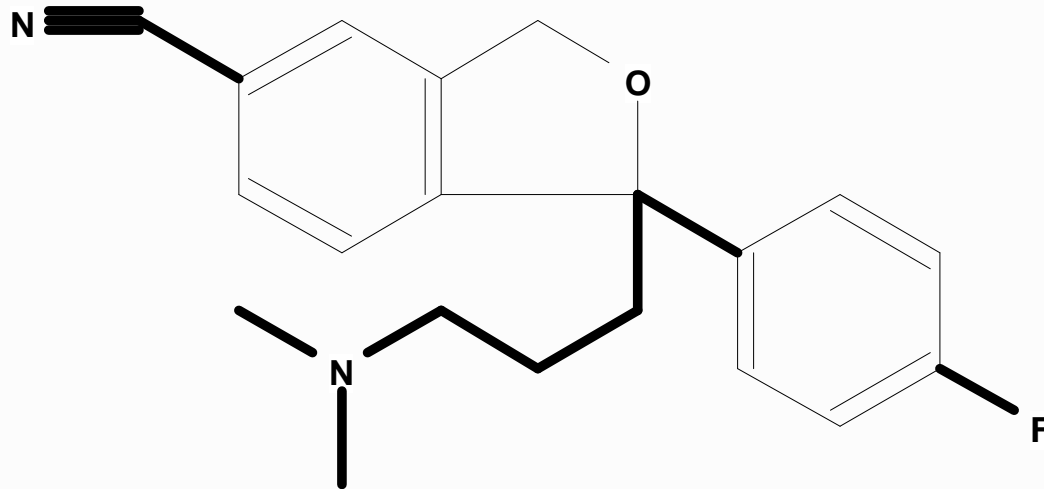


# 4. Block



**Acrobat-Dokument**

# SSRI Celexa



# **HIV und AIDS**

# Funktionen der HIV-Genteile

**Table 1.** HIV-gene functions

Genes	Functions
<b>Structural</b>	
<i>gag</i>	matrix, virion maturation and stability, capsid, virus particle maturation and release
<i>pol</i>	protease, reverse transcriptase, integrase
<i>env</i>	external envelope, receptor binding, virion infectivity
<b>Regulatory</b>	
<i>tat</i>	transcription transactivator of gene expression
<i>rev</i>	regulator of protein expression
<i>tev/tnv</i>	undefined
<i>nef</i>	negative factor, virus propagation
<i>vpr</i>	early regulatory protein
<b>Accessory</b>	
<i>vif</i>	cell-free virus transmission, <i>env</i> processing
<i>vpu</i>	virus maturation/release

# Virus - Lebenszyklus

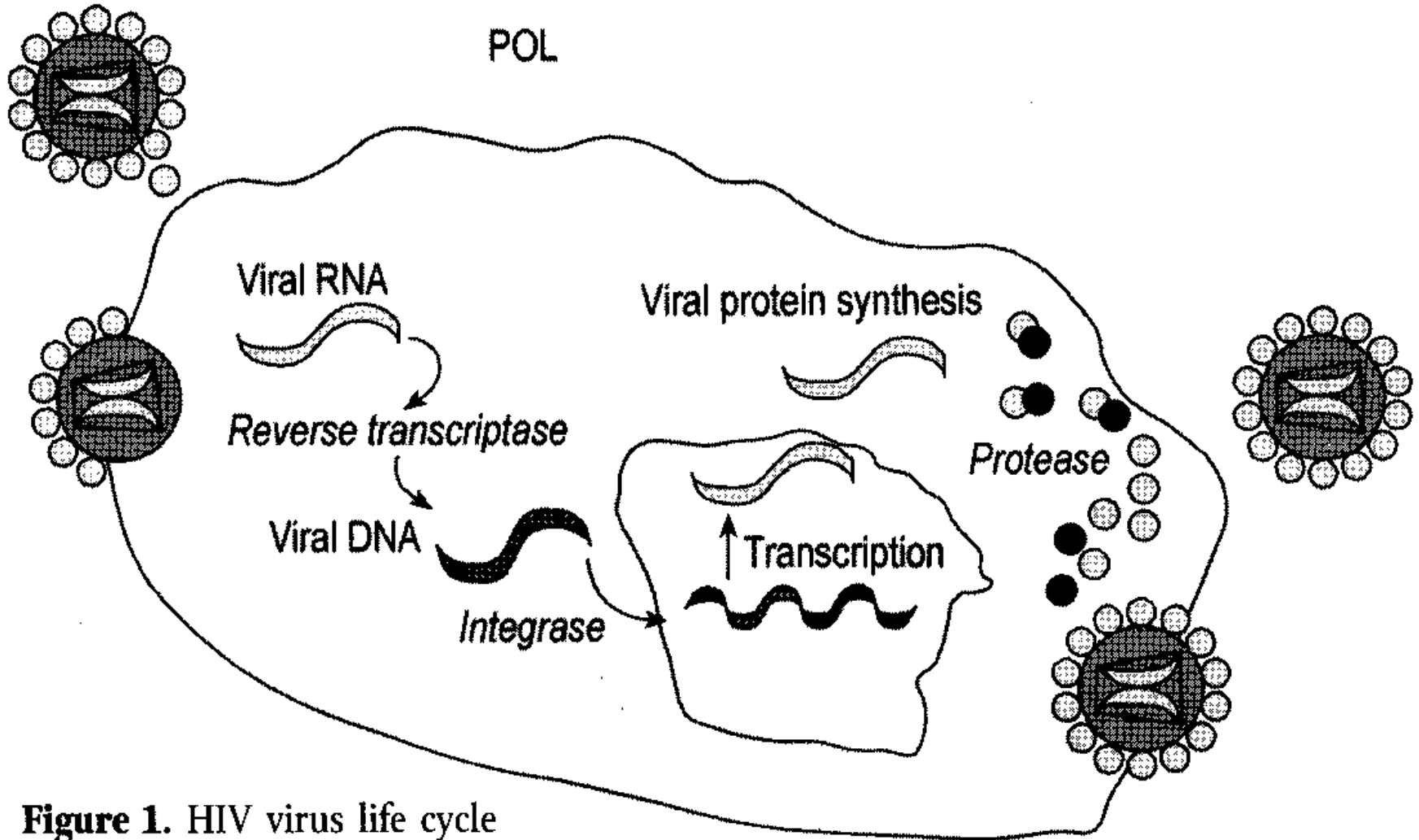
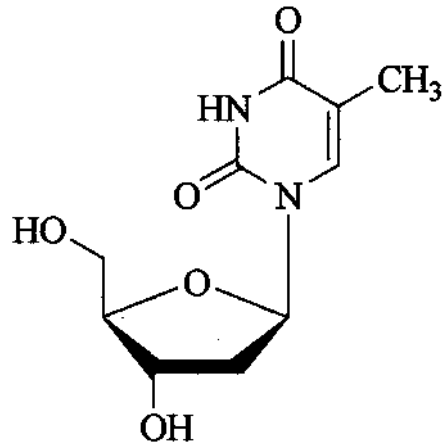


