

Iron-catalyzed Suzuki-Miyaura Coupling of Propargyl Electrophiles with Organoboron Compounds Derived from Alkenyl Bromides

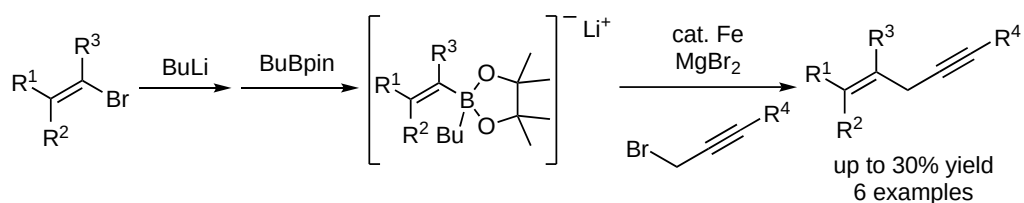
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Keywords: Cross-Coupling Reaction; Iron Catalyst; Urushiol; Stereoselectivity; Total Synthesis

Cross-coupling reactions between propargyl electrophiles and alkenylmetals are important methods to achieve stereochemical control in the synthesis of 1,4-enynes, which are versatile building blocks for complex molecular frameworks of natural and non-natural bioactive compounds. Our group has successfully developed the first iron-catalyzed Suzuki–Miyaura coupling of propargyl electrophiles with lithium alkenylborates to afford the corresponding 1,4-enynes in a regioselective and stereospecific manner.¹ The reaction was commenced from alkenylboronate, whose preparation involved the use of environmentally harmful heavy metal catalysts. On the other hand, it is well known that alkenyl bromides, a class of highly versatile compounds, can be synthesized by environmentally benign routes and could therefore serve as the starting materials to develop a promising green method. With this knowledge, we envisioned a new one-pot synthetic process of 1,4-enynes starting from the borate formation and followed by the cross-coupling reaction, which would be feasible by utilizing alkenyl bromide as the starting substrate.

The new one-pot procedure was established as follows: a solution of alkenyl bromide (1.4 eq) in THF was firstly treated with BuLi solution (1.4 eq) at $-78\text{ }^{\circ}\text{C}$, then BuBpin (1.5 eq) was added at the same temperature, and the reaction mixture was allowed to stir at $0\text{ }^{\circ}\text{C}$ for the borate formation. The formation of alkenylborate at this stage was confirmed by ^1H and ^{11}B NMR analyses. The catalytic reaction was carried out by sequential addition of primary propargyl bromide (1 eq), catalytic amounts of iron salt, ligand, and MgBr_2 to the borate solution at $-78\text{ }^{\circ}\text{C}$ then reacted at $0\text{--}60\text{ }^{\circ}\text{C}$ (Scheme 1). Both *Z/E*-alkenyl bromide can stereospecifically give the corresponding 1,4-enyne product in 15 to 30% NMR yield.

In this presentation, we will report on the screening of reaction conditions, ligands, the scope of substrates, and the synthesis of natural urushiol contents.



1) Agata, R.; Siming, L.; Matsuda, H.; Isozaki, K.; Nakamura, M. *Org. Biomol. Chem.* **2020**, *18*, 3022.