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# Preparation of a Resin-Based Chromium Catalyst for Effecting [6$\pi$ + 2$\pi$] Cycloaddition Reactions

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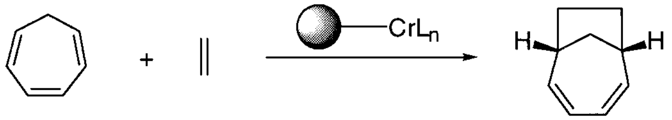
## ABSTRACT

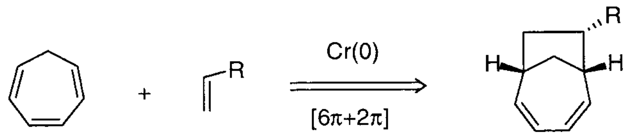


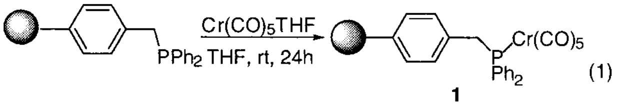
**A resin-based chromium catalyst for performing [6$\pi$ + 2$\pi$] cycloaddition reactions has been prepared from chloromethylated polystyrene. The catalyst provides cycloadducts in yields comparable to the photochemical and thermal versions of these transformations, and the process is effective with a wide range of 6$\pi$ and 2$\pi$ reaction partners.**

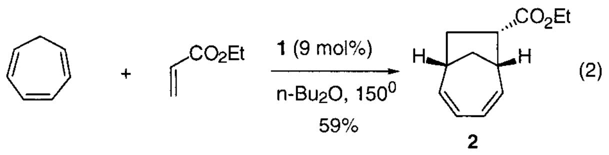
In recent years there has been a renewed interest in polymer-bound metal catalysts as the need for developing environmentally sound, economical, and experimentally convenient organic synthesis methods has increased.[1,2] Immobilized, metal-based reagents can offer numerous advantages over their solution-phase counterparts, including ease of separation from the product mix, reduced waste disposal problems, and the potential for recycling the catalyst system.

Chromium(0)-promoted higher-order cycloaddition reactions have emerged as powerful new methods for the rapid assembly of structurally elaborate polycyclic systems (Scheme 1).[3] Since these processes are capable of being executed using substoichiometric quantities of Cr(0) under thermal activation,[4] it was reasoned that they would also be amenable to polymer-supported catalysis. A significant potential benefit of performing these cycloadditions with resin-supported Cr(0) would be the facility with which chromium removal from the product mix could be accomplished. It was envisioned that simple filtration of the reaction mixture would remove the resin accompanied by virtually all of the chromium species. Successful implementation of this strategy has now been achieved in the [6$\pi$ + 2$\pi$] cycloaddition series.[5]

**Scheme 1**







Initial efforts in this investigation have focused on preparing and evaluating the reactivity of solid-supported catalysts in which the chromium(0) center is attached to a commercially available chloromethylated polystyrene resin (PS-DVB) (Merrifield resin, 2% cross-linked) via an appropriate phosphine linker.[6] The first generation version of this resin-bound Cr(0) complex was prepared by exposing the corre-

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(1) For recent reviews of this area, see: (a) Shuttleworth, S. J.; Allin, S. M.; Wilson, R. D.; Nasturica, D. *Synthesis* **2000**, 1035. (b) Lindner, E.; Schneller, T.; Auer, F.; Mayer, H. A. *Angew Chem., Int. Ed.* **1999**, *38*, 2154. (c) Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217.

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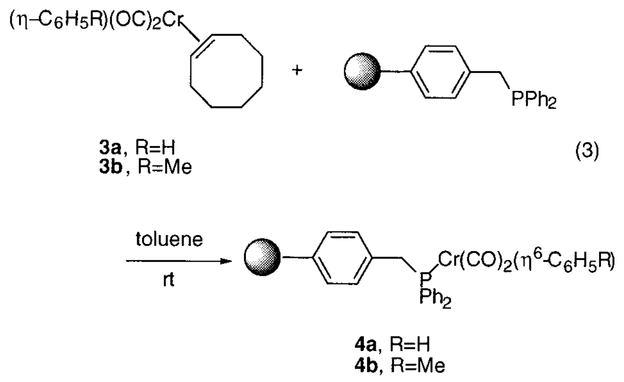
sponding phosphine-terminated system to $Cr(CO)_5THF$. The resultant complex was formulated primarily, but not exclusively, as structure **1** on the basis of elemental analysis and IR spectroscopy (eq 1). Heating a mixture of cycloheptatriene (CHT) and excess ethyl acrylate with catalyst **1** (9 mol %)[7] in di-*n*-butyl ether at 150° (sealed tube) afforded the expected [6 + 2] cycloadduct **2**[8] in 59% isolated yield (eq 2). Efforts to reuse this particular catalyst for promoting a second cycloaddition under the same conditions failed to deliver more than a trace amount of adduct **2**. This inability to recycle complex **1** in a productive fashion was attributed to a thermal "denaturation" of the system that rendered the metal center inaccessible for further reaction.

