

Neither the cycloadduct derived from the *Z* isomer nor the azatricyclo[5.2.1.0^{4,8}]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^{4,8}]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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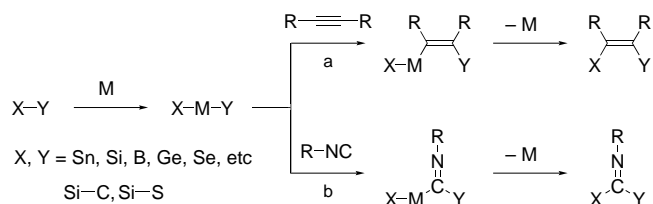
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Cyanamide Synthesis by the Palladium-Catalyzed Cleavage of a Si–N Bond**

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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.^[1] 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



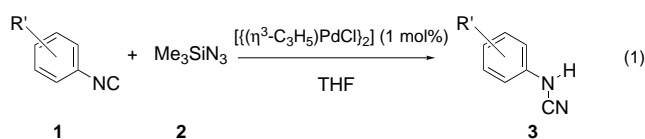
Scheme 1. Transition-metal-catalyzed addition of X–Y bonds to unsaturated bonds.

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metal–metal bond is found in silicon-containing derivatives such as Si–Si, Si–Sn, Si–B, Si–Se.^[2, 3] The geminal addition of Si–Sn,^[4] Si–Si,^[5] and Si–B^[6] 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.^[7–12] The vicinal addition (route a) of Si–C^[7–9] and Si–S^[10] 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.^[13] 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–N₃ bond to isocyanides **1**. The reaction of **1** with Me₃SiN₃ (**2**) in the presence of [((η³-C₃H₅)PdCl)₂] 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 [((η³-C₃H₅)PdCl)₂] (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).^[15] 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

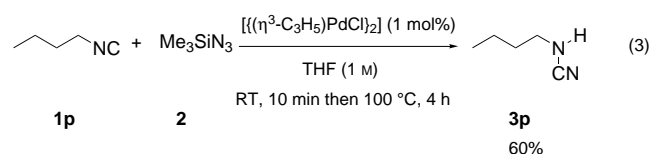
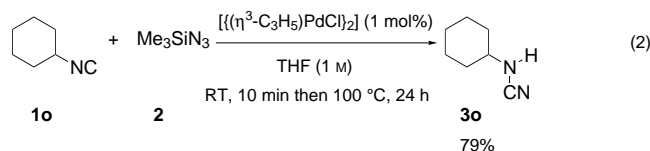
Table 1. Palladium-catalyzed formation of cyanamides.^[a]

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

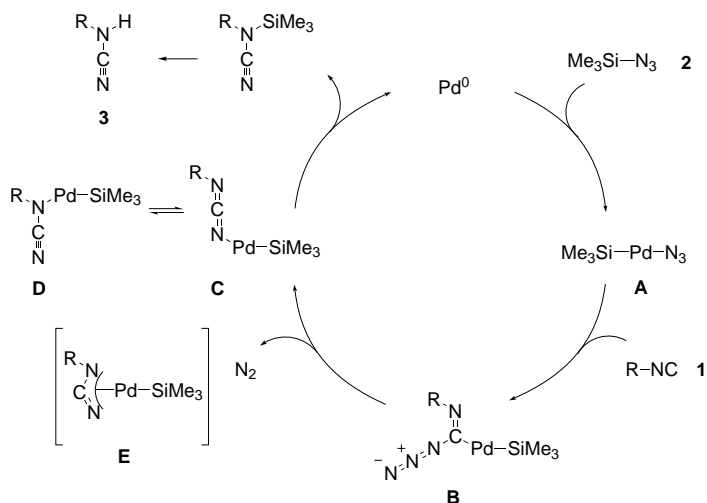
[a] A solution of **2** (1.2 equiv) in THF (1 M) was added to a mixture of **1** and [((η³-C₃H₅)PdCl)₂] (1 mol %). The mixture was stirred at RT for 10 min and then at 60 °C for the period shown in Table 1. [b] Isolated. [c] The reaction was conducted at 100 °C.

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.^[16] 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)].



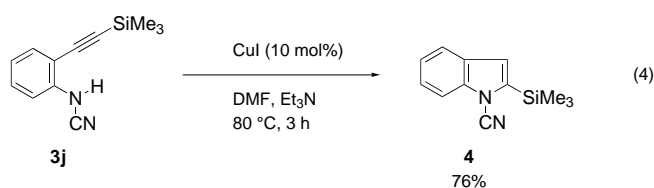
Scheme 2 shows the most probable mechanism for the present transformation. First, oxidative addition of Pd⁰ to trimethylsilyl azide (**2**) produces the Me₃Si–Pd–N₃ complex (**A**). Then, the insertion of isocyanide **1** in the Pd–N₃ bond of complex **A** gives the intermediate **B**. The 1,2-migration of the



Scheme 2. Proposed mechanism for the formation of cyanamides.

Me₃Si–Pd group from the carbon atom to the α nitrogen atom followed by concomitant elimination of N₂ affords the palladium–carbodiimide complex **C** (the Me₃Si–Pd mimic of the Curtius rearrangement).^[13, 17] 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 Pd⁰ 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 CuI gave the corresponding indole **4** in 76% yield.^[18]



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 Pd⁰ and of the geminal addition of a Si–N bond to isocyanides. In addition, we have shown that a Me₃Si–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 μL, 0.6 mmol) was added under an argon atmosphere to a solution (0.5 mL) of **1a** (66.6 mg, 0.5 mmol) and [η^3 -(C₃H₅)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 → 1/3) to afford **3a** in 85% yield (63.0 mg).

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