Catalytic Chromium(0)-Promoted [6π + 4π] Cycloaddition Reactions

James H. Rigby* and Christian Fiedler

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

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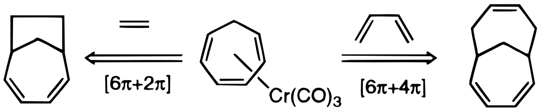
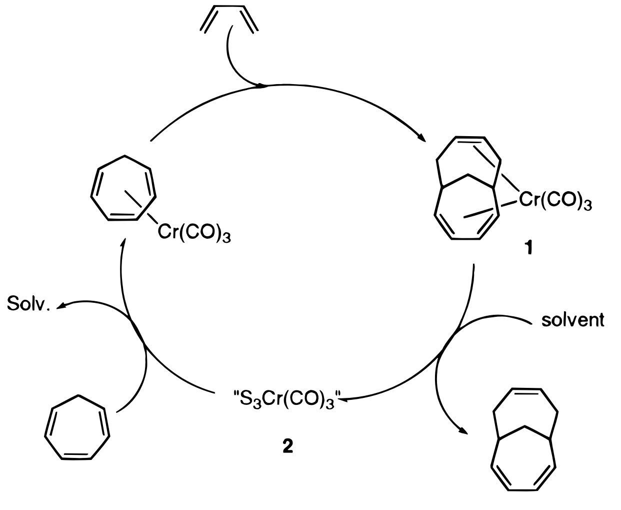
Chromium(0)-promoted higher-order cycloaddition reactions have emerged as powerful methods for the stereocontrolled assembly of structurally elaborate polycyclic systems,[1] and a number of applications of these transformations to problems of synthetic importance have recently been reported.[2] Among these processes, the Cr(0)-mediated [6π + 4π] reaction is of particular significance since it affords the versatile, and often difficult to prepare, bicyclo[4.4.1]undecane system in diastereomerically homogeneous form.[3]



(1)

While the typical photocycloaddition conditions that are stoichiometric in metal have proven to be quite effective for delivering these bicyclic systems, the synthetic utility of these transformations would be greatly enhanced if conditions could be identified that employ only *substoichiometric* quantities of the metal center during the cycloaddition event. A catalytic version of the corresponding Cr(0)-promoted [6π + 2π] process has previously been reported,[4] but efforts to extend this capability to the [6π + 4π] reaction have been futile until now. Indeed, little or no [6 + 4] cycloadduct could be isolated under reaction conditions that afforded virtually quantitative yields of product in the [6 + 2] series.[4] A possible catalytic cycle can be envisioned for the [6 + 4] process that reveals the principal obstacle to achieving a viable catalytic reaction in this series is the rather robust nature of the adduct−metal complex **1** (Scheme 1). The stability of this complex appears sufficient to significantly inhibit the decomplexation step, which is the crucial event for catalyst turnover via species **2**. Labile complexes of this latter type may serve as the actual catalysts in these reactions.[5] Under these circumstances, oxidation of the active Cr(0) species to an inactive Cr(III) oxidation state appears to be competitive with the desired cycloaddition process and rapidly shuts down the reaction. We now report that routine catalytic [6π + 4π] cycloadditions can be brought to practice by including an appropriate reducing agent in the reaction mixture to ensure that the chromium center is maintained at the requisite oxidation level throughout the reaction process. Judicious solvent selection has also been found to influence the efficiency of these reactions. Furthermore, it was envisioned that the metal center required for mediating these reactions would be introduced in the form of a relatively stable "precatalyst" that could be converted into an active catalytic species, such as **2**, during the reaction.

Scheme 1



Identification of a reducing agent capable of maintaining the Cr catalyst at the active oxidation level while not reacting with organic functionality present in the reaction mixture was critical to achieving a viable catalytic version of the [6 + 4] reaction. After some experimentation, magnesium powder was found to effectively participate in this capacity without compromising potentially reducible organic functions.[6] Analysis of the catalytic cycle in Scheme 1 suggested that the choice of the reaction medium would be critical to successful cycloaddition as well. The key in this situation was to employ coordinating solvents nucleophilic enough to decomplex cycloadduct complex **1** (Scheme 1) while being sufficiently labile ligands in the Cr(0) coordination sphere to allow rapid recomplexation of the triene reactant with the metal. Di-*n*-butyl ether and valeronitrile have been identified for this purpose, and eqs 2−4 depict typical catalytic reactions in the [6 + 4] series.[7] In each case 10 mol % of a chromium(0) "precatalyst" was employed.[8]

