Pergamon

Tetrahedron Letters 41 (2000) 5131–5134

TETRAHEDRON LETTERS

Novel synthesis of chiral terminal allenes via palladium(0)-catalyzed reduction of mesylates of 2-bromoalk-2-en-1-ols bearing a protected amino group, using diethylzinc

Hiroaki Ohno,[a] Ayako Toda,[b] Shinya Oishi,[b] Tetsuaki Tanaka,[a,*] Yoshiji Takemoto,[b] Nobutaka Fujii[b] and Toshiro Ibuka[b,†]

[a]*Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan*
[b]*Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan*

Received 19 April 2000; revised 11 May 2000; accepted 12 May 2000

Abstract

A novel palladium(0)-catalyzed synthetic route to a series of chiral terminal allenes bearing an *N*-protected amino alkyl group has been developed. The palladium(0)-catalyzed reaction of mesylates of 2-bromoalk-2-en-1-ols bearing an amino functionality, with diethylzinc affords the corresponding terminal allenes in good yields. Both (*E*)- and (*Z*)-bromomesylates can equally be used for the present reaction, yielding the desired allenes in comparable yields.

Keywords: allenes; palladium catalysis; diethylzinc; reduction.

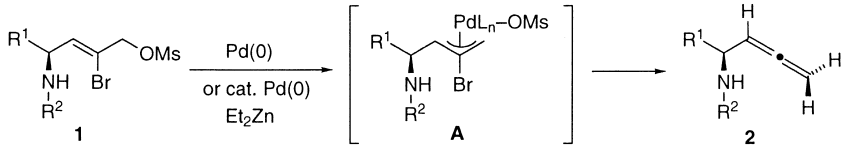
Amino allenes are potentially useful synthetic intermediates for biologically important three-,[1] four-,[2] five-,[3,4] and six-membered azacycles.[5] In addition, certain amino allenes have attracted much attention due to their potent inhibitory activity against monoamine oxidase (MAO).[6] In connection with a program directed towards the reactions of amino allenes,[1,2a] we required a reliable method for the synthesis of terminal amino allenes in enantiomerically pure form.

Although the synthesis of certain amino allenes from amino acids has appeared recently,[7,8] selective synthetic methods for terminal amino allenes in an enantiomerically or diastereomerically pure form are still scarce, notwithstanding their potential value in a number of synthetic intermediates.[4a,b,9]

This report describes a novel palladium-catalyzed synthetic method for terminal amino allenes by reduction of allyl bromomesylates with diethylzinc.[10,11] Although an unusual double substitution reaction of 2,3-dihaloprop-1-ene derivatives with some nucleophiles in the presence of catalytic Pd(0) or Pt(0) was reported,[12–14] there have been no reports describing synthesis of the allene of the type **2** from the bromo allylic mesylate **1** via π-allylpalladium intermediate **A** (Scheme 1).[15]

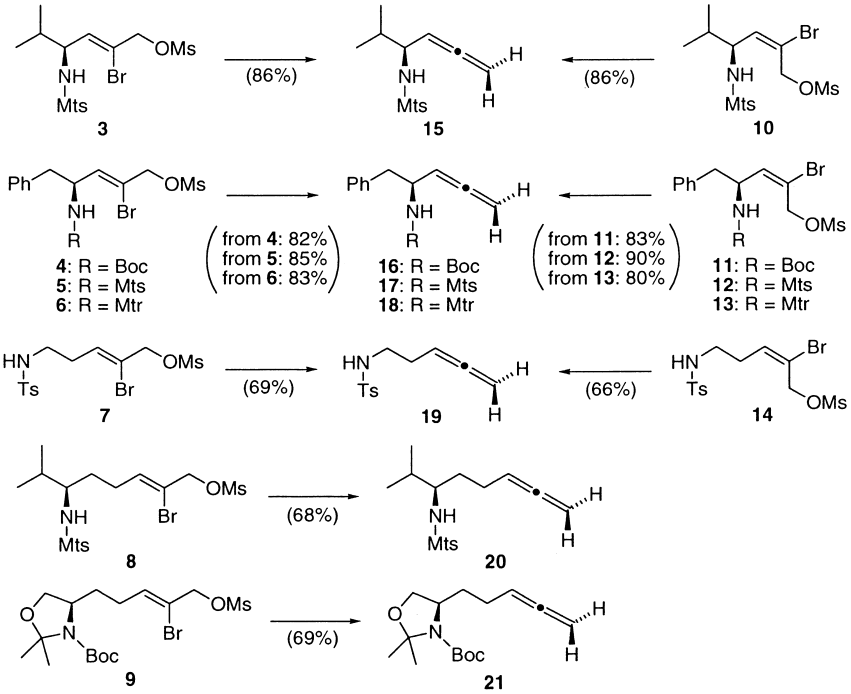
* Corresponding author.
† Deceased 20 January, 2000.

