

PREPARATION OF VINYL BORONIC ESTERS VIA A HOMOLOGATION REACTION: BIDIRECTIONAL SYNTHESIS OF MACHILLENE

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Vinyl boronic esters are privileged motifs in organic synthesis due to the range of transformations in which they participate [1]. Most prominently, they are an important class of reagent for the Suzuki-Miyaura cross-coupling reaction, which is one of the most utilized chemical reactions in medicinal chemistry [2]. Usually, vinyl boronic esters are prepared from either alkynes or vinyl halides which, whilst of reasonable commercial availability, are somewhat limited in terms of additional functionality [3]. In order to expand the range of accessible vinyl boronic esters, we have developed a synthetic approach *via* homologation of boronic esters (Figure 1A). This methodology and its scope will be discussed, as will its application in natural product synthesis.

Machillene, isolated by Chen *et al.*, caught our attention because of its micromolar anticancer activity *in vitro* and because both its relative and absolute stereochemistry were unknown [4]. Based on the available characterization data and subsequent analytical work by Breit *et al.*, we have predicted the stereochemistry and intend to prove the structure through a short and bidirectional synthesis (Figure 1B) [5].

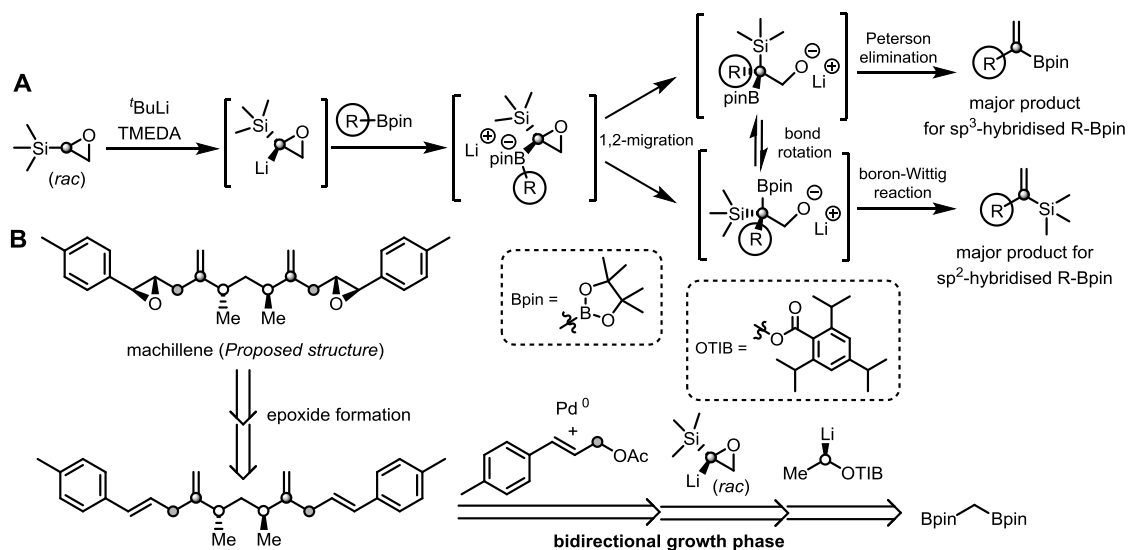


Figure 1. A) Outline of methodology. B) Outline of application.

[1] Morken *et al.*, *J. Am. Chem. Soc.* **2017**, *139*, 5027.

[2] Suzuki *et al.*, *Chem. Rev.* **1995**, *95*, 2457.

[3] Miyaura *et al.*, *J. Am. Chem. Soc.* **2017**, *139*, 5736. Srebnik *et al.*, *Organometallics* **1996**, *14*, 3127.

[4] Chen *et al.*, *Phytochemistry* **2005**, *66*, 1180.

[5] Breit *et al.*, *Chem. Eur. J.* **2012**, *18*, 7071.