

# Tandem and Concurrent Cycloaddition/Annulation Reactions of Chromium Alkynyl Carbene Complexes<sup>†</sup>

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**Abstract:** The Diels–Alder reaction of  $\alpha,\beta$ -acetylenic chromium carbene complexes readily occurs with a number of dienes at ambient temperatures. These alkynyl complexes can serve as synthons for substituted propiolate esters since the chromium pentacarbonyl group of the cycloadducts can be easily oxidatively removed with  $\text{Me}_2\text{SO}$ . The cyclohexa-2,5-dienyl chromium carbene complexes which are obtained from the Diels–Alder reactions are found to undergo annulation reactions with acetylenes to give dihydronaphthols or decalatrienones. The cycloaddition and annulation reactions may be carried out in tandem or concurrently with the alkynyl carbene complex, the diene, and the acetylene all in one pot. The alkynyl carbene complex will chemoselectively react with a diene in the presence of an acetylene, and the resultant cycloadduct will chemoselectively react with an acetylene in the presence of a diene to give up to as high as 92% yield of dihydronaphthol products. Some specific examples of the tandem and concurrent cycloaddition/annulation sequences are reported which suggest attractive applications to be made in synthetic organic chemistry.

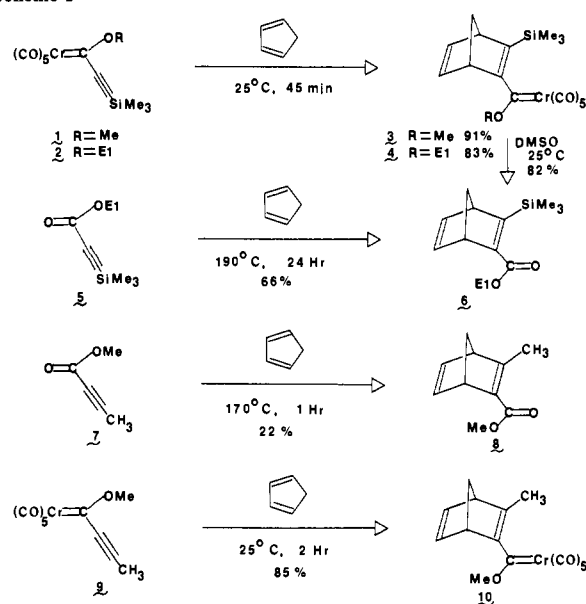
The chemistry of chromium carbene complexes has been developed to the point where there are a number of reactions<sup>1</sup> that may be drawn upon for applications to problems in synthetic organic chemistry. We recently reported on the facile Diels–Alder reactions of alkenyl carbene complexes.<sup>2</sup> Other important reactions include the benzannulation<sup>3</sup> and the cyclohexadienone annulation<sup>4</sup> reactions with acetylenes, cyclopropanation,<sup>5</sup> alkylations,<sup>6</sup>  $\beta$ -lactam formation with imines,<sup>7</sup> and aldol reactions.<sup>6,8</sup> We herein describe Diels–Alder reactions of alkynyl chromium carbene complexes and their utilization in tandem and concurrent cycloaddition/annulation sequences that portends a number of attractive applications to synthetic organic chemistry.

The (trimethylsilyl)ethynyl methoxy carbene complex **1**<sup>9a,10</sup> will react with great ease with cyclopentadiene at room temperature to give the cycloadduct **3** in 91% yield.<sup>12</sup> The structure of the cycloadduct is confirmed in the case of the ethyl complex **4** by oxidation with  $\text{Me}_2\text{SO}$ <sup>2,13</sup> to give the known norbornadienyl ester **6**.<sup>14</sup> There is a tremendous rate difference between the reaction of **2** and its closest carbon analogue ethyl trimethylsilylpropiolate **5**, which has been reported at 190 °C and 24 h to give **6** in 66% yield. The synthetic potential of these reactions is illustrated by the reactions of the propynyl complex **9**.<sup>9b</sup> Methyltetrolate **7** is known to react with cyclopentadiene at 170 °C but to give only a 22% yield of the cycloadduct **8**.<sup>15</sup> The reaction of the propynyl chromium carbene complex **9** on the other hand proceeds rapidly at room temperature to give **10** in 85% isolated yield. The reaction of **9** with cyclopentadiene is faster than that of 2-butyne which has been reported to occur in 4 days at ambient temperature.<sup>16</sup>