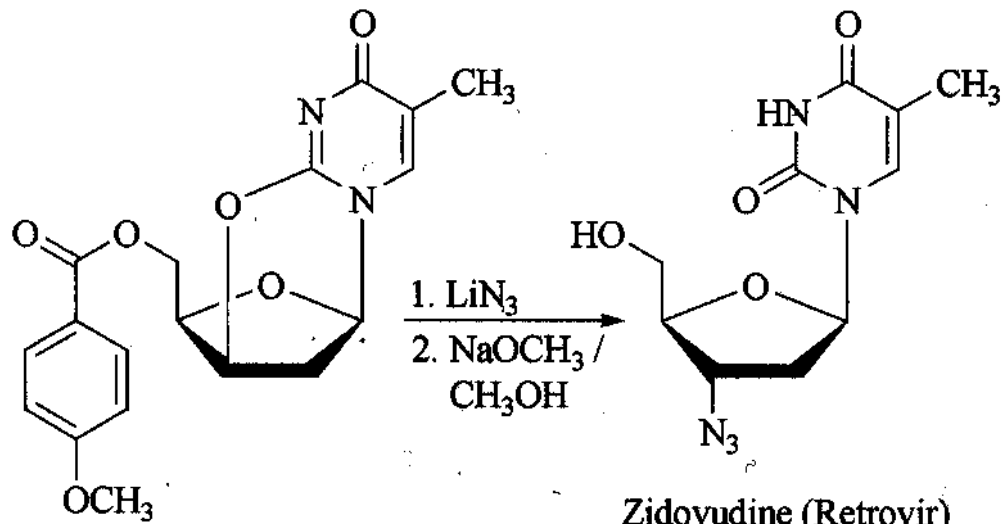
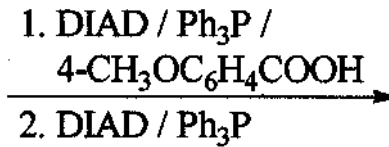
Figure 1. HIV virus life cycle

