Transition Metal-Promoted Three-Component Triene/Alkyne Cycloaddition. Facile Construction of a Novel Polycyclic Ring System

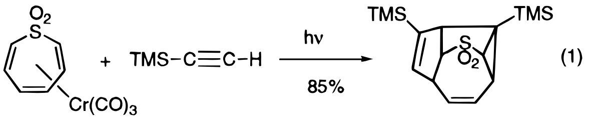
James H. Rigby,* Namal C. Warshakoon, and
Mary Jane Heeg†

Department of Chemistry, Wayne State University
Detroit, Michigan 48202-3489

Received March 25, 1996

Transition metal-mediated cycloaddition has emerged as an important means for assembling ring systems that are often difficult or impossible to make in other ways.[1] Construction of medium-sized rings through metal intervention has been a particularly fruitful area of investigation, and notable accomplishments in the preparation of seven- through ten-membered carbocycles have recently appeared.[2]

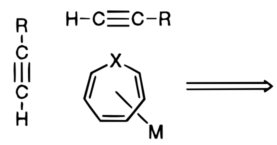
Rapid access to a higher level of molecular complexity can often be achieved through multicomponent cycloaddition processes promoted by transition metal templates. Examples include alkyne cyclotrimerization in several forms,[3] homo-Diels−Alder reactions (two component, but multiple π systems),[4] as well as several others.[2e,f,5] We wish to report a novel three-component, Cr(0)-promoted cycloaddition reaction involving the combination of two *terminal* alkyne units with cyclic trienes that delivers structurally elaborate cycloadducts in good to excellent yields in a process that can be viewed formally as two consecutive Cr(0)-mediated $[6\pi + 2\pi]$ cycloaddition events (Scheme 1).[6]



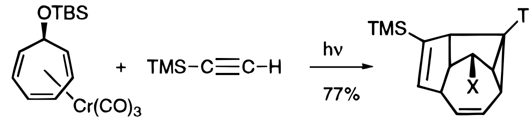
(1)

1 **2**

Scheme 1



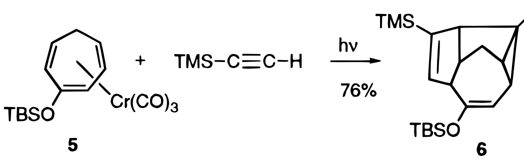
In a typical example, irradiation (450 W Canrad-Hanovia medium pressure Hg-lamp, U-glass filter) of a mixture of (η^6-thiepin-1,1-dioxide)tricarbonylchromium(0) (**1**)[7] and excess trimethylsilylacetylene (10 equiv) afforded an 85% isolated yield of the tetracyclic product **2**[8,9] (eq 1). In addition to the high level of chemical efficiency, several features of this reaction are noteworthy, including the fact that fully five bonds and three rings are created in a single operation and that only one regioisomer of product was isolated. The regioselectivity exhibited by the second alkyne addition is likely a consequence of steric interactions that develop between the TMS group and the proximate alkene carbon of the seven-membered ring in the alternative regioisomer. The course of this transformation can be contrasted with the usual pathway followed by *internal* alkynes in their reactions with similar complexes, which provides only 1:1 adducts.[2j,10,11] Not surprisingly, in our hands internal alkynes (Ph_2C_2, $TMSC_2Ph$) also afforded only the expected 1:1 adducts under these reaction conditions.



(2)

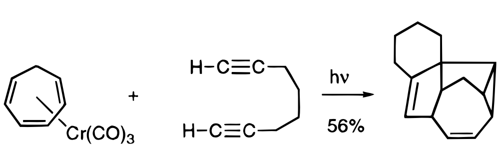
3 **4**, X=OTBS

The three-component cycloaddition process is also effective with cycloheptatriene−$Cr(CO)_3$ complexes as illustrated by the transformation in eq 2. In this instance adduct **4**,[8] available from complex **3**,[2n] in 77% yield, is produced as a single diastereomer. This observation is consistent with previous results in related cycloadditions in which the facial integrity of the initial metal complex is transferred to the cycloadduct with complete fidelity.[12] Triene ligands with non-hydrogen substitution at other locations on the ring afford the corresponding adducts with complete regioselectivity as evidenced by the exclusive formation of compound **6**[8] when readily available complex **5**[2n] is treated with trimethylsilylacetylene under normal reaction conditions (eq 3).



(3)

5 **6**



(4)

7

A particularly interesting result was obtained by tethering the two participating alkyne units together via a four-atom spacer.

---

† Author to whom inquiries regarding X-ray determinations should be directed.

[1] For an excellent overview of the entire area of metal-mediated cycloaddition, see: Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.

