

NON -TECHNICAL ABSTRACT: *(State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project for California.)*

The start of the twenty-first century has seen dramatic developments in medicine that are a result of the collaboration between organic chemists and biologists. The HIV (Human Immunodeficiency Virus) drug Crixivan is a result of one such collaboration. Crixivan is a protease inhibitor. Discovered by Merck in 1988, Crixivan had revolutionized the treatment of HIV. Crixivan, along with the drugs AZT and 3TC used in a cocktail, has the ability to reduce the amounts of HIV to below detectable levels. Before this treatment, HIV victims were dead within two years.

When Crixivan was discovered as a drug candidate, organic chemists were charged with the difficult task of synthesizing the large amounts needed of the drug. One kilogram was needed to keep a patient alive and well for a year.

The large scale, optimized synthesis of Crixivan utilizes a chiral epoxide as a key intermediate. Currently the Jacobsen asymmetric epoxidation that makes use of a chiral manganese salen catalyst is the best method for making the epoxide intermediate. The Jacobsen catalyst is derived from L-tartaric acid. Our project seeks new chiral salen catalysts based upon vanadium and the amino acid L-phenylalanine. We hope these changes in the design of the catalyst will lead to improved product yields and selectivity. These two factors will allow the Crixivan drug, along with numerous other drugs that utilize chiral epoxides as intermediates, to be synthesized more economically. It is hoped that these improvements in synthetic efficiency will allow Crixivan and other pharmaceutical drugs to be more widely available to medium and lower class populations.