# Nukleoside Analoge

# Zidovudine–erster Hemmstoff

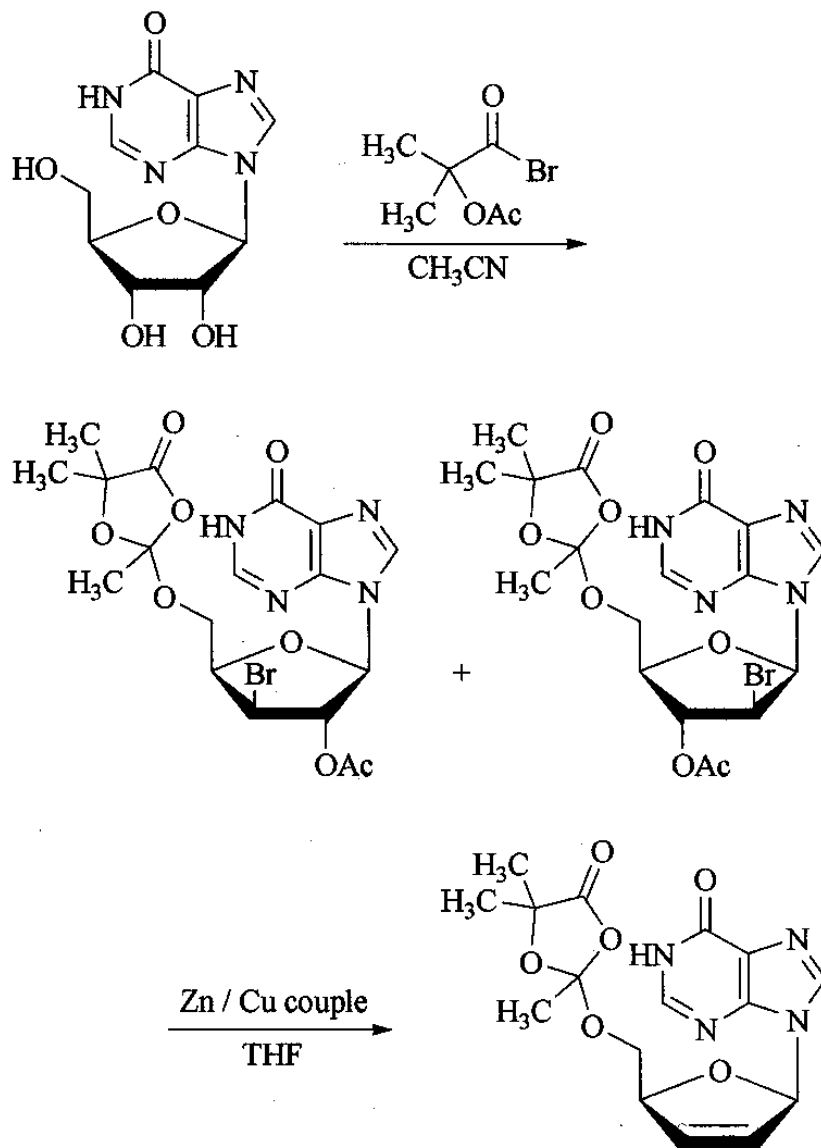


Thymidine



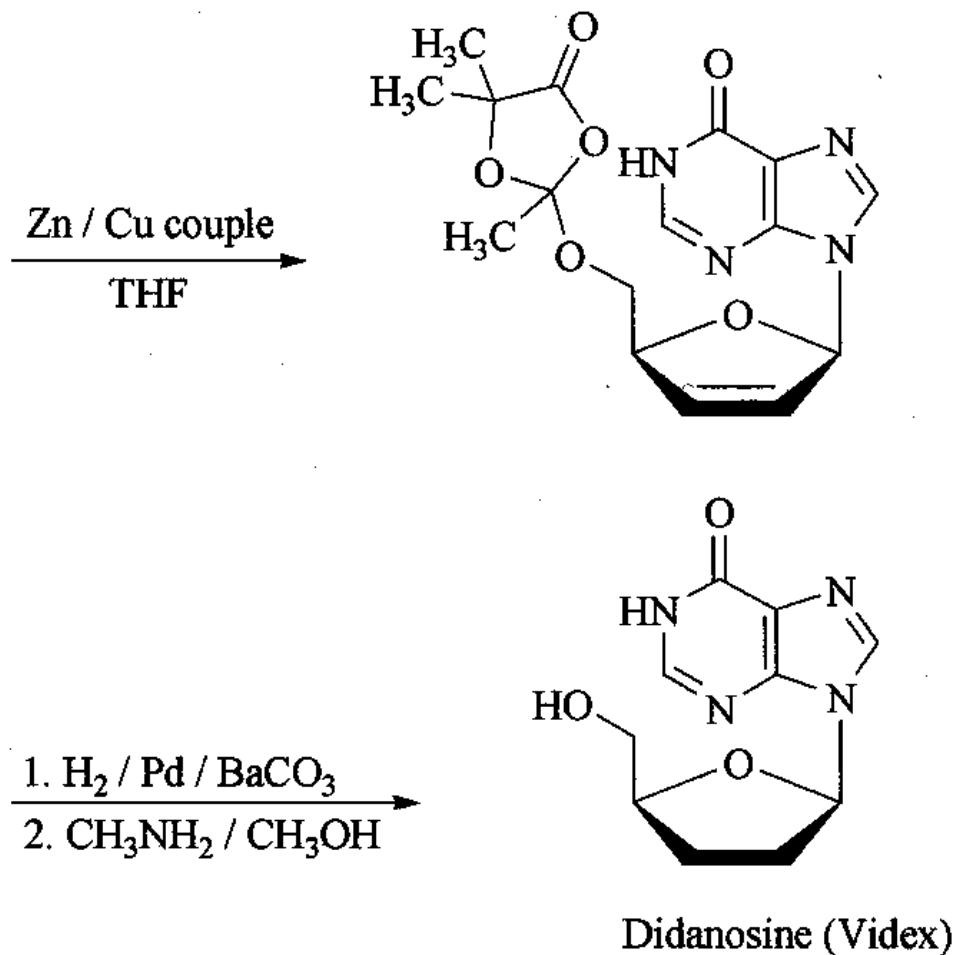
Zidovudine (Retrovir)

# Didanosine



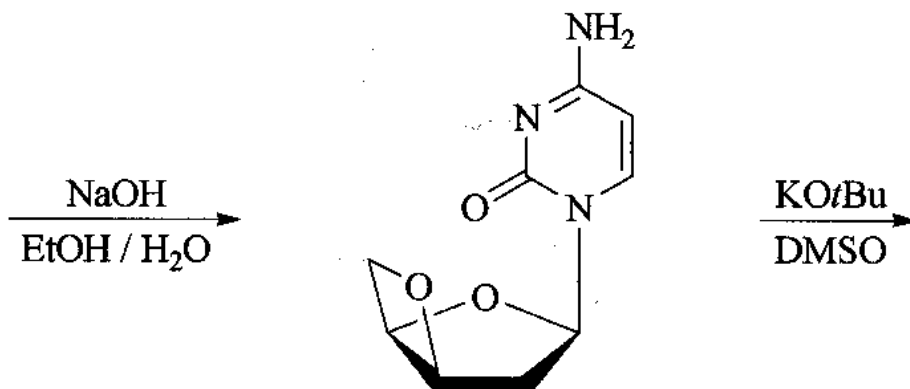
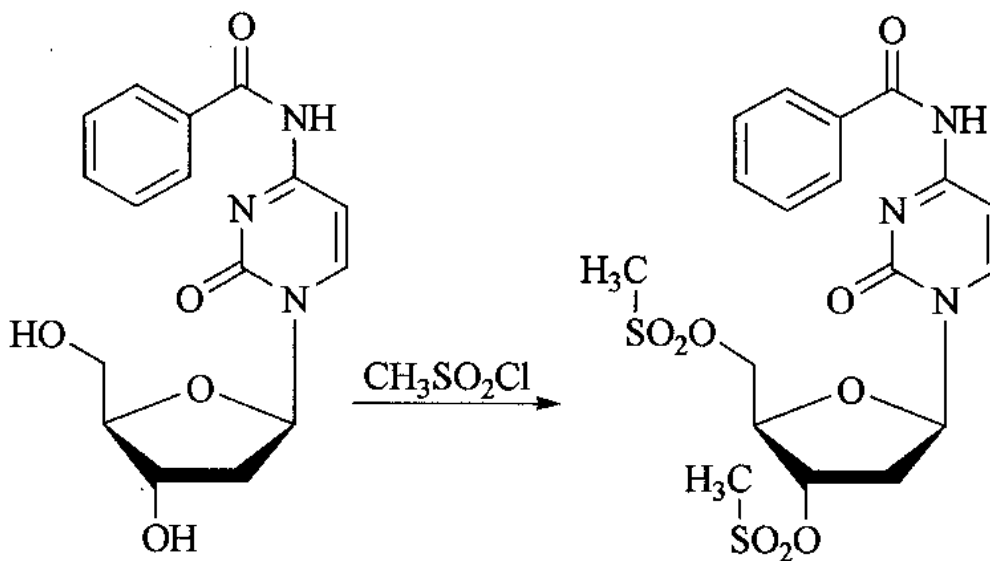


