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Expedient Access to Underexplored Chemical Space: Deoxygenative C(sp^3)–C(sp^3) Cross-Coupling
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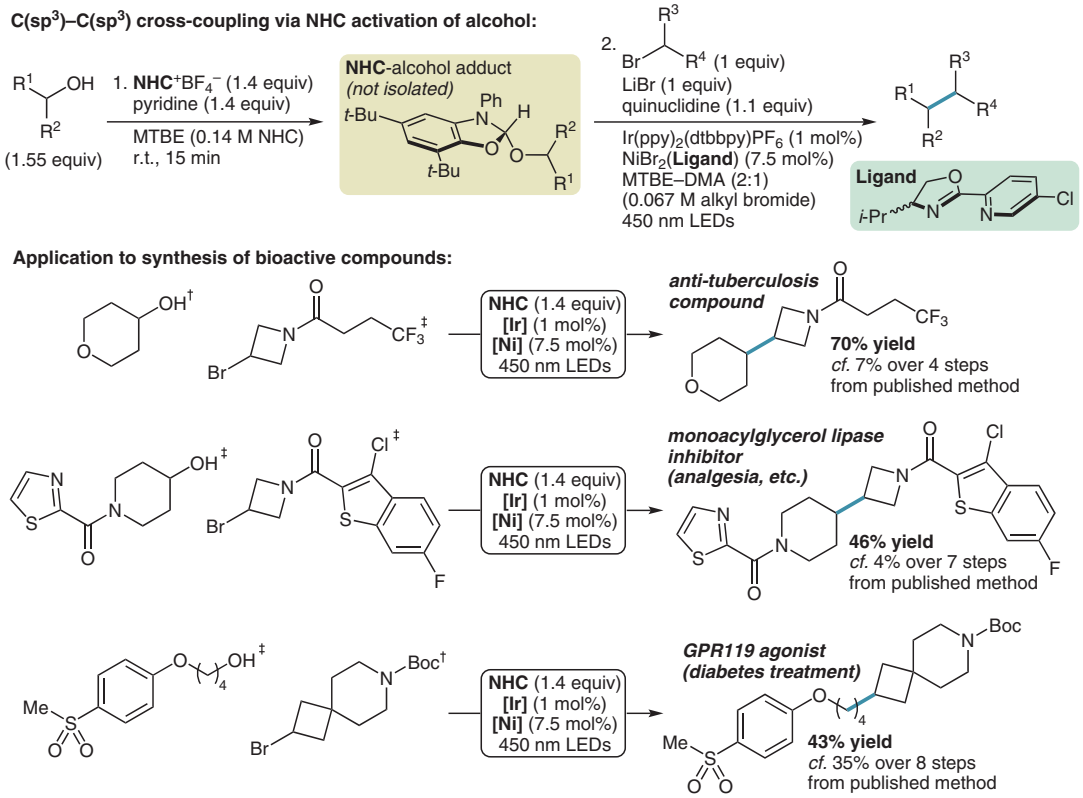
Alcohols as Substrates for Metallaphotoredox-Catalyzed C(sp^3)–C(sp^3) Cross-Coupling



† Commercially available. ‡ Synthesized in one step from commercially available starting materials.

Significance: Nickel catalyzes C(sp^3)–C(sp^3) cross-couplings efficiently without deleterious β-hydride elimination, unlike palladium. Still, the nucleophilic coupling partners of these reactions are often tedious to synthesize and difficult to handle. MacMillan and co-workers have previously demonstrated that alcohols can act as precursors of nucleophilic alkyl radicals in [metalla]photoredox processes by activation with an N-heterocyclic carbene (NHC). Here, this strategy is used to accomplish C(sp^3)–C(sp^3) cross-couplings with alkyl bromides. Primary and secondary alcohols and alkyl bromides are coupled in fair to good yields. Highly strained structures are well tolerated. Several bioactive compounds were concisely synthesized in yields superior to published methods.

Comment: Photoredox catalysis often enables transformations in a single step that would otherwise take several chemical steps to be accomplished using traditional methods. By leveraging alcohols as precursors for nucleophilic radicals, new retrosynthetic disconnections can be made that expedite the syntheses of several compounds of pharmaceutical interest. Despite yields less than 50% in some cases, alcohols can be used directly, whereas organometallic/organoboron coupling partners typically require one or more steps to prepare. The abundance of alcohols as a chemical feedstock enhances the appeal of this approach.

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