0040-4039/00/$ - see front matter
PII: S0040-4039(00)00790-5



Scheme 1.

The requisite mesylates **3**–**14**, shown in Scheme 2, were prepared according to our procedure published recently.[16] We initiated our study by converting the mesylate **3** into the allene **15** under various reaction conditions (Scheme 2). Treatment of the mesylate **3** with one equivalent of $Pd(PPh_3)_4$ in THF at room temperature gave the desired allene **15** in 82% yield as the sole product. It was found that only a catalytic amount of $Pd(PPh_3)_4$ was required when 2 equivalents of Et_2Zn was used as a reducing agent (86% yield). Although $Pd(OAc)_2$–$4PPh_3$ gave a satisfactory result (85% yield), $Pd(OAc)_2$ alone or $Pd(OAc)_2$–$4PBu_3$ was ineffective for the present transformation reaction, yielding only a trace quantity of the desired allene **15**.



Scheme 2. Reagent and conditions: $Pd(PPh_3)_4$ (10 mol%), Et_2Zn (2 equiv.), THF, room temperature, 20–60 min. Abbreviations: Mts = 2,4,6-trimethylbenzenesulfonyl; Mtr = 4-methoxy-2,3,6-trimethylbenzenesulfonyl

Having established the optimized reaction conditions, we next examined various substrates for the palladium-catalyzed reduction. As shown in Scheme 2, the mesylates **4**–**14** were converted into the corresponding amino allenes **15**–**21** in high yields by exposure to $Pd(PPh_3)_4$ (10 mol%) and Et_2Zn (2 equiv.) in THF for 20 min to 1 h at room temperature. From the above results, it is clear that a simple and efficient synthesis of terminal amino allenes could be realized irrespective of the (*E*)- or (*Z*)-geometry of the substrates.

One plausible mechanism for this palladium(0)-catalyzed reduction is shown in Fig. 1.[14a] The mesylate **3** and Pd(0) would form an allylpalladium intermediate **B** or **C**, which then could decompose to yield the allene **15** and a Pd(II) species. The generated Pd(II) complex would be reduced by Et_2Zn to regenerate a Pd(0) species.

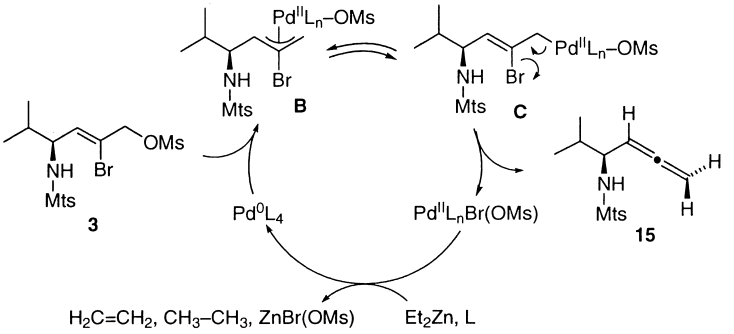


Figure 1.

In conclusion, we have demonstrated a novel synthetic method of amino allenes by palladium(0)-catalyzed reduction of allylic bromomesylates, using diethylzinc. Both (*Z*)- and (*E*)-mesylates were efficiently converted into the corresponding amino allenes in high yields. The scope and limitations of this unusual palladium-catalyzed reduction with diethylzinc are under investigation in this laboratory.

Acknowledgements

This article is dedicated to the memory of Professor Toshiro Ibuka, the conceptual originator of this treatise, died in a traffic accident in Japan on January 20, 2000. This article was supported in part by a Grant-in-Aid for Scientific Research (B) and (C) from the Ministry of Education, Science, Sports and Culture, Japan and the Japan Health Science Foundation.

