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Novel [2 + 2 + 2]Annulation of 1,6-Diynes Mediated by Methallylchromate or Methallylmagnesium Chloride under $CrCl_3$ Catalysis

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Organochromium reagents have significant roles in organic synthesis. The Nozaki−Hiyama−Kishi reaction utilizing $CrCl_2$ to generate allyl- or alkenylchromium species has served as a pivotal reaction in many total syntheses of naturally occurring compounds.[1] Arene−chromium complexes provide a regio- and stereoselective method to construct aromatic compounds.[2] However, organochromium ate complexes have received little attention from synthetic chemists so far.[3]

η^3-Allylmetallocene-mediated [2 + 2 + 2]- and [3 + 2 + 2]-allyl/alkyne annulations have been extensively explored by Stryker et al. and others.[4] Now we found that organochromates exhibit a unique reactivity toward diynes. Herein we wish to disclose a novel chromium-induced [2 + 2 + 2]annulation of 1,6-diynes which provides cyclohexadienylmethylmetals efficiently. The resulting bicyclic compound has a reactive carbon−metal bond that can be used for further elaboration.

We examined the reaction of 1,6-diynes with allylchromates (Scheme 1). Allylchromate was easily prepared by mixing $CrCl_3$ and allylmagnesium chloride in a 1:4 molar ratio.[5,6] Treatment of diyne **1a** with 1.5 equiv of the resulting chromium reagent provided the indan derivative **2** exclusively, although the yield was not satisfactory.[7] The starting material was recovered in 85% yield. After several investigations, tetramethallylchromate proved the most reactive toward 1,6-diyne **1a** and gave bicyclo[4.3.0]-nonadiene derivative **3a** in good yield.[8] Deuterium was incorporated in one of the methyl groups (90% *d*), when DCl/D_2O was added before quenching the reaction. This result clearly indicates the existence of cyclohexadienylmethylchromium **4a** as an intermediate. Unfortunately, the initial trial to trap the intermediary organochromium species **4a** with electrophiles failed.[9]

Scheme 1

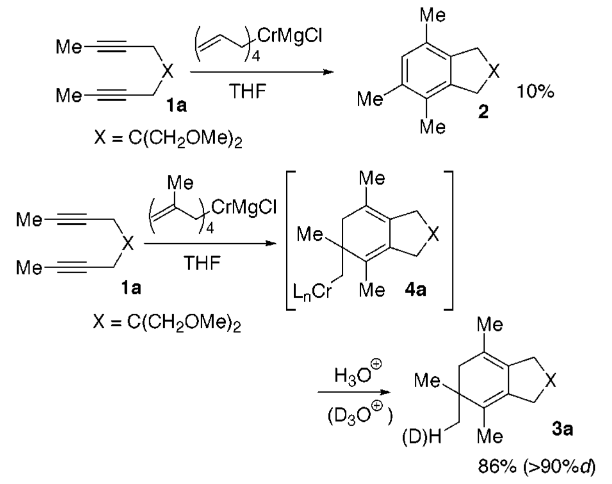
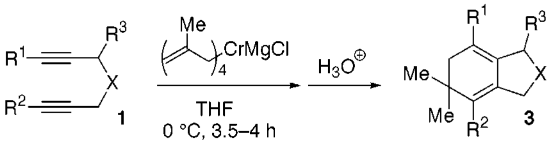


Table 1. Methallylchromate-Induced Bicyclization of 1,6-Diynes[a]



entry	diyne	X	R^1	R^2	R^3	**3**	yield (%)
1	**1a**	$C(CH_2OMe)_2$	Me	Me	H	**3a**	86
2	**1b**		Ph	Ph	H	**3b**	86
3	**1c**		Me	Ph	H	**3c**	91[b]
4	**1d**	CH_2	Me	Me	H	**3d**	66
5	**1e**	NBn	Ph	Ph	H	**3e**	83
6	**1f**	O	Me	Ph	n-C_5H_{11}	**3f**	58[c,d]

[a] Tetramethallylchromate (1.5 equiv), prepared from $CrCl_3$ (1.5 equiv) and methallylmagnesium chloride (6.0 equiv, 0.96 M THF solution), was employed in THF at 0 °C. [b] Regioselectivity (10/1). [c] Regioselectivity (11/1). [d] The chromate reagent (2.0 equiv) was used.

The bicyclization of various 1,6-diynes **1** with tetramethallylchromate is summarized in Table 1. The reaction of 1,6-diynes **1** with the chromate reagent provided the desired cyclohexadiene derivatives in good to excellent yields. It is noteworthy that the annulation of **1c** or **1f**, which might provide a regioisomeric mixture, yielded **3c** or **3f** regioselectively. Both nitrogen- and oxygen-tethered diynes **1e** and **1f** are equally good substrates for this chromate-mediated reaction.