# Didanosine

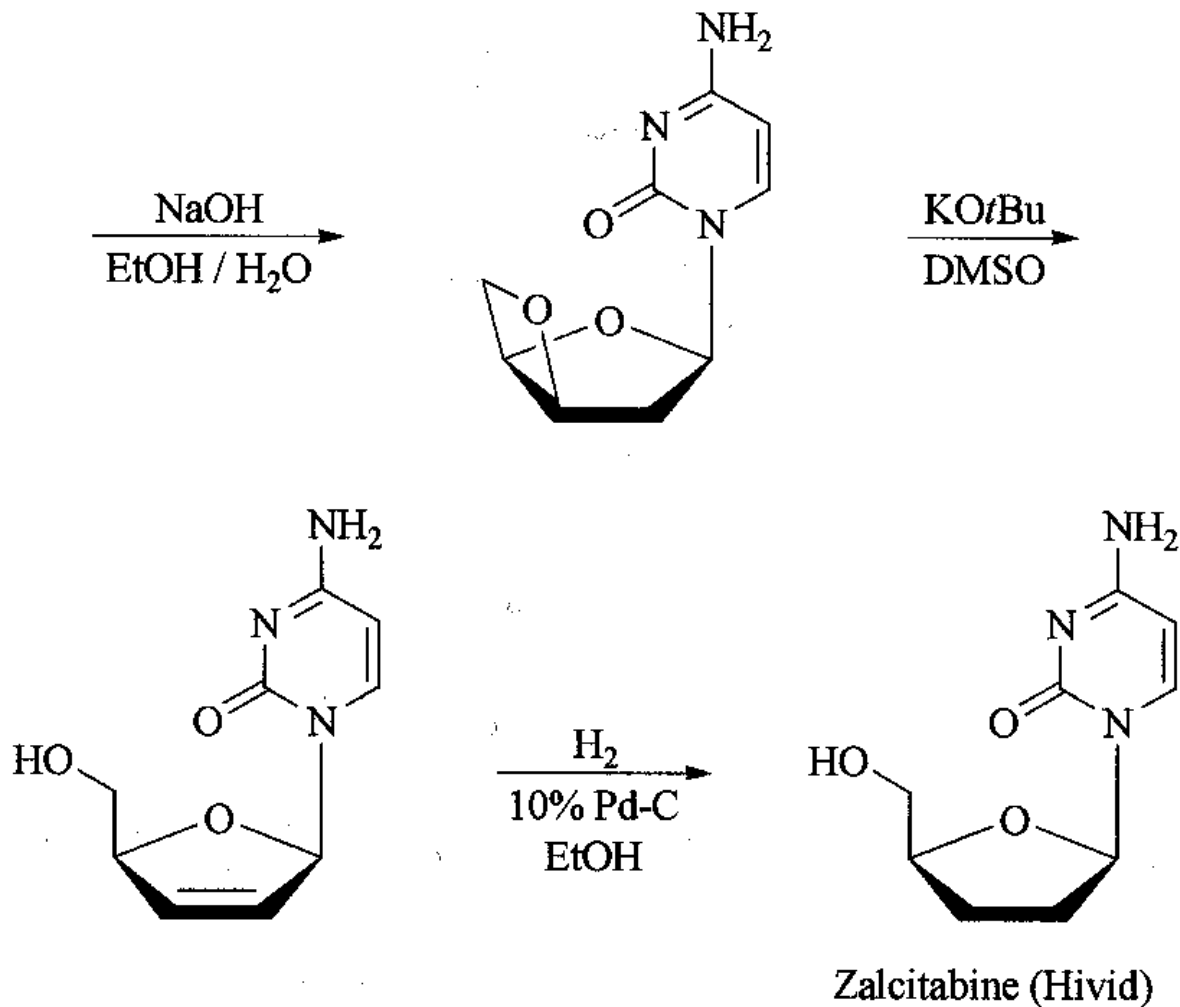


*Trade name: Videx (Bristol-Myers Squibb).*

# Zalcitabine

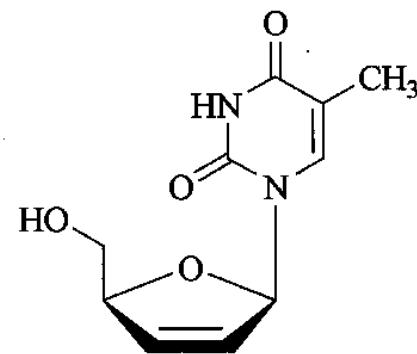
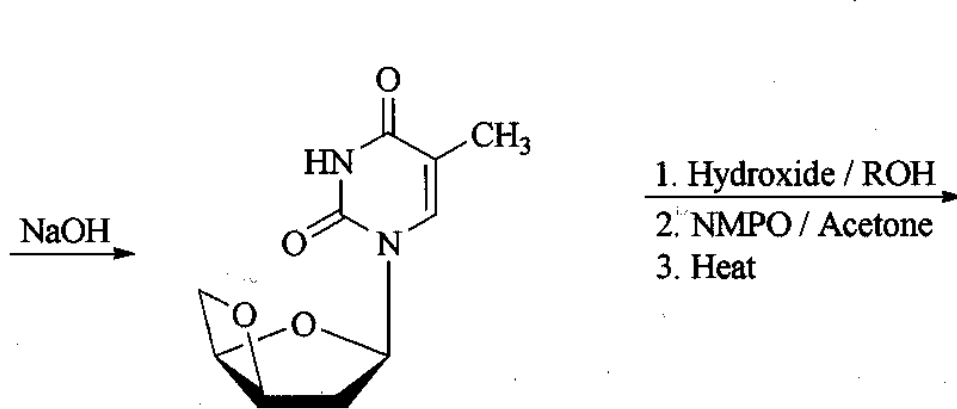
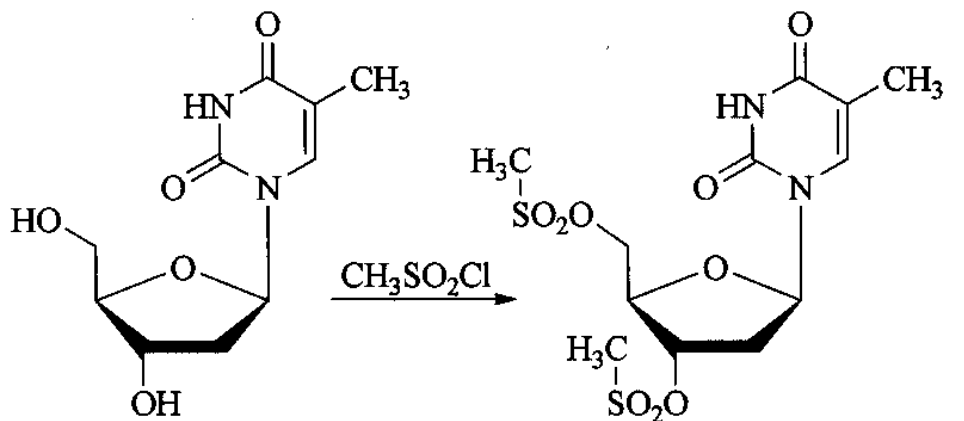


