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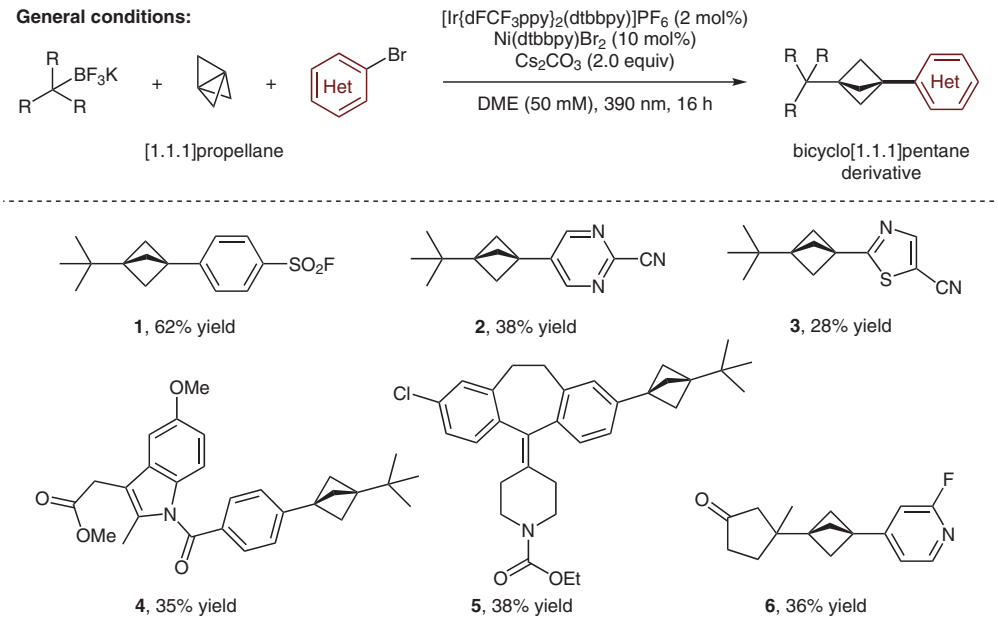
Dicarbofunctionalization of [1.1.1]Propellane Enabled by Nickel/Photoredox Dual Catalysis: One-Step Multicomponent Strategy for the Synthesis of BCP-Aryl Derivatives
J. Am. Chem. Soc. **2022**, *144*, 12961–12969, DOI: 10.1021/jacs.2c05304.

Photoredox Cross-Coupling for Propellane-Curious Chemists



Significance: The escape from flatland can be a treacherous adventure. Our familiar cross-couplings are often useless when faced with the dreaded sp^3-hybridized carbon. It is even more challenging when that sp^3 carbon belongs to [1.1.1]propellane. Although bicyclo[1.1.1]pentanes (BCPs; the products of reactions with [1.1.1]propellane) are touted as isosteres for *para*-phenylenes that might improve solubility and metabolic stability, it can be challenging to implement them generally in synthesis of heterocyclic compounds. Generation of a metalated or otherwise activated BCP is first necessary (J. Kanazawa, M. Uchiyama *Synlett* **2019**, *30*, 1). The mild conditions developed by Molander and co-workers quickly assemble molecules containing a BCP core from [1.1.1]propellane itself. Of note, this report includes a variety of pharmaceuticals (including **4** and **5**) rescued from flatland by using this method. Although it is limited to tertiary trifluoroboronates, due to the inherent reactivity of the resulting propellane radical, this represents a practical advancement in BCP synthesis.

Comment: [1.1.1]Propellane, with its unique internal bond, is fascinating in its own right. This paper reports both an interesting utilization of that internal bond and a clear understanding of its reactivity. By walking the tightrope between reactivity and inertness, some useful reactive electrophiles, including a sulfonylfluoride **3** and a molecule containing both a ketone and a 2-fluoropyridine group **6**, were left unscathed during the transformation, which is not possible with typical BCP coupling methods. Nucleophiles such as amines or alcohols, however, were suspiciously absent from the scope, and a pyrrole and primary amide substrate were reported to fail. [1.1.1]Propellane was only involved in the reaction if tertiary trifluoroboronates were used, which is a key scope limitation. Despite this, for specific syntheses, this protocol could be used to eliminate several synthetic steps from a BCP preparation, as the authors have clearly shown that this reaction is tolerant of diverse and synthetically useful coupling partners.

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Synfacts 2022, 18(10), 1067 Published online: 20.09.2022
DOI: 10.1055/s-0042-1752983; **Reg-No.:** V11122SF

Category
Synthesis of Heterocycles

Key words
propellanes
photoredox reaction
nickel catalysis
bicyclopentanes