal alkynes, it was considered that chemoselection between two different terminal alkynes may be possible if one of the terminal alkynes is protected. Thus, the reaction of alkenyl complex **28** was carried out in the presence of 1-hexyne and 1-octyne and different silylated terminal alkynes (Scheme 7). Silicon-substituted alkynes are normal substrates for the benzannulation reaction[1] but in some cases bulky silyl groups can lead to the isolation of ketene complexes rather than the expected benzannulated product.[11] We find here that a

(11) Moser, W. H.; Sun, L.; Huffman, J. C. *Org. Lett.* **2001**, *3*, 3389.

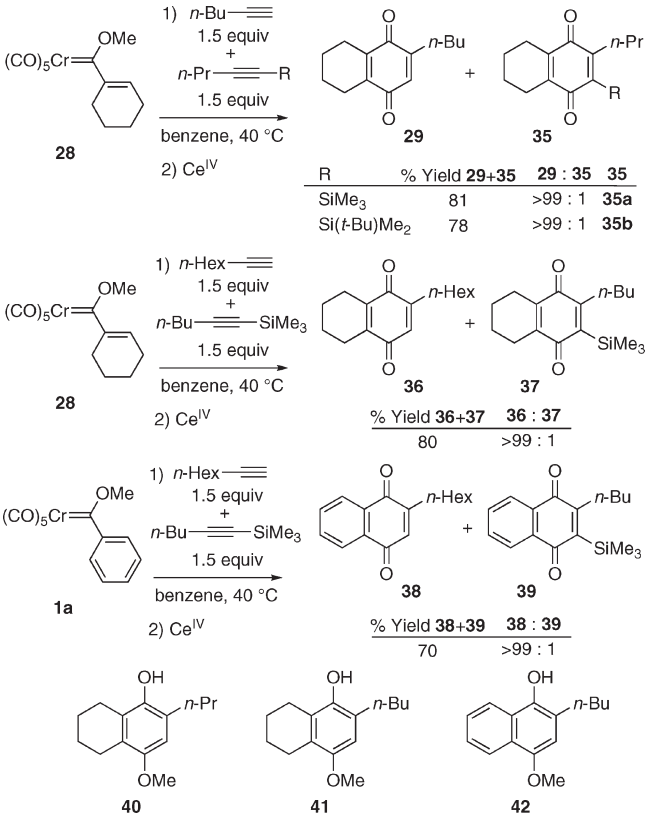
SCHEME 6



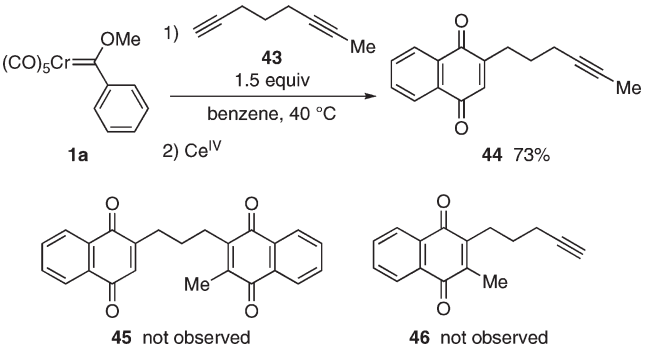
silicon substituent provides an excellent method for effecting chemoselection between two different terminal alkynes. This is illustrated in Scheme 7 where it was found that both trimethylsilyl and *tert*-butyldimethylsilyl groups are sufficient to lead to complete chemoselection between 1-hexyne and 1-pentyne in reaction with the carbene complex **28** when 1-pentyne is protected with a silyl substitutent.[11] Both silyl protecting groups provide the quinone **29** in >99:1 selectivity over quinone **35**. Under the same conditions, complex **28** will also display complete selection between 1-octyne and trimethylsilyl-1-hexyne giving >99:1 selectivity in favor of quinone **36** over quinone **37**. Again the stereoselectivities were determined by GC−MS with the aid of authentic samples of the silylated quinone **35**, **37**, or **39** that were prepared independently. These competition experiments were deliberately designed such that the silylated and nonsilylated terminal alkynes were not the same. This is because it is possible that the silylated phenol products could suffer protodesilylation to give the phenols **40**−**42** prior to oxidative workup. In each case it was determined that the quinones from these phenols were not formed. For example, quinone **35** (R = H) was not detected in the reaction where quinone **29** was formed and quinone **29** was not formed in the reaction where **36** was formed. Neither quinone **15** nor quinone **39** was observed in the reaction where quinone **38** was formed, indicating that both aryl and alkenyl complexes can be used in the chemoselective benzannulation of terminal alkynes in the presence of silylated alkynes.

The fact that high chemoselectivity is seen between terminal and internal alkynes with only 1.5 equiv of each alkyne suggests that it should be possible to achieve chemoselectivity in the reactions of molecules containing two different alkyne functions. Indeed, the reaction of the phenyl complex **1a** with the diyne **43** gave the quinone **44** in which the terminal alkyne was selectively incorporated (Scheme 8). No evidence for the presence of an isomer of **44** could be detected in the crude reaction mixture by GC−MS analysis. Also,

SCHEME 7



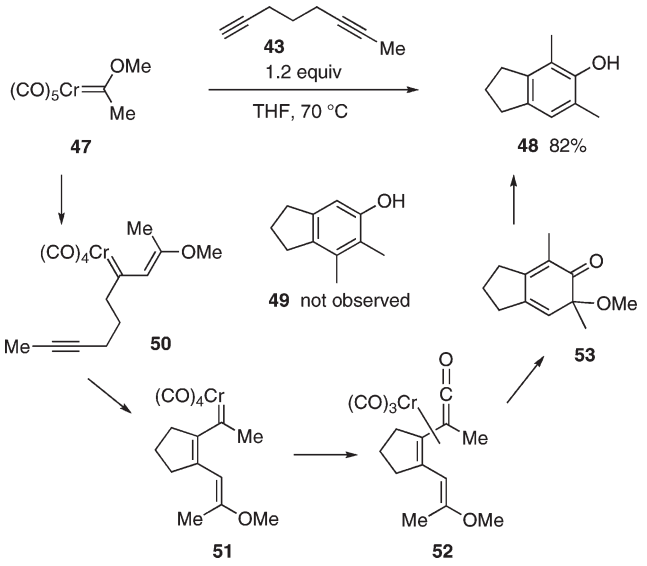
SCHEME 8



none of the bis-benzannulated product **45** could be detected in the crude reaction mixture by ^{1}H NMR spectroscopy or TLC before quinone **44** was purified.