# Zalcitabine



*Trade name:* Hivid (Hoffmann-LaRoche).

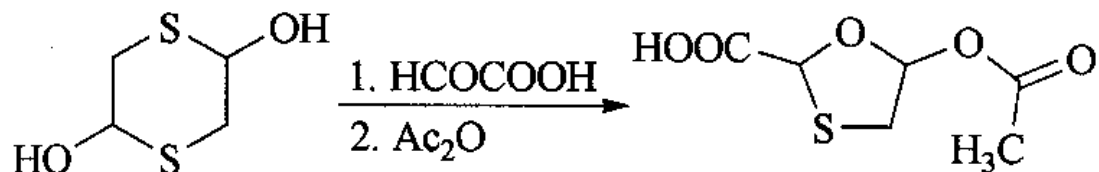
# Stavudine



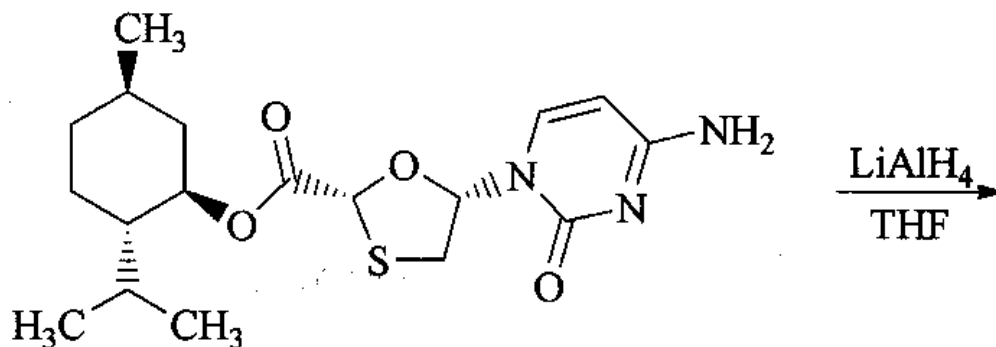
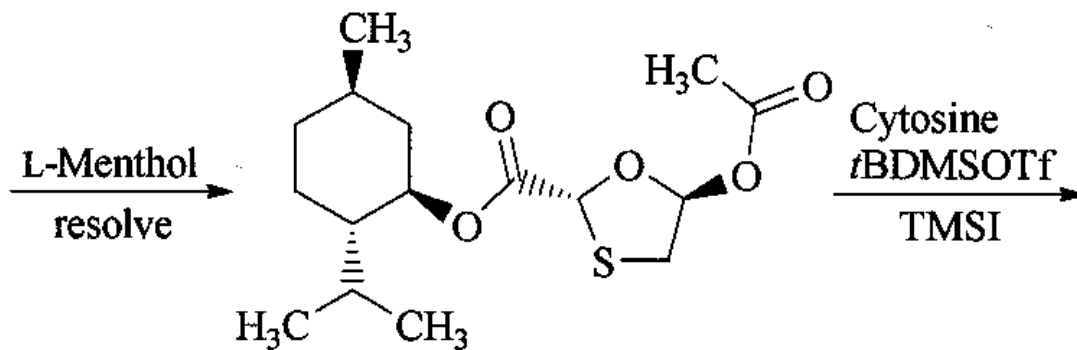
Stavudine (Zerit)

Trade name: Zerit (Bristol-Myers Squibb).

