

The Crixivan Story

June 7, 2013

- Some HIV/AIDS statistics, briefly.
- A simplified view of the HIV life cycle.
- Crixivan: retrosynthesis and selected transformations.

Announcements

Final Exam Practice Problems and a **Final Exam Review Sheet** have been posted.

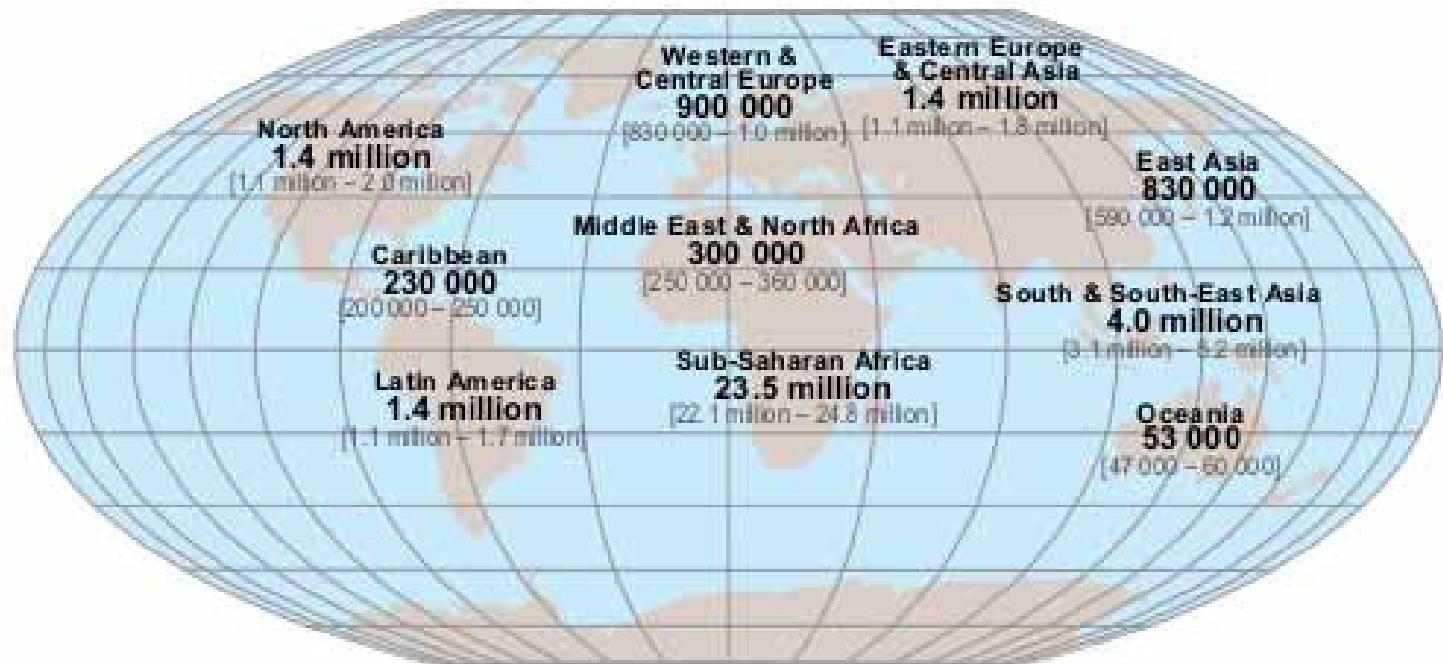
The **take-home final exam questions** will focus primarily on 41c material, but material from earlier quarters is certainly fair game. You will be allowed to only use the following when working your final exam: a calculator, molecular models, Loudon's text & solutions manual, and any paper or electronically archived class notes associated with 41a-c. Internet access is not allowed. A final exam review session will take place today from 4-5:30 PM in Crellin 151. The final will be distributed in Noyes 153 at 9:00 am on Monday, June 10. It will be due in the Crellin 357 drop box no later than 5:00 PM on Friday, June 14.

Be sure to provide course feedback via the Teaching Quality Feedback Report (TQFR) system, which is now open.

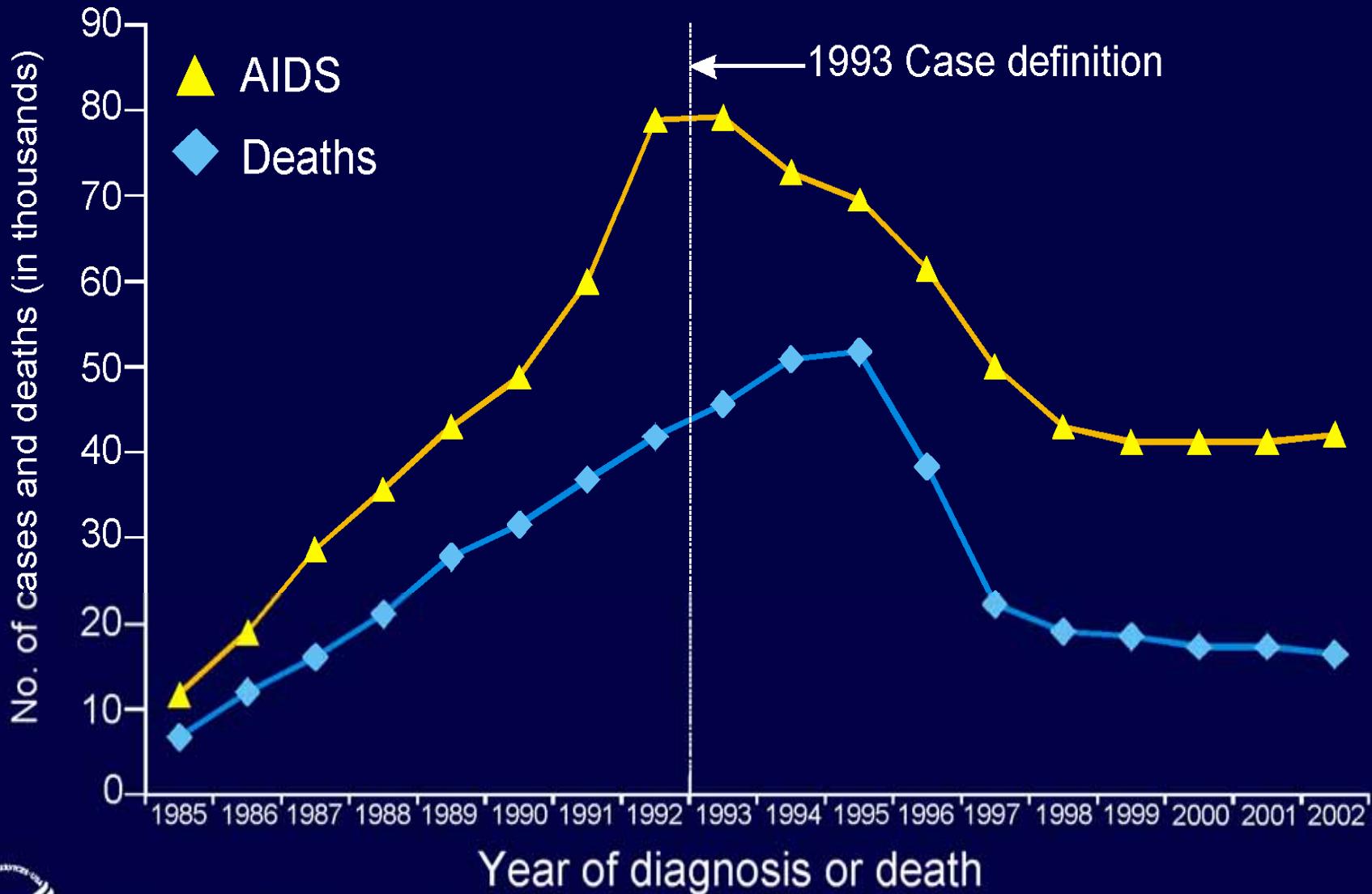
TA Office Hours during Finals Week: Ben Suslick (UTA) - Lloyd Lounge; Monday June 10 2-3 pm. If additional OH are required between now and then, please contact a TA or me and make an appointment.

