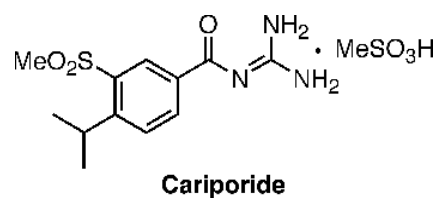


## Progress toward cariporide analogs for sodium-proton exchange inhibition

### ORGN 653

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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 IC<sub>50</sub> activity) NHE inhibitor, to address these temporal and delivery challenges. The preparation and biological activities of our cariporide analogs will be discussed.



[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

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