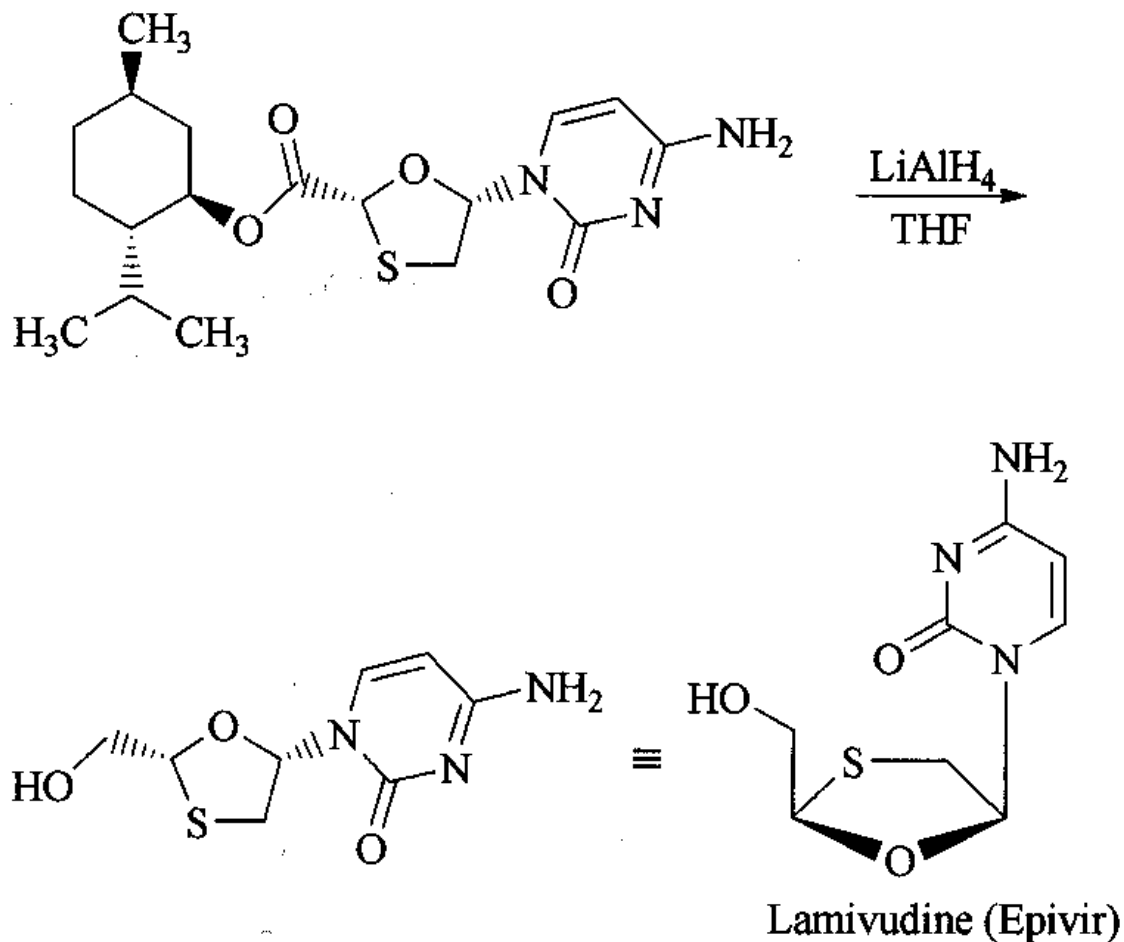
# Lamivudine



Mixture of diastereomers

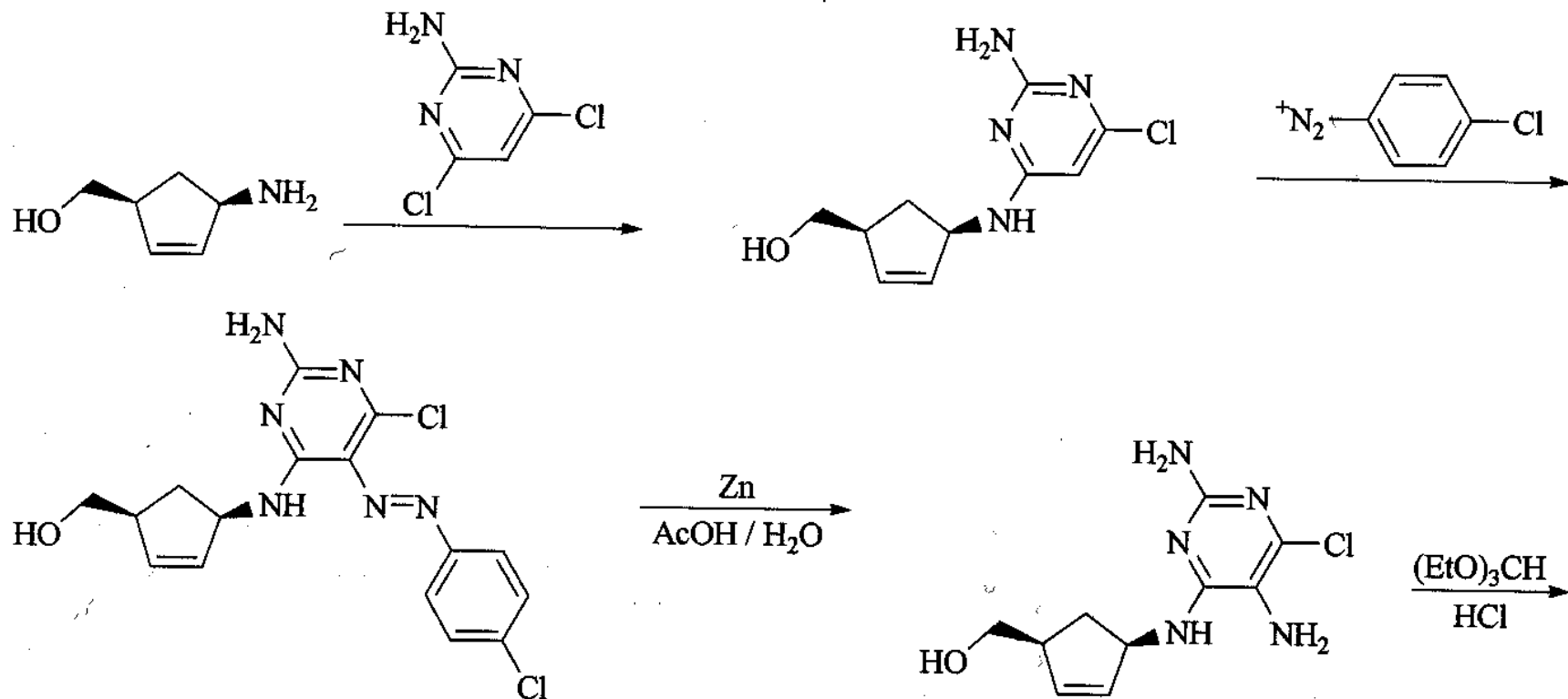


# Lamivudine