The Diels–Alder reactions of alkynyl carbene complexes with dienes will generate new carbene complexes of the type **12** which have a double bond in conjugation with the chromium–carbene carbon bond. These types of  $\alpha,\beta$ -unsaturated complexes are of high synthetic value by virtue of their annulation reactions with acetylenes to give the chromium tricarbonyl complexed phenols **13**<sup>3a,17</sup> when  $\text{R}_2 = \text{H}$  or the cyclohexadienones **14**<sup>4</sup> when  $\text{R}_2 = \text{Me}$ . Such an approach to the synthesis of complexes of the type **12** via cycloaddition reactions would be a welcome alternative to the only general approach currently available which involves the addition of cyclohexenyl lithiums to chromium carbonyl.

The coupling of the cycloaddition reactions of **11** and the annulation reactions of **12** is conceptually attractive, and to this end we were particularly interested in the trimethylsilyl-substituted complexes **15** which should follow directly from the cycloaddition reactions of the (trimethylsilyl)ethynyl complex **1**. Given the greater migratory propensity of silicon over hydrogen, the benzannulation of the cycloadduct **15** would be expected to give the

Scheme I



(trimethylsilyloxy)arene chromium tricarbonyl complex **16**. If this is in fact the case, another dimension could be added to these

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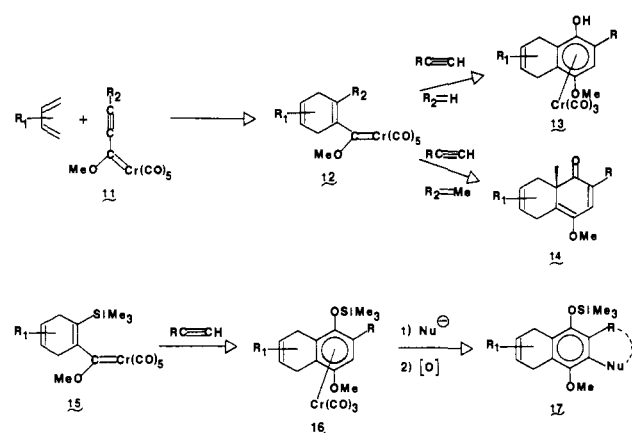
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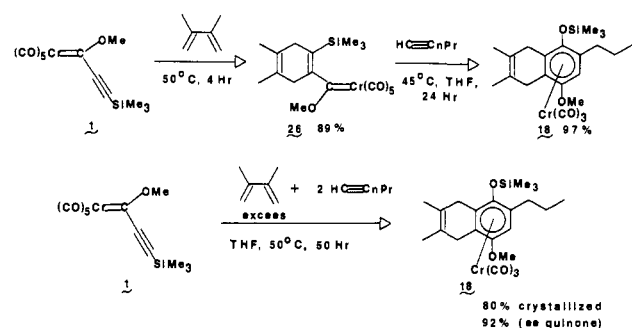
(9) (a) The complex **1** is prepared by the standard Fischer method<sup>11</sup> involving the addition of ((trimethylsilyl)ethynyl)lithium to chromium carbonyl followed by methylation with methane fluorosulfonate. Flash chromatography on silica gel with hexane ( $R_f = 0.39$ ) in air gives 78–82% yield of pure material: mp 26–27 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0.31 (s, 9 H), 4.35 (s, 3 H); IR ( $\text{CHCl}_3$ )  $\nu$  2065 w, 1990 w, 1959 s; mass spectrum,  $m/e$  (% rel intensity) 332  $\text{M}^+$  (3), 276 (3), 248 (3), 220 (5), 192 (20), 149 (80). Anal. ( $\text{C}_{12}\text{H}_{12}\text{O}_6\text{CrSi}$ ) C, H. (b) Complex **9** can be prepared in the same manner in 70% yield: m.p. 43.5–44.5 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  2.47 (s, 3 H), 4.31 (s, 3 H); IR ( $\text{CHCl}_3$ )  $\nu$  2060 m, 1995 w, 1950 s; mass spectrum,  $m/e$  (% rel intensity) 274  $\text{M}^+$  (12), 246 (12), 218 (13), 190 (19), 162 (36), 134 (100), 91 (82), 52 (100). Anal. ( $\text{C}_{10}\text{H}_6\text{O}_6\text{Cr}$ ) C, H.