Suggested Problems for Chapter 26: 26.42, 26.46, 26.48, 26.62(a-g), 26.66(a-d), 26.70.

Adults and children estimated to be living with HIV | 2011



Estimated Incidence of AIDS and Deaths among Adults and Adolescents with AIDS, 1985–2002—United States

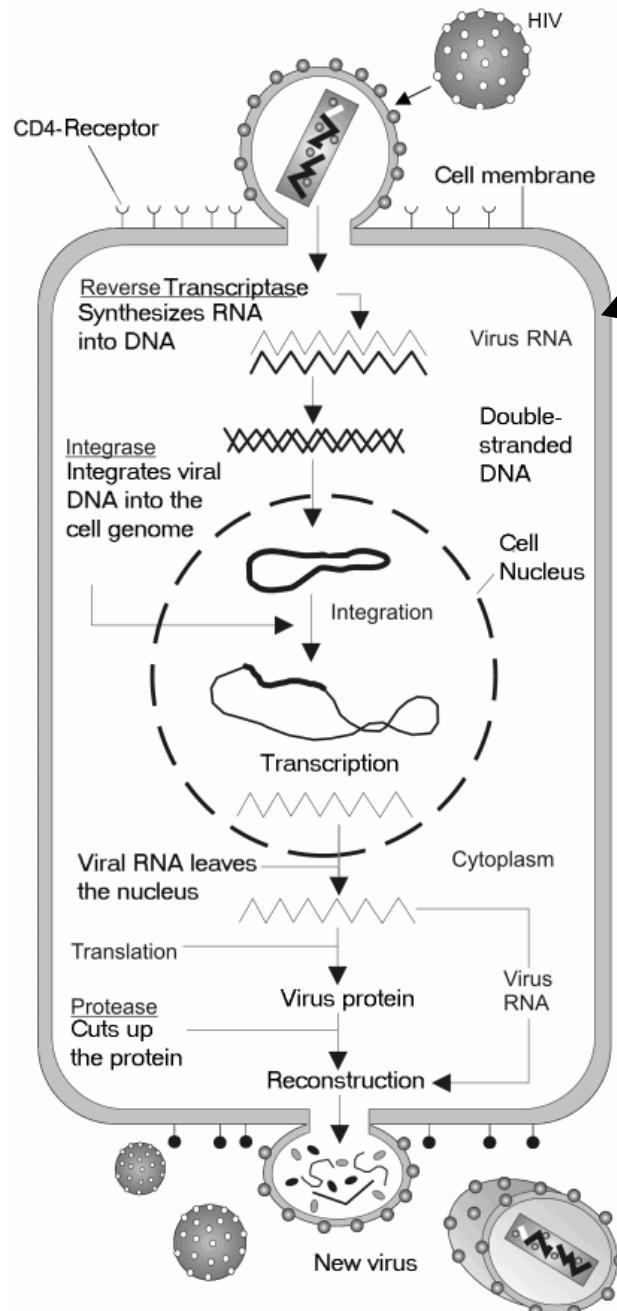


Note. Adjusted for reporting delays.