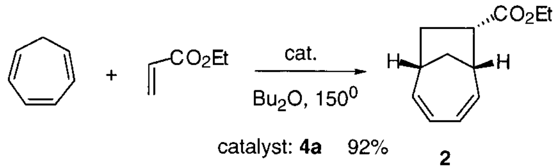
To overcome this obstacle, the coordination sphere around chromium was modified in a fashion designed to facilitate the formation of a coordinatively unsaturated metal center and then to promote coordination of the reactants prior to the ring-forming event. The selection of specific modifications at this juncture was guided by mechanistic considerations of the metal-promoted cycloaddition reactions themselves.[4b,9] In the event, complexes **3a**,**b** were employed to produce catalysts formulated as **4a**,**b** (on the basis of IR spectroscopy) using a modification of literature methods (eq 3).[10,11] Heating **4a** (R = H) with CHT and ethyl acrylate as before afforded adduct **2** in 92% yield (yield for photochemical reaction with stoichiometric Cr(0) is also 92%), and the corresponding toluene complex **4b** was found to give a 60% yield of **2** under identical conditions (eq 4). The lower activity of **4b** may be due to the relative electron-donating properties of toluene vs benzene.[12]



**3a**, R=H
**3b**, R=Me

(3)

**4a**, R=H
**4b**, R=Me



(4)

catalyst: **4a** 92%
**4b** 60%

**2**

Significantly, the catalyst could be recovered by simple filtration followed by washing with toluene, ether, and hexane and reused several times with relatively little erosion of efficacy. Indeed, successive elemental analyses of the resin revealed that only 0.7% of the chromium present initially on the solid support was lost after five reuses. Furthermore, the IR spectra of the recovered resin indicated a minimal reduction in the intensity of the metal−CO stretching bands located at 1890 and 1831 $cm^{-1}$. Perhaps the most important observation made regarding these reactions was that there was less than 0.53 ppm of trace chromium found in the cycloadducts after the resin and solvent had been removed. Thus, one of our most important initial objectives has been achieved, that is, simple filtration of the reaction mixture succeeds in removing all but trace amounts of chromium residue from the reaction product. This is a significant advance in that chromium removal can be problematic in the other versions of this reaction.

The results of a number of $[6\pi + 2\pi]$ cycloadditions mediated by solid-supported Cr(0) are collected in Table 1. The reaction process appears to be quite general with regard to the triene and trienophile participants. The reasonable diastereoselectivity observed in the reaction (entry 4) employing 8-phenylmenthol as a chiral auxiliary is noteworthy, particularly in light of the fact that the reaction is performed at 150 °C.

A particularly intriguing question that remains to be answered about this process is whether the chromium, in fact, dissociates from the linker and then effects a solution-phase cycloaddition or remains attached to the resin throughout the reaction. To gain insight into this issue, resin **5**, exhibiting a much longer linker chain, was prepared as shown

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(2) (a) Comely, A. C.; Gibson, S. E.; Hales, N. J. *J. Chem. Soc., Chem. Commun.* **2000**, 305. (b) Leadbeater, N. E.; Scott, K. A.; Scott, L. J. *J. Org. Chem.* **2000**, *65*, 3231. (c) Zhang, T. Y.; Allen, M. J. *Tetrahedron Lett.* **1999**, *40*, 5813. (d) Buchmeiser, M. R.; Wurst, K. *J. Am. Chem. Soc.* **1999**, *121*, 11101. (e) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657. (f) Angelino, M. D.; Laibinis, P. E. *Macromolecules* **1998**, *31*, 7581. (g) Fenger, I.; LeDrian, C. *Tetrahedron Lett.* **1998**, *39*, 4287.

(3) (a) Rigby, J. H. In *Advances in Cycloaddition*; Harmata, M., Ed.; JAI Press: Greenwich, 1999; Vol. 6, pp 97−118. (b) Rigby, J. H. *Tetrahedron* **1999**, *55*, 4521. (c) Rigby, J. H. *Acc. Chem. Res.* **1993**, *26*, 579.

(4) (a) Rigby, J. H.; Fiedler, C. *J. Org. Chem.* **1997**, *62*, 6106. (b) Rigby, J. H.; Short, K. M.; Ateeq, H. S.; Henshilwood, J. A. *J. Org. Chem.* **1992**, *57*, 5290.

(5) (a) Rigby, J. H.; Pigge, F. C. *J. Org. Chem.* **1995**, *60*, 7392. (b) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Henshilwood, J. A.; Short, K. M.; Sugathapala, P. M. *Tetrahedron* **1993**, *49*, 5495. (c) Rigby, J. H.; Henshilwood, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 5122.

(6) (a) Evans, G. O.; Pittman, C. U.; McMillan, R.; Beach, R. T.; Jones, R. *J. Organomet. Chem.* **1974**, *67*, 295. (b) Dumont, W.; Poulin, J.-C.; Dang, T.-Ph.; Kagan, H. B. *J. Am. Chem. Soc.* **1973**, *95*, 8295.