Several features of these transformations are noteworthy. For example, (η^6-cycloheptatriene)tricarbonylchromium[9] was found to be a particularly useful "precatalyst" in these reactions since it is shelf-stable and easily handled, while the more labile (η^6-naphthalene)tricarbonylchromium(0)[10] was even more effective in certain

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[1] (a) Rigby, J. H. *Acc. Chem. Res.* **1993**, *26*, 579. (b) Chafee, K.; Huo, P.; Sheridan, J. B.; Barbieri, A.; Aistars, A.; Lalancette, R. A.; Ostranden, R. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 1900. (c) Rigby, J. H.; Rege, S. D.; Sandanayaka, V. P.; Kirova, M. *J. Org. Chem.* **1996**, *61*, 842. (d) Rigby, J. H.; Warshakoon, N. C.; Heeg, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6094. (e) Chen, W.; Chafee, K.; Chung, H.-J.; Sheridan, J. B. *J. Am. Chem. Soc.* **1996**, *118*, 9980.

[2] (a) Rigby, J. H.; Pigge, F. C. *J. Org. Chem.* **1995**, *60*, 7392. (b) Rigby, J. H.; Niyaz, N. M.; Short, K.; Heeg, M. J. *J. Org. Chem.* **1995**, *60*, 7720. (c) Rigby, J. H.; Warshakoon, N. C. *J. Org. Chem.* **1996**, *61*, 7644.

[3] For a review of [6 + 4] cycloaddition reactions, see: Rigby, J. H. *Org. Reac. (N.Y.)* **1997**, *49*, 331.

[4] (a) Rigby, J. H.; Short, K. M.; Ateeq, H. S.; Henshilwood, J. A. *J. Org. Chem.* **1992,** *57*, 5290. (b) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Henshilwood, J. A.; Short, K. M.; Sugathapala, P. M. *Tetrahedron* **1993**, *49*, 5495.

[5] Closely related "Cr(CO)$_3$" catalysts have been invoked in the 1,4-reduction of dienes in coordinating solvents: Yagupsky, G.; Cais, M. *Inorg. Chim. Acta* **1975**, *12*, L27.

[6] Relevant standard reduction potentials (*Handbook of Chemistry and Physics*; CRC Press: Boca Raton, FL, 1986; pp D-157−8) are the following:

reaction	*E*°, V
$Mg^{2+} + 2e \rightarrow Mg$	−2.372
$Cr^{3+} + 3e \rightarrow Cr$	−0.744

[7] All cycloadducts have been prepared and fully characterized previously: Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Cuisiat, S. V.; Ferguson, M. P.; Henshilwood, J. A.; Krueger, A. C.; Ogbu, C. O.; Short, K. M.; Heeg, M. J. *J. Am. Chem. Soc.* **1993**, *115*, 1382.

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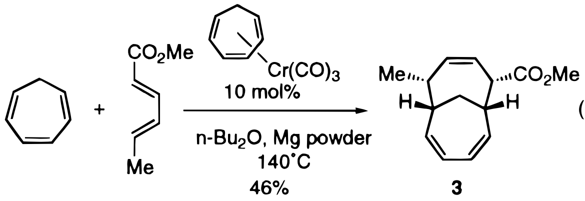
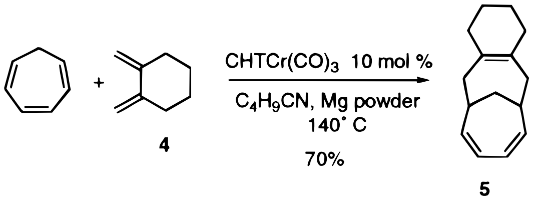


(2)