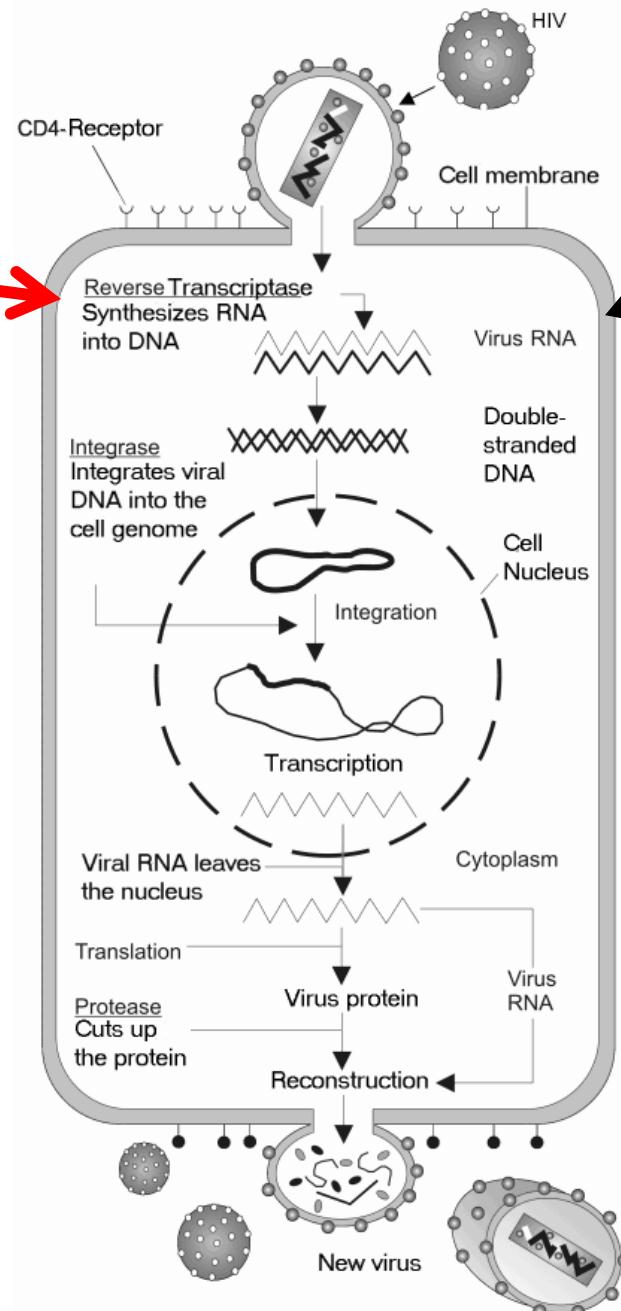


Macrophage or T-cell

HIV Life Cycle



Reverse
Transcriptase
Inhibitors



Macrophage or
T-cell

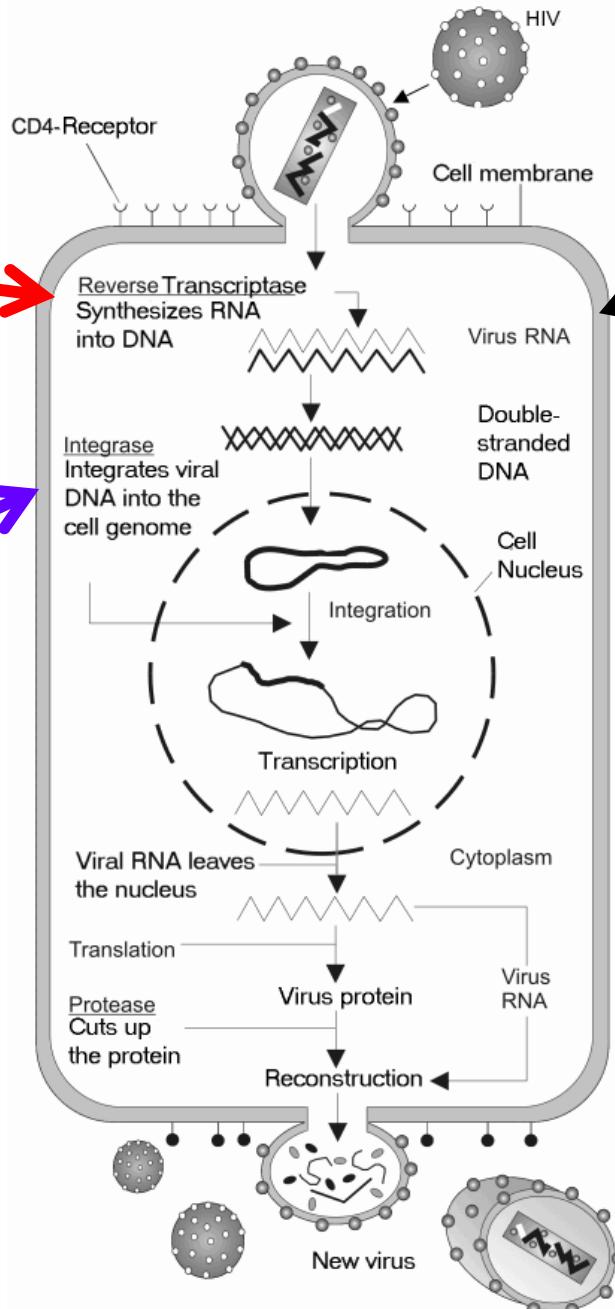
HIV Life Cycle

Reverse
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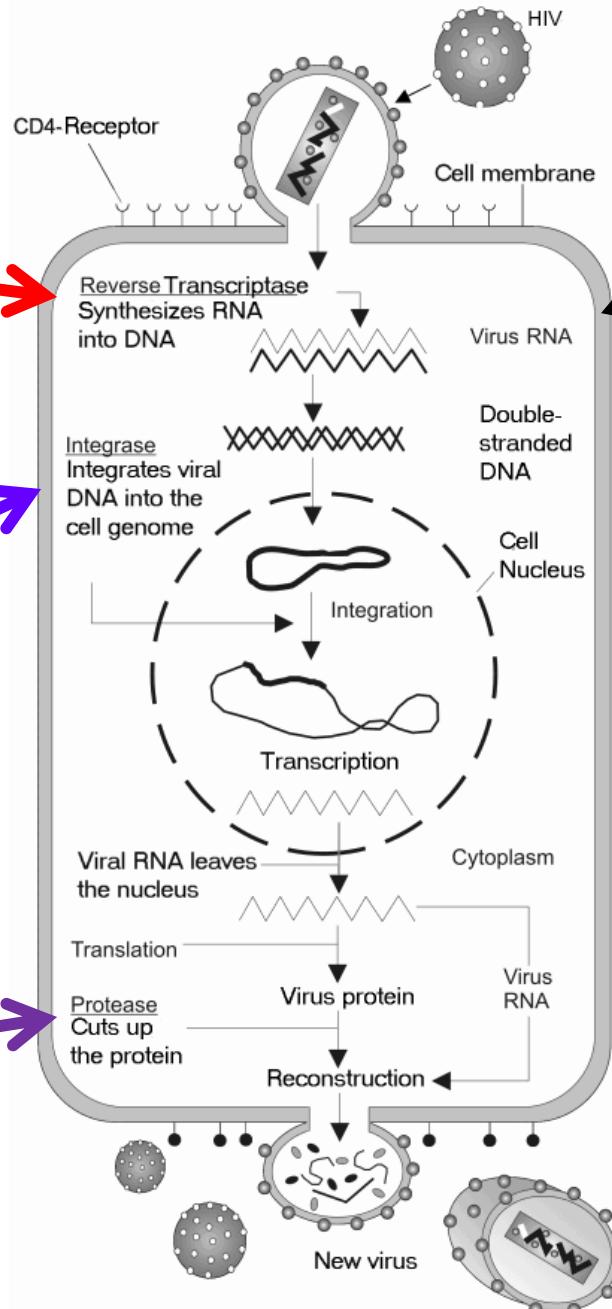
Reverse
Transcriptase
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Integrase
Inhibitors

