

Co(III)-catalyzed Three-Component C–H Bond Addition of Acrylamides to Dienes and Aldehydes

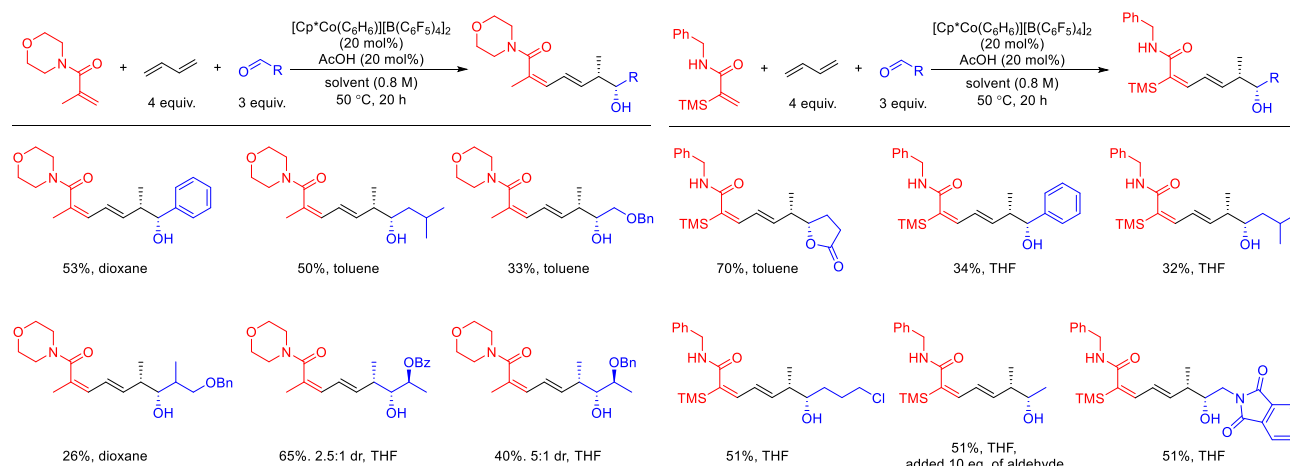
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Introduction

The Ellman group has been focusing on transition-metal catalyzed C–H bond addition cascades as a way of quickly assembling simple precursors into complex products. The three-component coupling of C–H bonds with dienes and aldehydes was among these studies, but couplings with aryl C–H bond substrates were primarily explored (*Nat. Catal.* **2018**, *1*, 673). If instead alkenyl C–H bond substrates could be employed, the resulting scaffolds would be valuable frameworks for further elaboration towards polyketide natural products. Hence, we have worked toward developing new three component coupling reactions with acrylamides. As a result, we developed a Co(III)-catalyzed three-component coupling of acrylamides with butadiene and aldehydes.

Results

The C–H bond addition of morpholine amides prepared from 2-methyl and 2-trimethylsilyl acrylic acids proceeded efficiently, and the three-component coupling with butadiene and various aldehydes proceeded in moderate to good yield.



In next study, we synthesized complex molecule **3** containing six stereocenters by Sharpless dihydroxylation of the chiral pool product **1**, followed by auto-lactonization, and hydrogenation of **2** (33%, 3 steps from aldehyde). This compound is a valuable framework for further elaboration towards complex macrolide and ionophore natural product synthesis.

Future Plan

We plan to optimize reaction conditions, examine substrate scope in regard to alkenyl C–H bond substrates, dienes, and aldehydes, and diversify products for demonstrating synthetic utility. Also, we will conduct mechanistic studies of this reaction. Once these are completed, we will prepare a manuscript for submission in a peer-reviewed journal.

