Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters 49 (2008) 3567–3569

Tetrahedron Letters

Novel copper hydride-promoted 1,3-rearrangement of α-allenylcyclopropane systems to methylenecyclopentenes

Kunio Hiroi *, Fumiko Kato, Takamasa Oguchi, Shinya Saito, Takanori Sone

Ohu University, The School of Pharmaceutical Sciences, 31-1 Misumido, Tomitamachi, Koriyama, Fukushima 963-8611, Japan

Received 19 February 2008; revised 1 April 2008; accepted 7 April 2008
Available online 9 April 2008

Abstract

α-Allenylcyclopropanedicarboxylates, for which a novel synthetic method has been devised by conjugate addition of a copper hydride (Stryker) reagent to α-cyclopropylpropargylic esters, have been newly found to be smoothly converted to methylenecyclopentene derivatives under mild reaction conditions by further treatment with the copper hydride reagent. The mechanistic pathway is discussed.

Keywords: Allene; Cyclopropane; Copper hydride; 1,3-Rearrangement

An organometal-catalyzed reaction of allenes[1] has provided useful methodologies for the functionalization of molecules by the direct elongation of a three-carbon unit in organic synthesis.[2] For instance, much attention has been paid to the efficient construction of molecules by means of palladium-catalyzed reactions of allenes in recent years.[3]

A cyclopropane skeleton[4] has been well known to be a useful functional group also for the elongation of a three-carbon unit by its palladium-catalyzed reaction. In particular, a palladium-catalyzed reaction of α-vinylcyclopropanes[5] with carbo- and heteronucleophiles provides products exemplified by intra- or intermolecular carbon–carbon and –heteroatom bond formation via π-allylpalladium complexes derived from them. So, similarly, we have taken much interest in the chemistry of allenylcyclopropane combined conjugate systems. Hitherto, few reports of organometal-catalyzed reactions of simple α-allenylcyclopropane systems have been published; only iridium,[6] rhodium,[7] and cobalt catalysts[8] (with CO) have been reported to be applicable to the reactions of simple α-allenylcyclopropanes, providing 1,3-rearrangement products such as α-alkylidenecyclopentene, or -cyclohexenone, and benzene derivatives. A thermal reaction of a simple α-allenylcyclopropane, in general, needs a high temperature of 380 °C for the accomplishment of the 1,3-rearrangement, resulting in the formation of methylenecyclopentene, 1,3-cyclohexadiene, and benzene derivatives.[9]

On the other hand, no report has appeared on organometal-catalyzed or thermal reactions of α-allenylcyclopropanes with electron-withdrawing groups on the rings, which stems from the difficulty in their approach. The α-allenylcyclopropane systems were not accessible from normal nucleophilic conjugate addition reactions of alkylmagnesium, zinc, or copper reagents to α-cyclopropylpropargylic esters. We have developed a new synthetic method to α-allenylcyclopropanes by the reactions of α-cyclopropylpropargylic esters with a copper hydride reagent.[10] We wish to communicate herein a novel copper hydride-promoted transformation of the α-allenylcyclopropanes into methylenecyclopentenes by 1,3-rearrangement, presumably, via cyclic dialkylcopper intermediates.

1-Cyclopropyl-2-propynyl acetates (**3**) were prepared by normal reaction sequences; cyclopropanation of α,β-unsaturated ketones with bromomalonate (NaH) followed by alkynylation of ketones (**1**) resulted with lithium

---

* Corresponding author. Tel.: +81 24 932 9212; fax: +81 24 933 7372.
E-mail address: k-hiroi@pha.ohu-u.ac.jp (K. Hiroi).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.04.031

3-trimethylsilylacetilide, acetylation with acetyl chloride, and desilylation of **2** by treating with tetrabutylammonium fluoride.

The studies on copper hydride-promoted reactions of 1-cyclopropyl-2-propynyl acetates (**3a**–**k**) obtained above were conducted with 0.5 equiv of $[\mathrm{CuH(PPh_3)}]_6$ (Stryker reagent) in toluene at room temperature in the presence of a small amount of H_2O under an atmosphere of argon for 3 h, providing unexpectedly methylenecyclopentene derivatives (**5a**–**k**) (49–71%) as the main products by 1,3-rearrangement via copper-coordinated intermediates with the formation of a small amount of α-allenylcyclopropanes (**4a**–**k**). The results are summarized in Table 1[11] (Scheme 1).