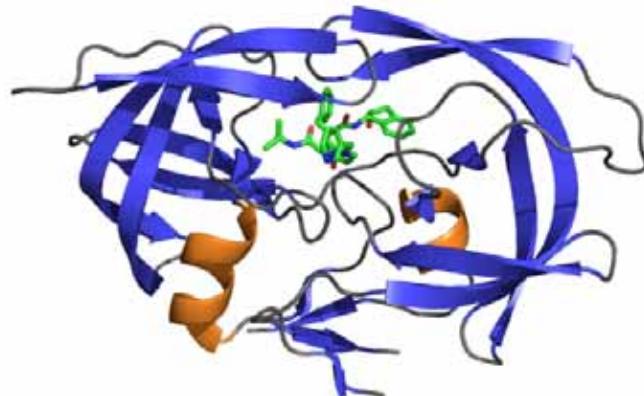
Protease
Inhibitors

Macrophage or
T-cell

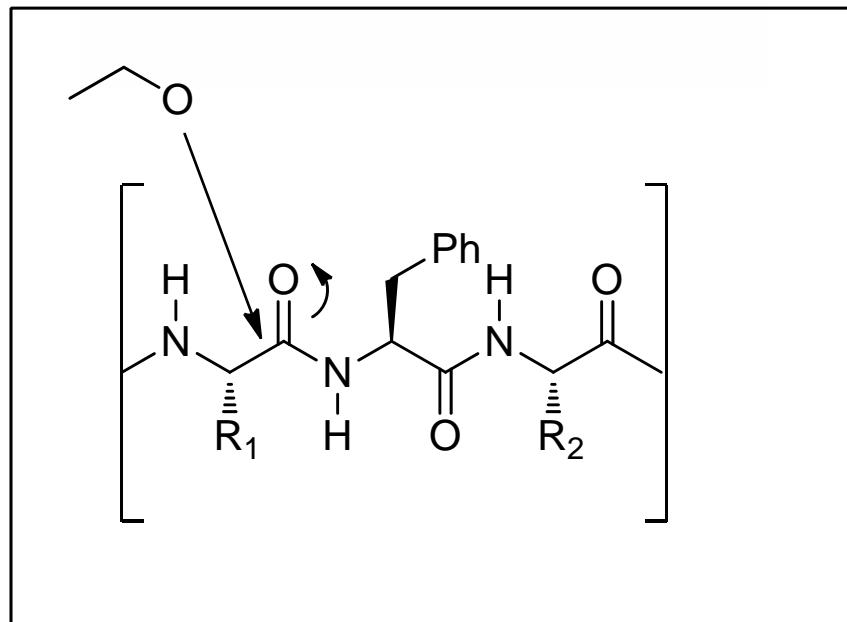
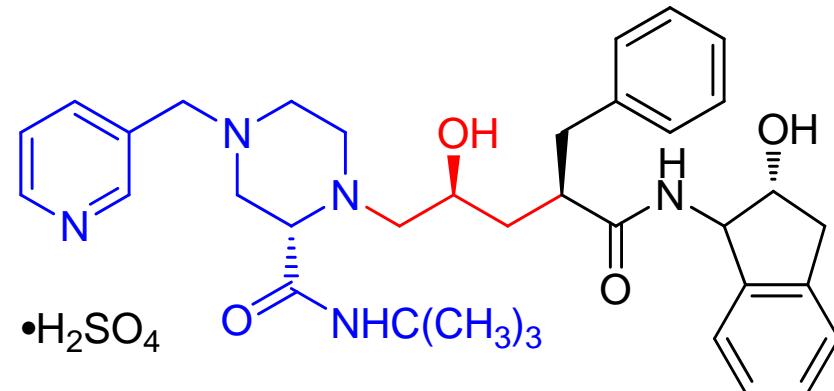
HIV Life Cycle