It is necessary to employ the combination of methallylmagnesium chloride and $CrCl_3$ in a 4:1 ratio. $(Methallyl)_3Cr$, $(methallyl)_2CrCl$, and $(methallyl)CrCl_2$ afforded none of the desired product **3**. Only the chromium ate complex can mediate this bicyclization. The reaction solvent is also crucial. The use of ether instead of THF resulted in quantitative recovery of the starting diyne **1**.

The use of a stoichiometric amount of $CrCl_3$ for this process requires a large excess of Grignard reagent. We then focused on the catalytic use of chromium chloride (Scheme 2). Fortunately, we found that treatment of 1,6-diynes **1a** and **1b** with methallylmagnesium chloride (4.0 equiv) in the presence of a catalytic amount of $CrCl_3$ (20 mol %) provided the desired products **3a** and **3b** in good yields.

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(1) (a) Fürstner, A. *Chem. Rev.* **1999**, *99*, 991. (b) Saccomano, N. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 1, Chapter 1.6, p 173. (c) Takai, K. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; p 1266.

(2) (a) Davies, S. G.; Coote, S. J.; Goodfellow, C. L. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: London, 1991; Vol. 2, p 1. (b) Uemura, M. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: London, 1991; Vol. 2, p 195. (c) Semmelhack, M. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, Chapter 2.4, p 517.

(3) Hojo, M.; Sakuragi, R.; Okabe, S.; Hosomi, A. *J. Chem. Soc., Chem. Commun.* **2001**, 357.

(4) (a) Schwiebert, K. E.; Stryker, J. M. *J. Am. Chem. Soc.* **1995**, *117*, 8275. (b) Dzwiniel, T. L.; Etkin, N.; Stryker, J. M. *J. Am. Chem. Soc.* **1999**, *121*, 10640. (c) Etkin, N.; Dzwiniel, T. L.; Schweibert, K. E.; Stryker, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 9702. (d) Lutsenko, Z. L.; Petrovski, P. V.; Bezrukova, A. A.; Rubezhov, A. Z. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988**, *4*, 855. (e) Tang, J.; Shinokubo, H.; Oshima, K. *Organometallics* **1998**, *17*, 290.

(5) Ethereal solution of allylmagnesium bromide afforded no trace of the desired product. Allylmagnesium chloride in THF is easily prepared according to the reported procedure. Lipshutz, B. H.; Hackmann, C. *J. Org. Chem.* **1994**, *59*, 7437.

(6) For preparation of triallylchromium, see: (a) Becconsall, J. K.; Job, B. E.; O'Briens, S. *J. Chem.* Soc. *A* **1967**, 423. (b) Kurras, E.; Klimsh, P. *Monatsber. Dtsch. Akad. Wiss. Berlin* **1964**, *6*, 736.

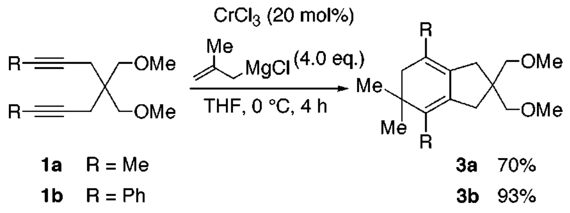
(7) This result might be attributed to instability of the chromate reagent. Thermal decomposition of $(allyl)_3Cr$ into $(allyl)_4Cr_2$ was reported. Aoki, T.; Furusaki, A.; Tomiie, Y.; Ono, K.; Tanaka, K. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 545.

(8) The structure of **3a** was confirmed by X-ray diffraction of the Diels−Alder adduct of the diene **3a** with maleimide. See Supporting Information.

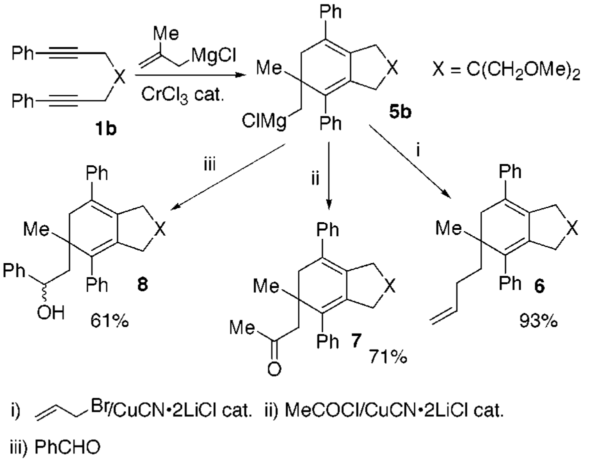
(9) The addition of electrophiles such as benzaldehyde or allyl bromide afforded none of the desired coupling products.

