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A Novel Chromium(0)-Promoted Four-Component Cycloaddition Reaction

James H. Rigby,* Charles R. Heap, Namal C. Warshakoon, and Mary Jane Heeg[†]

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

jhr@chem.wayne.edu

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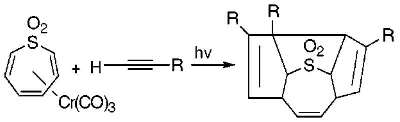
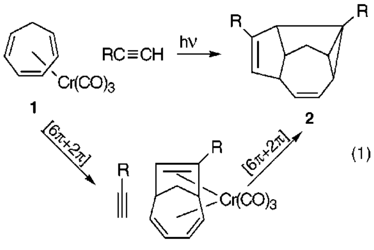
ABSTRACT



Reaction of (η^6-thiepin-1,1-dioxide)tricarbonylchromium(0) with excess terminal alkynes under photoactivation conditions affords novel pentacyclic adducts formally derived from a sequential [6π + 2π]/[6π + 2π]/[2σ + 2π] cycloaddition process.

Cycloaddition reactions mediated by various transition metals have become an important area of investigation in recent years.[1] The capability of effecting ring formation in environments wherein traditional thermal or photochemical transformations are either difficult or even impossible is one of the principal virtues of these processes. A particularly successful illustration of this feature has been metal intervention in the execution of so-called higher-order cycloaddition reactions. Notable advances in this area include Cr(0)-promoted [6π + 4π] cycloadditions,[2] Mn(I)-based [5 + 4] additions,[3] and Ni(0)-promoted [4π + 4π] combinations,[4] as well as Rh(I)-based [5 + 2][5] and numerous cobalt-mediated[6] higher-order cycloaddition processes.

Recently, we reported an extension of this concept that brought to practice a novel and quite powerful three-component higher-order cycloaddition that featured two consecutive [6π + 2π] cycloadditions mediated by chromium(0) (eq 1).[7,8] This transformation constitutes one of the most rapid increases in molecular complexity known for a one-pot process and provides adducts that exhibit substantial



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[†] To whom inquiries regarding X-ray structure determinations should be addressed.

(1) For a recent review of metal-mediated cycloaddition reactions, see: Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.

(2) (a) Rigby, J. H. *Tetrahedron* **1999**, *55*, 4521. (b) Rigby, J. H. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 4, pp 89–127. (c) Rigby, J. H. *Acc. Chem. Res.* **1993**, *26*, 579.

(3) (a) Kreiter, C. G.; Lehr, K.; Leyendocker, M.; Sheldrick, W. S.; Exner, R. *Chem. Ber.* **1991**, *124*, 3. (b) Kreiter, C. G.; Lehr, K. *J. Organomet. Chem.* **1991**, *406*, 159.

(4) (a) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, *108*, 4678. (b) Wender, P. A.; Snapper, M. L. *Tetrahedron Lett.* **1987**, *28*, 2221. (c) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904. (d) Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089.

(5) (a) Wender, P. A.; Husfield, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 1940. (b) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720.

(6) (a) Lautens, M.; Tam, W.; Sood, C. *J. Org. Chem.* **1993**, *58*, 4513. (b) Lautens, M.; Tam, W.; Edwards, L. G. *J. Org. Chem.* **1992**, *57*, 8. (c) Lautens, M.; Edwards, L. G. *J. Org. Chem.* **1991**, *56*, 3761. (d) Lautens, M.; Tam, W.; Lautens, J. C.; Edwards, L. G.; Cruddem, C. M.; Smith, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6863.

(7) Rigby, J. H.; Warshakoon, N. C.; Heeg, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6094.

(8) For selected examples of other metal-promoted, multicomponent cycloadditions, see: (a) Etkin, N.; Dzwiniel, T. L.; Schweibert, K. E.; Stryker, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 9702. (b) Grotjahn, D. B.; Vollhardt, K. P. C. *Synthesis* **1993**, 579. (c) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771. (d) Lecker, S. H.; Nguyen, N. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 856. (e) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539.

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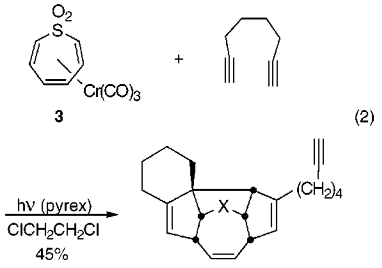
structural and stereochemical information.[9] Indeed, as many as four rings and up to six stereogenic centers can be created in a single operation, and the reaction is general with regard to the constitutions of the participating trienes and alkyne partners.

