

Neither the cycloadduct derived from the *Z* isomer nor the azatricyclo[5.2.1.0<sup>4,8</sup>]decane regioisomer was observed in the reaction mixture.

The success of the dipolar cycloaddition reaction with a relatively complex substrate **10** to form **11** prompted an investigation into the utility of the sulfonylation of vinylogous amides as azomethine ylide precursors for the synthesis of functionalized *N*-heterocycles in general. Thus, a series of intermolecular cycloadditions were performed with DMAD, dimethyl maleate, or dimethyl fumarate as the dipolarophile and a variety of vinylogous amides to serve as 1,3-dipole precursors. Acyclic vinylogous amides (see Table 1, entries 1–3) undergo the transformation efficiently, generating highly substituted pyrrolidines. As seen in the synthesis of **11**, vinylogous amides derived from 2-pyrrolidinones (Table 1, entries 4 and 5) provide facile access to pyrrolizidines. Furthermore, highly functionalized indolizidines can be prepared from vinylogous amides derived from 2-piperidinones (Table 1, entries 6 and 7).

In summary, the first enantiospecific synthesis of the bridged pyrrolizidine core of asparagamine **A** has been accomplished. The synthetic approach highlights an intramolecular 1,3-dipolar cycloaddition of an azomethine ylide derived from the sulfonylation of a vinylogous amide. This strategy allows concomitant installation of the angular *E*-1-butenyl side chain during the assembly of the azatricyclo[5.3.0.0<sup>4,8</sup>]decane skeleton of **1**. The use of vinylogous amides in this capacity can be extended to the preparation of a variety of highly functionalized pyrrolidines, pyrrolizidines, and indolizidines.

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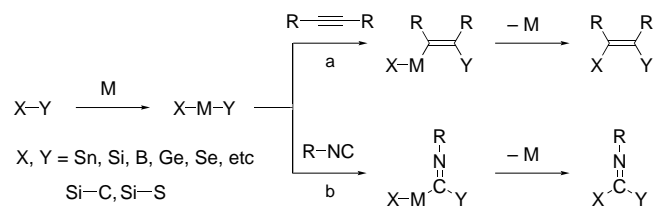
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## Cyanamide Synthesis by the Palladium-Catalyzed Cleavage of a Si–N Bond\*\*

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Studies on the transition-metal-catalyzed reaction of main-group-element–element bonds with unsaturated bonds have spread widely and extensively because of the synthetic utilities of the resulting products.<sup>[1]</sup> Various element–element bonds (X–Y) add to unsaturated C–C bonds, such as alkynes, 1,3-dienes, and allenes, in the presence of a transition-metal catalyst (route a in Scheme 1, vicinal addition). Among the bimetallic compounds, perhaps the most well-studied



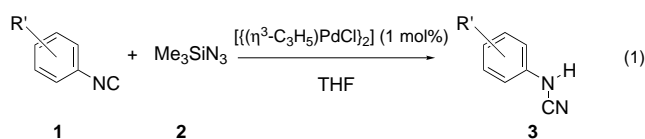
Scheme 1. Transition-metal-catalyzed addition of X–Y bonds to unsaturated bonds.

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metal–metal bond is found in silicon-containing derivatives such as Si–Si, Si–Sn, Si–B, Si–Se.<sup>[2, 3]</sup> The geminal addition of Si–Sn,<sup>[4]</sup> Si–Si,<sup>[5]</sup> and Si–B<sup>[6]</sup> to isocyanides is also known (route b in Scheme 1). However, only limited studies on the transition-metal-catalyzed addition of a Si–R bond (R = organic group) have been done.<sup>[7–12]</sup> The vicinal addition (route a) of Si–C<sup>[7–9]</sup> and Si–S<sup>[10]</sup> bonds is known. Quite recently, we have found that the geminal addition (route b) of the C–N bond takes place in the presence of a palladium catalyst.<sup>[13]</sup> However, the metal-catalyzed addition of a Si–N bond, either in a vicinal or in geminal mode, is not known. We now report the first example of the catalytic geminal addition of a Si–N<sub>3</sub> bond to isocyanides **1**. The reaction of **1** with Me<sub>3</sub>SiN<sub>3</sub> (**2**) in the presence of [((η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl)<sub>2</sub>] as a catalyst gave cyanamides **3** [Eq. (1)], possibly through the proposed intermediate **B** (see Scheme 2) formed through the geminal addition mode (route b, Scheme 1).