Crixivan: an HIV Protease Inhibitor

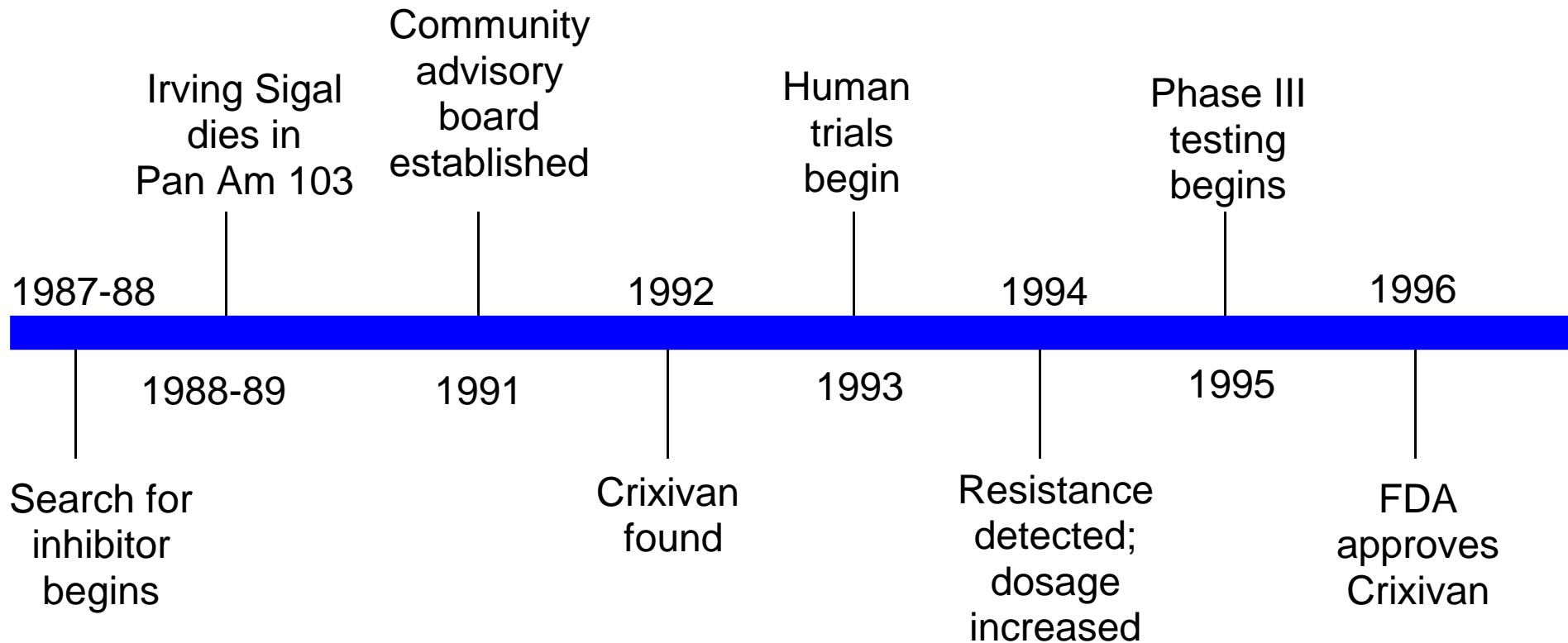


http://en.wikipedia.org/wiki/File:2avo_Indinavir.png

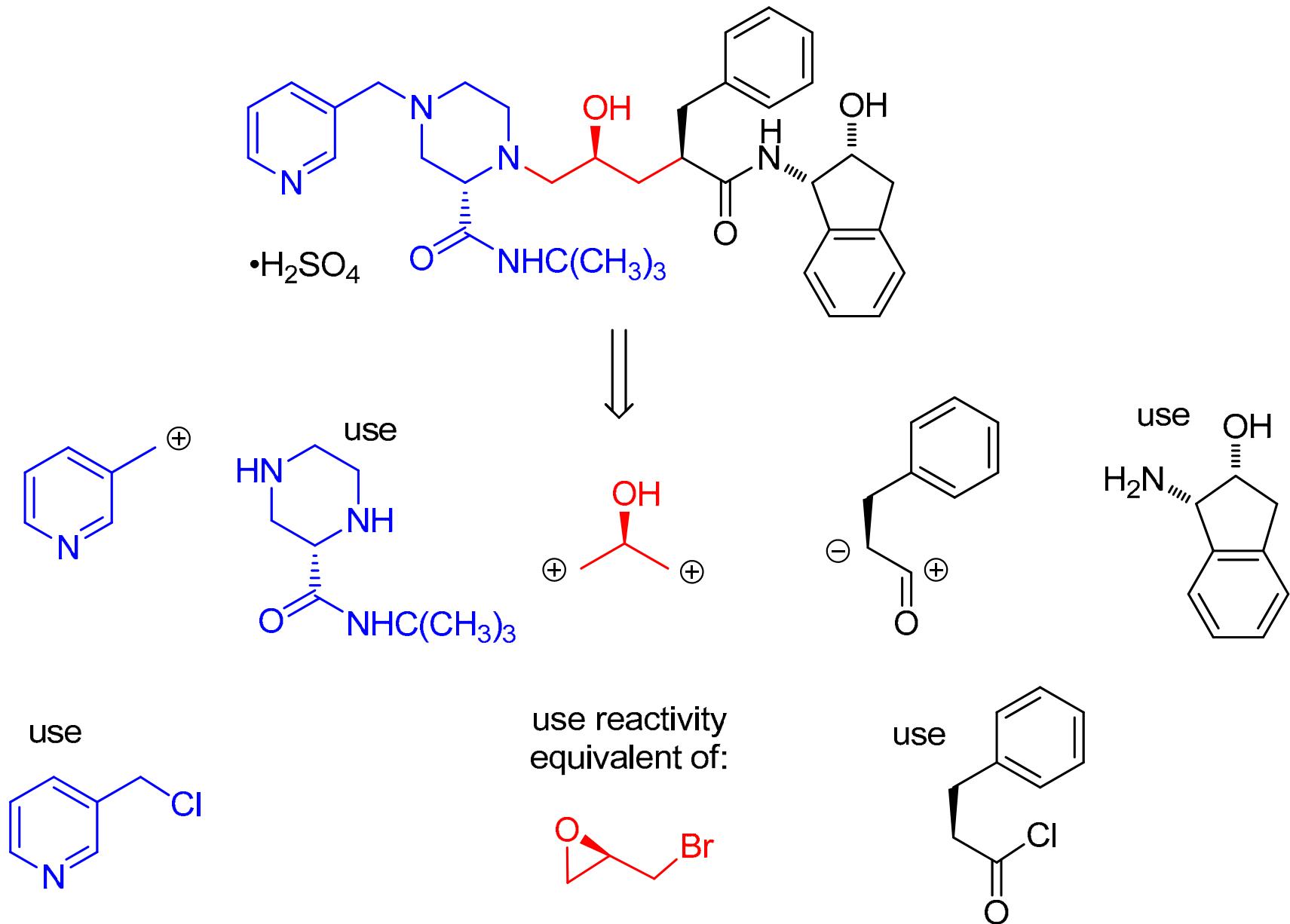


BOX: protease active site

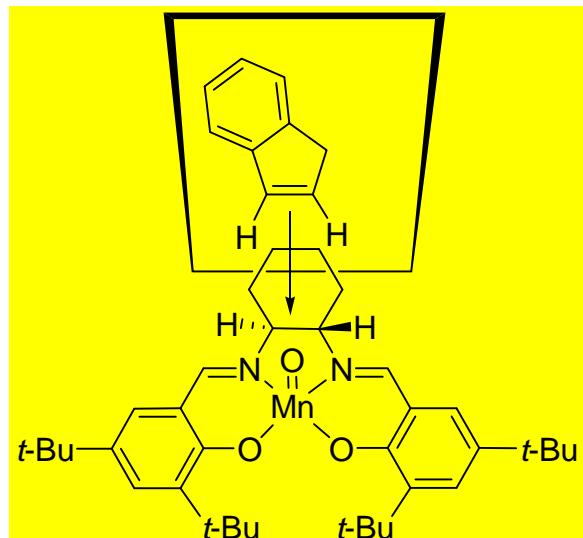
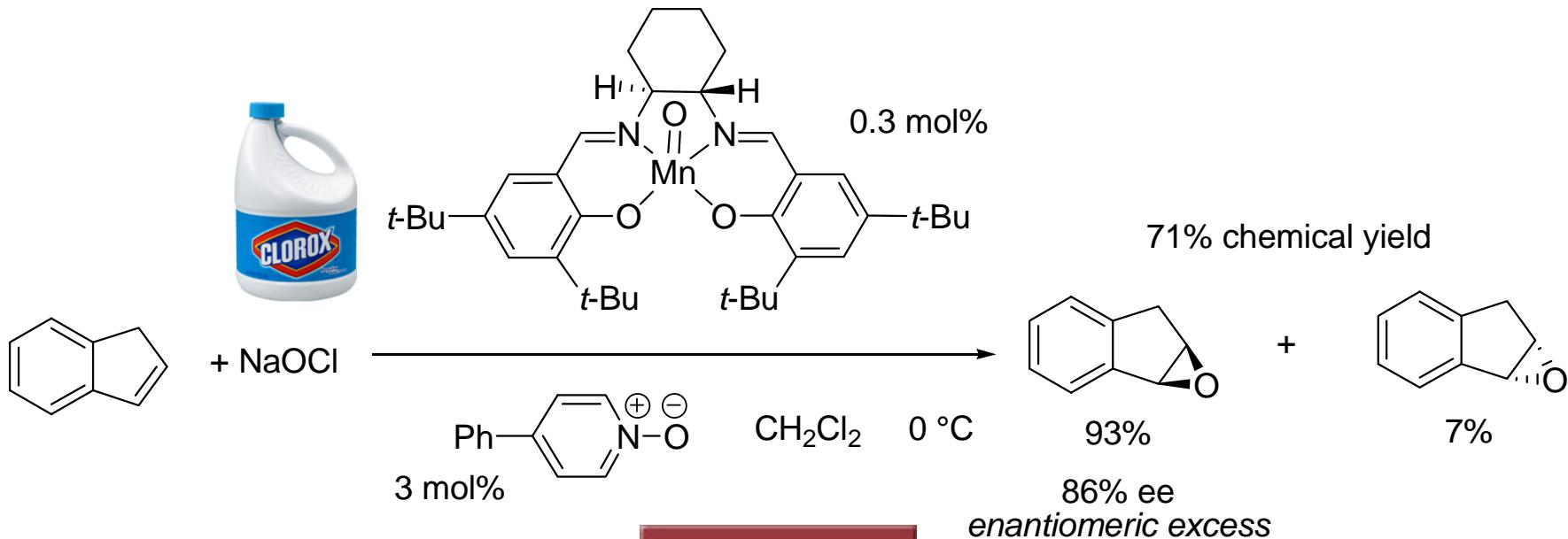
Timeline for Development of Merck's Protease Inhibitor



