

Intramolecular Carbocyclization of Allenoate-aldehydes with Hexamethylditin Catalyzed by Palladium Complex: Synthesis of Cyclic Dienes[†]

Wonjae Seong, Suyeon Gong, Seok-Hoon Woo, and Chan-Mo Yu*

Department of Chemistry, Sungkyunkwan University, Suwon 440-746, Korea. *E-mail: cmyu@chem.skku.ac.kr
Received January 4, 2010, Accepted February 9, 2010

Key Words: Allenoate, Carbocyclization, Diene, Lactone, Palladium

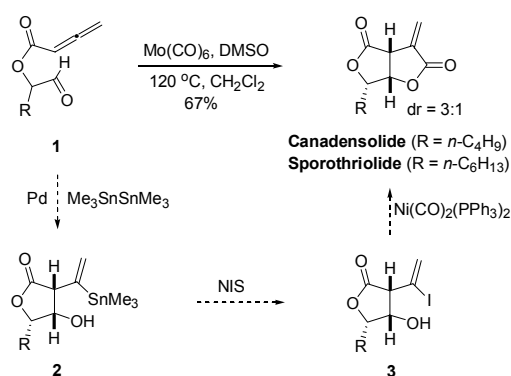
Development of new synthetic methods in the construction of cyclic system is an important subject in organic chemistry. Among a variety of synthetic methodologies for the construction of cyclic compounds, chemical transformations involving the use of transition metal catalysts are some of the most attractive methodologies because reactions can directly construct complex molecules from relatively simple starting materials.¹ As a consequence, many advances in the cyclization mediated by transition metals have been made through a variety of ways in synthetic strategy.² Of particular interest is a cyclization strategy between carbonyl and unsaturated bonds to find practical way of chemical routes for the preparation of lactones mainly because the chemical process could dominate over the classical methods in simple trial.³ In this regard, an allene has been proven to be a useful substrate for a variety of transition metal catalytic reactions, particularly for the cyclizations in the construction of carbo- and heterocycles.⁴ Recently, we disclosed our discovery of direct cyclization methods for the synthesis of avenacilolide,⁵ as a part of the allylic transfer strategy utilizing an allene as substrates or intermediates.⁶ To extend this protocol, we reported a cyclization of allenoate-aldehydes **1** mediated by molybdenum carbonyl in the presence of DMSO to direct access naturally occurring canadensolide as shown in Scheme 1.⁷ Although the reaction produced canadensolide and analogues in reasonable yields, products were always contaminated with diastereomers in a 3:1 mixture presumably due to a high reaction temperature.

The characteristic features of this protocol in terms of chemical efficiency through a three component coupling process

and structural features of products have encouraged us to carry out further investigations to design synthetic routes, which would improve stereoselectivity and utility of method. As a consequence, we became quite interested in carrying out investigation with stepwise reaction based on our previous studies^{6c} because it was expected to achieve better diastereoselectivity due to a lower reaction temperature.

With this issue in mind, several allene-aldehydes were prepared by a method developed by our laboratory.⁷ As a starting point, the allenoate-aldehyde **1a** (R = *n*-C₄H₉) was selected as a model substrate because a synthesis of canadensolide was expected from **1a** by the three steps sequence from our laboratory.^{6c}

Initial attempts to cyclocarbonylation of **1a** under the previous conditions employed for simple allene-aldehydes indicated that the conversion to the corresponding lactone **2a** could not be satisfied in terms of chemical conversion, although carbocyclization was occurred. Reaction produced the dehydrated **4a** as a single product (Table 1, entry 1). After surveying numerous conditions for orienting experiments as summarized in Table 1, several key findings were emerged as follows: i) the desired **2a** was not produced under the various conditions appeared in Table 1; ii) the use of Lewis acid additives such as BF₃·OEt₂ and TiCl₄ resulted in the decomposition;⁸ iii) addition of base *i*Pr₂NEt turned out to reduced chemical yield; iv) the use of CH₂Cl₂ was superior to other solvents such as toluene,



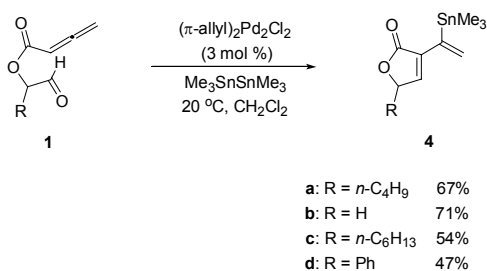
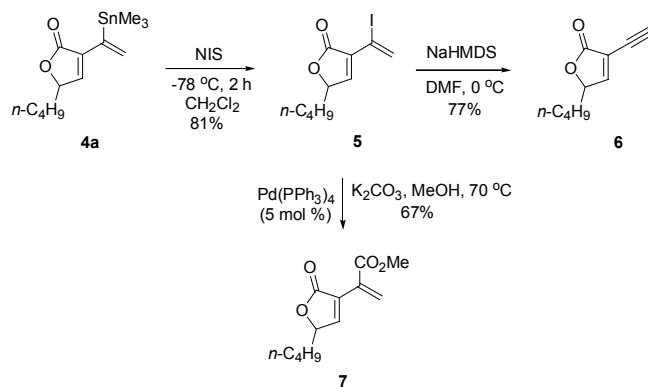
Scheme 1. General strategy

Table 1. Preliminary investigations with **1a**

entry	solvent	additive	T/°C	t/h	yield, 4a ^a
1	CH ₂ Cl ₂	none	-40	7	41
2	CH ₂ Cl ₂	BF ₃ ·OEt ₂	-40	7	decomposed
3	CH ₂ Cl ₂	TiCl ₄	-40	7	decomposed
4	CH ₂ Cl ₂	<i>i</i> Pr ₂ NEt	-40	7	23
5	CH ₂ Cl ₂	none	20	3	67
6	toluene	none	20	7	33
7	ether	none	20	7	37
8	CF ₃ Ph	none	20	4	48

^arefer to isolated product.