As shown in Table 1, it should be noted that no substituent in the systems (**3a**: $R^1 = R^2 = H$) retarded the 1,3-rearrangements of the resulting α-allenyl intermediates, giving an allene **4a** (64% yield) as a main product. However, substitutions at the α sites of propargylic acetates (**3b**–**j**) accelerated the rearrangements at room temperature to give methylenecyclopentenes **5b**–**j** as the main products along with a very small amount of allenylcyclopropanes **4b**–**j**. Lowering of the reaction temperature at 0 °C retarded the rearrangement; the reaction of **3b** at 0 °C provided α-allenylcyclopropane **4b** without any formation of **5b**. On the other hand, the introduction of a methyl group (**3k**: $R^1 = H$, $R^2 = Me$) at the α position of the cyclopropyl group disturbed presumably sterically the 1,3-rearrangement to give an α-allenylcyclopropane (**4k**) as a main product (46%) along with methylenecyclopentene (**5k**) (21%).

Copper-promoted reactions of chemically pure α-cyclopropylallenes (**4**) isolated by thick-layer chromatography over silica gel were studied in toluene at room temperature or 40 °C or 3 h. Use of the Stryker reagent in these cases accelerated the smooth conversion of the allenes to cyclopentene derivatives, upon treatment with the reagent at 40 °C or room temperature, giving **5a** (51%) and **5b** (74%), respectively (Table 2).

However, other normal ionic copper catalysts such as copper(I) chloride, copper(II) dichloride, or ditriflate were not effective for the rearrangement of α-allenylcyclopropanes, even though at high reaction temperature (50, 60, or 100 °C) the starting allenes were recovered. It was also confirmed that no reaction occurred without the copper reagent (Stryker) at room temperature or at a much higher reaction temperature (50 or 110 °C).

Thus, it can be certainly concluded that the copper(I) and (II) catalysts such as those mentioned above could not accelerate the reactions, while the copper hydride reagent would play an important role for the smooth acceleration of the rearrangements.

Based on these results, we propose, for rationalization of the results, a plausible mechanism of the 1,3-rearrangement via a cyclic copper complex **6c**, formed by the inser-

Table 1
Studies on copper hydride-promoted reactions of alkynylcyclopropanes[a]

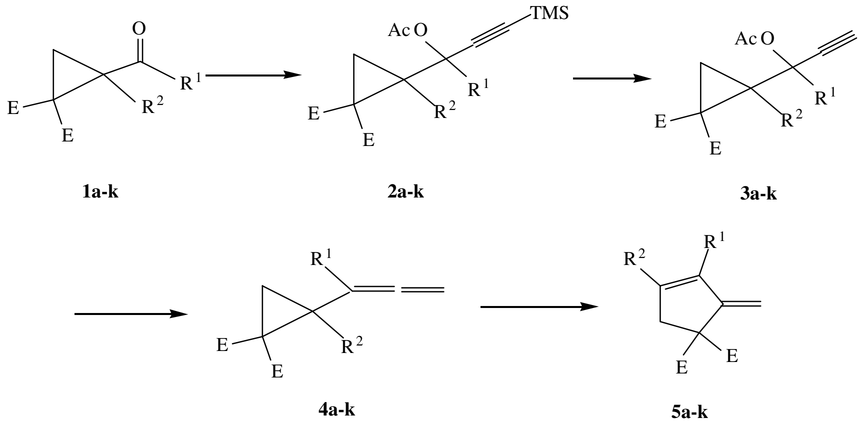
3a–k	R^1	R^2	Reaction temp (°C)	Yield of **4** (%)	Yield of **5** (%)
3a	H	H	rt	64	—
3a	H	H	50	24	21
3b	Me	H	0	46	—
3b	Me	H	rt	8	70
3c	Et	H	rt	8	55
3d	*i*-Pr	H	rt	Trace	71
3e	*i*-Bu	H	rt	Trace	57
3f	*t*-Bu	H	rt	7	59
3g	*c*-Hexyl	H	rt	17	60
3h	Ph	H	rt	Trace	52
3i	Bzl	H	rt	6	49
3j	$PhCH_2CH_2$	H	rt	Trace	62
3k	H	Me	rt	46	21

[a] The reactions of **3a**–**k** with Stryker reagent [hydride(triphenylphosphine)copper] hexamer, 0.5 equiv were carried out in toluene for 3 h.

