

## Iterative Cross-Coupling: A Simple Strategy for Complex Small Molecule Synthesis

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A simple and highly modular strategy for small molecule synthesis involving the iterative cross-coupling of B-protected bifunctional haloboronic acids is reported. Enabling this approach, we have newly discovered that the pyramidalization of boronic acids via complexation with the trivalent ligand N-methyliminodiacetic acid inhibits their reactivity towards cross-coupling and affords products which are highly crystalline, free flowing solids that are easily purified and are stable to long-term storage at room temperature under air. This ligand is remarkably stable to anhydrous Suzuki-Miyaura conditions yet is readily cleaved using mild aqueous base. Although the reactivity of aryl, heteroaryl, alkenyl, and alkyl boronic acids can vary dramatically, this methodology is effective for protecting and deprotecting all four classes of nucleophiles. Harnessing this potential, we achieved the first total synthesis of the natural product ratanhine using the Suzuki-Miyaura reaction iteratively to bring together a collection of easily synthesized and highly robust building blocks.