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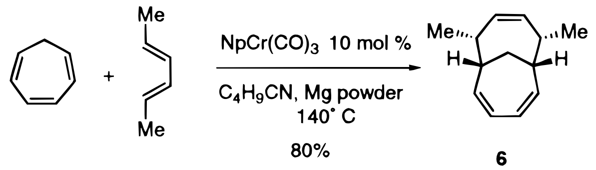
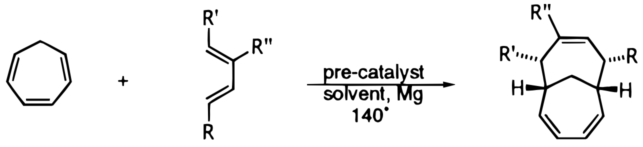


(4)

NpCr(CO)$_3$ = (η^6-naphthalene)tricarbonylchromium(0)

instances. Finally, it should be emphasized that the thermal, conditions employed in these catalytic reactions afforded exactly the same adduct structures (including stereochemistry) as did the corresponding photocycloadditions. These results suggest that a related stepwise process prevails under both sets of reaction conditions. Discussion of these mechanistic details have appeared elsewhere.[7] Finally, it is noteworthy that few, if any, byproducts derived from competitive uncatalyzed, thermal cycloaddition events were observed during the course of these reactions, which is consistent with previous results from our laboratory.[7]

Table 1. Catalytic [6π + 4π] Cycloaddition Reactions



entry	R, R′, R″	precatalyst[a]	solvent	yield (%)[d]
1	R, R′ = Me; R″ = H	CHTCr(CO)$_3$[b]	n-Bu$_2$O	46
2	R, R′ = Me; R″ = H	CHTCr(CO)$_3$	C$_4$H$_9$CN	52
3	R, R′ = Me; R″ = H	NpCr(CO)$_3$[c]	C$_4$H$_9$CN	80
4	R, R′ = H; R″ = Me	CHTCr(CO)$_3$	n-Bu$_2$O	40
5	R, R′ = H; R″ = Me	CHTCr(CO)$_3$	C$_4$H$_9$CN	50
6	R, R′ = H; R″ = Me	NpCr(CO)$_3$	C$_4$H$_9$CN	67
7	R = Me; R′, R″ = H	CHTCr(CO)$_3$	n-Bu$_2$O	32
8	R = Me; R′, R″ = H	CHTCr(CO)$_3$	C$_4$H$_9$CN	49
9	R = TMSO; R′, R″ = H	CHTCr(CO)$_3$	n-Bu$_2$O	50
10	R = TMSO; R′, R″ = H	CHTCr(CO)$_3$	C$_4$H$_9$CN	53
11	R = CO$_2$Me; R′ = Me; R″ = H	CHTCr(CO)$_3$	C$_4$H$_9$CN	58

[a] Precatalyst loading 10 mol % in each case. [b] CHTCr(CO)$_3$ = (cycloheptatriene)tricarbonylchromium. [c] NpCr(CO)$_3$ = (naphthalene)tricarbonylchromium. [d] Yield of isolated, metal-free cycloadduct.

Several other results of this study that illustrate the generality of these reaction conditions are collected in Table 1. Some intriguing effects of solvent and precatalyst can be noted by comparing and contrasting entries 1–3 and 4–6 in the table. It is interesting to note that in many instances valeronitrile emerged as the solvent of choice for maximizing reaction efficiency. As can be seen by examining entries 10 and 11, both electron rich and electron deficient 4π partners effectively participate in the catalytic reaction. This insensitivity to the electronic nature of the reactants was also a salient feature of the stoichiometric photocycloadditions reported previously.[7]

In summary, [6π + 4π] cycloaddition can be effectively performed with substoichiometric quantities of metal by carefully selecting the precatalyst, solvent, and reducing agent employed. This development should enhance the preparative utility of these powerful cycloaddition reactions.

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(8) **General Procedure for Conducting Catalytic [6π + 4π] Cycloaddition Reactions:** A Carius tube is flushed with dry nitrogen and then charged with the appropriate Cr(0) precatalyst (0.1 equiv), freshly distilled solvent (10–20 mL), magnesium powder (0.1 equiv), cycloheptatriene (1 equiv), and the diene (10–12 equiv). This mixture was carefully degassed using the freeze-pump-thaw technique, and the tube was then sealed and heated at 140 °C for 2–5 days. After cooling to room temperature, the resulting suspension was filtered through Celite. The filtrate solvent was removed *in vacuo*, and column chromatography afforded the product.

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