R. De Gasparo, O. Halgas, D. Harangozo, M. Kaiser* E. F. Pai*, R. L. Krauth-Siegel, F. Diedrich* (ETH Zurich, Switzerland)

Targeting a Large Active Site: Structure-Based Design of Nanomolar Inhibitors of Trypanosoma brucei Trypanothione Reductase


Nanomolar Inhibitor of Trypanosoma brucei Trypanothione Reductase

Significance: The parasitic protozoa responsible for trypanosomiasis, Chagas’ disease, and leishmaniasis require the reduction of trypanothione disulfide to trypanothione, which the parasites use in several essential processes. Target molecule N is the strongest competitive inhibitor in vitro of trypanothione reductase from Trypanosoma cruzi reported to date.

Comment: Note the construction of highly hindered amine E by nucleophilic substitution of benzotriazole from N,N-acetal B by the organomagnesium reagent D.