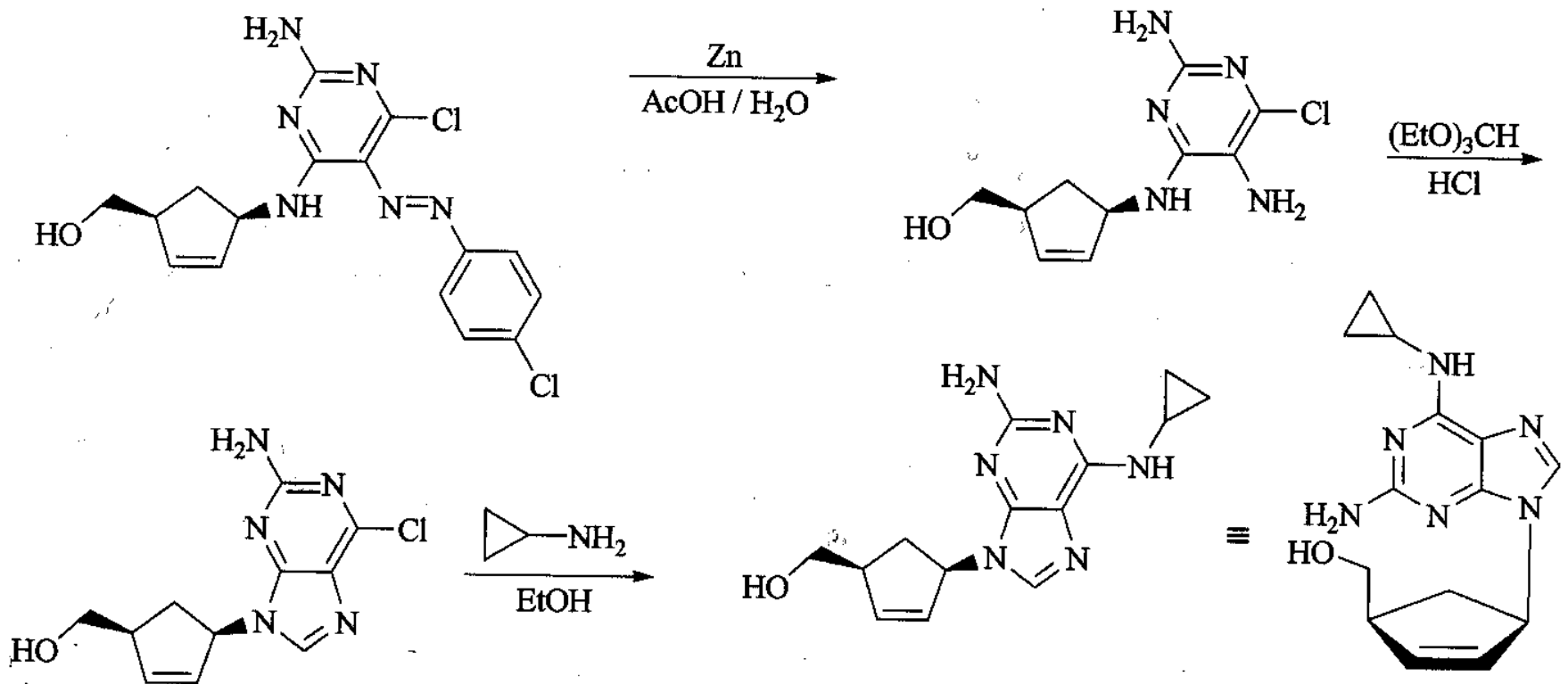


*Trade names:* Epivir (BioChem Pharma, Glaxo Wellcome), Combivir (lamivudine and zidovudine combination tablets, Glaxo Wellcome).