The two-alkyne annulation provides for a synthesis of phenols starting with an alkyl carbene complex.[8] This reaction can be effected either with 2 equiv of an alkyne in an intermolecular fashion or, more efficiently, with a diyne leading to an intramolecular process. The reaction of the alkyl carbene complex with the first equivalent of the alkyne generates an α,β-unsaturated carbene complex in situ of the type **50** that then undergoes the benzannulation reaction with the second equivalent of the alkyne (Scheme 9). The penultimate product is a cyclohexadienone of the type **53**, which can be isolated under certain cases but most often is reduced to a phenol by chromium(0). A few cases are known in which this reaction has been carried out with unsymmetrical diynes, and in each case a single product has been reported and is

SCHEME 9



that resulting from reaction of the terminal alkyne in preference to the internal alkyne.[8] Neither the presence nor absence of the product resulting from the reaction of the internal alkyne is indicated in these reports. We decided to examine the reaction of the methyl complex **47** with the diyne **43** and determine if, along with the expected phenol **48**, we could obtain any evidence for the isomeric phenol **49** that would result from reaction of the internal alkyne first. The optimal solvent for this reaction is THF, and a slightly higher temperature is needed given that CO dissociation from an alkyl carbene complex is slower than for α,*β*-unsaturated complexes. The reaction of complex **47** with diyne **43** led to the isolation of the phenol **48** in 82% yield. Analysis of the crude reaction mixutre by GC−MS and by ^{1}H NMR with the aid of the expected shifts for the phenol **49** led to the conclusion that the phenol **49** is not formed in this reaction or, if it is, the selectivity for **48** over **49** is at least 50:1.

Discussion

The observations made in the present work can be interpreted in terms of the mechanistic scenario outlined in Scheme 10 that can be taken as our best understanding of the possibilities and issues associated with the mechanism of the benzannulation reaction at this point.[1,4,5a,6] There seems to be a consensus that the first and rate-limiting step of the benzannulation reaction is loss of CO to give the unsaturated tetracarbonyl complex **54**. Although not rate-limiting, the next step involves a bimolecular reaction of intermediate **54** with an alkyne to give either the alkyne complex **55** by coordination or, with carbon−carbon bond formation, to give the η^1,η^3-vinyl carbene complexed intermediate **8A**. It is not known conclusively whether the formation of **55** and/or **8A** from **54** is reversible or irreversible, although some computational studies suggest that it is not reversible.[6d] The next step is generally believed to involve an insertion of a carbon monoxide ligand in vinyl carbene complex **8A** to give the η^4-vinyl ketene complex **9A**. There is some evidence to suggest that this CO insertion step is irreversible.[4,6d,12] The origins of the selectivity between 1-hexyne and 3-hexyne must lie either in the kinetic formation of **55** or **8A** or, if the formation of **55** and/or **8A** are reversible, in the relative stability of **8A** derived from 1-hexyne and 3-hexyne. Thermodynamically, 1-hexyne would be expected to give **8A** with lower energy given the close contacts between R_S (H vs Et) and the carbon monoxide ligand (**8B** in Scheme 2) and between R_S and the alkoxy substituent (**8A** in Scheme 10). The same expectation would pertain to the transition state for the formation of **8A** under kinetic conditions. Therefore, the reaction with 1-hexyne would be expected to be more favored and thus much faster.

The chemoselectivity between 1-hexyne and 3-hexyne can be seen to be a function of the size of the alkoxy group. For example, the reaction of methoxy substituted complex **1a** gives a 95:5 ratio of quinones **15** to **16** (Table 1, entry 4) whereas, the isopropoxy substituted complex **1b** gives complete selectivity for the quinone **15** (> 99:1) as indicated by entry 11 in Table 1. The bulkier isopropoxy group would be expected to induce a stronger interaction with the substituent R_S in the η^1,η^3-vinyl carbene complexes intermediate **8A** than the methoxy group. Thus, differentiation between 1-hexyne (R_S = H) and 3-hexyne (R_S = Et) in the guise of intermediate **8A** would be expected to be more pronounced when OR is an isopropoxy group than when it is a methoxy group.

The solvent and temperature both had an effect on the competition between the reactions with 1-hexyne and 3-hexyne as indicated by the data for the reaction with the phenyl complex **1** (Table 1). Where there was a response to the temperature, not unexpectedly the selectivity decreased with increasing temperature (entries 8 vs 11). It was interesting to find that the chemoselectivity increased with the coordinating ability of the solvent, and this was true for both the methoxy and isopropoxy complexes **1a** and **1b**. This suggests that the 16 e$^-$ unsaturated species **54** can be intercepted by solvent to give the saturated intermediate **56**. If complex **56** can react with the alkyne in an associative manner to give the η^1,η^3-vinyl carbene complexed intermediate **8A**, then it might be expected that this associative process would be more sensitive to the sterics of the alkyne than a process that involves direct coordination of an alkyne with **54** to give **8A.**[13] This could be expected to lead to increased chemoselection between 1-hexyne and 3-hexyne with coordinating solvents.

The biggest effect of the solvent is the dramatic drop in yields of the quinone **15** (Table 1). It is well-known that the yields of the benzannulation reaction are higher in noncoordinating solvents such as benzene and hexane.[1,6b,c,g] Polar and/or coordinating solvents lead to the formation of several different side-products including indenes[6b] and cyclobutenones,[6g] and this is certainly a possible explanation for the loss of mass balance in the reactions in THF and MeCN. Indene products were detected by GC−MS in the crude reactions mixtures of the reactions indicated in Table 1, but only the amounts of the quinone **15** were quantified. Cyclobutenones may not survive the thermal conditions of GC analysis.

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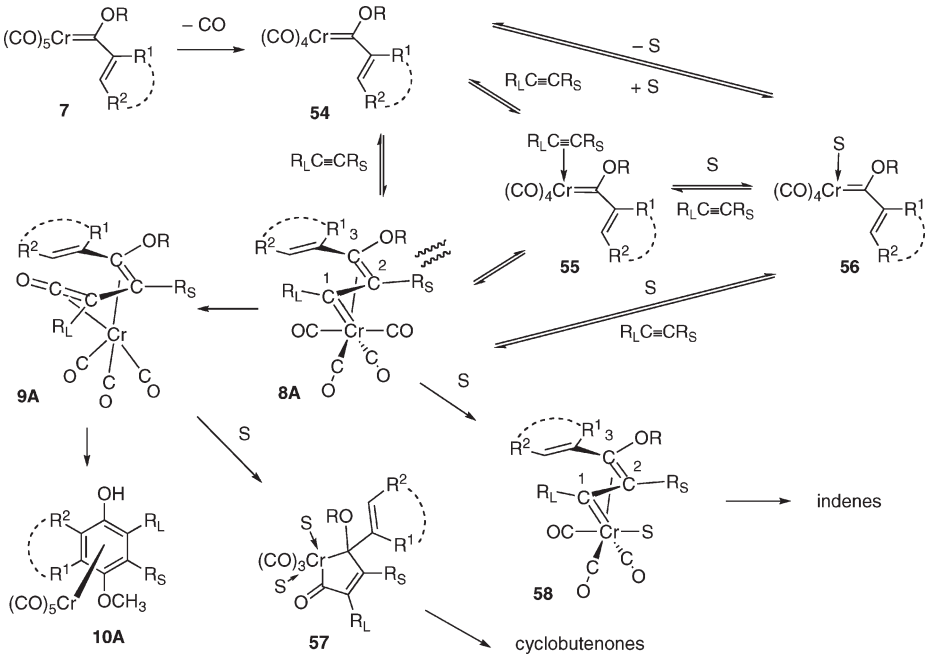
(13) A reviewer suggested the interesting possibility that intermediate **56** in Scheme 10 could also react with an alkyne in a dissociative process. If this involved loss of a CO ligand, then the solvent effect would be expressed in the differential rates of addition of terminal and internal alkynes to intermediate **54** and to the intermediate generated from **56** by loss of CO.

