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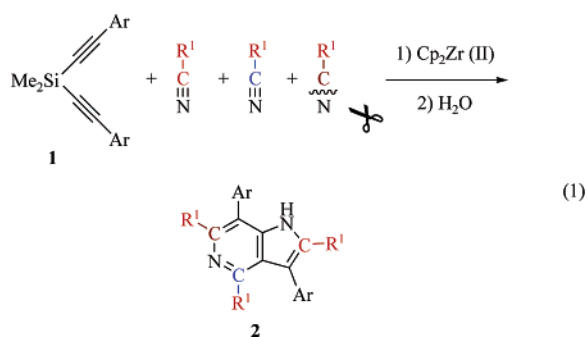
# Zirconocene-Mediated Intermolecular Coupling of One Molecule of Si-Tethered Diyne with Three Molecules of Organonitriles: One-Pot Formation of Pyrrolo[3,2-*c*]pyridine Derivatives via Cleavage of C≡N Triple Bonds of Organonitriles

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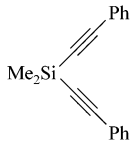
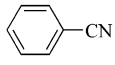
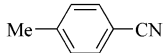
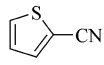
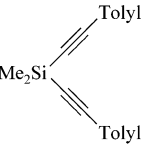
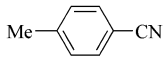
Transition-metal-mediated reaction of organonitriles has attracted much attention, since novel reaction patterns of the C≡N triple bonds can be developed and synthetically useful methodologies for construction of C–C, C–N, and C–O bonds can be expected.<sup>1</sup> Particularly, transition-metal-mediated coupling of organonitriles with other unsaturated organic substrates such as alkynes is of great synthetic interest.<sup>2–5</sup> In this paper, we report a zirconocene-mediated coupling reaction of organonitriles with alkynes, in which one Si-tethered diyne **1** is coupled in one pot with three molecules of nitriles promoted by a low-valent zirconocene species (eq 1). Along with coupling, cleavage of one of the three C≡N triple bonds and cleavage of the two Si–C bonds took place, affording pyrrolo[3,2-*c*]pyridine derivatives **2** after hydrolysis.<sup>6</sup>



A typical procedure is as follows. To a toluene solution (10 mL) of Cp<sub>2</sub>ZrBu<sub>2</sub> (Negishi reagent), generated in situ from the reaction of 1 mmol of Cp<sub>2</sub>ZrCl<sub>2</sub> and 2 mmol of *n*-BuLi at –78 °C, was added 1 mmol of bis(phenylethynyl)dimethylsilane (**1a**, Ar = Ph).<sup>7</sup> The reaction mixture was warmed to 50 °C and stirred at this temperature for 3 h. A zirconacyclobutene–silacyclobutene fused ring compound (**3a**, Ar = Ph) as a reactive organometallic intermediate was formed (eq 2), as previously reported by Takahashi and co-workers.<sup>7</sup> Benzonitrile (3.5 mmol) was then added and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was then cooled to room temperature and quenched with saturated aqueous NaHCO<sub>3</sub>. Normal workup procedure afforded the fused-ring compound **2a** (Ar = R<sup>1</sup> = Ph) in 70% isolated yield.

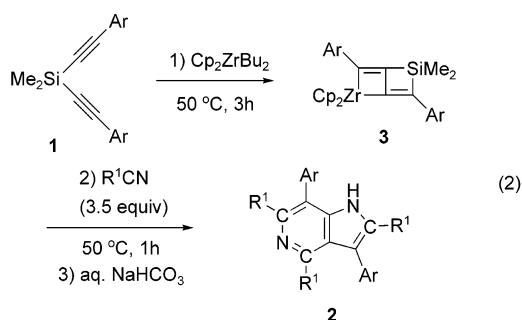
Listed in Table 1 are representative results obtained from the zirconocene-mediated coupling of bis(alkynyl)silanes and organonitriles. Both aliphatic and aromatic nitriles could be used to afford the final products in high isolated yields. The structures of compounds **2b** (Ar = Ph, R<sup>1</sup> = tolyl) and **2c** (Ar = Ph, R<sup>1</sup> =

**Table 1.** Zirconocene-Mediated Coupling of a Bis(alkynyl)silane with Three Molecules of Organonitriles Affording Pyrrolo[3,2-*c*]pyridine Derivatives

Bis(alkynyl)silane <b>1</b>	Organo-nitrile (R <sup>1</sup> CN)	Yield of product 2/% <sup>a</sup>
 <b>1a</b>	 Ph-CN	<b>2a</b> 70
<b>1a</b>	 Me-Ph-CN	<b>2b</b> 81
<b>1a</b>	 2-Thiophenyl-CN	<b>2c</b> 66
<b>1a</b>	Pr-CN	<b>2d</b> 72
<b>1a</b>	Bu-CN	<b>2e</b> 64
 <b>1b</b>	 Me-Ph-CN	<b>2f</b> 46
<b>1b</b>	Pr-CN	<b>2g</b> 67

<sup>a</sup> Isolated yields. Reaction conditions are given in eq 2.

