

Extended Abstract

Design and Synthesis of Cysteine Proteases Inhibitors [†]

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Cysteine proteases belonging to the papain superfamily have been recognized as interesting therapeutic targets for the search for new drugs against infectious tropical diseases such as malaria (falcipain), Chagas' disease (curtain), leishmaniasis, and Sleeping sickness (rhodesian), and a number of human pathologies, including cancer, Alzheimer's disease, and osteoporosis (cathepsins). We have reported irreversible inhibitors Dipeptidyl epoxiesters (k_{inac}/K_i up to $92,090 \text{ M}^{-1}\text{s}^{-1}$) [1], Dipeptidyl enoates (k_{inac}/K_i up to $1,530,000 \text{ M}^{-1}\text{s}^{-1}$) [2,3], Aminoacyl epoxysulfones [4], and also reversible inhibitors Dipeptidyl nitroalkenes (IC_{50} up to 0.44 nM) [5] as inhibitors of parasitic cysteine proteases and cathepsins. Inhibition kinetics and computational studies have been used to study the mode of action of these inhibitors.

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