

Cationic Palladium Catalyzed Enyne Cycloreductions

Chang Ho Oh* and Sung Yong Um

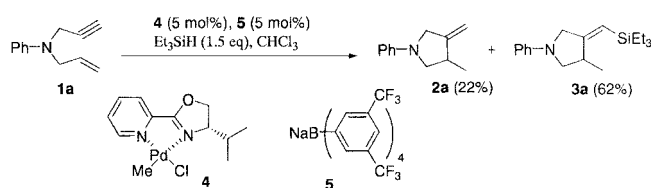
Department of Chemistry, Hanyang University, Seoul 133-791, Korea

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Effective construction of exomethylnecyclopentanes has been a major challenge in synthetic organic chemistry due to the large appearance of biologically active natural products possessing 5-membered rings.¹ Most of the approaches to date involve olefination of cyclopentanone,² radical cyclization of halodienes or enynes,³ palladium catalyzed cycloreduction of enynes,⁴ cycloisomerization of 1,6-dienes.⁵ Although these methods are well working for various enyne substrates, few methods can apply to nitrogen-containing enynes. Ito and his coworkers reported an enantioselective cycloisomerization of nitrogen-containing enynes, but no groups have studied their cycloreductions.⁶ Various cationic palladium compounds have been utilized for catalytic cyclizations of 1,6-dienes.⁷ Recently, Widenhoefer and his coworkers have reported a good method for enantioselective diene cycloisomerizations using cationic palladium chiral compounds.⁸ We have long been interested in searching an efficient and selective methodology for enyne and enediyne cycloreductions using transition metal catalysts.⁹ While we were looking for a catalyst for cycloreduction of nitrogen-containing enynes, we postulated that cationic palladium compounds might be of good choice to catalyze such nitrogen-containing enynes. Here, we wish to report our preliminary results on cationic palladium catalyzed cycloreduction of enynes for the first time. We have chosen *N,N*-allylpropargylaniline as the first substrate since this substrate has not been well cyclized under our previously reported conditions mainly due to the cleavage of a C-N bond. When Pd₂(dba)₃, Pd(OAc)₂, Pd(PPh₃)₄, or other allylpalladium chloride dimer was mixed with triethylsilane and acetic acid, formic acid, or silver triflate, the combined catalyst systems did not catalyze cycloreduction of the enyne. We thought that inert reactivity could arise from poor coordination of the enynes with palladium catalysts. Thus, we tested a diene-coordinated palladium compound which might easily undergo ligand substitutions by the enynes. A combined system of (COD)PdMeCl and silver triflate in the presence of triethylsilane reacted quickly with the enyne, but only reduction at the triple bond occurred.

Then, (dppe)PdMeCl was prepared for test, but no suc-



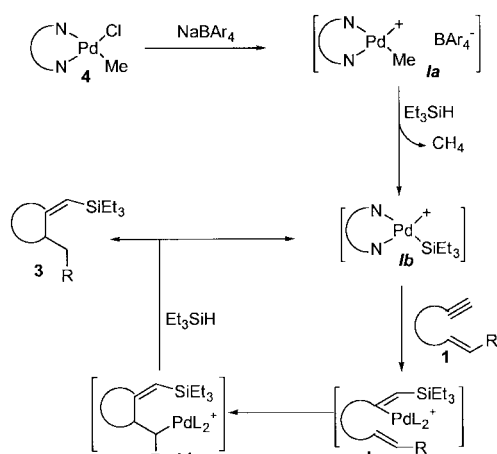
Scheme 1

cessful cycloreductions were obtained. Finally, (N-N)Pd-MeCl [N-N=4-isopropyl-2-(2-pyridinyl)-2-oxazoline] (**4**) and NaBAr₄ [Ar=3,5-C₆H₃(CF₃)₂] (**5**) were tested with the enyne **1a** in the presence of 1.5 equivalent of triethylsilane (Scheme 1).^{7,10} We isolated the cycloreduced product **2a** and its silylated product **3a** in 22% and 62% yields, respectively. It is worth to note that a cationic palladium catalyst system was used for cycloreduction of enynes for the first time. The above conditions were applied to the structurally diverse enynes (**1b-1k**) as summarized in Table 1.

Several features are to be noted. The cationic palladium species catalyzed cycloreductions of various enynes to the corresponding cycloreduced products.¹¹ Among them, cycloreduction of nitrogen-containing enynes (**1a**, **1j**, and **1k**) are the most informative for expanding the synthetic methodology.

Table 1. Cycloreductions of enynes using cationic palladium catalyst and triethylsilane

Entry	Substrates	solvent	Temp (°C)/ time (h)	Products	Yields
1	1b	CH ₂ Cl ₂	RT/18	2b	88 (24% ee)
2	1c	CH ₂ Cl ₂	RT/24	2c	79
3	1d	CHCl ₃	RT/6	2d	65
4	1e	CHCl ₃	50/2	2e	53
5	1f	CH ₂ Cl ₂	RT/36	2f	93
6	1g	CH ₂ Cl ₂	RT/6	2g	90
7	1h	CHCl ₃	50/6	2h	76
8	1i	CH ₂ Cl ₂	RT/20	2i	81
9	1j	CH ₂ Cl ₂	RT/5	2j, 3j	35, 50
10	1k	CH ₂ Cl ₂	50/2	2k, 3k	10, 57



Scheme 2

Second, isolation of the silylated products gave an important clue for the cycloaddition mechanism. When the silylated product **3a** was subjected to the same reaction conditions, we isolated the desilylated product **2a**. Third, asymmetric cycloaddition of an enyne **1b** under the present conditions was accomplished in a limited success (24% ee). Mechanistically, formation of the silylated product **3** could be rationalized as shown in Scheme 2.

The cationic methylpalladium complex (**Ia**), formed from methylpalladium chloride and sodium tetraarylborate, might react with triethylsilane first to form triethylsilylpalladium (**Ib**), which then undergo silapalladation with the more reactive triple bond of the enynes **1** to form the triethylsilylvinylpalladium intermediate (**Ic**). Further carbopalladation with a pendant double bond and then subsequent reduction of alkylpalladium intermediate (**Id**) by triethylsilane would give the products **3** and triethylsilylpalladium for next catalytic cycle. Although we could not understand how the cycloaddition products **2** were formed from the products **3**, it should be noted that the silylated product would be an important intermediate. It implied that the triethylsilane play a dual role both in reductive cleavage of alkylpalladium intermediates and in activating palladium catalyst to silapalladate the terminal triple bond.

In summary, a 1 : 1 mixture of (N-N)PdMeCl [N-N=4-isopropyl-2-(2-pyridinyl)-2-oxazoline] and NaBAR₄ [Ar=3,5-C₆H₃(CF₃)₂] could catalyze cycloaddition of various enynes via silapalladation/cycloaddition under mild conditions.

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- All new compounds **2a-k** were characterized by ¹H NMR, ¹³C NMR, IR and high resolution mass spectroscopy.