Progress toward cariporide analogs for sodium-proton exchange inhibition

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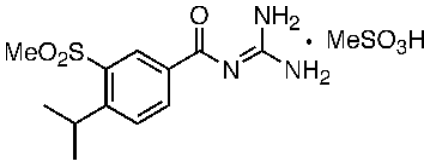
The sodium proton exchanger (NHE) is particularly important in maintaining the intracellular pH in human heart and brain. Under anaerobic conditions (i.e., ischemia), a shift from oxidative to nonoxidative glycolysis occurs. The resultant decrease in the intracellular pH activates NHE, which increases the intracellular sodium, initiating the sequence of physiological events that lead to cell death. Thus, there has been great interest in the development of compounds that inhibit NHE. Indeed, potent NHE inhibitors are available. However, a fundamental impediment to the field is the delivery of these compounds to poorly vascularized tissues during the early phases of ischemia when NHE inhibition is most beneficial. We have synthesized analogs of cariporide, a potent (e.g., nanomolar IC50 activity) NHE inhibitor, to address these temporal and delivery challenges. The preparation and biological activities of our cariporide analogs will be discussed.



Cariporide

Materials, Devices and Switches, Metal-Mediated Reactions, Asymmetric Reactions, Total Synthesis, Biologically-Related Molecules and Processes
7:00 PM-9:00 PM, Wednesday, April 9, 2008 Morial Convention Center -- La Louisiane, Blrm. C, Poster

Sci-Mix
8:00 PM-10:00 PM, Monday, April 7, 2008 Morial Convention Center -- Hall A, Sci-Mix

Division of Organic Chemistry

The 235th ACS National Meeting, New Orleans, LA, April 6-10, 2008