(7) The amount of resin to be employed in these reactions is determined on the basis of the results of elemental analysis, which in this particular case indicated 2.08% Cr by weight (56% of maximum calculated chromium loading).

(8) This compound has been prepared and fully characterized previously in our laboratory, see: ref 5b.

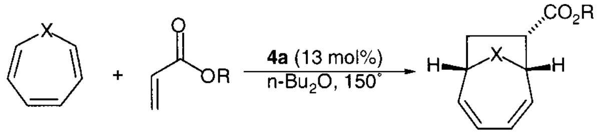
(9) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Cuisiat, S. V.; Ferguson, M. D.; Henshilwood, J. A.; Krueger, A. C.; Ogbu, C. O.; Short, K. M.; Heeg, M. J. *J. Am. Chem. Soc.* **1993**, *115*, 1382.

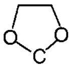
(10) Howell, J. A. S.; Palin, M. G.; McArdle, P.; Cunningham, D.; Goldschmidt, Z.; Gottlieb, H. E.; Herzoni-Langerman, D. *Organometallics* **1993**, *12*, 1694.

(11) Elemental analysis revealed that ~95% of the calculated amount of Cr had been incorporated into catalyst **4a**. The infrared spectra of the yellow resins **4a**,**b** exhibited intense metal carbonyl stretching at 1890, 1831 $cm^{-1}$ and 1884, 1826 $cm^{-1}$, respectively, which are quite similar to related nonresin−based arene dicarbonyl phosphine complexes: Bitterwolf, T. E. *Polyhedron* **1988**, *7*, 1377.

(12) The electronic properties of arene ligands are known to exert a profound influence on the catalytic activities of chromium carbonyl complexes in other situations: Frankel, E. N.; Butterfield, R. O. *J. Org. Chem.* **1969**, *34*, 3930.

**Table 1.** Solid-Supported Cr(0)-Mediated [$6\pi + 2\pi$] Cycloaddition

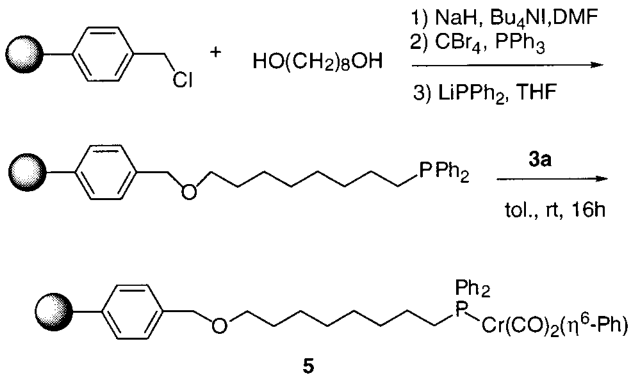


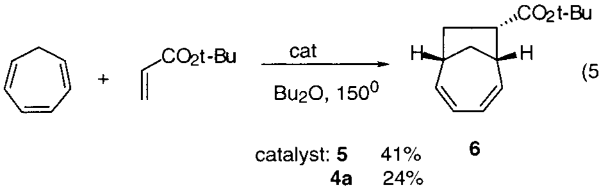
| Entry | X | R | Yield (%)[a] |
|---|---|---|---|
| 1 | $CH_2$ | Et | 92 |
| 2 | $CH_2$ | $C_4H_9$ | 82 |
| 3 | $CH_2$ | (-)-menthyl | 81[b] |
| 4 | $CH_2$ | (-)-8-phenylmenthyl | 79[c] |
| 5 | $NCO_2Et$ | Et | 64 |
| 6 |  | Et | 80 |

[a] All compounds have been prepared and fully characterized previously, see Ref. 5b. [b] Diastereomer ratio = 2:1. [c] Diastereomer ratio = 4:1

in Scheme 2. Heating **5** with CHT/ethyl acrylate under normal conditions afforded adduct **2** in 90% yield, essentially the same result as seen with resin **4a** (eq 4). However, when catalyst **5** was heated with CHT and *tert*-butyl acrylate, a 41% yield of adduct **6**[8] was obtained (eq 5). In contrast, **4a** gave only a 24% yield of this adduct, suggesting that the steric environment in the vicinity of the supported metal may play a significant role when hindered reactants are involved. A second experiment was performed in which the resin was heated to 150 °C ($n$-$Bu_2O$) in the absence of substrate and filtered. The resulting filtrate was then heated with cycloheptatriene and ethyl acrylate to determine if any catalytic activity remained in solution. None of the expected cycloadduct was detected, suggesting that little or no chromium(0) dissociated from the resin into the solvent under these conditions. These observations provide circumstantial evidence supporting the notion that the metal is retained on the resin throughout the reaction.

**Scheme 2**





(5)

In conclusion, a viable resin-supported chromium(0) catalyst for promoting [$6\pi + 2\pi$] cycloadditions has been developed. Key features of the process include high chemical yields of products, the ability to recycle the catalyst, and ease of removing all but trace amounts of chromium residue from the organic products.

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