



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

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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. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: allenes; palladium catalysis; diethylzinc; reduction.

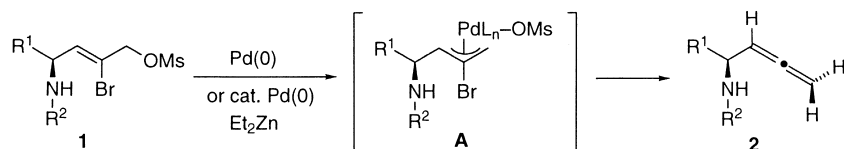
Amino allenes are potentially useful synthetic intermediates for biologically important three-,¹ four-,² five-,^{3,4} and six-membered azacycles.⁵ In addition, certain amino allenes have attracted much attention due to their potent inhibitory activity against monoamine oxidase (MAO).⁶ In connection with 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

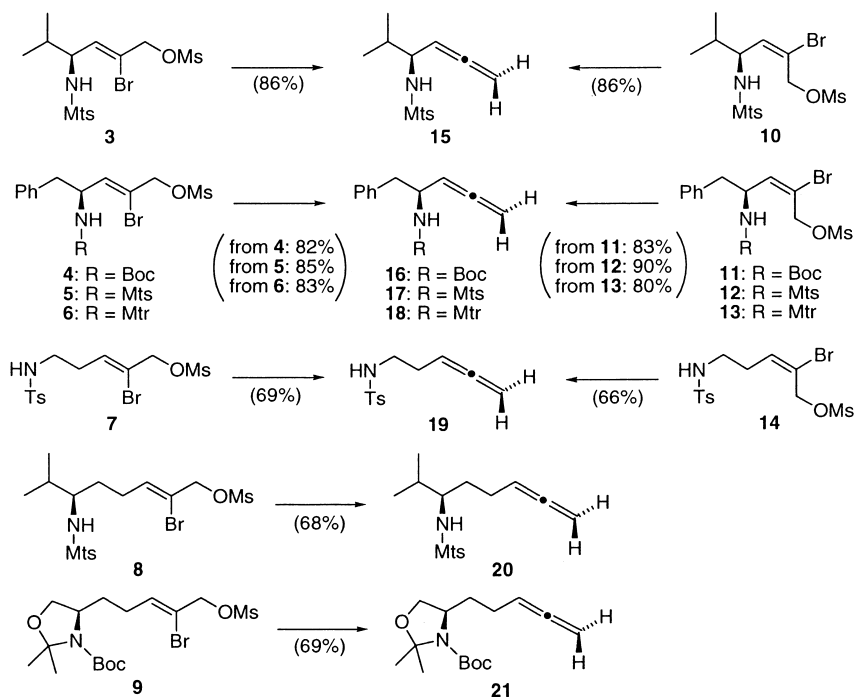
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Scheme 1.

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(PPh₃)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(PPh₃)₄ was required when 2 equivalents of Et₂Zn was used as a reducing agent (86% yield). Although Pd(OAc)₂–4PPh₃ gave a satisfactory result (85% yield), Pd(OAc)₂ alone or Pd(OAc)₂–4PBu₃ was ineffective for the present transformation reaction, yielding only a trace quantity of the desired allene **15**.



Scheme 2. Reagent and conditions: Pd(PPh₃)₄ (10 mol%), Et₂Zn (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(PPh₃)₄ (10 mol%) and Et₂Zn (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 Et₂Zn to regenerate a Pd(0) species.

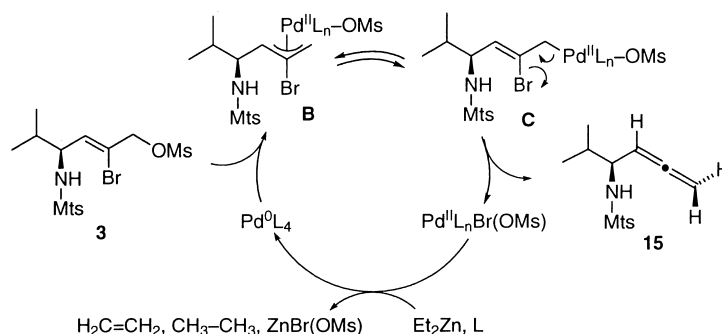


Figure 1.

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.

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