<sup>†</sup> This paper is dedicated to Professor Josef Fried whose enthusiasm is contagious to all.

Scheme II



Scheme III



reactions by taking advantage of the electron-withdrawing chromium tricarbonyl group put on the arene ring by the benzannulation reaction and carrying out aromatic nucleophilic substitution reactions<sup>18</sup> on **16** to introduce functionality at the C-3 position. Migration of silicon to oxygen in **16** may be crucial since similar nucleophilic substitutions of **13** ( $R_3 = H$ ) would require 2 equiv of nucleophile, one of which would deprotonate the phenol and thus perhaps offset the electron-withdrawing effect of the chromium tricarbonyl group and forego the aromatic nucleophilic substitution reaction. Such elaborations of **16** at C-3 would be of value since the annulation reactions (of **12**) are nonregioselective with disubstituted unsymmetrical alkynes, but they are highly regioselective with terminal alkynes in the direction indicated in Scheme II.<sup>17,19</sup>

The Diels-Alder reaction of the (trimethylsilyl)ethynyl complex **1** readily occurs with a number of dienes as indicated in Table I, and in each case the subsequent benzannulation of the cycloadduct does proceed with migration of silicon to oxygen. The cycloaddition of **1** with 2,3-dimethylbutadiene is over in 4 h at 50 °C, and after purification by flash chromatography the corresponding cycloadduct is obtained in 89% yield. Subsequent

Table I. Tandem Cycloaddition/Annulations of **1** and **9**

Complex	Diene	Yield of D. A. Adduct <sup>a</sup>	Alkyne <sup>b</sup>	Annulation Product	Yield <sup>c</sup>
<b>1</b>		89 %	$nPrC\equiv CH$		97% <sup>d</sup>
		50 °C, 4 Hr			52 %
<b>1</b>		67 %	$nPrC\equiv CH$		95 %
		25 °C, 1 d			56 %
<b>1</b>		91 %	$nPrC\equiv CH$		58 % <sup>e</sup>
		25 °C, 30 min			67 % <sup>f</sup>
<b>1</b>		49 % <sup>h</sup>	$nPrC\equiv CH$		67 % <sup>i</sup>
		25 °C, 5 d			47 % <sup>i</sup>
<b>1</b>		85 %	$nPrC\equiv CH$		33 % <sup>l</sup>
		25 °C, 2 Hr			
<b>1</b>		100 % <sup>i</sup>	$nPrC\equiv CH$		80 % <sup>j</sup>
		25 °C, 10 min			92 % <sup>j</sup>

<sup>a</sup>Unless otherwise specified all Diels-Alder reactions were carried out with neat diene at the temperature indicated. <sup>b</sup>All of the annulation reactions were carried out at 0.05 M in THF at 50 °C for 24 h. <sup>c</sup>Unless otherwise indicated all yields refer to isolated material. <sup>d</sup>Removal of solvent and alkyne under vacuum gave a 97% yield of essentially pure **18**, which can be crystallized from hexane.<sup>20</sup> <sup>e</sup>70 °C, 2 days. <sup>f</sup>One-pot reaction carried out at 0.03 M in THF with 8 equiv of diene and 1.5 equiv of acetylene. <sup>g</sup>Diels-Alder reaction performed under 3 atm of carbon monoxide. <sup>h</sup>Workup by flash chromatography on silica gel of the directly filtered crude reaction mixture. <sup>i</sup>2 M in benzene with 1 equiv of diene; <sup>1</sup>H NMR yield.

reaction of the cycloadduct with 1-pentyne gives the protected chromium tricarbonyl complexed phenol **18**<sup>20</sup> in essentially quantitative yield. The other cycloaddition/annulation reactions of complex **1** indicated in Table I behave similarly and in most cases were taken to the free phenol by simple oxidation in air. It was noted that the benzannulation step was uncharacteristically slower for a disubstituted acetylene, an observation not previously made for this reaction.<sup>3b,17</sup>