[2] Seven-membered ring synthesis: (a) Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. (b) Hoffmann, H. M. R. *Angew Chem., Int. Ed. Engl.* **1984**, *23*, 1. (c) Trost, B. M.; MacPherson, D. T. *J. Am. Chem. Soc.* **1987**, *109*, 3483. (d) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720. (e) Schwiebert, K. E.; Stryker, J. M. *J. Am. Chem. Soc.* **1995**, *117*, 8275. Eight-membered ring synthesis: (f) Brenner, W.; Heimbach, P.; Hey, H.; Muller, E. W.; Wilke, G. *Justus Liebigs Ann. Chem.* **1969**, *727*, 161. (g) Diercks, R.; Stamp, L.; tom Dieck, H. *Chem. Ber.* **1984**, *117*, 1913. (h) Lautens, M.; Tam, W.; Sood, C. *J. Org. Chem.* **1993**, *58*, 4513. (i) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, *108*, 4678. (j) Davis, R. E.; Dodds, T. A.; Hseu, T.-H.; Wagnon, J. C.; Devon, T.; Tancrede, J.; McKennis, J. S.; Pettit, R. *J. Am. Chem. Soc.* **1974**, *96*, 7562. (k) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Henshilwood, J. A.; Short, K. M.; Sugathapala, P. M. *Tetrahedron* **1993**, *49*, 5495. Nine-membered rings: (l) Kreiter, C. G.; Lehr, K.; Leyendecker, M.; Sheldrick, W. S.; Exner, R. *Chem. Ber.* **1991**, *124*, 3. Ten-membered rings: (m) Özkar, S.; Kurz, H.; Neugebauer, D.; Kreiter, C. G. *J. Organomet. Chem.* **1978**, *160*, 115. (n) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Cuisiat, S. V.; Ferguson, M. D.; Henshilwood, J. A.; Krueger, A. C.; Ogbu, C. O.; Short, K. M.; Heeg, M. J. *J. Am. Chem. Soc.* **1993**, *115*, 1382.

[3] (a) Vollhardt, K. P. C. *Angew Chem., Int. Ed. Engl.* **1984**, *23*, 539. (b) Sato, Y.; Nishimata, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133. (c) Neidlein, R.; Kux, U. *Helv. Chim. Acta.* **1994**, *77*, 1051. (d) Negishi, E.; Harring, L. S.; Owczarczyk, Z.; Mohamud, M. M.; Ay, M. *Tetrahedron Lett.* **1992**, *33*, 3253.

[4] Lautens, M.; Tam, W.; Lautens, J. C.; Edwards, L. G.; Crudden, C. M.; Smith, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6863 and references cited therein.

[5] (a) Wilson, A. M.; Waldman, T. E.; Rheingold, A. L.; Ernst, R. D. *J. Am. Chem. Soc.* **1992**, *114*, 6252. (b) Wang, C.; Sheridan, J. B.; Chung, H.-J.; Coté, M. L.; Lalancette, R. A.; Rheingold, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 8966. (c) Herndon, J. W.; Zora, M.; Patel, P. P. Chatterjee, G.; Matasi, J. J.; Tumer, S. U. *Tetrahedron* **1993**, *49*, 5507. (d) Grevels, F.-W.; Schnieder, K. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 410.

[6] A similar ring system has been prepared previously in an Fe(0)-mediated process: Goddard, R.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1979**, 711.

[7] Rigby, J. H.; Ateeq, H. S.; Krueger, A. C. *Tetrahedron Lett.* **1992**, *33*, 5873.

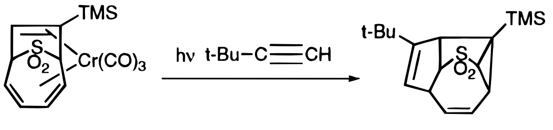
[8] This compound exhibited spectral (^{1}H NMR, ^{13}C NMR, IR) and analytical (combustion analysis and/or HRMS) data consistent with the assigned structure.

[9] The structure of this compound was determined by single-crystal X-ray analysis.

S0002-7863(96)00951-1 CCC: $12.00

Thus, reaction of (η^6-1,3,5-cycloheptatriene)tricarbonylchromium(0) with 1,7-octadiyne under standard photochemical conditions afforded the *pentacyclic* adduct **7**[8] in good yield (eq 4). This example clearly demonstrates the capability of this new reaction to rapidly build up molecular complexity.

A number of other examples that illustrate the scope of this three-component cycloaddition process are compiled in Table 1. It is particularly noteworthy that the reaction can also be effected under thermal activation conditions although the yields are somewhat lower than with photoactivation (entries 3, 5). This feature of these transformations parallels observations made previously with other Cr(0)-mediated two-component cycloadditions.[10a,13] Trimethylsilylacetylene is not the only 2π species able to participate in this multicomponent coupling since a range of terminal alkynes have been shown to be serviceable partners in the reaction (entries 1, 6, 8, 9).

