



## Palladium Catalyzed Hydroamination of Conjugated Enynes

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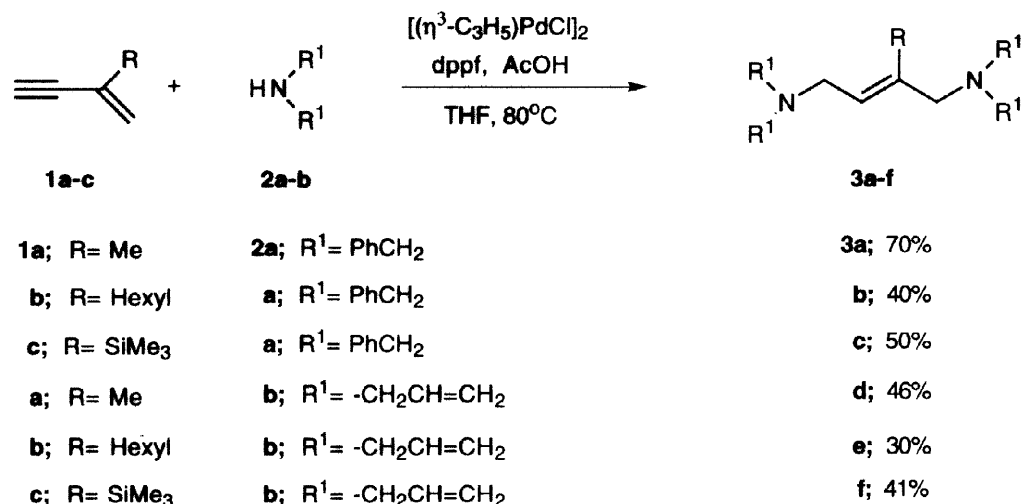
**Abstract:** The  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf-AcOH}$  catalytic system effected the hydroamination of conjugated enynes **1** leading to the formation of (E)-isomer of alkenic 1,4-diamines in stereoselective fashion.

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The transition metal mediated nucleophilic addition across carbon-carbon multiple bonds is a convenient process for the functionalization of unsaturated organic molecules and also in the synthesis of heterocyclic molecules.<sup>1</sup> Among various reactions, hydroamination reaction is one of the most useful methods for the carbon-nitrogen bond formation.<sup>2</sup> There are few reports on the hydroamination of alkenes, alkynes, allenes and dienes assisted by transition metals, lanthanides and actinides.<sup>3</sup> In recent years, palladium catalyzed hydroamination reactions attract more attention.<sup>3a-c</sup> However, most of them are intramolecular reactions. There is no report on the intermolecular stereoselective hydroamination of conjugated enynes. Recently, the palladium catalyzed hydroamination of allenes has been reported from this laboratory.<sup>4</sup> Herein we report the first stereoselective hydroamination of conjugated enynes in the presence of palladium catalyst (Scheme 1). A remarkable feature of the hydroamination of the conjugated enynes is the formation of reactive allenes as intermediates which undergo further addition of amine.

In the course of our investigation on the palladium catalyzed hydroamination of enynes, we have found that certain palladium catalysts catalyze the hydroamination of 2-substituted conjugated enynes in a stereoselective manner. Our studies were initiated by the addition of dibenzyl amine (1 equiv) to the mixture containing  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf}$ , enyne **1a** (1 equiv) and AcOH in THF. It was found that at reflux conditions the reaction gave (E)-isomer of alkenic 1,4-diamine **3a** in 26% yield. The increase in the yield (up to 70%) was observed when 4 equiv of dibenzyl amine was employed.

During the optimization of reaction conditions, we found that there was no product formation if any one of the substances was excluded. Further, we examined this reaction with various catalyst systems such as  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf}$ ,  $\text{Pd(OAc)}_2\text{/dppf}$ ,  $\text{Pd}_2\text{dba}_3\text{.CHCl}_3\text{/dppf}$  and  $\text{Pd(PPh}_3)_4\text{/P(o-tolyl)}_3$ . Among them  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf}$  gave the best result. THF was found to be a better solvent for this reaction. The reaction was found to be a general one and other enynes were also converted to the corresponding alkenic 1,4-diamines in moderate yields. The results are presented in Scheme 1.<sup>5</sup> The products were identified by NMR and Mass spectral data analysis and the stereochemistry of the product was confirmed by NMR study.