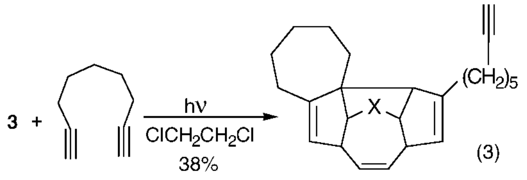
We now wish to report the successful implementation of a remarkable *four*-component chromium(0)-mediated cycloaddition process involving (η^6-thiepin-1,1-dioxide)tricarbonylchromium(0) (**3**) and various tethered diyne reaction partners. In a typical example of this process, photocycloaddition of the readily available complex **3**[10] with excess 1,7-octadiyne ($CH_2CH_2Cl_2$, $h\nu$ (Pyrex filter)) afforded the pentacyclic triene sulfone **4**[11,12] in 45% yield (eq 2).



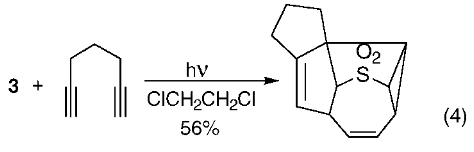
3 (2)

4, X = SO$_2$

1,8-Nonadiyne has also proven to be an effective participant in this multicomponent cycloaddition. In this instance, adduct **5**[11] was produced in 38% yield. In contrast, 1,6-heptadiyne, in which the two alkyne moieties are connected by only three methylene units, failed to provide any of the corresponding four-component adduct, yielding only the three-component cycloadduct **6**[11] in 56% yield.



5, X = SO$_2$



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In considering a mechanism for this fascinating process, the first two steps involved in this overall transformation were presumed to parallel the pathway observed for the previously described [$6\pi + 2\pi$], [$6\pi + 2\pi$] process (eq 1).[7] However, in this instance a third cycloaddition event has occurred in which an additional alkyne component has been incorporated across the cyclopropane unit via what would appear to be a novel (metal-mediated) [$2\sigma + 2\pi$] cycloaddition. To the best of our knowledge this type of reaction finds no relevant precedent in Cr(0)-based cycloaddition chemistry, although a substantial literature exists for related [3 + 2] cycloadditions in the chemistry of Pd and Ni.[13] A somewhat related process has also been suggested as being involved in the Rh(I)-mediated [5 + 2] cycloaddition.[5]

The production of single regioisomeric adducts **4** and **5** in their respective reactions and the apparent inability of heptadiyne, which possesses a shorter carbon spacer, to undergo the [3 + 2] cycloaddition step are suggestive of a pathway in which the third alkyne reaction partner is directed to the cyclopropane site prior to bond formation by some sort of delivery mechanism. Figure 1 depicts a plausible intermediate that rationalizes these empirical results. The key feature of this species is that one of the terminal alkyne moieties is precoordinated to the metal center as a prelude to ring formation. At this juncture of the investigation, our working hypothesis assumes that each step in this reaction process is metal-mediated, although no substantive evidence supporting this contention is available, particularly regarding the putative final step in the sequence.[14]

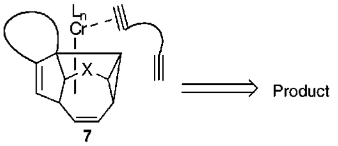

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Figure 1. Possible intermediate in the four-component cycloaddition process.

While the involvement of a coordinated intermediate such as **7** appears quite reasonable for explaining many of the features of these reactions, the role of chromium(0) in promoting the critical [$2\sigma + 2\pi$] cycloaddition event is less clear. Further mechanistic work is currently underway in our laboratory in an attempt to more fully understand the details of this novel and potentially powerful ring-forming process.

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[9] For related processes, see: (a) Chen, W.; Chaffees, K.; Chung, H.-J.; Sheridan, J. B. *J. Am. Chem. Soc.* **1996**, *118*, 9980. (b) Goddard, R.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1979**, 711.

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

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

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

[13] (a) Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77. (b) Binger, P.; Schuchardt, U. *Chem. Ber.* **1980**, *113*, 3334. (c) Binger, P.; Schuchardt, U. *Chem. Ber.* **1981**, *114*, 3313. (d) Binger, P.; Wedemann, P. *Tetrahedron Lett.* **1983**, *24*, 5847. (e) Binger, P.; Brinkmann, A.; Wedemann, P. *Chem. Ber.* **1983**, *116*, 2920. (f) Motherwell, W. B.; Shipman, M. *Tetrahedron Lett.* **1991**, *32*, 1103. (g) Lautens, M.; Ren, Y.; Delanghe, P. H. M. *J. Am. Chem. Soc.* **1994**, *116*, 8821.

[14] It should be noted that no evidence for the formation of either a three- or four-component cycloadduct can be seen when the photocycloaddition is performed in the absence of a Cr(0) center.