SCHEME 10



The benzannulation reactions of alkenyl complexes are well-known[1,6c,g] to be far less sensitive to solvent than are the reactions of aryl complexes, and this is one of the reasons that the competition reactions for the alkenyl complexes indicated in Scheme 4 were not examined in other solvents. One interesting feature of the reactions in Scheme 4 is that all complexes give complete selection for 1-hexyne over 3-hexyne except for the *trans*-propenyl complex **23**. This may be related to the steric interactions associated with the interaction of an alkyne with intermediate **54** and the expectation that they would be larger when R^1 is non-hydrogen than when it is hydrogen.

Conclusions

This study for the first time gives a quantitative look at the relative rate of terminal and internal alkynes in the benzannulation reaction of Fischer carbene complexes. While the alkyne is not under normal conditions involved in the rate-limiting step of the reaction, the step at which the alkyne is incorporated is apparently much faster for a terminal alkyne than for an internal alkyne. This leads to a greater than 99:1 selectivity for incorporation of the terminal alkyne over the internal alkyne for most of the carbene complexes studied and the major exception is with aryl methoxy complexes, which display a 95:5 selectivity. This high selectivity includes trimethylsilyl substituted internal alkynes that can serve as surrogates for terminal alkynes since selectivity between different terminal alkynes is low to nonexistent. Armed with the information gained from the present work, the synthetic chemist can proceed with the utmost assurance that the benzannulation reaction of a Fischer carbene with a molecule containing two alkyne functions will selectively occur at the terminal alkyne.

Experimental Section

The preparation and characterization of most of the carbene complexes employed in this study have been previously described, including the aryl complexes **1a**[14a] and **1b**,[14b] the isopropenyl complex **20a**,[15] the *trans*-propenyl complexes **23a**[16] and **23b**,[17] the *sec*-butenyl complex **25a**,[15b] the cyclohexenyl complex **28**,[18] and the methyl complex **47**.[19]

Preparation of Isopropenyl Isopropoxy Chromium Carbene Complex 20b. To a flame-dried round-bottom flask filled with argon was added isopropenyl bromide (1.8 mL, 20 mmol) in THF (0.1 M). The solution was cooled to −78 °C, and then 1 equiv of *n*-BuLi was added dropwise. The resulting solution was stirred at −78 °C for 30 min and then transferred by cannula to a flask containing 1.1 equiv of $Cr(CO)_6$ in THF (0.05 M) at room temperature. The solution was allowed to stir at room temperature for 2 h. The resulting solution of the lithium acylate was concentrated *in vacuo* and allowed to stand under high vacuum for 10 min. The lithium acylate was dissolved in 20 mL water, and then 1.5 equiv of Me_4NBr was added with vigorously shaking. The solution was stirred at room temperature for 30 min. After this time, the crude ammonium acylate salt was extracted three times with CH_2Cl_2. The organic layer was dried over $MgSO_4$, and then the solvent was removed *in vacuo* to give the ammonium salt (4.14 g, 12.4 mmol) in 62% yield.

A portion of the ammonium acylate salt (0.50 g, 1.4 mmol) was dissolved in dry CH_2Cl_2, and 1.5 equiv of freshly prepared isopropyltriflate[20] was added as a concentrated solution in CH_2Cl_2. The reaction was stirred at room temperature for 30 min. The reaction was quenched by pouring the mixture into a separatory

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funnel containing saturated aq $NaHCO_3$ and pentane. The aqueous layer was separated and extracted with pentane until no red color was seen in the aqueous layer. The combined organic layers were washed twice with brine, and then dried over $MgSO_4$. The dried solution was filtered through a fritted funnel dry packed with Celite 503. The product carbene complex was purified by silica gel chromatography using pure pentane as eluent to give carbene complex **20b** (0.302 g, 0.99 mmol) in 71% yield. Red solid, mp 63−64 °C; $R_f = 0.30$ (hexanes). Spectral data for **20b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.49 (d, 6 H, $J = 5.4$ Hz), 1.85 (s, 3 H), 4.83 (br, 1 H), 4.98 (br, 1 H), 5.50 (br, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.5, 22.7, 85.2, 157.3, 216.4, 224.1, 349.8 (1 sp^2 C not located); IR (neat) 1980s, 1920brs, 1611w cm^{-1}; MS *m*/*z* (% rel intensity) 304 M^+ (3), 276 (14), 248 (10), 164 (100), 122 (42). Anal. Calcd for $C_{12}H_{12}CrO_6$: C, 47.38; H, 3.98. Found: C, 47.68; H, 4.30.

Preparation of the *sec*-Butenyl Isopropoxy Chromium Carbene Complex 25b. Carbene complex **25b** was prepared with the same procedure described above for the preparation of complex **20b**. The intermediate ammonium acylate salt was obtained in 84% yield (5.88 g, 16.8 mmol) from (*E*)-2-bromobut-2-ene (1.85 mL, 20 mmol). The carbene complex **25b** was obtained in 94% yield (0.896 g, 2.81 mmol) from 1.02 g (3.0 mmol) of the ammonium acylate salt. Red oil; $R_f = 0.29$ (pentane). Spectral data for **25b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.46 (s, 3 H), 1.50 (d, 6 H, $J = 6.1$ Hz), 1.85 (s, 3 H), 4.93 (br, 1 H), 5.09 (br, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.0, 20.1, 22.6, 23.03, 83.2, 113.7, 146.1, 216.6, 224.5, 356.3; IR (neat) 2986, 2084, 1991, 1379, 1254, 1178, 1082, 988, 878, 711, 661, 621 cm^{-1}; MS *m*/*z* (% rel intensity) 318 M^+ (1), 178 (31), 136 (28), 135 (41), 126 (42), 107 (28), 105 (20), 84 (100), 83 (83), 80 (18), 67 (26), 55 (93). Anal. Calcd for $C_{13}H_{14}CrO_6$: C, 49.06; H, 4.43. Found: C, 49.01; H, 4.60.

