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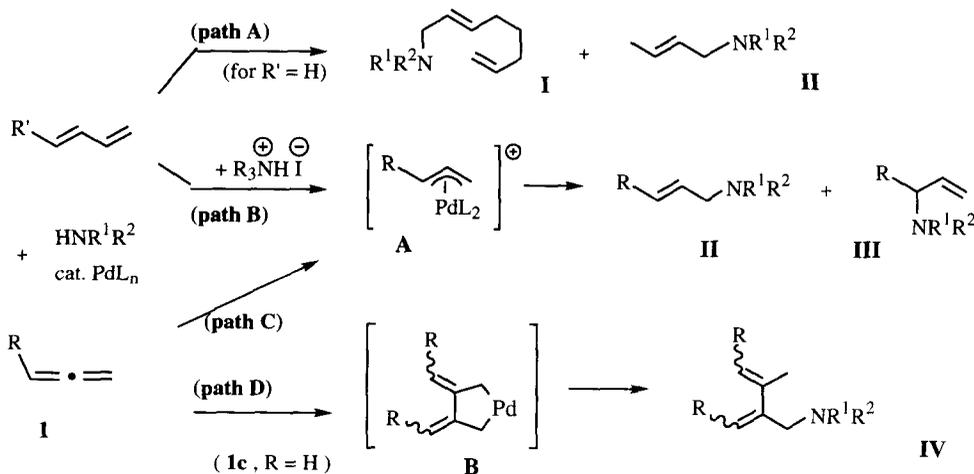
## Synthesis of Allylic Amines Through the Palladium-Catalyzed Hydroamination of Allenes.

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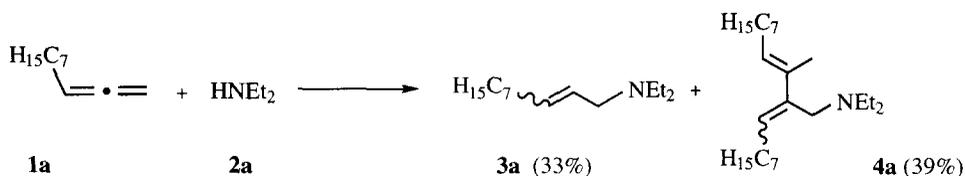
**Abstract** : The palladium-catalyzed addition of amines to allenes in the presence of triethylammonium iodide leads to allylic amines.

Allylic amines are important organic compounds, on account of their use as synthetic intermediates<sup>1</sup> and of their occurrence as natural substances.<sup>2</sup> Synthetic routes to these compounds are numerous<sup>3,4</sup> and often lead to mixture of regio and stereoisomers ; more recent efforts have focused on stereoselective methodologies.<sup>5,6</sup> Among these, several palladium-catalyzed transformations from allylic substrates<sup>7</sup>, alkenes<sup>8</sup>, alkynes<sup>6</sup> and 1,3-dienes<sup>8,9</sup> have been described. Considerable work with the latter unsaturated compounds has shown that telomerization in the presence of an amine leads to octadienylamines **I** (1:2 adduct) or allylic amines **II** (1:1 adduct) when the palladium catalysts are used in association with monodentate or bidentate phosphine ligands, respectively (path A). More recently, Dieck *et al.*<sup>10</sup> demonstrated the beneficial effect of adding an amine hydroiodide salt which resulted in the formation of allylic amines **II** and **III** via an intermediate  $\pi$ -allyl complex **A** (path B). Allene **1c** (R=H) is also known to telomerize under palladium catalysis leading to dienic amines **IV** (R=H), presumably through the palladacyclopentane intermediate **B** (path D).<sup>11</sup>



We report herein on the palladium-catalyzed hydroamination of allenic compounds to substituted allylic amines **II** in the presence of 0.2 equivalent of triethylammonium iodide, which may involve hydropalladation<sup>12</sup> of the allenic functionality (path C).

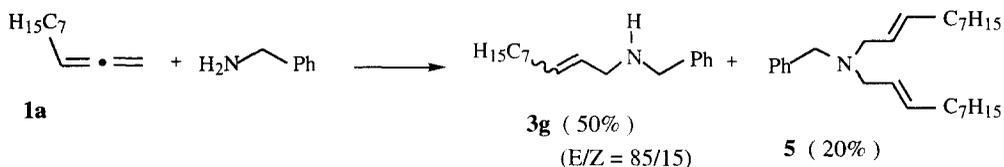
Initial experiments with 1,2-decadiene **1a** and diethylamine **2a** were carried out to find a suitable catalyst-ligand-solvent system for the desired transformation. Mixtures of allylic amine **3a** (as a mixture E + Z) and the dienic amine **4a** were obtained with palladium diacetate-triphenylphosphine in dimethylformamide (entry 1 and 2 in Table).



