

# BORYLATIONS FROM CARBOXYLIC ACIDS

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## INTRODUCTION

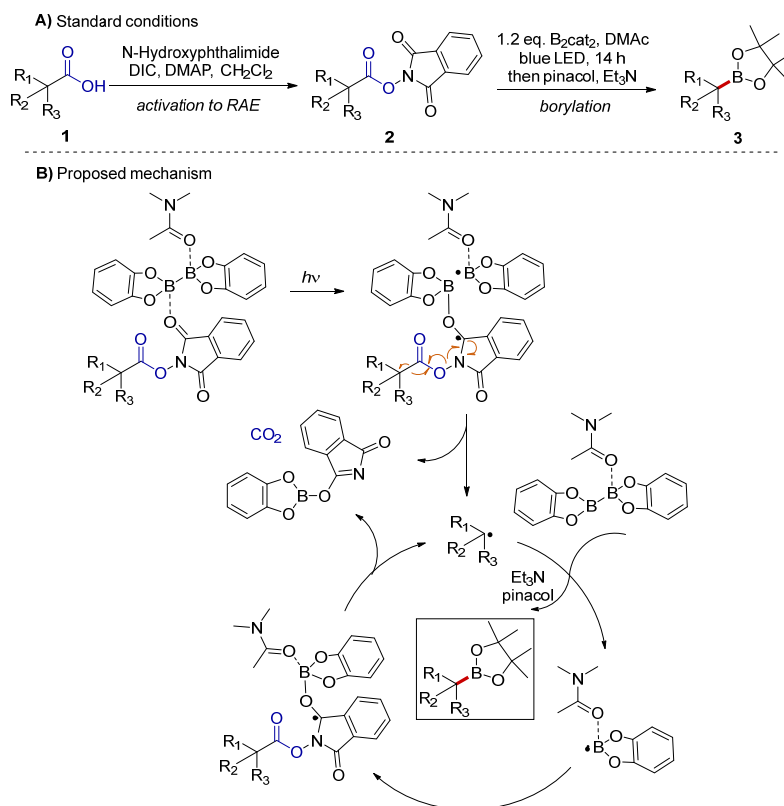
The C–B bond is a versatile motif across sub-disciplines of chemistry owing to its Lewis acidity and unique electronic configuration. Organoboron molecules have shown better drug potency and pharmacokinetics making them of use to medicinal chemists<sup>1</sup>, are employed as a transmetallating agent in the ubiquitous Suzuki-Miyaura cross-coupling reaction for C–C bond formation and are a motif in polymers with an array of properties useful for material scientists.<sup>2</sup> Common strategies to synthesize C–B bonds include transmetallation with an organomagnesium or organolithium reagent, hydroboration of alkenes, and Miyaura borylation of halides. Conventionally, incorporation of the C–B bond occurs early limiting possibilities of late-stage modifications to make organoboronic species. Being able to borylate ubiquitous carboxylic acids would open the doors to gauging the reactivity of underexplored organoboron drug targets. In recent years, methods relying on single electron transfer (SET) or metal initiated processes to form C–B bonds from the C–C bonds of carboxylic acids have been developed.

## RADICAL INITIATED DECARBOXYLATIVE BORYLATION

Common intermediates in decarboxylative borylation are the *N*-acyloxyphthalimides (**2**) redox active esters (RAEs) derived from carboxylic acids. In 2017, Li and co-workers reported a visible light photoinduced decarboxylative borylation that uses [Ir(ppy)<sub>2</sub>(dtbpy)]PF<sub>6</sub> as a photocatalyst, B<sub>2</sub>pin<sub>2</sub> or B<sub>2</sub>(OH)<sub>4</sub> as the boron source, and **2** as an alkyl radical precursor for decarboxylative coupling.<sup>3</sup>

Activation of the carboxylic acid to the RAE allows for the iridium photocatalyst to generate a radical anion that then is decarboxylated giving an alkyl radical that recombines with the boron source. These mild conditions allowed for the formation of primary and secondary alkyl boronic esters that are tolerant of ether and carbonyl functionality. In the same year, Aggarwal and coworkers developed a metal-free and additive-free blue-light

### Scheme 1: Photoinduced decarboxylative borylation

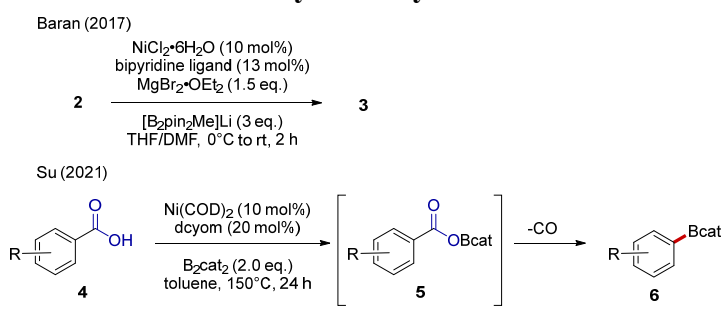


photoinduced decarboxylative borylation (Scheme 1). This method utilizes the same RAE intermediate (**2**) and is tolerant of tertiary carboxylic acids and a wide variety of functional groups including bromides and carbonyls.<sup>4</sup> A limitation of the Li and Aggarwal methods is the lack of demonstrated aryl borylations. This gap was filled by Glorius and co-workers in 2017 with their photoinduced decarboxylative borylation of RAE **2** to make aryl boronic esters.<sup>5</sup> Using an alternative RAE to *N*-acyloxyphthalimide, Han and co-workers developed a method that uses a peroxyanhydride intermediate derived from reacting a carboxylic acid with *m*CPBA. A single electron transfer mechanism analogous to the one proposed by Aggarwal (Scheme 1B) furnished an array of alkyl organoboron products.<sup>6</sup>

## TRANSITION METAL-CATALYZED BORYLATION

Baran and co-workers reported a decarboxylative borylation using catalytic Ni and RAE **2** (Scheme 2).<sup>7</sup> Recently, Su and co-workers developed a method that does not require activation of the carboxylic acid to an RAE albeit needs higher thermal temperatures to proceed (Scheme 2).<sup>8</sup> Rather than generating a radical that results in decarboxylation, the (acyloxy)boron intermediate **5** oxidatively adds to Ni then releases carbon monoxide upon reductive elimination with catecholborane.

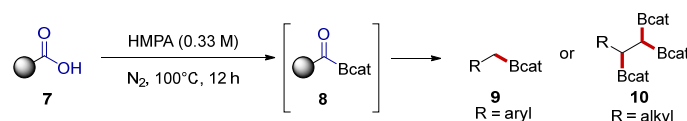
### Scheme 2: TM catalyzed borylation



## DEOXYGENATIVE BORYLATION

In 2021, Li and co-workers developed a deoxygenative method that directly uses carboxylic acids and retains the carbonyl carbon of the carboxylic acid rather than decarboxylation (Scheme 3).<sup>9</sup> Their method relies on high thermal

### Scheme 3: Deoxygenative borylation



temperatures that forms acylboronate species **8**. B<sub>2</sub>cat<sub>2</sub> adds across the carbonyl double bond resulting in a triboronated intermediate that further reacts with water and B<sub>2</sub>cat<sub>2</sub> to give the monoboronated product **9** for aryl carboxylic acids or the triboronated product **10** for aliphatic ones.

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