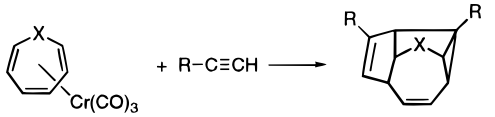


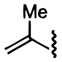
8 **9**

(5)

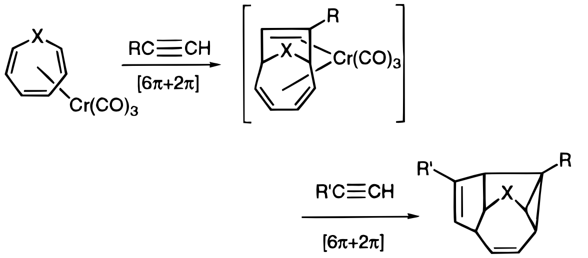
In an effort to gain some insight into the mechanistic features of this process, a small quantity of the crude 1:1 adduct complex **8**[14] was reacted under normal photochemical conditions in the presence of a large excess of *tert*-butylacetylene. This afforded the mixed tetracyclic adduct **9** in low yield along with some recovered 1:1 adduct (eq 5).[15] This result is consistent with the notion that the transformation may proceed through an initial metal-promoted $[6\pi + 2\pi]$ cycloaddition across the cyclic, conjugated triene followed by a second, rapid Cr(0)-mediated $[6\pi + 2\pi]$ cycloaddition event involving the newly created triene system to produce the observed adduct (eq 6). Each of these bond-forming events is assumed to be a stepwise process as is the case in other metal-mediated cycloadditions. Some aspects of this putative reaction pathway are reminiscent of Sheridan's Mn-mediated double-alkyne addition reaction reported recently.[5b]

Table 1. Cr(0)-Promoted Three-Component Cycloaddition of Terminal Alkynes and Cyclic Trienes



entry	X	R	conditions[a]	yield (%)[b]
1	SO_2		A	32
2	SO_2	TMS-	B	35
3	SO_2	TMS-	C	32
4	CH_2	TMS-	A	75[c]
5	CH_2	TMS-	C	40
6	CH_2	n-Bu-	A	40
7	CH_2CH_2	TMS-	A	52
8	SO_2	t-Bu-	A	70
9	CH_2	t-Bu-	A	87

[a] Typical reaction conditions: (A) $h\nu$, U-glass filter, $ClCH_2CH_2Cl$, 1 h. (B) $h\nu$, Pyrex filter, $ClCH_2CH_2Cl$, 1 h. (C) 160 °C, sealed tube, Bu_2O, 12 h. [b] Isolated yield after column chromatography. [c] Reference 9.



(6)

In summary, chromium(0)-promoted cycloaddition between terminal alkynes and cyclic trienes affords structurally elaborate tetra- and pentacyclic products with good to excellent efficiency. The structural features of the resultant products present numerous opportunities for post-cycloaddition manipulations that could be exploited to synthetic advantage. Future work along these lines is currently underway.

Acknowledgment. We thank the National Institutes of Health (GM-30771) for their generous financial support of this research.

Supporting Information Available: Typical experimental procedures and complete spectroscopic data for all new compounds and details of the crystal structure determinations, diagrams, and selected bond lengths and angles (15 pages). See any current masthead page for ordering and Internet access instructions.

JA9609516

---

[10] (a) Chaffee, K.; Huo, P.; Sheridan, J. B.; Barbieri, A.; Aistars, A.; Lalancette, R. A.; Ostrander, R. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 1900. (b) Brammer, L.; Dunne, B. J.; Green, M.; Moran, G.; Orpen, A. G.; Reeve, C.; Schaverien, C. J. *J. Chem. Soc., Dalton Trans.* **1993**, 1747. (c) Klein, R.; Sedmera, P.; Čejka, J.; Mach, K. *J. Organomet. Chem.* **1992**, *436*, 143. (d) Chaffee, K.; Sheridan, J. B.; Aistars, A. *Organometallics* **1992**, *11*, 18. (e) Fischler, I.; Grevels, F.-W.; Leitich, J.; Özkar, S. *Chem. Ber.* **1991**, *124*, 2857. (f) Mach, K.; Antropiusová, H.; Petrusová, L.; Hanuš, V.; Tureček, F. *Tetrahedron* **1984**, *40*, 3295. (g) Nagashima, H.; Matsuda, H.; Itoh, K. *J. Organomet. Chem.* **1983**, *258*, C15.

[11] Efforts to arrest the current reaction at the 1:1 adduct stage by employing 1 equiv of alkyne were only partially successful (see ref 14).

[12] Rigby, J. H.; Sugathapala, P.; Heeg, M. J. *J. Am. Chem. Soc.* **1995**, *117*, 8851.

[13] Rigby, J. H.; Short, K. M.; Ateeq, H. S.; Henshilwood, J. A. *J. Org. Chem.* **1992**, *57*, 5290.

[14] Complex **8** was prepared by reacting complex **1** with 0.1 equiv of trimethylsilylacetylene under standard photochemical conditions. Excess **1** was removed chromatographically to afford crude **8** in low yield.

[15] This observation suggests that two different alkyne partners could be reacted sequentially on a preparative scale if the rapid second addition could be slowed sufficiently. Work on this intriguing possibility is currently underway.