Other conditions met with little success (entries 3, 5) and showed that the presence of chloride ion has a detrimental effect (entries 4, 5). Finally, the catalyst bis(dibenzylideneacetone)palladium, Pd(dba)<sub>2</sub>, with two equivalents of triphenylphosphine in refluxing THF allowed formation of amine **3a** and a minor amount (<10%) of the dienic amine<sup>13</sup> **4a** (entries 7, 8); the donor ligand tri-*n*-butylphosphine inhibited the reaction (entry 6).

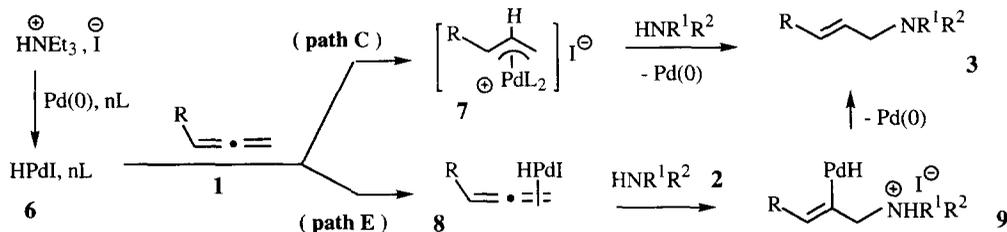
These conditions seemed general<sup>14</sup> for the synthesis of 98% pure (E)-allylic tertiary amine **3** from a monosubstituted allene and a secondary amine (entries 7-12); allene **1c** was prone to telomerization<sup>11</sup> and gave a 55% yield of the dienic amine **4f** (entry 13). 6,7-Tridecadiene, as a model of 1,3-disubstituted allene, gave no reaction.

Another reaction with benzylamine as a primary amine and allene **1a** in the same conditions gave allylic amine **3g** (50%) and the bisallylic amine **5** (20%), indicating a good overall transformation of the allenic substrate.

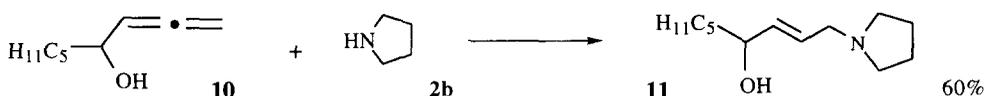


Two plausible explanations can be proposed, each involving as the initial step formation of a hydropalladium iodide species **6**. This species could hydropalladate allene **1** (path C) giving a  $\pi$ -allyl palladium complex **7** which is known to lead to the allylic amine **3**. An alternative pathway (path E) might involve a  $\pi$ -complex **8** between HPdI and the terminal double bond of allene **1**, which undergoes nucleophilic attack of amine **2** to give **9**; reductive elimination would then afford the allylic amine **3**, together with regenerated catalyst. Two similar pathways have been proposed by Yamamoto<sup>15</sup> and our group<sup>16</sup> for the palladium-catalyzed addition of malonate type compounds to allenes under neutral or basic conditions. However it seems presently uneasy to favour one of these pathways.<sup>15</sup>





Further studies on the mechanistic aspects of this new hydroamination reaction of allenes are in progress, as well as synthetic application to functionalized allenes, e.g. allenic alcohols. Thus 1,2-nonadien-4-ol **10** gave a 60% yield of the allylic aminoalcohol **11** under the above described conditions.



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- In all the cases the dienic amine **4a**, the product of the telomerization-functionalization of allene **1a**, was obtained as a 70/30 mixture of two of its stereoisomers which were not separated by flash-chromatography.
- Typical procedure is as follows* : N-(3-phenyl-2-propenyl) pyrrolidine **3e** (entry 12) Pd(dba)<sub>2</sub> (0.13mmol), triphenylphosphine (0.26 mmol) and Et<sub>3</sub>NHI (0.44 mmol) were mixed in THF (3 ml) under nitrogen during 15 minutes. Phenylallene **1b** (2.6 mmol) and pyrrolidine **2b** (2.88 mmol, 1.1 equiv) were then added and the mixture heated to 60°C for 32h. Hydrolysis with water (10 ml) was followed by extraction with CH<sub>2</sub>Cl<sub>2</sub> (4x15 ml) and drying over Na<sub>2</sub>SO<sub>4</sub>. Purification by flash-chromatography on silicagel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH : 95/5 + 0.1% NH<sub>4</sub>OH) yielded 190 mg (89%) of amine **3e**.  
<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>), δ (ppm) : 1.05 (t, J = 7.1 Hz, 6H) ; 2.56 (q, J = 7.1 Hz, 4H) ; 3.23 (d, J = 6.5 Hz, 2H) ; 6.29 (dt, J<sub>trans</sub> = 15.9 Hz and J = 6.5 Hz, 1H) ; 6.50 (d, J<sub>trans</sub> = 15.9 Hz, 1H) ; 7.14-7.38 (m, 5H).
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