Synthesis in a Boron World

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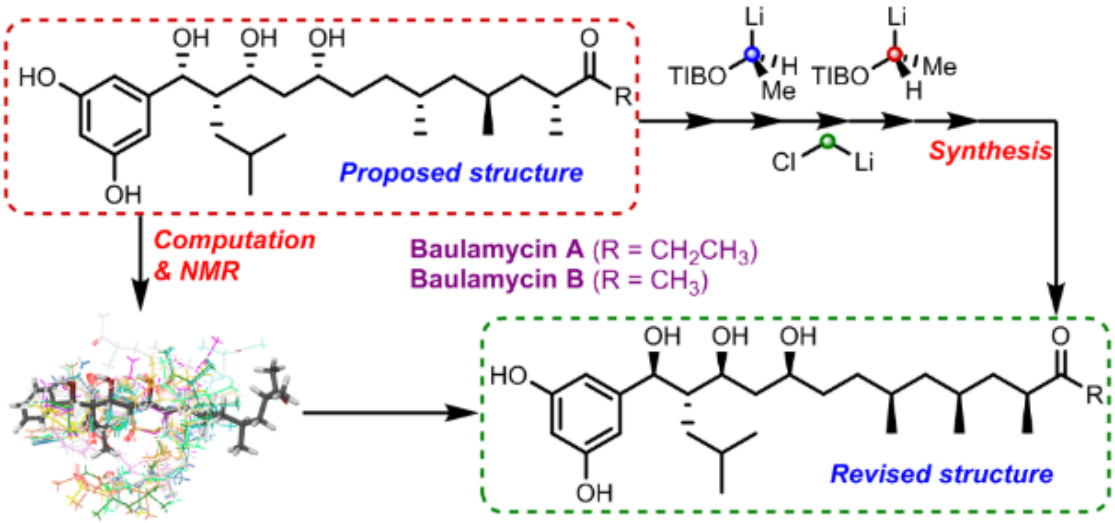
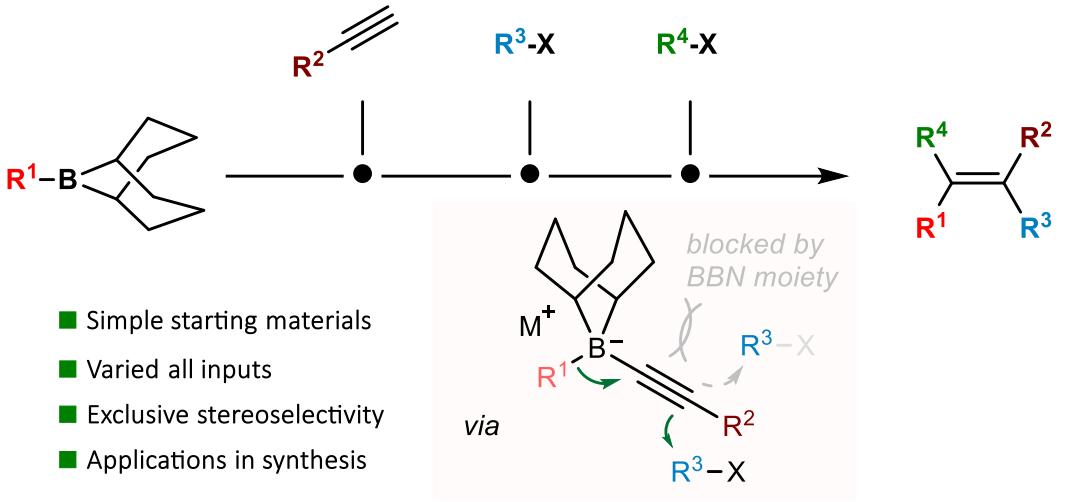
Nature has evolved highly sophisticated machinery for organic synthesis, many of which resemble molecular assembly-line processes. So far chemists have been able to apply this type of approach in the synthesis of peptides, oligonucleotides and polysaccharides but it is much more difficult to apply iterative methodologies to organic synthesis.

Here, we describe the application of iterative homologation of boronic esters using chiral lithiated carbamates and chloromethyllithium enabling us to grow carbon chains with control over both relative and absolute stereochemistry. Application of this strategy to the synthesis of the proposed structure of baulamycin and the real structure will be presented as well as other complex targets.



Cross coupling, particularly Suzuki cross coupling, is one of the most important reactions in medicinal chemistry. Most couplings involve sp2-sp2 bond formation but this invariably leads to flat molecules. With increasing interest in accessing three dimensional space (escape from flatland), there is increasing interest in broadening this coupling reaction to include sp2-sp3 and even sp3-sp3 coupling. In this lecture I will show how new variations of the Zweifel olefination reaction enable sp2-sp3 couplings (alkenes with alkyl boronic esters) and an extension of this reaction which enable aromatics to be coupled with hindered secondary and even tertiary boronic esters. I will also discuss how this chemistry can be applied to the stereocontrolled synthesis of tetrasubstituted alkenes and how we can even extend this work to stereocontrolled sp3-sp3 couplings, where stereochemistry can essentially be dialled in.



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