References

1. Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1999**, *64*, 2992.
2. (a) Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 7393. (b) Rutjes, F. P. J. T.; Tjen, K. C. M. F.; Wolf, L. B.; Karstens, W. F. J.; Shoemaker, H. E.; Hiemstra, H. *Org. Lett.* **1999**, *1*, 717.
3. For a review, see: Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199.
4. (a) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4253. (b) Fox, D. N. A.; Gallagher, T. *Tetrahedron* **1990**, *46*, 4697. (c) Davies, I. W.; Scopes, D. I. C.; Gallagher, T. *Synlett* **1993**, 85. (d) Karstens, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **1997**, *38*, 6275. (e) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421. (f) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633.
5. (a) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871. (b) Ha, J. D.; Lee, D.; Cha, J. K. *J. Org. Chem.* **1997**, *62*, 4550. (c) Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 10012.
6. (a) Halliday, R. P.; Davis, C. S.; Heotis, J. P.; Pals, D. T.; Watson, E. J.; Bickerton, R. K. *J. Pharm. Sci.* **1968**, *57*, 430. (b) Massey, V.; Hemmerich, P. *The Enzymes* **1975**, *12*, 466.

7. (a) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; Ibuka, T. *Tetrahedron Lett*. **1999**, *40*, 349. (b) Ohno, H.; Toda, A.; Fujii, N.; Takemoto, Y.; Tanaka, T.; Ibuka, T. *Tetrahedron* **2000**, *56*, 2811.
8. Dexter, C. S.; Jackson, R. F. W.; Elliott, J. *J. Org. Chem*. **1999**, *64*, 7579. Dexter, C. S.; Lackson, R. F. W. *Chem. Commun*. **1998**, 75. Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Turner, D. *J. Org. Chem*. **1995**, *60*, 2210. For an excellent synthesis of terminal allenes from propargyl alcohols by treatment with *o*-nitrobenzenesulfonylhydrazine–PPh_3–DEAD, see: Myers, A. G.; Zheng, B. *J. Am. Chem. Soc*. **1996**, *118*, 4492.
9. Fox, D. N. A.; Gallagher, T. *Tetrahedron* **1990**, *46*, 4697. Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Chem. Soc., Chem. Commun*. **1989**, 1073. Karstens, W. F. J.; Stol, M.; Rutjes, F. P. J. T.; Hiemstra, H. *Synlett* **1998**, 1126.
10. Reduction of benzylic halides with diethylzinc using $Pd(PPh_3)_4$ as catalyst, see: Agrios, K. A.; Srebnik, M. *J. Org. Chem*. **1993**, *58*, 6908.
11. Semmelhack et al. reported that undesired allene was produced by treatment of bromo-mesylate with 2.4 equivalents of a Ni reagent, see: Semmelhack, M. F.; Brickner, S. J. *J. Am. Chem. Soc*. **1981**, *103*, 3945.
12. Organ, M. G.; Miller, M.; Konstantinou, Z. *J. Am. Chem. Soc*. **1998**, *120*, 9283.
13. (a) Castaño, A. M.; Aranyos, A.; Szabó, K. J.; Bäckvall, J.-E. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 2551. (b) Ohe, K.; Matsuda, H.; Morimoto, T.; Ogoshi, S.; Chatani, N.; Murai, S. *J. Am. Chem. Soc*. **1994**, *116*, 4125. For a report of the palladium-catalyzed reaction of a derivative of 1-oxygenated-2-bromoprop-2-ene, see: Trost, B. M.; Oslob, J. D. *J. Am. Chem. Soc*. **1999**, *121*, 3057.
14. For related works, see: (a) Lukas, J.; Visser, J. P.; Kouwenhoven, A. P. *J. Organomet. Chem*. **1973**, *50*, 349; (b) Lupin, M. S.; Powell, J.; Shaw, B. L. *J. Chem. Soc. (A)* **1966**, 1687.
15. While this manuscript was being prepared, an independent report by Bäckvall et al. appeared, describing a reverse reaction of our allene synthesis. Thus, palladium(II)-catalyzed 1,2-oxidation of a certain allene with *p*-benzoquinone in the presence of LiBr affords, only an isolated example, 2,3-dibromoprop-1-ene derivative, see: Jonasson, C.; Karstens, W. F. J.; Hiemstra, H.; Bäckvall, J.-E. *Tetrahedron Lett*. **2000**, *41*, 1619.
16. (a) Ohno, H.; Toda, A.; Fujii, N.; Ibuka, T. *Tetrahedron: Asymmetry* **1998**, *9*, 3929. (b) Ohno, H.; Toda, A.; Takemoto, Y.; Fujii, N.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2949.