Procedure A. Competitive Benzannulation of Carbene Complexes with Two Different Alkynes. Illustrated for the reaction of **1a** in benzene at 40 °C with 15 equiv of 1-hexyne and 15 equiv of 3-hexyne. To a 50 mL flame-dried pear-shaped single-necked flask in which the 14/20 joint was replaced by a high vacuum T-shaped Teflon valve was added carbene complex **1a** (0.157 g, 0.50 mmol) in 5 mL of benzene. To this were added 1-hexyne (0.75 mL, 6.5 mmol) and 3-hexyne (0.70 mL, 6.2 mmol). The system was deoxygenated by the freeze−thaw method, and after the third cycle the flask was backfilled with argon at room temperature. The flask was sealed by closing the Teflon valve, and the flask was then heated at 40 °C for 22 h (or 80 °C for 16 h). The crude reaction mixture was diluted with Et_2O and treated with 10 equiv of 0.5 M ceric ammonium nitrate solution. The two phase mixture was stirred for 3 h at room temperature. At this point, the reaction was poured into a 125 mL separatory funnel and diluted with Et_2O. A saturated aq $NaHCO_3$ solution was added to the funnel and then separated without shaking to avoid an emulsion. The organic layer was washed with saturated $NaHCO_3$ (2 × 10 mL). The aqueous layer was then back extracted with ether (2 × 10 mL). The combined organic layers were then washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in 20 mL Et_2O, and 1 mL of this solution was reserved for GC and GC−MS analysis. The other 95% of the crude reaction mixture was loaded onto a silica gel chromatography column (2 × 25 cm) and eluted with 5% EtOAc in hexanes to give the purified quinone **15** (0.0703 g, 0.33 mmol) in 69% yield. This isolated yield was adjusted to account for the 5% that had been removed as an analytical sample. The ratio of quinone **15** to quinone **16** was determined to be 95:5 by GC analysis on an Alltech ECONO-CAP SE 54 capillary column (30 m × 0.53 mm i.d. × 1.2 μm) with the aid of an authentic sample of quinone **16** that was prepared as described below. GC−MS analysis confirmed the presence of **16** and also indicated the presence of trace amounts of compounds that by molecular weight were consistent with the indene **17** and the cyclopentenedione **18**. This reaction was repeated in THF, MeCN, and hexane as solvents at 40 and at 80 °C and also with the same four solvents for the isopropoxy complex **1b** at both temperatures, and the results are presented in Table 1. The optimal conditions for the isopropoxy complex **1b** was also in benzene at 40 °C and gave quinone **15** in 74% yield with a greater than 99:1 selectivity for quinone **15** over quinone **16**. Spectral data for 2-*n*-butylnaphthalene-1,4-dione **15**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.93 (t, 3 H, $J = 7.3$ Hz), 1.38−1.42 (m, 2 H), 1.52−1.56 (m, 2 H), 2.55 (td, 2 H, $J = 7.9$, 1.3 Hz), 6.77 (t, 1 H, $J = 1.3$ Hz), 7.69−7.71 (m, 2 H), 8.03−8.09 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.8, 22.5, 29.3, 30.1, 126.0, 126.6, 132.1, 132.3, 133.6, 133.6, 134.7, 152.0, 185.2, 185.3. These data match those previously reported for this compound.[21]

Procedure B: Preparation of Authentic Samples of the Minor Quinones. Illustrated for the synthesis of quinone **16** via the benzannulation reaction of carbene complex **1b** with 3-hexyne. To a 50 mL flame-dried pear-shaped single-necked flask in which the 14/20 joint was replaced by a high vacuum T-shaped Teflon valve was added carbene complex **1b** (0.153 mg, 0.45 mmol) in 5 mL of benzene. To this was added 2 equiv of 3-hexyne. The system was deoxygenated by the freeze−thaw method, and after the third cycle, the flask was backfilled with argon at room temperature. The flask was sealed by closing the Teflon valve, and the flask was then heated at 80 °C for 16 h. The crude reaction mixture was diluted with Et_2O and treated with 10 equiv of a 0.5 M ceric ammonium nitrate solution. The two-phase mixture was stirred for 3 h at room temperature. At this point, the reaction was poured into a 125 mL separatory funnel and diluted with Et_2O. A saturated aq $NaHCO_3$ solution was added to the funnel and then separated without shaking to avoid an emulsion. The combined organic layer was washed with saturated aq $NaHCO_3$ (2 × 10 mL). The aqueous layer was then back extracted with ether (2 × 10 mL). The combined organic layers were then washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (2 × 25 cm) with 5% EtOAc in hexanes as eluent to give quinone **16** (0.869 g, 0.406 mmol) in 90% yield as a yellow solid. Spectral data for 2,3-diethylnaphthalene-1,4-dione 1**6**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.13 (t, 6 H, $J = 7.5$ Hz), 2.62 (q, 4 H, $J = 7.5$ Hz), 7.66 (dd, 2 H, $J = 5.8$, 3.3 Hz), 8.04 (dd, 2 H, $J = 5.7$, 3.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 20.1, 126.1, 132.2, 133.2, 148.1, 185.0. These data match those previously reported for this compound.[18]

Phenyl Carbene Complexes 1a and 1b with 1-Hexyne and 3-Hexyne. This competition experiment was carried out with carbene complex **1a** (0.107 g, 0.34 mmol), 1-hexyne (0.060 mL, 0.52 mmol), and 3-hexyne (0.058 mL, 0.51 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **15** (0.0540 g, 0.252 mmol) in 78% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **15**:**16** was 96:4. The same reaction with the isopropoxy complex **1b** (0.128 g, 0.38 mmol), 1-hexyne (0.065 mL, 0.57 mmol), and 3-hexyne (0.065 mL, 0.57 mmol) gave **15** (0.0580 g, 0.271 mmol) in 75% yield with a >99:1 ratio of **15**:**16**. The data for **15** matched that presented in Procedure A above.

Phenyl Carbene Complexes 1a and 1b with 1-Hexyne and 3-Heptyne. This competition experiment was carried out with carbene complex **1a** (0.101 g, 0.32 mmol), 1-hexyne (0.055 mL, 0.48 mmol), and 2-heptyne (0.062 mL, 0.48 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **15** (0.0525 g, 0.245 mmol) in 81% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **15**:**19** was 97:3, which was determined with the aid of an authentic sample of **19** prepared as indicated below. The same reaction with the isopropoxy complex **1b** (0.101 g, 0.30 mmol),

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1-hexyne (0.052 mL, 0.45 mmol), and 2-heptyne (0.058 mL, 0.45 mmol) gave **15** (0.0521 g, 0.243 mmol) in 85% yield with a >99:1 ratio of **15**:**19**. The data for **15** matched that presented in Procedure A above.

Synthesis of Quinone 19 from Phenyl Carbene Complex 1b and 3-Heptyne. Quinone **19** (0.0500 g, 0.22 mmol, 73%) was prepared from carbene complex **1b** (0.102 mg, 0.30 mmol) and 2-heptyne according to Procedure B. Spectral data for 2-butyl-3-methylnaphthalene-1,4-dione **19**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.93 (t, 3 H, J = 7.1 Hz), 1.41−1.46 (m, 4 H), 2.17 (s, 3 H), 2.61−2.64 (m, 2 H), 7.66−7.68 (m, 2 H), 8.05−8.07 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.6, 13.9, 23.1, 26.8, 30.9, 126.2, 126.3, 132.2, 132.2, 133.3, 133.3, 143.1, 147.6, 184.7, 185.4. These data match those previously reported for this compound.[22]

Isopropenyl Carbene Complexes 20a and 20b with 1-Hexyne and 3-Hexyne. This competition experiment was carried out with carbene complex **20a** (0.170 g, 0.616 mmol), 1-hexyne (0.141 mL, 1.23 mmol), and 3-hexyne (0.1.40 mL, 1.23 mmol) in 6.2 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **21** (0.0642 g, 0.360 mmol) in 62% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **21**:**22** was 99:1, which was determined with the aid of an authentic sample of **22** prepared as indicated below. The same reaction with the isopropoxy complex **20b** (0.157 g, 0.50 mmol), 1-hexyne (0.115 mL, 1.0 mmol), and 3-hexyne (0.114 mL, 1.0 mmol) gave **21** (0.0620 g, 0.348 mmol) in 73% yield with a >99:1 ratio of **21**:**22**. Spectral data for 2-butyl-5-methylcyclohexa-2,5-diene-1,4-dione **21**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.91 (t, 3 H, J = 7.2 Hz), 1.33−1.37 (m, 2 H), 1.43−1.48 (m, 2 H), 2.01 (d, 3 H, J = 1.6 Hz), 2.36−2.40 (m, 2 H), 6.52 (t, 1 H, J = 1.5 Hz), 6.56 (q, 1 H, J = 1.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.8, 15.4, 22.4, 28.4, 29.9, 132.4, 133.6, 145.5, 149.6, 187.8, 188.3. These data those previously reported for this compound.[23]