The cycloaddition and annulation reactions may also be carried out concurrently with the carbene complex, the diene, and the acetylene all in one pot (Scheme III). Complex **1** will chemoselectively react with 2,3-dimethylbutadiene in the presence of 1-pentyne, and the resulting cycloadduct **28** will chemoselectively react with 1-pentyne to give the phenol complex **18** in 80% crystallized yield from hexane in two crops (the corresponding quinone can be isolated chromatographically in 92% yield).<sup>21</sup> A more functionalized example is the concurrent reaction of **1** with (2-trimethylsilyloxy)butadiene and 1-pentyne which provides for the one-pot construction of the highly functionalized tetralone **22** in 58% yield as the only regioisomer that could be detected. In

(20) Compound **18**: mp 121–123.5 °C (hexane); <sup>1</sup>H NMR (500 MHz)  $\delta$  0.34 (s, 9 H), 1.04 (t, 3 H,  $J$  7.3 Hz), 1.63 (m, 2 H), 1.77 (s, 3 H), 1.80 (s, 3 H), 2.28 (m, 1 H), 2.59 (m, 1 H), 3.05–3.30 (m, 4 H), 3.70 (s, 3 H), 4.93 (s, 1 H); IR (CHCl<sub>3</sub>)  $\bar{\nu}$  1945, 1865, 1850 sh; mass spectrum,  $m/e$  (% rel intensity) 454 M<sup>+</sup> (20), 398 (15), 370 (100), 353 (10), 325 (30). Anal. (C<sub>22</sub>H<sub>30</sub>O<sub>5</sub>CrSi) C, H, Cr.

(21) The one-pot chemoselective tandem cycloaddition/annulations were carried out at 0.03 M in THF at 50 °C with 1.5 equiv of 1-pentyne (1.2 equiv of **26**) with excess diene; 15 equiv of 2-(trimethylsilyloxy)butadiene and 80 equiv of 2,3-dimethylbutadiene.

(10) Satisfactory spectral data and elemental analysis or high-resolution mass spectra were obtained for all new compounds.

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(12) Unless otherwise indicated, all yields refer to pure compounds isolated by flash chromatography on silica gel with hexane in air.

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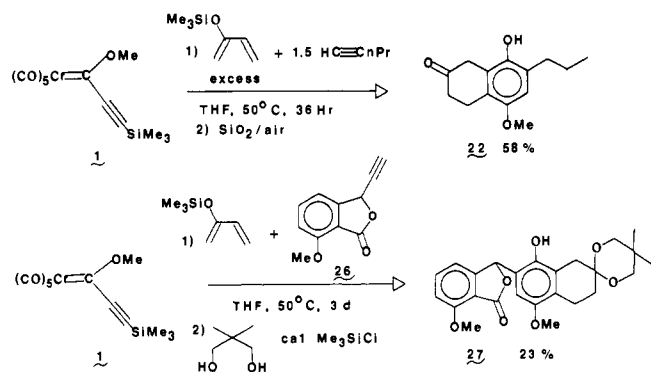
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(b) Semmelhack, M. F. *Pure Appl. Chem.* **1981**, *53*, 2379. (c) Semmelhack, M. F. *Proc. IUPAC Symp. Org. Synth.* **1981**, *3*, 63.

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Scheme IV



a similar manner the concurrent reaction of complex **1**, (2-trimethylsilyloxy)butadiene, and acetylene **26** gives after ketalization<sup>22</sup> the phenol **27** in 23% (unoptimized) overall yield.<sup>21</sup> We have previously employed the phenol **27** as an intermediate in anthracyclinone synthesis,<sup>3a</sup> and the concurrent cycloaddition/annulation sequence offers an alternate and comparably efficient approach to these intermediates.

The Diels-Alder reactions of the propynyl complex **9** proceed in good to excellent yields with reactive dienes (Table I). The reaction with the less reactive 2,3-dimethylbutadiene proceeds at 25 °C in 5 days to give only a 49% yield of the cycloadduct. This reaction was run under 3 atm of carbon monoxide and is somewhat improved from the 37% yield obtained under an argon atmosphere. The reason for the reduced yield with 2,3-dimethylbutadiene is not understood at this time. In accord with our recent report<sup>4</sup> describing the cyclohexadienone annulation of  $\beta,\beta$ -disubstituted  $\alpha,\beta$ -unsaturated carbene complexes such as **12** ( $R_2 \neq H$ ), the cycloadducts obtained from **9** will react with 1-pentyne to give the cyclohexadienones **23-25**. Thus the application of the cycloaddition/annulation sequence to carbon-substituted alkynyl complexes such as **9** provides for a direct synthetic approach to some interesting bicyclic 2,4-cyclohexadienones which are suggestive of attractive approaches to the synthesis of a number of natural products.