Crixivan: A Retrosynthetic Analysis



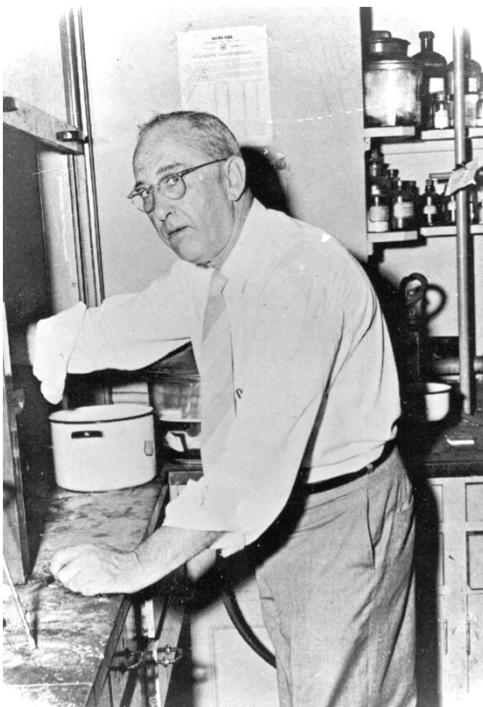
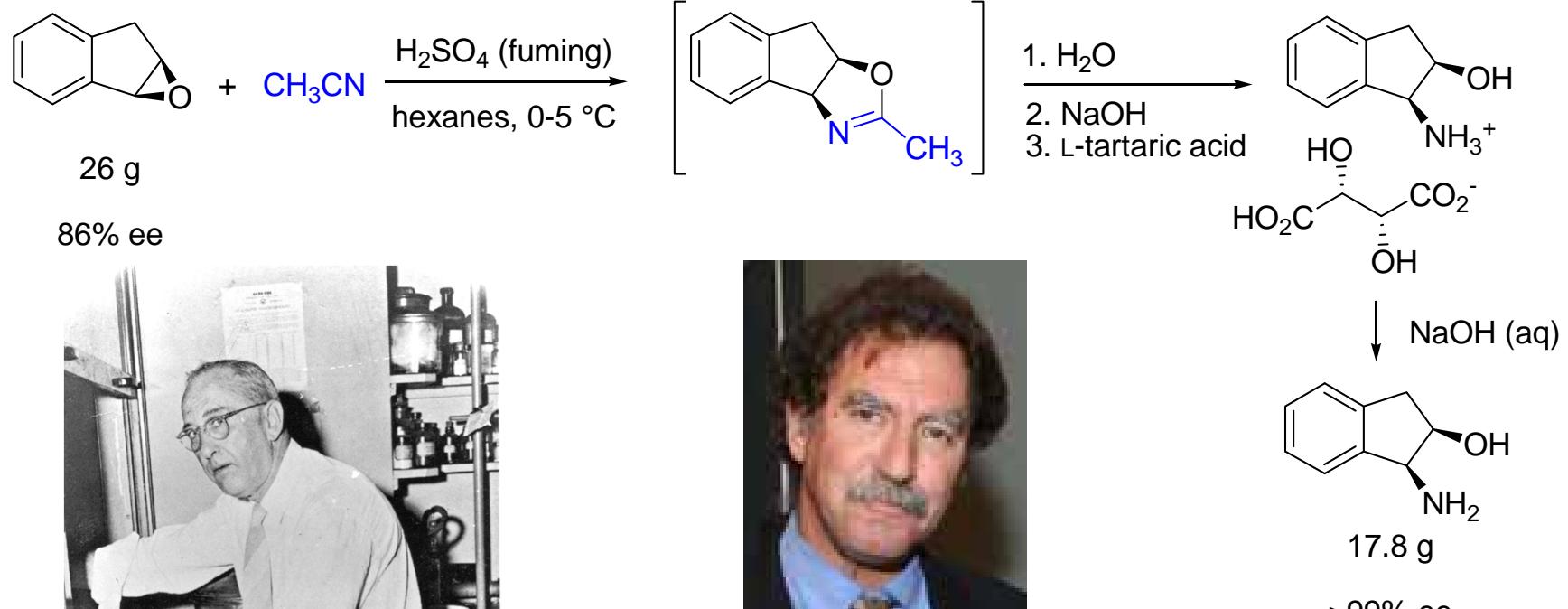
Jacobsen Asymmetric Epoxidation of Indene



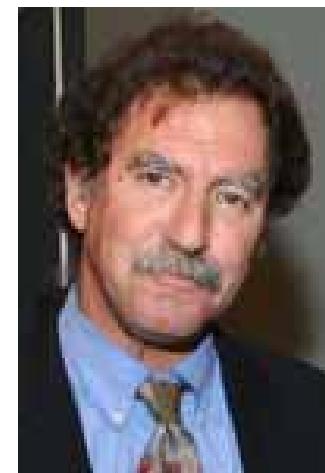
*Prof. Eric N. Jacobsen
Harvard University*

- Enantioselectivity explained by side-on approach
- Jacobsen, et al. *JACS*, **1991**, *113*, 7063.
- Jacobsen, Reider et al. *Org. Syn.* **1998**, *76*, 47.

