

Catalytic Cycloaddition Reactions between Propargylic Alcohol Derivatives and Hydrazones

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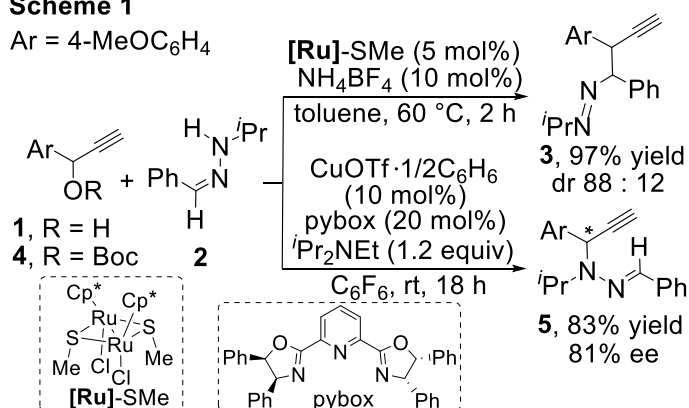
Transition metal-catalyzed propargylic substitution reactions of propargylic alcohol derivatives with nucleophiles have been attracting much attention as synthetic tools for the carbon–carbon and carbon–heteroatom formation in organic synthesis.¹ On the other hand, hydrazones are known to serve not only as nitrogen-centered nucleophiles but also as carbon-centered nucleophiles, leading to multiple applications in organic synthesis in recent years.² As an extensive study, we have focused on the use of hydrazones as nucleophiles for the transition metal-catalyzed propargylic substitution reactions of propargylic alcohol derivatives, and further examined their application to cycloaddition reactions.

The reaction of a propargylic alcohol (**1**) with a hydrazone (**2**) in the presence of 5 mol% of thiolate-bridged diruthenium complex **[Ru]-SMe** and 10 mol% of NH_4BF_4 in toluene at 60 °C for 2 h gave the corresponding *C*-propargylic substituted product (**3**) in 97% yield, whereas the reaction of a propargylic ester (**4**) with **2** in the presence of 10 mol% of $\text{CuOTf} \cdot 1/2\text{C}_6\text{H}_6$ and 20 mol% of a chiral pybox in hexafluorobenzene at room temperature for 18 h gave the corresponding *N*-propargylic substituted product (**5**) in 83% yield with 81% ee (Scheme 1).

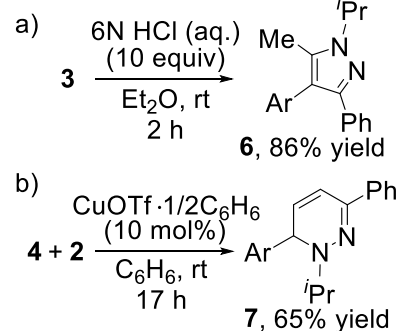
Further treatment of **3** with 10 equiv of HCl in ether at room temperature for 2 h brought about the intramolecular cycloaddition to afford a 5-methyl-1*H*-pyrazole derivative (**6**) in 86% yield (Scheme 2a). In contrast, the reaction of **4** with **2** in the presence of 10 mol% of $\text{CuOTf} \cdot 1/2\text{C}_6\text{H}_6$ in benzene at room temperature for 17 h gave a 1,6-dihydropyridazine derivative (**7**) in 65% yield (Scheme 2b). The difference in the reactivity of hydrazone toward the ruthenium- and copper-catalyzed reaction systems was also investigated in details.

Scheme 1

Ar = 4-MeOC₆H₄



Scheme 2



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