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 and of their occurrence as natural substances. Synthetic routes to these compounds are numerous and often lead to mixture of regio and stereoisomers; more recent efforts have focused on stereoselective methodologies. Among these, several palladium-catalyzed transformations from allylic substrates, alkenes, alkynes and 1,3-dienes have been described. Considerable work with the latter unsaturated compounds has shown that telomerization in the presence of an amine leads to octadienylamines (1:2 adduct) or allylic amines (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. demonstrated the benificial effect of adding an amine hydroiodide salt which resulted in the formation of allylic amines II and III via an intermediate n-allyl complex A (path B). Allene (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).
We report herein on the palladium-catalyzed hydroamination of allenic compounds to substituted allylic amines \( \text{II} \) in the presence of 0.2 equivalent of triethylammonium iodide, which may involve hydropalladation\(^\text{12}\) 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, \( \text{Pd(dba)}_2 \), with two equivalents of triphenylphosphine in refluxing THF allowed formation of amine 3a and a minor amount (<10%) of the dienic amine\(^\text{13}\) 4a (entries 7, 8); the donor ligand tricyclohexylphosphine inhibited the reaction (entry 6).

These conditions seemed general\(^\text{14}\) for the synthesis of 98% pure (E)-allylic tertiary amine 3 from a monosubstituted allene and a secondary amine (entries 7-12); allene 1e was prone to telomerization\(^\text{11}\) 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\(^\text{15}\) and our group\(^\text{16}\) 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.\(^\text{15}\)
Table

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\begin{align*}
\text{R} & + \text{HNR}^1\text{R}^2 \xrightarrow{\text{Palladium salt}} \text{R} & \text{NR}^1\text{R}^2 + \text{NR}^1\text{R}^2 \\
1 & 2 & 3 & 4 \\
\text{1a} & \text{HNET}_2 & 4\% \text{Pd(OAc)}_2 + 2 \text{PPh}_3 & \text{DMF} - 65^\circ\text{C} - 19\text{h} & 3\text{a} & 4\text{a} \\
\text{2a} & \text{HNET}_2 & 4\% \text{Pd(OAc)}_2 + 2 \text{PPh}_3 + \text{TMEDA} & \text{DMF} - 65^\circ\text{C} - 18\text{h} & (16) (50/50) & (15) \\
\text{3} & \text{3a} & 5\% \text{Pd(PhCN)}_2\text{Cl}_2 + \text{PPh}_3 & \text{MeOH} - 65^\circ\text{C} - 18\text{h} & - & - \\
\text{4} & \text{3a} & 4\% \text{PdCl}_2 + 4 \text{PPh}_3 + 4\% \text{AgBF}_4 & \text{CH}_3\text{CN} - 60^\circ\text{C} - 20\text{h} & 59 (95/5) & - \\
\text{5} & \text{3a} & 4\% \text{Pd(dba)}_2 + 2 \text{PPh}_3 & \text{THF} - 65^\circ\text{C} - 18\text{h} & (38) (92/8) & (8) \\
\text{6} & \text{3a} & 4\% \text{Pd(dba)}_2 + 2 \text{P(nBu)}_3 & \text{THF} - 65^\circ\text{C} - 18\text{h} & - & - \\
\text{7} & \text{3a} & 5\% \text{Pd(dba)}_2 + 2 \text{PPh}_3 & \text{THF} - 65^\circ\text{C} - 18\text{h} & 55 (96/4) & 9 \\
\text{8} & \text{3a} & 10\% \text{Pd(dba)}_2 + 2 \text{PPh}_3 & \text{THF} - 65^\circ\text{C} - 18\text{h} & 70 (96/4) & 8 \\
\text{9} & \text{3a} & 5\% \text{Pd(dba)}_2 + 2 \text{PPh}_3 & \text{THF} - 65^\circ\text{C} - 17-22\text{h} & 3\text{b} 53 (98/2) & - \\
\text{10} & \text{3a} & - & - & 3\text{c} 64 (98/2) & 4\text{c} 14 \\
\text{11} & \text{3a} & - & - & 3\text{d} 72 (98/2) & 4\text{d} 19 \\
\text{12} & \text{3a} & - & - & 3\text{e} 89 (98/2) & - \\
\text{13} & \text{3a} & - & - & 4\text{f} 55 \\
\end{align*}
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Yield \(^a\) and (E/Z) \(^b\) values are provided for each entry. Further details are provided in the text below.

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\(^a\) Yields refer to materials isolated by column chromatography, except those in parentheses which are determined through GLC (hexadecane as internal standard).

\(^b\) E/Z ratios were determined through GLC or \(^1\)H NMR.
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.

References and notes:

1. For recent uses in organic synthesis, see for example:
12. A hydroboration step has been postulated in the Pd-catalyzed addition of an acid function to propargylic acetate to give allylic gem-dicarboxylate:
13. In all cases the dicarboxylic acid 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.
14. Typical procedure is as follows: N-(3-phenyl-2-propenyl) pyrrolidine 3e (entry 12)
   Pd(dba)2 (0.13 mmol), triphenylphosphine (0.26 mmol) and Et3N (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 CH2Cl2 (4x15 ml) and drying over Na2SO4. Purification by flash-chromatography on silicagel (CH2Cl2/MeOH : 95/5 + 0.1% NH4OH) yielded 190 mg (89%) of amine 3e.
   1H NMR (200 MHz, CDC13), δ (ppm): 1.05 (t, J = 7.1 Hz, 6H); 2.56 (q, J = 7.1 Hz, 2H); 3.23 (d, J = 6.5 Hz, 2H); 6.29 (dt, Jtrans = 15.9 Hz and J = 6.5 Hz, 1H); 6.50 (d, Jtrans = 15.9 Hz, 1H); 7.14-7.38 (m, 5H).

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