The results are summarized in Table 1. Trimethylsilyl azide (**2**) was added to a solution of 4-methoxyisocyanobenzene (**1a**) and [((η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl)<sub>2</sub>] (1 mol %) in THF. The mixture was stirred at room temperature for 10 min and then at 60 °C for 6 h to give (4-methoxyphenyl)cyanamide (**3a**) in 85 % yield (entry 1).<sup>[15]</sup> We carried out reactions with the isocyanides **1b** and **1c** which have an electron-donating group on the aromatic ring. The corresponding aryl cyanamides **3b** and **3c** were obtained in high yields (entries 2 and 3). The reaction of isocyanobenzene **1d** was complete in only 2 h to afford phenylcyanamide (**3d**) in high yield (entry 4). We next carried out the reactions with the isocyanides **1e–g** having an electron-withdrawing group at the *para* position. All these reactions were complete within 3 h to give the corresponding cyanamides **3e–g** in high yields (entries 5–7). The reactions

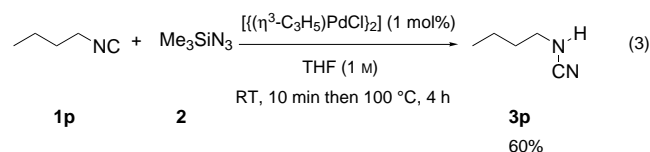
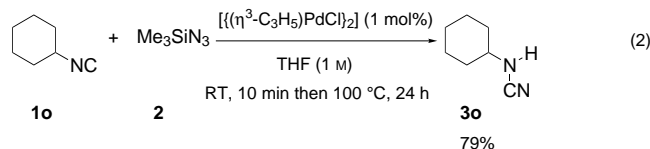
Table 1. Palladium-catalyzed formation of cyanamides.<sup>[a]</sup>

Entry	<b>1</b>	R'	Time [h]	<b>3</b>	Yield [%] <sup>[b]</sup>
1	<b>1a</b>	4-MeO	6	<b>3a</b>	85
2	<b>1b</b>	4- <i>i</i> Pr	5	<b>3b</b>	84
3	<b>1c</b>	4-morpholino	8	<b>3c</b>	87
4	<b>1d</b>	H	2	<b>3d</b>	84
5	<b>1e</b>	4-CO <sub>2</sub> Me	3	<b>3e</b>	80
6	<b>1f</b>	4-CN	2	<b>3f</b>	81
7	<b>1g</b>	4-Cl	3	<b>3g</b>	81
8	<b>1h</b>	4-Me <sub>3</sub> SiCC	2	<b>3h</b>	65
9	<b>1i</b>	3-Me <sub>3</sub> SiCC	2	<b>3i</b>	83
10	<b>1j</b>	2-Me <sub>3</sub> SiCC	3	<b>3j</b>	58
11	<b>1k</b>	2,6-dimethyl	13	<b>3k</b>	79
12	<b>1l</b>	2,4-dichloro	1.5	<b>3l</b>	79
13	<b>1m</b>	2,4-dimethoxy <sup>[c]</sup>	2	<b>3m</b>	94
14	<b>1n</b>	3,4,5-trimethoxy <sup>[c]</sup>	2	<b>3n</b>	88

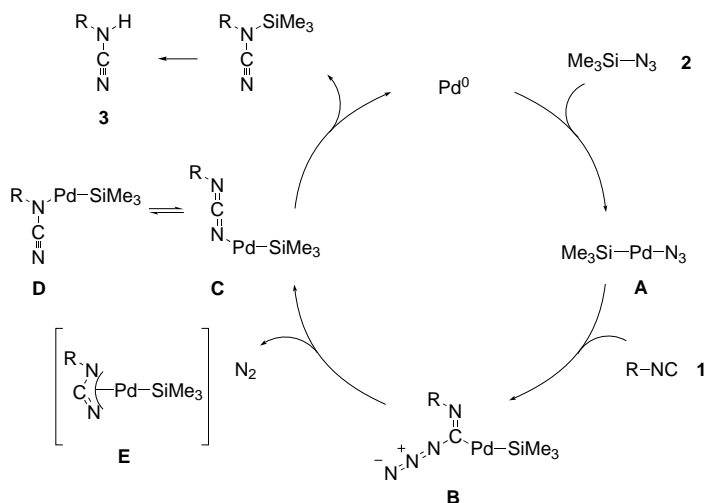
[a] A solution of **2** (1.2 equiv) in THF (1 M) was added to a mixture of **1** and [((η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl)<sub>2</sub>] (1 mol %). The mixture was stirred at RT for 10 min and then at 60 °C for the period shown in Table 1. [b] Isolated. [c] The reaction was conducted at 100 °C.