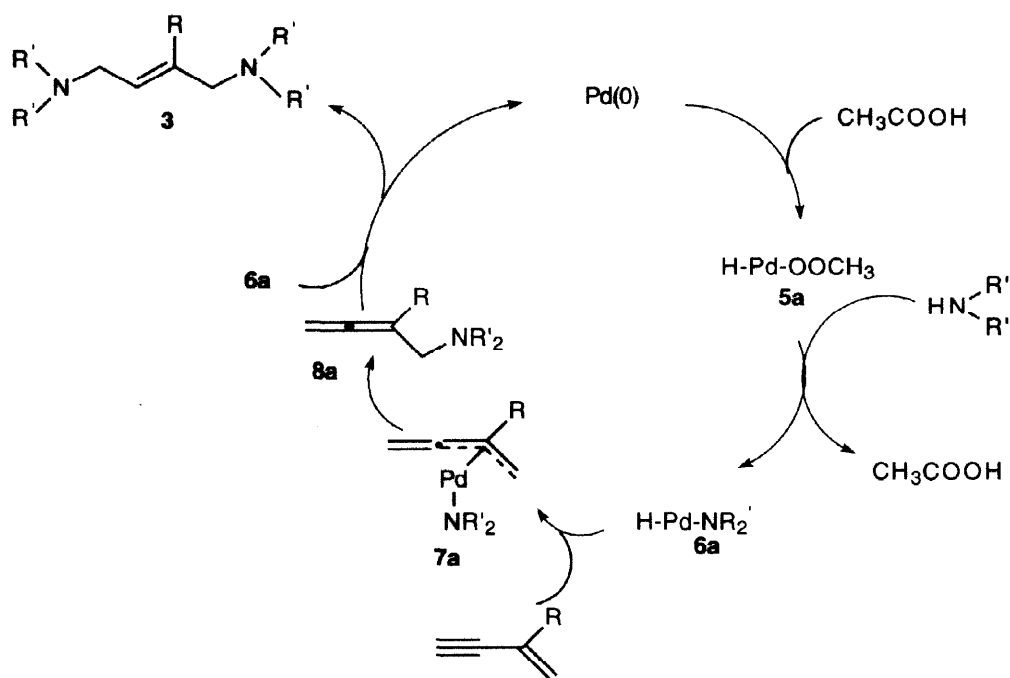


Scheme 1

The typical procedure is as follows: To a mixture of  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2$  (0.025 mmol, 26 mg), dppf (0.06 mmol, 33 mg), and THF (1 ml) which was kept in a reaction vial under argon atmosphere, were added acetic acid (0.5 mmol, 33 mg), enyne **1a** (0.5 mmol, 33 mg) and dibenzyl amine (2.0 mmol, 394 mg). The reaction mixture was heated to 80°C and stirred for 18h. The contents were filtered through a short column of alumina to remove suspended particles. After concentration, the residue was subjected to silica gel column chromatography. Ethyl acetate (1%) in hexane eluted diamine **3a** in 70% yield (161 mg).

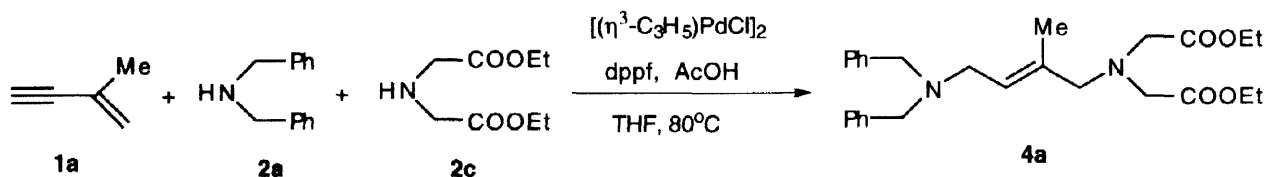
Recently, Cazes's et.al reported the palladium catalyzed intermolecular hydroamination of allenes with aliphatic amines in the presence of triethylammonium iodide.<sup>6</sup> In order to compare the reactivity of this catalytic system, we examined the reaction of enyne **1a** with dibenzyl amine using their catalytic system. However, the reaction did not give fruitful results. These results show that our catalytic system is the most suitable for the hydroamination of enynes.

A possible reaction pathway for this palladium (0) catalyzed hydroamination is shown in Scheme 2, although it is speculative. The reaction may consist of five steps, initiated by the oxidative addition of acetic acid to palladium (0) leading to the formation of hydrido palladium species **5a**.<sup>7</sup> This species **5a** on the reaction with an amine would lead to the formation of the hydrido amino palladium species **6a**.<sup>8</sup> Addition of this **6a** to an enyne would give the amino allene **8a** via exo-methylene  $\pi$ -allyl palladium complex **7a** as an intermediate. Even though it is a strained one a related species has been reported in the literature.<sup>9</sup> Further addition of **6a** to **8a** and regeneration of the catalyst would give the alkenic 1,4-diamine **3** as a product.<sup>4</sup>



Scheme 2

Unfortunately, the reaction did not give fruitful results with dibutyl amine, toluene sulfonamide and diethyl iminodiacetate. Probably, in the case of diethyl iminodiacetate **2c**, the initially formed allenic amine did not react with another equivalent of amine. Instead it underwent decomposition before reacting with another amine. It was thought that the initially formed allenic amine can be reacted with another reactive amine such as dibenzyl amine to produce unsymmetrically substituted 1,4-diamine. Indeed, the reaction of dibenzyl amine (1 equiv) with enyne **1a** (1 equiv) in the presence of excess (4 equiv) of diethyl iminodiacetate **2c** gave unsymmetrically substituted alkenic 1,4-diamine **4a** (41%) besides **3a** (10%). The structure of alkenic 1,4-diamine **4a** was established by NMR (COLOC, NOE) and Mass spectral studies.



Further investigation on this reactivity with other amines will be fruitful for the synthesis of mixed 1,4-diamino-2-butenes.

In summary, we have developed a single pot protocol for the stereoselective double hydroamination of enynes. These types of allylic amines are important organic compounds on account of their use as synthetic intermediates and their use as inhibitors.<sup>10</sup> Hence, this procedure will find potential use in organic synthesis.

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**References and notes:**

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