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The Diels-Alder reactions of chromium carbene complexes occur with reactivities, regioselectivities, and stereoselectivities that are normally only associated with Lewis acid catalyzed reactions.<sup>2</sup> The reactions of chromium carbene complexes with acetylenes is a proven and powerful annulation method that occurs with high regio- and stereoselectivity.<sup>3,4,17</sup> The coupling of these reactions in either a tandem or concurrent fashion provides for the overall selective formation of a large number of carbon-carbon bonds in the construction of complex and valuable synthetic intermediates under neutral conditions and at near ambient temperatures. We will report later on the synthetic applications of these cycloaddition/annulation reactions and on the results of our current efforts to utilize them in the preparation of arene chromium tricarbonyl complexes such as **16** which may be employed as starting materials in subsequent reactions mediated by the presence of the chromium tricarbonyl group.

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**Registry No.** **1**, 92314-81-3; **2**, 92314-82-4; **3**, 92314-83-5; **4**, 92314-84-6; **6**, 16205-82-6; **9**, 92314-85-7; **10**, 92314-86-8; **12** ( $R_1 = 4\text{-Me}_3\text{Si}$ ;  $R_2 = \text{Me}_3\text{Si}$ ), 92314-90-4; **18**, 92314-87-9; **19**, 92314-93-7; **20**, 92314-94-8; **21**, 92314-95-9; **22**, 92314-96-0; **23**, 92314-97-1; **24**, 92314-98-2; **25**, 92314-99-3; **28**, 92314-88-0;  $\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(\text{CH}_3)=\text{CH}_2$ , 513-81-5;  $\text{CH}_2=\text{C}(\text{OSiMe}_3)\text{CH}=\text{CH}_2$ , 38053-91-7;  $\text{CH}_2=\text{C}(\text{OSiMe}_3)\text{CH}=\text{CHOMe}$ , 59414-23-2;  $\text{CH}_3(\text{CH}_2)_2\text{C}\equiv\text{CH}$ , 627-19-0;  $\text{CH}_3\text{CH}_2\text{C}\equiv\text{CC}-\text{H}_2\text{CH}_3$ , 693-02-7; 1,3-cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 592-57-4; [[2-(trimethylsilyl)bicyclo[2.2.2]octa-2,5-dien-3-yl]methoxymethylene]pentacarbonylchromium, 92314-89-1; [(2,4,5-trimethylcyclohexa-1,4-dien-1-yl)methoxymethylene]tetracarbonylchromium, 92314-91-5; [[2-methyl-6-methoxy-4-(trimethylsilyloxy)cyclohexa-1,4-dien-1-yl)methoxymethylene]pentacarbonylchromium, 92314-92-6.

**Supplementary Material Available:** Spectral and physical characterization of all new compounds in addition to experimental procedures are included (14 pages). Ordering information is given on any current masthead page.

## Photoreduction of *N*-Methylphthalimide with 2,3-Dimethyl-2-butene. Evidence for Reaction through an Electron Transfer Generated Ion Pair

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**Abstract:** The photoreduction of *N*-methylphthalimide (NMP) in the presence of 2,3-dimethyl-2-butene (DMB) gives a pair of products (**1** and **2**) which could formally arise by hydrogen abstraction by the imide followed by coupling of the resultant radical pair at either of the two allylic positions on the 1,1,2-trimethylallyl radical. Sensitization and quenching studies have shown that these products arise from the singlet state of NMP and not the triplet as previously suggested. Isotope effect studies with deuterium labeled DMB indicate that the reaction most probably proceeds by initial electron transfer to give the radical cation-radical anion pair. The ion pair either collapses to a zwitterionic precursor to **1** (**13**) or proton transfers to give a radical pair which subsequently collapses to **2**. Isotope effect experiments indicate that decay of **13** to NMP and DMB is an efficient process relative to product formation.

The photochemistry of phthalimides in the presence of alkenes is characterized by four processes:<sup>1</sup> the addition to give benz-

azepinediones (eq 1);<sup>2</sup> electron transfer to afford radical ion pairs which are trapped by alcohols (eq 2);<sup>3</sup> photoreduction (eq 3);<sup>4,5</sup>