[†]This paper is dedicated to Professor Sunggak Kim on the occasion of his honorable retirement.

**Scheme 2.** Synthesis of diene **4** from **1****Scheme 3.** Functional group transformations of **4**

ether, and CF₃Ph in terms of reactivity and chemical yields; v) reaction performed at 20 °C in CH₂Cl₂ resulted in the best chemical yield for the synthesis of **4a**.

Upon optimal conditions (Table 1, entry 5), the reaction was conducted by a dropwise addition of a mixture of **1a** (1 equiv) and Me₃SnSnMe₃ (1.2 equiv) in CH₂Cl₂ for 20 min to a solution of (π-allyl)₂Pd₂Cl₂ (3 mol %) at 20 °C in CH₂Cl₂. After 3 h at 20 °C, the reaction mixture was quenched by addition of saturated aqueous NaHCO₃. After usual workup procedure and then removal of volatile materials under reduced pressure, final purification was effected by column chromatography to yield **4a** in 67% yield.

We soon realized that the synthesis of functionalized cyclic dienes might be useful because the utilization of dienes can be foreseen for many functional group transformations.⁸ With the notion that this approach might lead to a general and efficient method for the synthesis of a cyclic diene **4**, we set out to determine the scope to produce structurally various products. Indeed, the method is successful with **1a-d** to yield the diene **4a-d** as a single adduct, respectively, in moderate to good yields as shown in Scheme 2.

Product **4** is readily amenable for further conversion to synthetically useful compounds by functional group transformations of vinylstannane as depicted in Scheme 3. For example, compound **4a** was converted to **5** by NIS at -78 °C in CH₂Cl₂.⁹ Elimination of **5** with NaHMDS in DMF yielded the enyne **7**. Carbonylation of **6** in the presence of Pd(0) in the presence of K₂CO₃ under CO pressure in MeOH gave **8** in good yield.¹⁰

In summary, this communication describes synthetic routes to the cyclic diene **4** from allenoate-aldehydes **1** with hexamethyl-ditin catalyzed by palladium complex in a general and efficient way which promises to be synthetically useful. Studies are in progress to incorporate with diene into multi-cyclic compounds by cycloaddition reaction related to a core skeleton of biologically active natural products.

Acknowledgments. Generous financial support from the Korea Research Foundation (KRF-2006-312-C00234; KRF-2005-005-J11901) and the Korea Science & Engineering Foundation (R01-2007-000-20315-0) is gratefully acknowledged.

References and Notes

- (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644.
- (a) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067. (b) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813.
- Reviews, see: (a) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695. (b) Ma, S. *Eur. J. Org. Chem.* **2004**, 1175.
- Mandai, T. In *Modern Allene Chemistry*, Vol. 2; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; pp 925-972.
- Yu, C.-M.; Youn, J.; Jung, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 1553.
- (a) Yu, C.-M.; Hong, Y.-T.; Lee, J. *J. Org. Chem.* **2004**, *69*, 8506. (b) Yu, C.-M.; Hong, Y.-T.; Yoon, S.-K.; Lee, J. *Synlett* **2004**, 1695. (c) Yu, C.-M.; Youn, J.; Lee, M.-K. *Org. Lett.* **2005**, *7*, 3733. (d) Yu, C.-M.; Youn, J.; Jung, H.-K. *Bull. Korean Chem. Soc.* **2006**, *27*, 463. (e) Ko, K.-J.; Kim, S. H.; Kim, Y.; Min, D.; Yu, C.-M. *Bull. Korean Chem. Soc.* **2007**, *28*, 1921. (f) Kim, S. H.; Oh, S.-J.; Ho, P.-S.; Kang, S.-C.; O, K.-J.; Yu, C.-M. *Org. Lett.* **2008**, *10*, 265.
- Kwon, J.; Gong, S.; Woo, S.-H.; Yu, C.-M. *Bull. Korean Chem. Soc.* **2009**, *30*, 773.
- For example: Katritzky, A. R., Taylor, R. J. K., Eds., In *Comprehensive Functional Group Transformations II*; Elsevier Pergamon: Amsterdam, 2005; pp 427-1310.
- (a) Britton, R. A.; Piers, E.; Patrick, B. O. *J. Org. Chem.* **2004**, *69*, 3068. (b) Paley, R. S.; De Dios, A.; Estroff, L. A.; Lafontaine, J. A.; Montero, C.; McCulley, D. J.; Rubio, M. B.; Ventura, M. P.; Weers, H. L.; de la Pradilla, R. F.; Castro, S.; Dorado, R.; Morente, M. *J. Org. Chem.* **1997**, *62*, 6326.
- Martin, L. D.; Stille, J. K. *J. Org. Chem.* **1982**, *47*, 3630.