Communication

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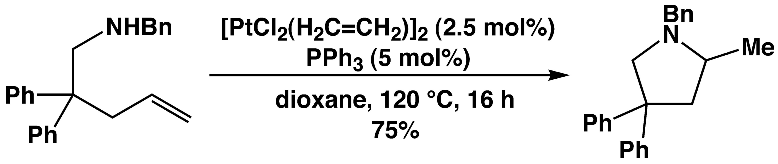

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Platinum-Catalyzed Intramolecular Hydroamination of Unactivated Olefins with Secondary Alkylamines

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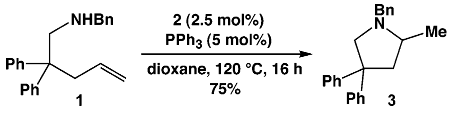
The prevalence of nitrogen heterocycles in naturally occurring and biologically active molecules,[1] coupled with the limitations associated with traditional methods for C−N bond formation,[2] has stimulated considerable interest in catalytic olefin amination as a route to nitrogen heterocycles.[3] However, despite significant progress in this area, the intramolecular hydroamination of unactivated olefins with alkylamines remains problematic.[3−11] For example, Pd(II) complexes catalyze the intramolecular oxidative amination of unactivated olefins with arylamines[4] and amides[5] but are not compatible with alkylamines.[6] Conversely, lanthanide metallocene[7] and amido[8] complexes catalyze the intramolecular hydroamination of unactivated olefins with alkylamines, but the synthetic utility of these protocols is compromised by the poor functional group compatibility and extreme moisture sensitivity of the lanthanide catalyst. A number of other systems for the hydroamination of unactivated olefins with alkylamines have been identified, but these are either of limited scope,[9] are restricted to the intermolecular hydroamination of vinyl arenes,[10] or require a stoichiometric amount of transition metal complex.[11]

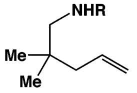
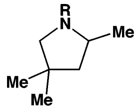
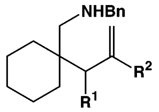
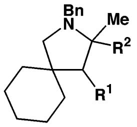
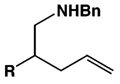
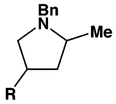
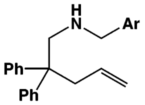
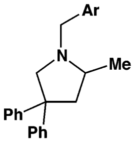
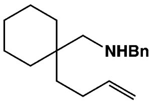
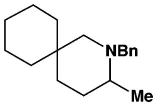
The attack of nucleophiles on olefins complexed to Pt(II) has been known for nearly a century.[12] However, efficient catalytic processes that exploit this reactivity have not been forthcoming, presumably due to the high kinetic and thermodynamic stability of platinum alkyl and olefin complexes.[13] Nevertheless, we have recently reported effective Pt(II)-catalyzed protocols for the addition of carbon,[14] nitrogen,[15] and oxygen[16] nucleophiles to unactivated olefins.[17] Although this group of transformations includes the Pt(II)-catalyzed hydroamination of ethylene with carboxamides,[15] all our attempts to achieve the hydroamination of ethylene with alkylamines have been unsuccessful. Despite these failures, we considered that the Pt-catalyzed hydroamination of unactivated olefins with alkylamines might be realized under intramolecular conditions. Indeed, here we report the Pt(II)-catalyzed intramolecular hydroamination of γ- and δ-amino olefins to form nitrogen heterocycles.

Heating a concentrated dioxane solution of γ-amino olefin **1** (0.5 M) with a catalytic mixture of $[PtCl_2(H_2C{=}CH_2)]_2$ (**2**) (2.5 mol %) and PPh_3 (5 mol %) at 120 °C for 16 h led to isolation of pyrrolidine **3** in 75% yield (eq 1). Platinum-catalyzed hydroamination of γ-amino olefins tolerated substitution at the allylic and internal olefinic carbon atoms and tolerated both primary and secondary N-bound alkyl groups (Table 1, entries 1−7). *gem*-Dialkyl substitution at the β-position of the γ-amino olefin facilitated hydroamination, but was not required (Table 1, entries 8 and 9). Platinum-catalyzed hydroamination tolerated a range of functionality including bromo, nitro, and cyano groups, carboxylic esters, acetals, and benzyl and silyl ethers (Table 1, entries 2, 6, and 10−14). Furthermore, neither the rate nor yield of hydroamination was affected by the presence of water (0.5 equiv) in the reaction mixture (Table 1, entries 4 and 5). δ-Amino olefins also underwent Pt-catalyzed hydroamination to form piperidine derivatives in moderate yield (Table 1, entry 15).



eq 1

Table 1. Hydroamination of Amino Olefins Catalyzed by a Mixture of $[PtCl_2(H_2C{=}CH_2)]_2$ (**2**) (2.5 mol %) and PPh_3 (5 mol %) in Dioxane at 120 °C

entry	alkenyl amine	heterocycle	time (h)	yield (%)[a]
				
1	R = Bn		9	65
2	R = CH_2CH_2OBn		22	70
3	R = Cy		17	57
				
4	$R^1 = R^2 = H$		2	82 (91)[c]
5[b]			2	(92)[c]
6	$R^1 = H$, $R^2 = Me$		14	79
7	$R^1 = OTBDMS$, $R^2 = H$		14	85 (3.5:1)[d]
				