of isocyanides **1e–g** with an electron-withdrawing group proceeded faster than those (**1a–c**) with an electron-donating group. The isocyanides **1h–j** conjugated with an alkynyl group afforded the corresponding cyanamides **3h–j** in good to high yields (entries 8–10). The above results indicate that the cyanamide-forming reaction tolerates a wide range of functional groups and proceeds well, irrespective of the position of the substituents. Even the disubstituted isocyanobenzene **1k** and **1l** afforded the corresponding cyanamides **3k** and **3l** in good to high yields (entries 11 and 12). The reaction of dimethoxyisocyanobenzene **1m** and trimethoxyisocyanobenzene **1n** afforded the corresponding cyanamides **3m** and **3n** in high yields, although elevated temperature was needed (entries 13 and 14).

We next investigated the reactivity of alkyl isocyanides.<sup>[16]</sup> The reaction of cyclohexyl isocyanide (**1o**) at 100 °C for 24 h gave the corresponding cyanamide **3o** in 79 % yield [Eq. (2)]. When the reaction was conducted at 60 °C, the yield was lowered and a longer reaction time was needed. The reaction of butyl isocyanide (**1p**) under similar conditions gave butylcyanamide **3p** in 60 % yield [Eq. (3)].



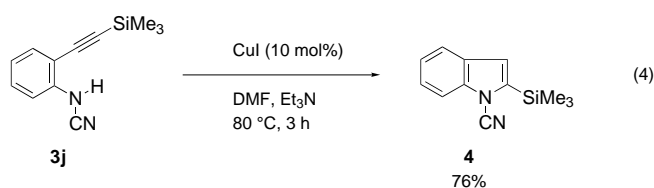
Scheme 2 shows the most probable mechanism for the present transformation. First, oxidative addition of Pd<sup>0</sup> to trimethylsilyl azide (**2**) produces the Me<sub>3</sub>Si–Pd–N<sub>3</sub> complex (**A**). Then, the insertion of isocyanide **1** in the Pd–N<sub>3</sub> bond of complex **A** gives the intermediate **B**. The 1,2-migration of the



Scheme 2. Proposed mechanism for the formation of cyanamides.

$\text{Me}_3\text{Si-Pd}$  group from the carbon atom to the  $\alpha$  nitrogen atom followed by concomitant elimination of  $\text{N}_2$  affords the palladium–carbodiimide complex **C** (the  $\text{Me}_3\text{Si-Pd}$  mimic of the Curtius rearrangement).<sup>[13, 17]</sup> The palladium–carbodiimide complex **C** could be in equilibrium with the palladium–cyanamide complex **D**, or, more probably, could be represented as **E**. Reductive elimination of  $\text{Pd}^0$  from the palladium intermediates **C–E** gives the corresponding trimethylsilyl-protected cyanamide, which is converted into **3** during chromatographic separation on silica gel.

An application of a cyanamide obtained by the above procedure to indole synthesis is shown in Equation (4). The reaction of (2-alkynylphenyl)cyanamide (**3j**) in the presence of catalytic amounts of  $\text{CuI}$  gave the corresponding indole **4** in 76% yield.<sup>[18]</sup>



We are now in a position to synthesize aryl and alkyl cyanamides **3** with a wide range of substituents in very high to good yields through the palladium-catalyzed reaction between isocyanides **1** and trimethylsilyl azide (**2**). This is the first example of Si–N bond cleavage catalyzed by  $\text{Pd}^0$  and of the geminal addition of a Si–N bond to isocyanides. In addition, we have shown that a  $\text{Me}_3\text{Si-Pd}$  mimic of the Curtius rearrangement could intervene in the catalytic cycle. Further studies on the synthetic application of this novel reaction and on the mechanistic detail are in progress.

### Experimental Section

Trimethylsilyl azide (80  $\mu\text{L}$ , 0.6 mmol) was added under an argon atmosphere to a solution (0.5 mL) of **1a** (66.6 mg, 0.5 mmol) and  $[\eta^3\text{-(C}_6\text{H}_5)_3\text{PdCl}]_2$  (1.8 mg, 0.005 mmol) in THF. The solution was stirred at room temperature for 10 minutes and then at 60 °C for 6 h. The reaction mixture was cooled to room temperature and filtered through a short Florisil pad and concentrated. The residue was purified by column chromatography (silica gel, hexane/ether 10/1  $\rightarrow$  1/3) to afford **3a** in 85% yield (63.0 mg).

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