Ritter Reaction on Epoxide Gives Aminoindanol After Hydrolysis & Enrichment of Desired Enantiomer *via* Tartrate Salt Formation



Prof. J.J. Ritter (NYU)

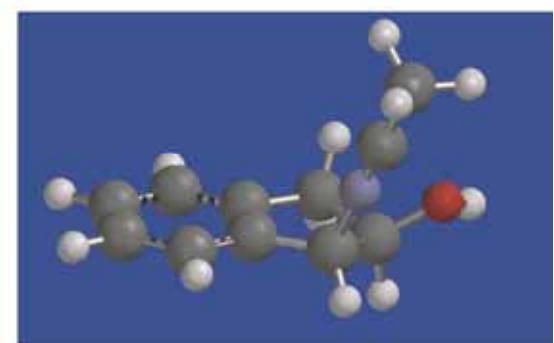
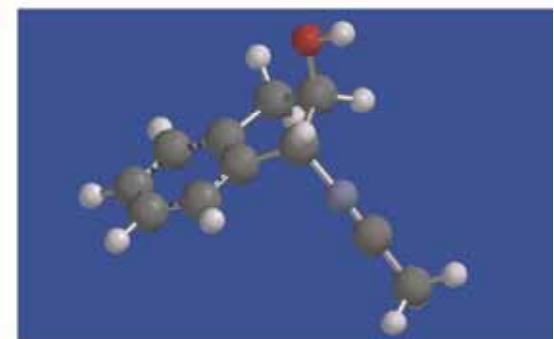
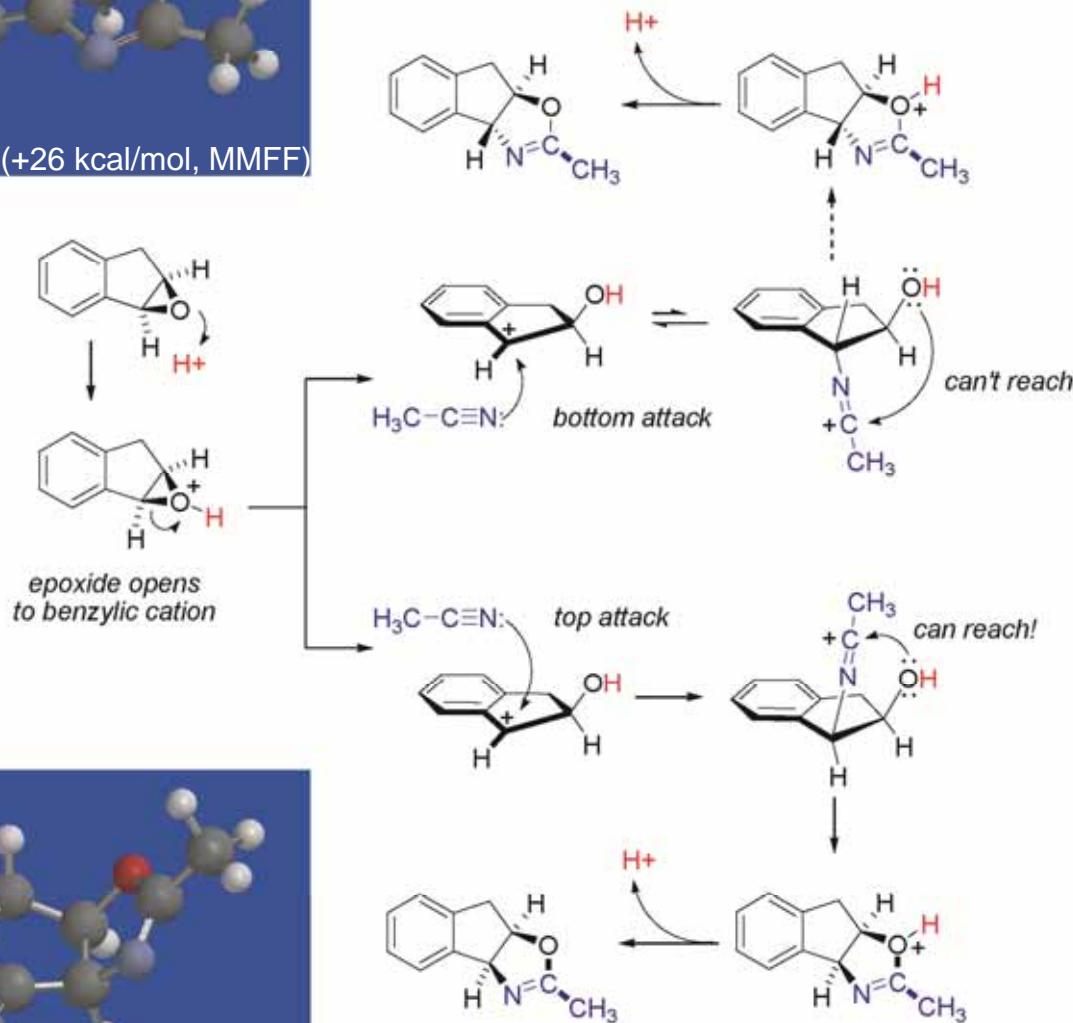
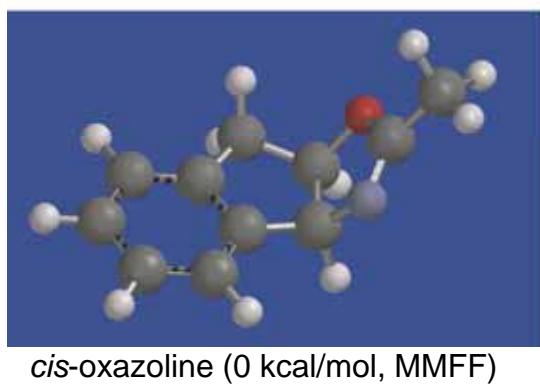
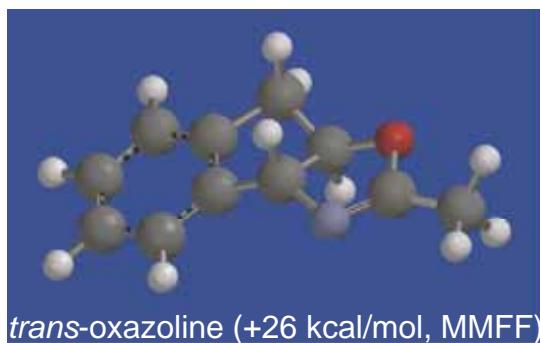


Paul Reider
Merck/Amgen/Princeton

Jacobsen, Reider, et al. *Org. Syn.* **1998**, 76, 47.