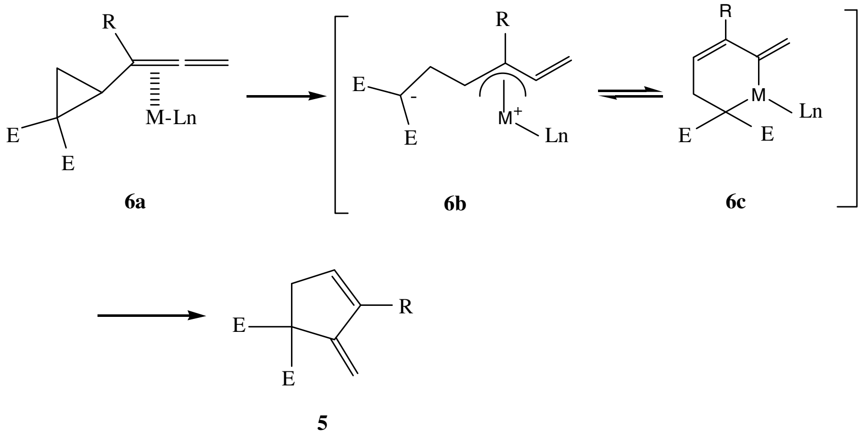
Table 2
Studies on copper hydride-promoted reactions of allenylcyclopropanes (**4**)[a]

Substrates	Reaction temp (°C)	Yield of **5** (%)
4a	40	51 (**5a**)
4b	rt	74 (**5b**)

[a] The reactions of **4a**,**b** with a copper hydride (Stryker) reagent (0.5 equiv) were carried out in toluene for 3 h in the presence of H_2O (0.5 equiv).



Scheme 1.



Scheme 2.

tion of the copper reagent to the cyclopropane rings via **6a**,**b**. The alkylcopper intermediate, prepared by the insertion of the copper reagent into the allenylcyclopropane part would undergo reductive elimination of the copper catalyst in **6c** to give methylenecyclopentenes **5** (Scheme 2).

Thus, we present here the first report for the synthesis of α-allenylcyclopropanedicarboxylates and the novel transformation of the cyclopropanes into methylenecyclopentene derivatives with a copper hydride (Stryker) reagent.

References and notes

1. (a) *Allenes in Organic Synthetsis*; Schuster, H. F., Coppola, G. M., Eds.; John Wiley & Sons: New York, 1984; (b) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VHC: Weinheim, 2004.
2. For reviews, see: (a) Ma, S. *Chem. Rev.* **2005**, *105*, 2829–2871; (b) Zimmer, R.; Dinesh, C.; Nandanan, E.; Khan, F. *Chem. Rev.* **2000**, *100*, 3067; (c) Marshall, J. *Chem. Rev.* **2000**, 3163; (d) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590; (e) Bates, R.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12; (f) Sydnes, L. *Chem. Rev.* **2003**, *36*, 701; (g) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207.
3. (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590–3593; (b) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed.* **1995**, *34*, 2589.
4. (a) de Meijere, A. *Angew. Chem.* **1979**, *91*, 867–884; (b) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411.
5. (a) Shimizu, I.; Ohashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 3825–3828; (b) Yamamoto, K.; Ishida, T.; Tsuji, J. *Chem. Lett.* **1987**, *6*, 1157–1158.
6. Murakami, M.; Itami, K.; Ubukata, M.; Tsuji, I.; Itoh, Y. J. *Org. Chem.* **1998**, *63*, 4–5.
7. Hayashi, M.; Ohmatsu, T.; Meng, Y.-P.; Saigo, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 837–839.
8. (a) Yoshida, M.; Sigimoto, K.; Ihara, M. *Tetrahedron* **2002**, *58*, 7839–7846; (b) Owada, Y.; Matsuo, T.; Iwasawa, N. *Tetrahedron* **1997**, *53*, 11069–11086; (c) Iwasawa, N.; Owada, Y.; Matsuo, T. *Chem. Lett.* **1994**, 115–116.
9. (a) Oison, L. P.; Gajewski, J. J. *Tetrahedron Lett.* **1993**, *34*, 2895–2898; (b) Minter, D. E.; Fonken, G. J. *Tetrahedron Lett.* **1977**, *20*, 1717–1720; (c) Minster, D. E.; Fonken, G. D. *Tetrahedron Lett.* **1977**, *48*, 4149–4152.
10. (a) Brestensky, D. M.; Huseland, D. E.; McGettigan, C.; Stryker, J. M. *Tetrahedron Lett.* **1988**, *29*, 3749–3752; (b) Chiu, P.; Li, Z.; Fung, K. C. M. *Tetrahedron Lett.* **2003**, *44*, 455–457.
11. *General procedure*: In a 25 ml two-necked flask equipped with a septum inlet $[CuH(PPh_3)]_6$ (366 mg, 0.185 mmol) was placed, and toluene (3 ml) was added under atmosphere of argon. A solution of **3b** (100 mg, 0.3730 mmol) in toluene (2 ml) and H_2O (0.035 ml) were added, and the reaction mixture was stirred at room temperature for 3 h. The reaction solution was diluted with ether, filtered with silica gel, and the filtrate was evaporated under reduced pressure. The residue was purified with flash column chromatography over silica gel (ethyl acetate–hexane 1:10) to give **5b** (70 mg, 70% yield) and **4b** (8 mg, 8% yield).