Synthesis of Quinone 22 from Isopropenyl Carbene Complex 23b and 3-Hexyne. Quinone **22** (0.032 g, 0.18 mmol, 36%) was prepared from carbene complex **23b** (0.152 mg, 0.50 mmol) and 3-hexyne according to Procedure B. Yellow oil, R_f = 0.35 (5% EtOAc in hexanes). Spectral data for 2,3-diethyl-5-methyl-[1,4]-benzoquinone **22**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.04 (t, 3 H, J = 7.4 Hz), 1.05 (t, 3 H, J = 7.4 Hz), 2.00 (d, 3 H, J = 1.5 Hz), 2.44 (q, 2 H, J = 7.4 Hz), 2.46 (q, 2 H, J = 7.4 Hz), 6.52 (q, 1 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9 (br, 2C), 15.8, 19.4, 19.7, 133.2, 145.3, 145.38, 145.5, 187.7, 188.0; MS m/z (% rel intensity) 178 M^+ (100), 164 (11), 163 (85), 149 (32), 135 (38), 121 (40), 107 (23), 91 (22), 79 (17), 77 (14), 67 (18), 53 (12).

***trans*-Propenyl Carbene Complexes 23a and 23b with 1-Hexyne and 3-Hexyne.** This competition experiment was carried out with carbene complex **23a** (0.138 g, 0.50 mmol), 1-hexyne (0.115 mL, 1.0 mmol), and 3-hexyne (0.114 mL, 1.0 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **24** (0.0350 g, 0.197 mmol) in 41% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **24**:**22** was 96:4, which was determined with the aid of an authentic sample of **22** prepared as described above. The same reaction with the isopropoxy complex **20b** (0.152 g, 0.50 mmol), 1-hexyne (0.115 mL, 1.0 mmol), and 3-hexyne (0.114 mL, 1.0 mmol) gave **24** (0.0270 g, 0.152 mmol) in 32% yield with a 98:2 ratio of **24**:**22**. Yellow oil; R_f = 0.30 (5% EtOAc in hexanes). Spectral data for 2-butyl-6-methyl-[1,4]-benzoquinone **24**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.91 (t, 3 H, J = 7.2 Hz), 1.34−1.38 (m, 2 H), 1.43−1.48 (m, 2 H), 2.03 (d, 3 H, J = 1.5 Hz), 2.40 (t, 2 H, J = 7.7 Hz), 6.47−6.48 (m, 1 H), 6.52−6.53 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 15.9, 22.3, 28.7, 29.8, 132.2, 132.9, 145.8, 149.5, 187.7, 187.8; IR (neat) 2959, 2932, 2874, 1653, 1614, 1294, 914 cm^{-1}; MS m/z (% rel intensity) 178 M^+ (79), 163 (63), 135 (100), 121 (11), 107 (26), 91 (22), 79 (12), 77 (11). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.54, H, 8.29.

***trans-sec*-Butenyl Carbene Complexes 25a and 25b with 1-Hexyne and 3-Hexyne.** This competition experiment was carried out with carbene complex **25a** (0.38 g, 1.31 mmol), 1-hexyne (0.226 mL, 1.97 mmol), and 3-hexyne (0.223 mL, 1.0 mmol) in 13 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **26** (0.0136 g, 0.708 mmol) in 57% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **26**:**27** was 99:1, which was determined with the aid of an authentic sample of **27** prepared as described below. The same reaction with the isopropoxy complex **25b** (0.268 g, 0.842 mmol), 1-hexyne (0.145 mL, 1.26 mmol), and 3-hexyne (0.143 mL, 1.26 mmol) in 8.4 mL of benzene gave **26** (0.1270 g, 0.66 mmol) in 83% yield with a >99:1 ratio of **26**:**27**. Spectral data for 5-*n*-butyl-2,3-dimethylcyclohexa-2,5-diene-1,4-dione **26**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3 H, J = 7.1 Hz), 1.28−1.43 (m, 4 H), 1.93 (s, 3 H), 1.95 (s, 3 H), 2.33 (t, 2 H, J = 7.4 Hz), 6.42 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.0, 12.3, 13.8, 22.3, 28.7, 29.9, 131.9, 140.3, 140.9, 149.0, 187.4, 187.5. These data those previously reported for this compound.[24]

Synthesis of Quinone 27 *trans-sec*-Butenyl Carbene Complex 25b and 3-Hexyne. Quinone **27** was prepared from carbene complex **25b** and 3-hexyne according to Procedure B. Spectral data for 2,3-diethyl-5,6-dimethylcyclohexa-2,5-diene-1,4-dione **27**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.04 (t, 6 H, J = 7.6 Hz), 1.98 (s, 6 H), 2.46 (q, 4 H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.3, 14.0, 19.7, 140.4, 145.0, 187.5. These data matched those previously reported for this compound.[25]

Cyclohexenyl Carbene Complex 28 with 1-Hexyne and 3-Hexyne. This competition experiment was carried out with carbene complex **28** (0.16 g, 0.5 mmol), 1-hexyne (0.115 mL, 1.0 mmol), and 3-hexyne (0.114 mL, 1.0 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **29** (0.075 g, 0.344 mmol) in 72% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **29**:**30** was 99:1, which was determined with the aid of an authentic sample of **30** prepared as described below. Spectral data for 2-*n*-butyl-5,6,7,8-tetrahydronaphthalene-1,4-dione **29**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.90 (td, 3 H, J = 7.3, 1.8 Hz), 1.33−1.37 (m, 2 H), 1.44−1.47 (m, 2 H), 1.65−1.67 (m, 4 H), 2.36−2.40 (m, 6 H), 6.44−6.45 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 20.9, 21.1, 22.2, 22.3, 22.6, 28.5, 29.9, 131.9, 141.9, 142.3, 149.0, 187.5, 187.7. These data those previously reported for this compound.[25]

Synthesis of Quinone 30 from Cyclohexenyl Carbene Complex 28 and 3-Hexyne. Quinone **30** was prepared from carbene complex **28** and 3-hexyne according to Procedure B. Spectral data for 2,3-diethyl-5,6,7,8-tetrahydronaphthalene-1,4-dione **30**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.04 (t, 6 H, J = 7.5 Hz), 1.63−1.65 (m, 4 H), 2.37−2.37 (m, 4 H), 2.44 (q, 4 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 19.5, 21.2, 22.5, 141.9, 145.0, 187.5. These data matched those previously reported for this compound.[26]

Phenyl Carbene Complex 1a with *n*-Butyl Acetylene and *tert*-Butyl Acetylene. This competition experiment was carried out with carbene complex **1a** (0.247 g, 0.79 mmol), 1-hexyne (0.136 mL, 1.19 mmol), and *tert*-butyl acetylene (0.142 mL, 1.19 mmol) in 8 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **15** (0.079 g, 0.369 mmol) in 49% isolated yield and quinone **31** (0.040 g, 0.187 mmol) in 25% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **15**:**31** was 2:1. The data for **15** matched that those presented for **15** in