10.1021/ja015746r CCC: $20.00

Scheme 2



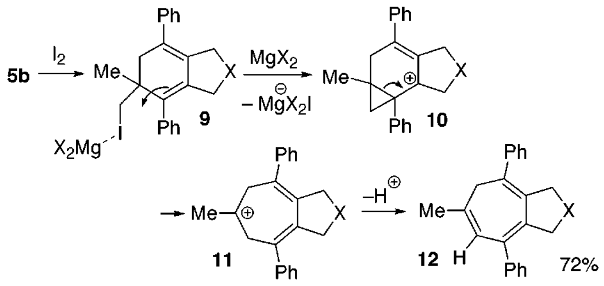
Scheme 3



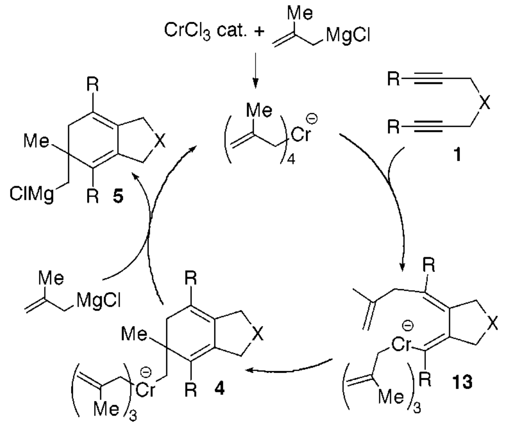
The use of catalytic chromium is also beneficial for the further functionalization of the metallic residue in the intermediate. The cyclohexadienylmethylmagnesium species **5b** reacts with various electrophiles efficiently (Scheme 3). As for trapping of **5b** with allyl bromide or acyl chloride, the addition of catalytic CuCN·2LiCl improved the yields of the coupling products **6** and **7**.[10] To our great surprise, the reaction of **5b** with iodine yielded the cycloheptatriene derivative **12** exclusively. This [3 + 2 + 2] annulation product might be formed via the cationic intermediate **10**, generated from the initial product **9** by the action of magnesium halide acting as a Lewis acid (Scheme 4).[11]

Stryker et al. have revealed that the [2 + 2 + 2]allyl/alkyne annulation is initiated by allylation of an alkyne ligand on the metal. We assume that this is also the case for our bicyclization. We propose a plausible catalytic cycle as follows (Scheme 5). The allylchromation of the carbon−carbon triple bond trigers the cyclization to yield the dienylchromium **13**.[12] The subsequent insertion of the terminal alkene into the carbon−chromium bond

Scheme 4



Scheme 5



provides **4**. Transmetalation of **4** from chromium into magnesium furnishes the cyclic magnesium compound **5** and regenerates the allylic chromium species.[13]

In conclusion, we have found that methallylchromate induces the [2 + 2 + 2]annulation of 1,6-diynes efficiently. Chromate reagents are quite readily available, because chromium chloride is inexpensive and Grignard reagents can be prepared easily. Moreover, this bicyclization is accomplished by the use of a catalytic amount of $CrCl_3$. This reaction represents not only a new reaction pattern of organochromium reagents but also a catalytic version of the allylmetal-mediated [2 + 2 + 2]annulation. Cyclohexadienylmethylmagnesium prepared by this method can be utilized for the subsequent functionalization. Further research on the use of chromium ate complexes in organic synthesis is currently under way in our laboratory.

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Supporting Information Available: General procedures and spectral data for all compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] General procedure for the catalytic reaction. A solution of methallylmagnesium chloride (1.67 mL, 0.96 M THF solution, 1.6 mmol) was added to a THF solution of $CrCl_3$ (13 mg, 0.08 mmol) at 0 °C. After being stirred for 20 min, **1b** (133 mg, 0.4 mmol) was introduced and the mixture was stirred for 4 h at 0 °C. To the mixture were added allyl bromide (1.8 mmol) and CuCN·2LiCl (0.08 mmol). After being stirred for another 45 min, the mixture was poured into 1 M HCl and extracted with ether. The organic layers were dried and concentrated. Purification by chromatography afforded **6** (159 mg, 0.37 mmol) in 93% yield.

[11] Direct rearrangement from **9** into **11** is also conceivable. However, we take account of **10** because of its stability.

[12] Addition of diallylchromium phosphine complex toward simple alkynes was reported, see: Betz, P.; Jolly, P. W.; Krüger, C.; Zakrzewski, U. *Organometallics* **1991**, *10*, 3520.

[13] The use of a decreased amount (10 mol %) of $CrCl_3$ with the Grignard reagent (3.0 equiv) yielded **3a** in 39% yield along with the recovered starting diyne. We assume that the coordination of diene moiety in **4** onto the chromium center causes the slow transmetalation.