Title:

Boron-containing Analogs of Fosmidomycin: Synthesis and Antibacterial Properties

Abstract:

With an alarming increase in antibiotic resistance, there is an urgent need to develop new classes of therapeutic agents with new mechanisms of action. Fosmidomycin is a potent antibiotic that inhibits the non-mevalonate isoprenoid biosynthesis (MEP) pathway with the molecular target being 1-deoxy-D-xylulose-5-phosphate reductoisomerase (IspC). The highly charged phosphonate moiety of fosmidomycin hinders absorption and leads to poor pharmacokinetic properties thus this compound has found limited utility as a therapeutic agent. Our work investigates the synthesis and evaluation of boron-containing compounds that may act as neutral phosphate/phosphonate isosteres. Here, we report the synthesis of a library of boron-containing analogs of fosmidomycin, their evaluation as inhibitors of IspC, and their antimicrobial activity.