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Procedure A above. Spectral data for 2-*tert*-butylnaphthalene-1,4-dione **31**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (s, 9 H), 6.81 (s, 1 H), 7.66-.769 (m, 2 H), 7.99−8.01 (m, 1 H), 8.04−8.06 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.4, 35.7, 125.6, 126.8, 131.5, 133.2, 133.5, 133.7, 133.8, 158.3, 184.9, 185.9. These data matched those previously reported for this compound.[27]

Cyclohexenyl Carbene Complex 28 with *n*-Butyl Acetylene and *tert*-Butyl Acetylene. This competition experiment was carried out with carbene complex **28** (0.236 g, 0.75 mmol), 1-hexyne (0.129 mL, 1.12 mmol), and *tert*-butyl acetylene (0.138 mL, 1.12 mmol) in 7.5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **29** (0.089 g, 0.408 mmol) in 57% isolated yield and quinone **32** (0.050 g, 0.229 mmol) in 32% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **29**:**32** was 2:1. The spectral data for **29** matched that those presented for **29** above. Spectral data for 2-*tert*-butyl-5,6,7,8-tetrahydronaphthalene-1,4-dione **32**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.23 (s, 9 H), 1.63−1.65 (m, 4 H), 2.35−2.38 (m, 4 H), 6.48 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.9, 21.3, 22.1, 22.8, 29.3, 35.1, 131.1, 140.9, 143.9, 155.6, 187.4, 188.4. These data matched those previously reported for this compound.[28]

Phenyl Carbene Complex 1a with *n*-Butyl Acetylene and Phenyl Acetylene. This competition experiment was carried out with carbene complex **1a** (0.156 g, 0.50 mmol), 1-hexyne (0.086 mL, 0.75 mmol), and phenyl acetylene (0.082 mL, 0.75 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **15** (0.0397 g, 0.186 mmol) in 39% isolated yield and quinone **33** (0.0204 g, 0.087 mmol) in 18% isolated yield in a 55:45 isolated ratio. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **15**:**33** was 1:1. The data for **15** matched that those presented for **15** in Procedure A above. Spectral data for 2-phenylnaphthalene-1,4-dione **33**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.04 (s, 1 H), 7.43−7.46 (m, 3 H), 7.54−7.56 (m, 2 H), 7.73−7.75 (m, 2 H), 8.07−8.09 (m, 1 H), 8.14−8.15 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 125.9, 127.0, 128.4, 129.4, 129.9, 132.0, 132.4, 133.3, 133.7, 133.8, 135.1, 148.0, 184.3, 185.0. These data matched those previously reported for this compound.[18]

Cyclohexenyl Carbene Complex 28 with *n*-Butyl Acetylene and Phenyl Acetylene. This competition experiment was carried out with carbene complex **1a** (0.158 g, 0.50 mmol), 1-hexyne (0.086 mL, 0.75 mmol), and phenyl acetylene (0.082 mL, 0.75 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **29** (0.0386 g, 0.180 mmol) in 38% isolated yield and quinone **34** (0.0333 g, 0.142 mmol) in 30% isolated yield in a 1:1 isolated ratio. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **29**:**34** was 1:1. The data for **29** match those presented for **29** above. Spectral data for 5,6,7,8-tetrahydro-2-phenylnaphthalene-1,4-dione **34**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.68−1.70 (m, 4 H), 2.43−2.47 (m, 4 H), 6.74 (s, 1 H), 7.37−7.40 (m, 3 H), 7.42−7.44 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.8, 21.1, 22.3, 22.8, 128.2, 129.1, 129.56, 132.3, 133.1, 142.1, 142.5, 145.5, 186.5, 187.5. These spectral data match those previously reported for this compound.[29]

Phenyl Carbene Complex 1a with 3-Hexyne and 2-Heptyne. This competition experiment was carried out with carbene complex **1a** (0.102 g, 0.33 mmol), 2-heptyne (0.076 mL, 0.66 mmol), and 3-hexyne (0.075 mL, 0.66 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A. The quinones could not be separated by chromatography on silica gel, and thus purification resulted in the isolation of a 1:1 mixture of **19** and **16** in a 62% combined yield (0.046 g of the mixture). The quinones were identified in the mixture with the aid of the ^{1}H NMR spectra of each of the quinones, which were prepared as described above.

Cyclohexenyl Carbene Complex 28 with 1-Hexyne and Trimethylsilyl-1-pentyne. This competition experiment was carried out with carbene complex **28** (0.158 g, 0.50 mmol), 1-hexyne (0.086 mL, 0.75 mmol), and 1-TMS-1-pentyne (0.138 mL, 0.75 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **29** (0.0884 g, 0.406 mmol) in 81% isolated yield as the only product. The ^{1}H NMR spectrum of the crude reaction mixture indicated that the ratio of **29**:**35a** was >99:1 as determined with the aid of an authentic sample of quinone **35a** prepared as described below. Quinone **35a** also could not be detected by GC−MS analysis of the crude reaction mixture. The data for quinone **29** match those presented for **29** above.

Synthesis of Quinone 35a from Carbene Complex 28 and Trimethylsilyl-1-pentyne. Quinone **35a** (45 mg, 0.145 mmol, 44%) was prepared from carbene complex **28** (103 mg, 0.33 mmol) and trimethylsilyl-1-pentyne according to Procedure B. Yellow oil; R_f = 0.51 (20:1:1 hexanes/Et_2O/CH_2Cl_2). Spectral data for 5,6,7,8-tetrahydro-2-(trimethylsilyl)-3-propylnaphthalene-1,4-dione **35a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.26 (s, 9 H), 0.93 (t, 3 H, J = 7.3 Hz), 1.35−1.40 (m, 2 H), 1.62−1.64 (m, 4 H), 2.33−2.37 (m, 4 H), 2.45−2.48 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 1.6, 14.3, 21.1, 21.2, 22.5, 22.6, 24.7, 30.7, 141.9, 143.5, 145.5, 156.5, 186.8, 192.0; IR 2942, 2874, 1644, 1273, 868, 844 cm^{-1}; MS m/z (% rel intensity) 276 M^+ (34), 262 (22), 261 (100), 233 (26). HRMS (CI) calcd for $C_{16}H_{25}O_2Si$ m/z 277.1624, meas 277.1619.

Cyclohexenyl Carbene Complex 28 with 1-Hexyne and *tert*-Butyldimethylsilyl-1-pentyne. This competition experiment was carried out with carbene complex **28** (0.158 g, 0.50 mmol), 1-hexyne (0.086 mL, 0.75 mmol), and 1-TBS-1-pentyne (0.138 g, 0.75 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **29** (0.0848 g, 0.389 mmol) in 78% isolated yield as the only product. No evidence for the presence of quinone **35b** could be obtained upon analysis of the crude reaction mixture by GC−MS or ^{1}H NMR spectroscopy. The data for quinone **29** match those presented for **29** above.