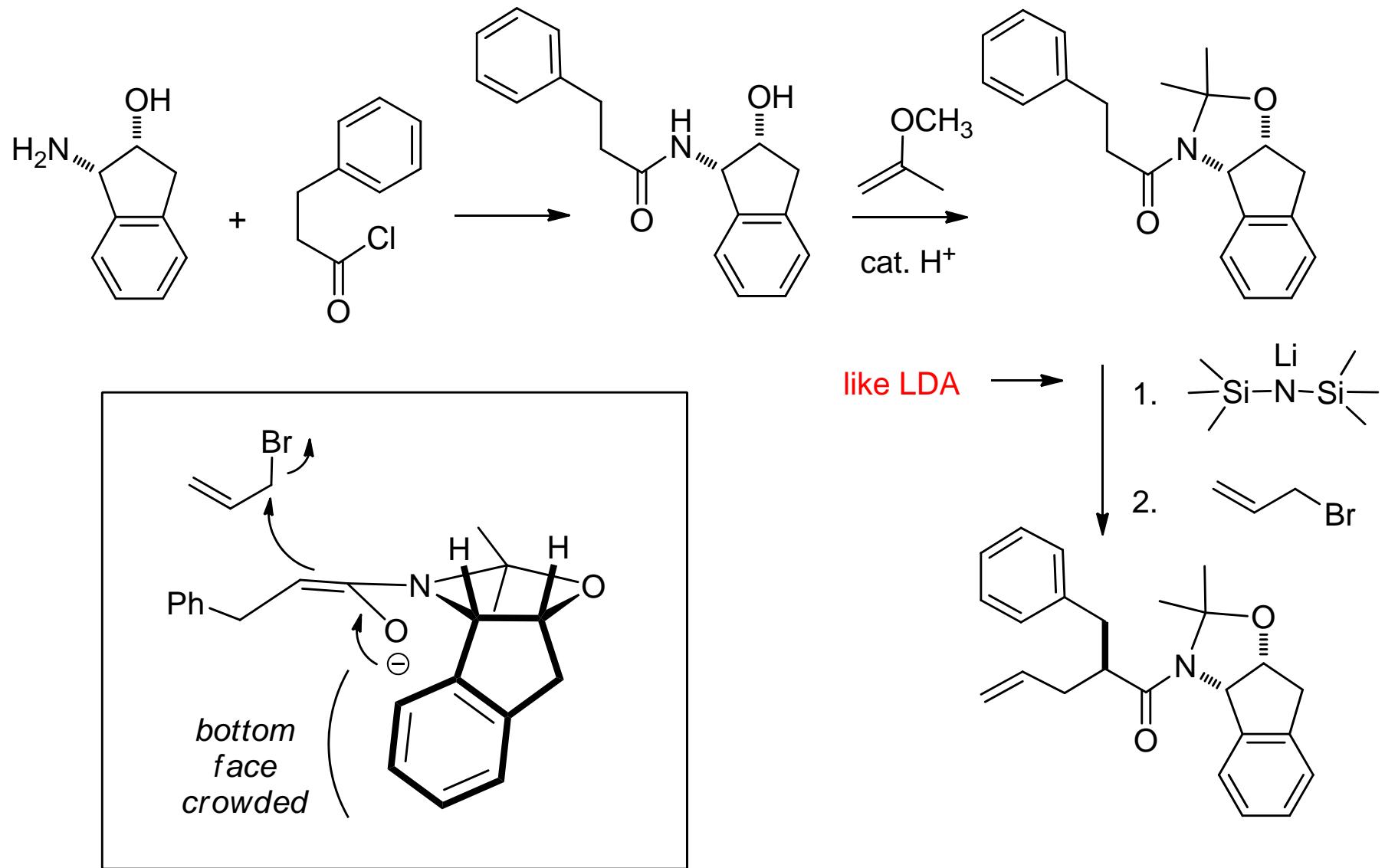
Ritter Reaction Mechanism:

Benzyllic Cation, Proximity, and Ring Strain.

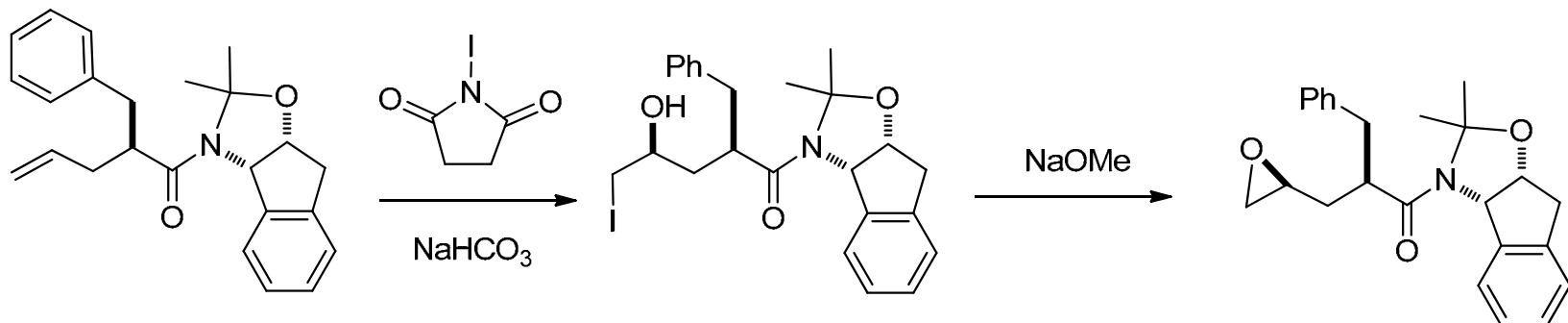


acetonitrile-benzyl cation adducts
(computed with HF/3-21G* theory)

A Built-In Chiral Auxiliary Sets a New Stereogenic Center



Crixivan End-Game Chemistry



*like a haloxydrin reaction, only a bit more complicated!