8	R = *i*-Pr		11	62 (1.2:1)[d]
9	R = 4-C_6H_4OMe		21	59 (1.5:1)[d]
				
10	Ar = 4-C_6H_4Br		18	70
11	Ar = 4-C_6H_4CN		40	64
12	Ar = 4-$C_6H_4NO_2$		40	72
13	Ar = 4-$C_6H_4CO_2Me$		36	77
14	Ar = 3,4-C_6H_3(-OCH_2O-)		20	71
15			6[e]	57

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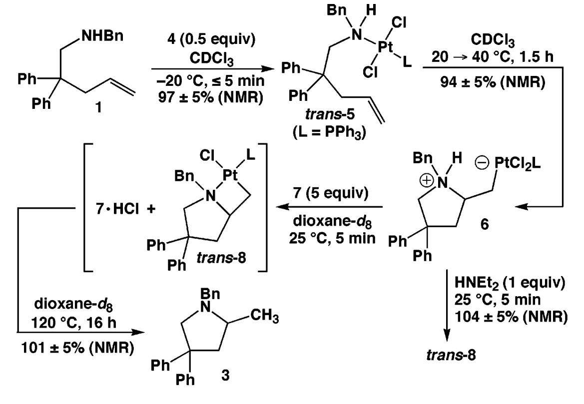
[a] Isolated product of ≥95% purity. [b] Reaction mixture contained water (0.5 equiv). [c] GC yield given in parentheses. [d] Diastereomeric ratio given in parentheses. [e] Substrate added slowly to reaction mixture.

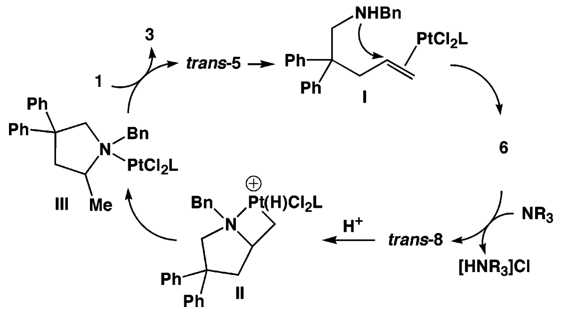
To gain insight into the mechanism of the Pt-catalyzed hydroamination of amino olefins, we investigated the stoichiometric reaction of **1** with the platinum phosphine dimer $[PtCl_2(PPh_3)]_2$ (**4**).[18] Reaction of **1** (15 mM) and **4** (0.5 equiv) in $CDCl_3$ at −20 °C led to rapid (≤5 min) formation of the platinum amine complex *trans*-**5** in 97 ± 5% yield (^1H NMR) (Scheme 1).[19] Warming a $CDCl_3$ solution of *trans*-**5** at 20 °C for 1 h and at 40 °C for 0.5 h led to formation of the zwitterionic complex **6** in 94 ± 5% yield (^1H NMR) (Scheme 1).[20] Thermolysis of a dioxane-d_8 solution of **6** at

10.1021/ja043278q CCC: $30.25

Scheme 1



Scheme 2



80 °C for 16 h led to decomposition without formation of pyrrolidine **3**. Conversely, treatment of a dioxane-d_8 solution of **6** (32 mM) with *N*-benzyl-4-pentenylamine (**7**; 5 equiv) at 25 °C for 5 min led to complete consumption of **6** and formation of the heterobicyclic platinum amine complex *trans*-**8** (Scheme 1);[19−21] subsequent thermolysis of this solution at 120 °C for 16 h formed **3** in 101 ± 5% yield from *trans*-**8** (^{1}H NMR). In a separate experiment, treatment of **6** with $HNEt_2$ (1 equiv) at 25 °C for 5 min formed *trans*-**8** in 104 ± 5% yield (^{1}H NMR) (Scheme 1).

The experiments described in the preceding paragraph support a mechanism for the platinum-catalyzed hydroamination of **1** initiated by formation of platinum amine complex *trans*-**5** (Scheme 2). C−N bond formation presumably occurs via intramolecular ligand exchange followed by outer-sphere attack[12] of the pendant amine on the olefin of **I** to form **6** (Scheme 2). Because thermolysis of **6** in the absence of **7** formed no detectable amounts of **3** and because **6** reacted rapidly and quantitatvely with amine to form *trans*-**8**, intramolecular protonolysis of the Pt−C bond of **6** appears unlikely. Rather, our data support a mechanism involving deprotonation/chloride displacement from **6** followed by intermolecular protonolysis of the Pt−C bond of *trans*-**8**,[22] presumably via a Pt(IV) hydride intermediate such as **II** (Scheme 2).[23] Ligand exchange from Pt-amine complex **III** would release **3** and regenerate *trans*-**5**.

In summary, we have developed an effective late-transition metal-catalyzed protocol for the intramolecular hydroamination of unactivated olefins with alkylamines and we have identified a number of potential intermediates in the catalytic cycle.

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Supporting Information Available: Experimental procedures and spectroscopic data for products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Complexes **4** and **2** were equally effective as catalysts for the conversion of **1** to **3**.
(19) See Supporting Information for details regarding the synthesis and characterization of complexes *trans*-**5**, **6**, and *trans*-**8**.
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