Cyclohexenyl Carbene Complex 28 with 1-Octyne and Trimethylsilyl-1-hexyne. This competition experiment was carried out with carbene complex **28** (0.0778 g, 0.25 mmol), 1-octyne (0.0404 mL, 0.38 mmol), and 1-TMS-1-hexyne (0.075 mL, 0.38 mmol) in 5 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **36** (0.0492 g, 0.20 mmol) in 80% isolated yield as a yellow oil; R_f = 0.30 (20:1:1 hexanes/Et_2O/CH_2Cl_2). The ^{1}H NMR spectrum of the crude reaction mixture indicated the presence of only a trace of quinone **37** with a ratio of **36**:**37** of >99:1 as determined with the aid of an authentic sample of quinone **37** prepared as described below. Spectral data for 2-*n*-hexyl-5,6,7,8-tetrahydro-[1,4]naphthoquinone **36**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.86 (t, 3 H, J = 6.6 Hz), 1.25−1.34 (m, 6 H), 1.45−1.48 (m, 2 H), 1.66 (m, 4 H), 2.35−2.40 (m, 6 H), 6.44 (t, 1 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 20.9, 21.1, 22.2, 22.4, 22.6, 27.7, 28.8, 28.9, 31.4, 131.9, 141.9, 142.3, 149.0, 187.5, 187.7; IR (neat) 2932, 2861, 1651, 1616, 1294 cm^{-1}; MS m/z (% rel intensity) 246 M^+ (50), 203 (38), 178 (24), 177 (100), 176 (33), 175 (21), 161 (26), 149 (15), 148 (23), 147 (15), 91 (16), 79 (16), 77 (16). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.84; H, 9.14.

Synthesis of Quinone 37 from Carbene Complex 28 and Trimethylsilyl-1-hexyne. Quinone **37** (50.1 mg, 0.155 mmol, 47%) was prepared from carbene complex **28** (103 mg, 0.33 mmol) and trimethylsilyl-1-hexyne according to Procedure B. Yellow oil; R_f = 0.41 (20:1:1 hexanes/Et_2O/CH_2Cl_2). Spectral data for 2-*n*-butyl-3-trimethylsilyl-5,6,7,8-tetrahydro-[1,4] naphthoquinone **37**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.26 (s, 9 H), 0.89 (t, 3 H, J = 7.1 Hz), 1.32−1.35 (m, 4 H), 1.62−1.64 (m, 4 H), 2.34−2.36 (m, 4 H), 2.47−2.49 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 1.6, 13.9, 21.1, 21.2, 22.5, 22.6, 23.1, 28.7, 33.5, 141.9, 143.5,

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145.4, 156.8, 186.8, 192.0; IR (neat) 2938, 1645, 1273, 868, 847 cm^{-1}; MS *m*/*z* (% rel intensity) 290 M^+ (10), 276 (35), 275 (36), 247 (18), 234 (31), 233 (84), 73 (18). HRMS (CI) calcd for $C_{17}H_{27}O_2Si$ $(M + H)^+$ *m*/*z* 291.1780, meas 291.1782.

Phenyl Carbene Complex 1a with 1-Octyne and Trimethylsilyl-1-hexyne. This competition experiment was carried out with carbene complex **1a** (0.109 g, 0.35 mmol), 1-octyne (0.0774 mL, 0.52 mmol), and 1-TMS-1-hexyne (0.105 mL, 0.52 mmol) in 6.9 mL of benzene at 40 °C for 22 h according to Procedure A to give quinone **38** (0.0596 g, 0.246 mmol) in 70% isolated yield. The ^{1}H NMR spectrum of the crude reaction mixture indicated the presence of only a trace of quinone **39** with a ratio of **38**:**39** of > 99:1 as determined with the aid of an authentic sample of quinone **39** prepared as described below. Spectral data for 2-hexylnaphthalene-1,4-dione **38**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.83−0.86 (m, 3 H), 1.25−1.29 (m, 4 H), 1.34−1.37 (m, 2 H), 1.50−1.55 (m, 2 H), 2.50−2.53 (m, 2 H), 6.74 (t, 1 H, J = 1.4 Hz), 7.66−7.68 (m, 2 H), 7.99−8.01 (m, 1 H), 8.03−8.05 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 22.5, 27.9, 29.0, 29.5, 31.5, 125.9, 126.5, 132.0, 132.3, 133.5, 133.5, 134.6, 151.9, 185.1, 185.2. These data match those previously reported for this compound.[21]

Synthesis of Quinone 39 from Phenyl Carbene Complex 1a and Trimethylsilyl-1-hexyne. Quinone **39** (27.8 mg, 0.087 mmol, 25%) was prepared from carbene complex **1a** (107 mg, 0.343 mmol) and trimethylsilyl-1-hexyne according to Procedure B. The major product of this reaction was tentatively identified as 3-*n*-butyl-2,3-dihydroinden-1-one (35.3 mg, 0.188), which was isolated in 55% yield. Spectral data for 2-*n*-butyl-3-(trimethylsilyl)naphthalene-1,4-dione **39**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.36 (s, 9 H), 0.93−0.95 (m, 3 H), 1.41−1.45 (m, 4 H), 2.67−2.70 (m, 2 H), 7.64−7.67 (m, 2 H), 7.96−7.98 (m, 1 H), 8.01−8.03 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 1.8, 13.9, 23.2, 29.2, 33.5, 126.0, 126.2, 132.2, 133.1, 133.3, 133.3, 148.8, 159.4, 184.6, 189.6. These data match those previously reported for quinone **39**.[30]

Synthesis of 1,6-Octadiyne 43 from 1,6-Heptadiyne. Preparation of 1-Trimethylsilyl-1,6-heptadiyne. 1,6-Heptadiyne (2.0 g, 21 mmol) was dissolved in 100 mL of dry THF, cooled to −78 °C, and then allowed to stir at this temperature for 10 min. A solution of lithium hexamethyldisilazide (21 mL, 1.0 M) was added, and the resulting mixture stirred for 45 min at −78 °C. Me_3SiCl (2.75 g, 25.2 mmol) in 5 mL dry THF was then added, and reaction was stirred for 2 h at the same temperature. Then 20 mL of saturated aqueous solution of ammonium chloride was added, and the mixture was warmed to room temperature and stirred for 30 min. The aqueous layer was extracted twice with 25 mL of Et_2O, the combined organic layer was dried on $MgSO_4$, and the solvent was evaporated under vacuum. The residue was distilled (bp 72−75 °C, 20 Torr) giving 3.56 g, 20 mmol (95% yield) of 1-trimethylsilyl-1,6-heptadiyne as a colorless liquid. Spectral data: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.15 (s, 9 H), 1.74 (pent, J = 7.5 Hz, 2 H), 1.96 (t, J = 2.5 Hz, 1 H), 2.29−2.32 (m, 2 H), 2.33−2.36 (m, 2 H).

