Rearrangements of Fluorinated Cyclopropylboronates as a Novel Approach towards Fluoroalkene-Based Peptidomimetics

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The aim of this research is to study new approaches towards fluoroalkene-based peptidomimetics using (gem-fluorohalocyclopropyl)boronates. Fluoroalkenes have high antiviral, antitumor or anti-HIV activity. Unfortunately, existing methods for fluoroalkenes synthesis require expensive reagents and catalysts, though still provide low substrate-scope. (gem-Fluorohalocyclopropyl)boronates are a new type of C3 fluorinated building blocks that was recently developed in our laboratory. They can be obtained from commercially available substrates. Also, they potentially have a variety of possible transformation pathways. This makes them promising reagents for synthesis of fluoroalkene-based peptidomimetics with a variety of substituents. My goal was to study different reactions and find their applications in synthesis of bioactive compounds. The reactions between (gem-fluorohalocyclopropyl)boronates and different nucleophiles does not proceed with weak (benzyl azide) and sterically hindered (BocNHOTs) nucleophiles. With more reactive nucleophiles, there is a competition between Matteson rearrangement on tetracoordinated boron and elimination of boron and halogen with formation of fluorocyclopropene. In case of bromamine T elimination is preferable, while CHCl2Li at decreased temperature gives rearrangement product. The synthesis of 3-fluorohomoallylic alcohols was also studied. After the isomerization of (gem fluorohalocyclopropyl)boronates, the mixture of vinyl- and allylboronates is formed, which can further react with aldehydes giving corresponding 3-fluorohomoallylic alcohols with high diastereoselectivity. These results allow to synthesize fluorinated analogues of different biologically active substances like Lacosamide, Funapide (painkillers), Tosedostat (antitumor).

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