2-thiophenyl) have been determined by single-crystal X-ray analysis (see Supporting Information).

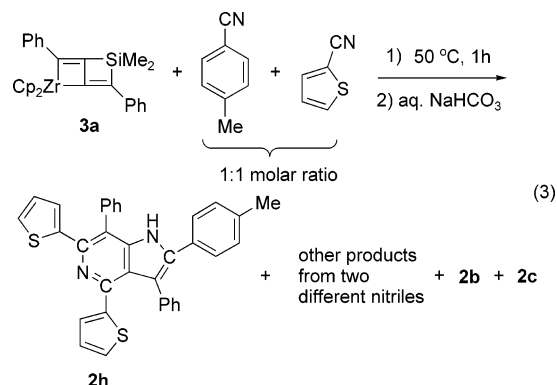


When a 1:1 molar ratio mixture of *p*-tolunitrile and 2-thiophenecarbonitrile was treated with **3a** (eq 3), compound **2h** was obtained

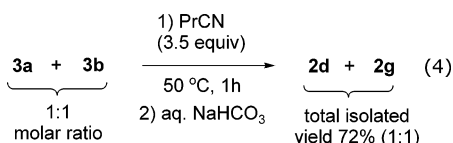
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as one of the products and has been structurally characterized by single-crystal X-ray analysis (see Supporting Information). This result indicates that three molecules of nitriles are incorporated into the product via a step-by-step manner.

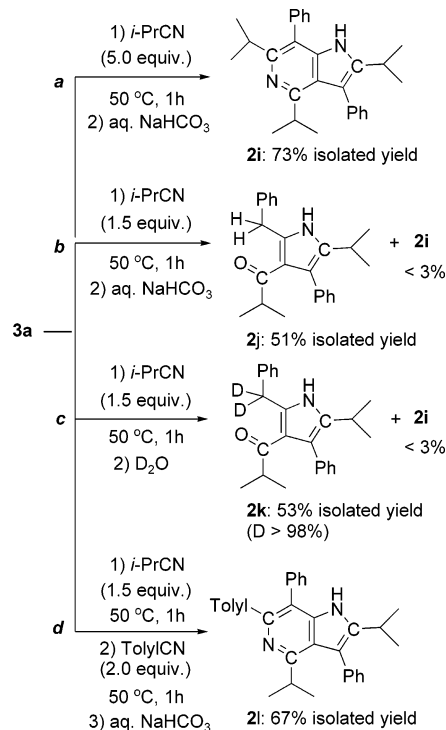


Addition of PrCN to a 1:1 molar ratio mixture of **3a** and **3b** (Ar = tolyl) afforded two products **2d** and **2g** in 72% (1:1) combined isolated yield (eq 4). No cross-coupled products were obtained, indicating that the coupling reaction and cleavage proceeded intramolecularly.



Interestingly, when *i*-PrCN was used, the reaction could be stopped after a second nitrile was incorporated into the reaction intermediate. As demonstrated in Scheme 1, the ketone derivative **2j** (Scheme 1, *b*) was obtained in 51% isolated yield and its structure was determined by single-crystal X-ray analysis (see Supporting Information). When the reaction mixture was quenched with D<sub>2</sub>O

**Scheme 1**



(Scheme 1, *c*), product **2k** containing a CD<sub>2</sub> moiety was obtained. Addition of *p*-tolunitrile as a third molecule of nitrile to the reaction intermediate of **3a** with two molecules of *i*-PrCN afforded product **2l** in 67% isolated yield (Scheme 1, *d*). This product **2l** was formed chemo- and regioselectively from two molecules of *i*-PrCN and one molecule of *p*-tolunitrile. These results are instructive for understanding the reaction mechanism (see Supporting Information for a proposed reaction mechanism). Further investigation to elucidate the reaction mechanisms and further applications of these novel and synthetically useful reactions are in progress.

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**Supporting Information Available:** Experimental details, characterization data, copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra for all isolated compounds and crystallographic data, positional and thermal parameters, and lists of bond lengths and angles for **2b**, **2c**, **2h**, **2j**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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