Methylation of 1-Trimethylsilyl-1,6-heptadiyne. 1-Trimethylsilyl-1,6-heptadiyne (3.56 g, 21 mmol) was dissolved in 100 mL of dry THF and then cooled to −78 °C. A solution of *n*-BuLi (14 mL of 1.6 M solution) in hexane was added via syringe, followed by 10 mL of HMPA. The reaction turned to a maroon color. The resulting mixture was stirred for 10 min, and then methyl iodide (3.64 g, 25.2 mmol) was added; after stirring for 30 min the color changed and became a pale yellow. The reaction was allowed to warm to room temperature and was quenched with 30 mL of a saturated aqueous solution of ammonium chloride, and the aqueous phase was extracted with diethyl ether. After drying of the combined organic layer with $MgSO_4$ and removal of the volatiles by a rotary evaporator, the residue was distilled (bp 95−102 °C, 15 Torr) to yield 1-trimethylsilyl-1,6-octadiyne in 89% yield (3.34 g, 18.7 mmol) as a colorless liquid. Spectral data: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.14 (s, 9 H), 1.68 (pent, J = 7 Hz, 2 H), 1.77 (t, J = 3 Hz, 3 H), 2.21−2.24 (m, 2 H), 2.34−2.30 (m, 2 H).

Preparation of 1,6-Octadiyne 43. 1-Trimethylsilyl-1,6-octadiyne (3.34 g, 18.7 mmol) was dissolved in 100 mL of dry THF, and then 20 mL of 1 M TBAF solution was added via syringe. The solution turned dark brown immediately. The mixture was stirred for 1 h at room temperature. Then, 30 mL of a saturated aqueous ammonium chloride solution was added, and the aqueous layer was extracted with diethyl ether. The combined organic phase was dried with $MgSO_4$ and then filtered. The solvent was evaporated on rotary evaporator, and then the residue was passed through silica gel with pentane to remove a brown residue. The pentane was removed under vacuum yielding 1,6-octadiyne **43** in 51% yield (1.02 g, 9.6 mmol) as a colorless liquid. The overall yield from 1,6-heptadiyne was 41% over 3 steps. On large scale the product can be distilled at bp 65−70 °C (15 Torr). Spectral data for **43**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.65 (pent, J = 7 Hz, 2 H), 1.73 (t, J = 2 Hz, 3 H), 1.91 (t, J = 3 Hz, 1 H), 2.21 (m, 2 H), 2.27 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 3.4, 17.5, 17.8, 27.9, 68.6, 77.0, 77.9, 83.7; IR (KBr) 3420w, 2958s, 2925vs, 2860s, 1456 m. These data matched those previously reported for this compound.[31]

Benzannulation of Phenyl Carbene Complex 1a with 1,6-Octadiyne 43. The reaction of carbene complex **1a** (0.2123 g, 0.68 mmol) and alkyne **43** (0.1083 g, 1.02 mmol) in 10 mL of dry benzene was carried out following Procedure B described above at 40 °C for 22 h. After the reaction was done, 10 equiv of a 0.5 M aqueous solution of ceric ammonium nitrate was added at room temperature along with 10 mL of diethyl ether, and resulting mixture was stirred for 6 h. Then, the reaction mixture was washed with aq $NaHCO_3$, and the aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, and the volatiles were removed by rotary evaporation. Analysis of the crude reaction mixture by GC−MS and ^{1}H NMR did not provide any evidence for the presence of quinone **46** or for quinone **45**. GC−MS analysis was performed on an Agilent JW Scientific DB-5 ms column (0.32 mm × 30 m) with an initial temperature of 60 °C with a ramp rate of 10 °C/min. Quinone **44** had a retention time of 12.48 min, but otherwise the baseline was flat from 2 to 18 min. Finally, quinone **44** was purified by preparative TLC (hexane/EtOAc = 5:1) on an Analtech 20 × 20 cm 1000 μm plate to give 0.1182 g of yellow needles (0.50 mmol, 73%). Spectral data for **44**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.74 (t, J = 2.5 Hz, 3 H), 1.78 (pent, J = 7.5 Hz, 2 H), 2.24 (m, 2 H), 2.69 (dt, J = 7.5 Hz, 1 Hz, 2 H), 6.83 (t, J = 1 Hz, 1 H), 7.73 (m, 2 H), 8.07 (m, 1 H), 8.10 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 3.4, 18.4, 27.2, 28.8, 76.8, 78.1, 126.1, 126.6, 132.2, 132.4, 133.6, 133.7, 135.1, 151.2, 185.1, 185.1; HRMS (ES+) calcd for $(C_{16}H_{14}O_2 + H)^+$ *m*/*z* 239.1072; meas 239.1081. Yellow needles, mp 49−50 °C. R_f = 0.59 (5:1 hexane/EtOAc).

Two-Alkyne Annulation of Methyl Carbene Complex 47 with 1,6-Octadiyne 43. The reaction of the carbene complex **47** (0.2126 g, 0.85 mmol) and the diyne **43** (0.1062 g, 1.02 mmol) in 23 mL of dry tetrahydrofuran was carried with Procedure B indicated above. After 16 h at 70 °C, the reaction was complete, the solution was transferred to a 50 mL flask, and 10 g of silica gel was added. The volatiles were removed by rotary evaporator for 30 min, and then the resulting impregnated silica gel powder was placed on top of 10 g of silica gel in a column and eluted with dichloromethane. All fractions were collected and combined, and the ^{1}H NMR spectrum of the crude reaction mixture was

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recorded. The ^{1}H NMR spectrum of the crude reaction mixture without filtering through silica gel is subject to severe signal broadening due to the presence of paramagnetic Cr(III) species. The phenol **48** was then purified by silica gel chromatography to give **48** in 82% yield (0.1142 g, 0.70 mmol). Spectral data for **48**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.05 (pent, J = 7.5 Hz, 2 H), 2.22 (s, 3 H), 2.80 (t, J = 7.5 Hz, 2 H), 2.83 (t, J = 7.5 Hz, 2 H), 2.17(s, 3 H), 4.43 (s, 1 H), 6.85 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.4, 16.1, 25.3, 31.8, 32.6, 119.0, 120.7, 123.4, 135.3, 142.2, 150.4. HRMS (ES−) calcd for $(C_{11}H_{14}O - H)^+$ m/z 161.0966; meas 161.0970. Yellow needles mp 79 °C. R_f = 0.47 (5:1 hexane/EtOAc).

Analysis of the ^{1}H NMR spectrum of the crude reaction mixture indicates that the phenol **48** is the exclusive product of the reaction and that the ratio of phenol **48** to phenol **49** is at least 50:1. The phenol **49** is a known compound, and the ^{1}H NMR spectrum of **49** is reported to have an aromatic singlet at 6.50 ppm.[32] The aryl singlet for the phenol **48** determined in the present work occurs at 6.85 ppm. This type of chemical shift difference is typical of what is expected for the shielding effect of a hydroxy group on a benzene ring. For example, the pair of compounds 2,3,4,6-tetramethylphenol **70a**[33] (aryl singlet at 6.78 ppm) and 2,3,4,5-tetramethylphenol **70b**[33a] (aryl singlet at 6.49 ppm) and the pair of compounds 2,4-dimethyltetra-2-lol **71a**[34] (singlet at 6.62 ppm) and 3,4-dimethyltetra-2-lol **71b**[32,35] (singlet at 6.33−6.36 ppm) also exhibited shielding effects of the hydroxyl group in the range of ~0.3 ppm. Analysis of the ^{1}H NMR spectrum of the crude reaction mixture revealed that there were no absorptions visible in the range of 6.3−6.6 ppm, and thus it can be concluded that the selectivity for phenol **48** over **49** is at least 50:1.

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Supporting Information Available: ^{1}H and ^{13}C spectra of the compounds discussed in this work. This material is available free of charge via the Internet at http://pubs.acs.org.

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