# Abacavir



# Abacavir



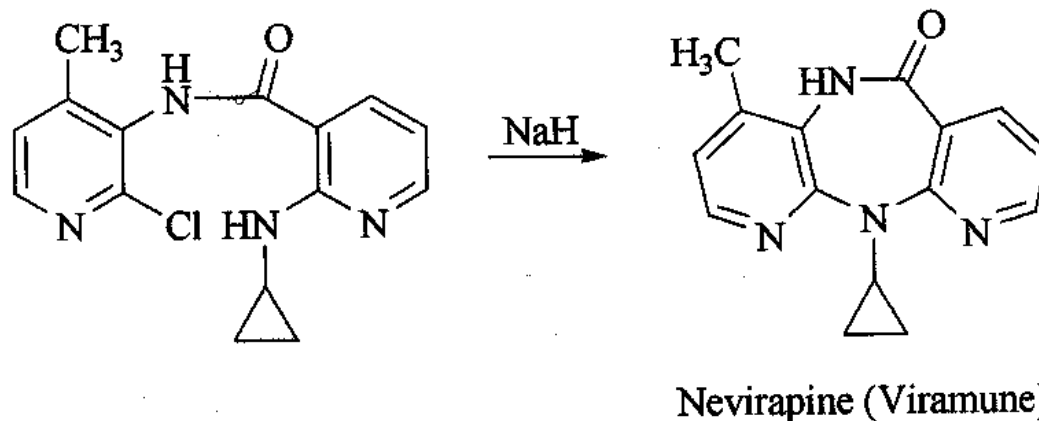
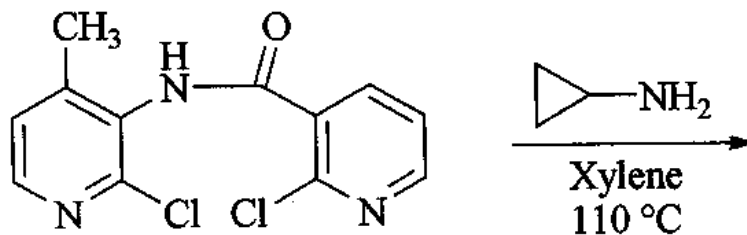
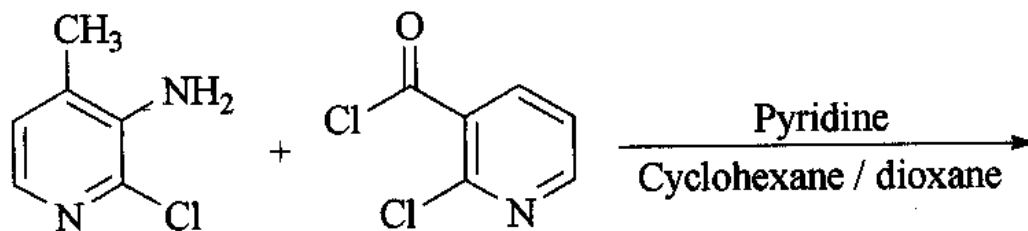
Trade name (abacavir sulfate): Ziagen, Glaxo Wellcome.

Abacavir (Ziagen)



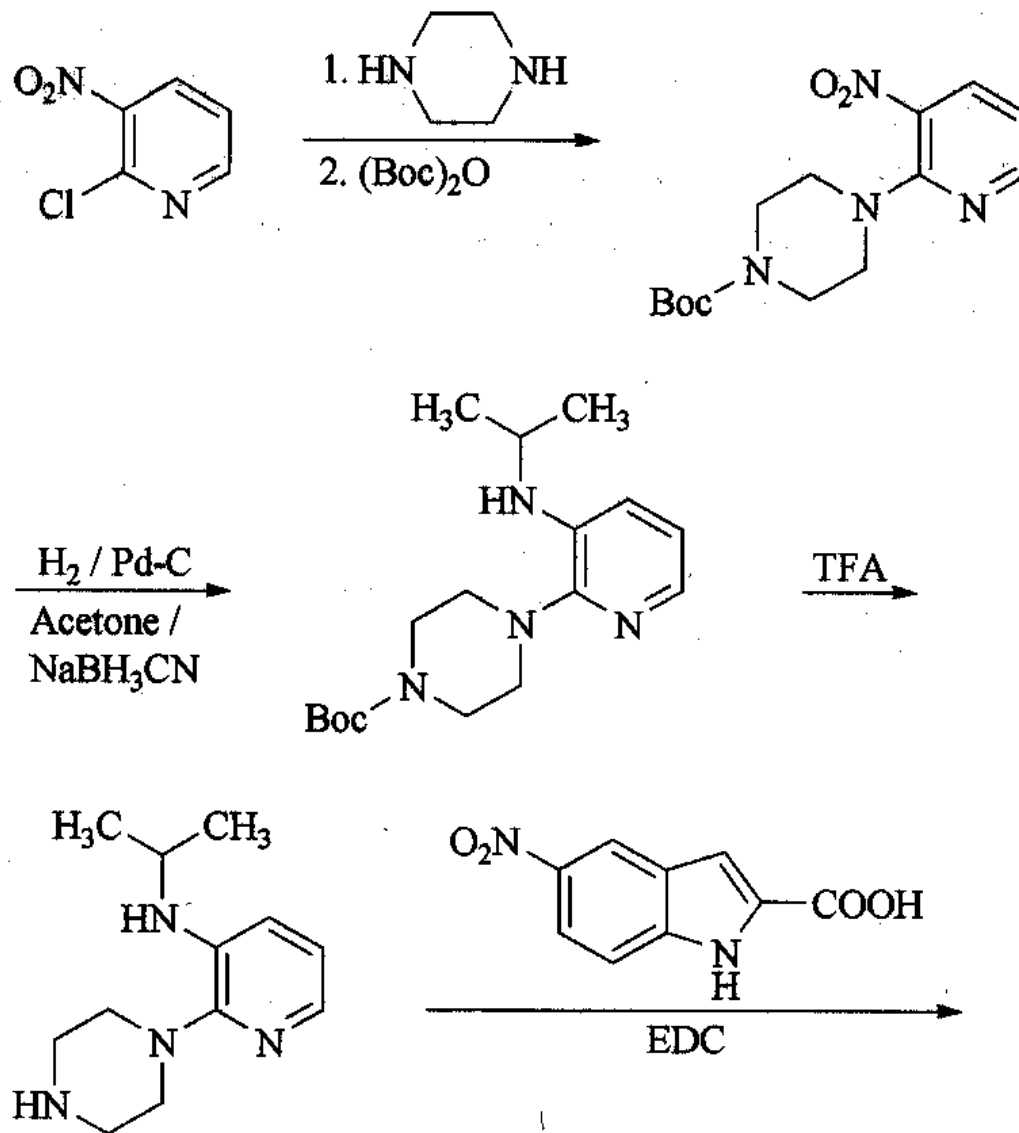
# Nonnukleoside Analoge

# Nevirapine

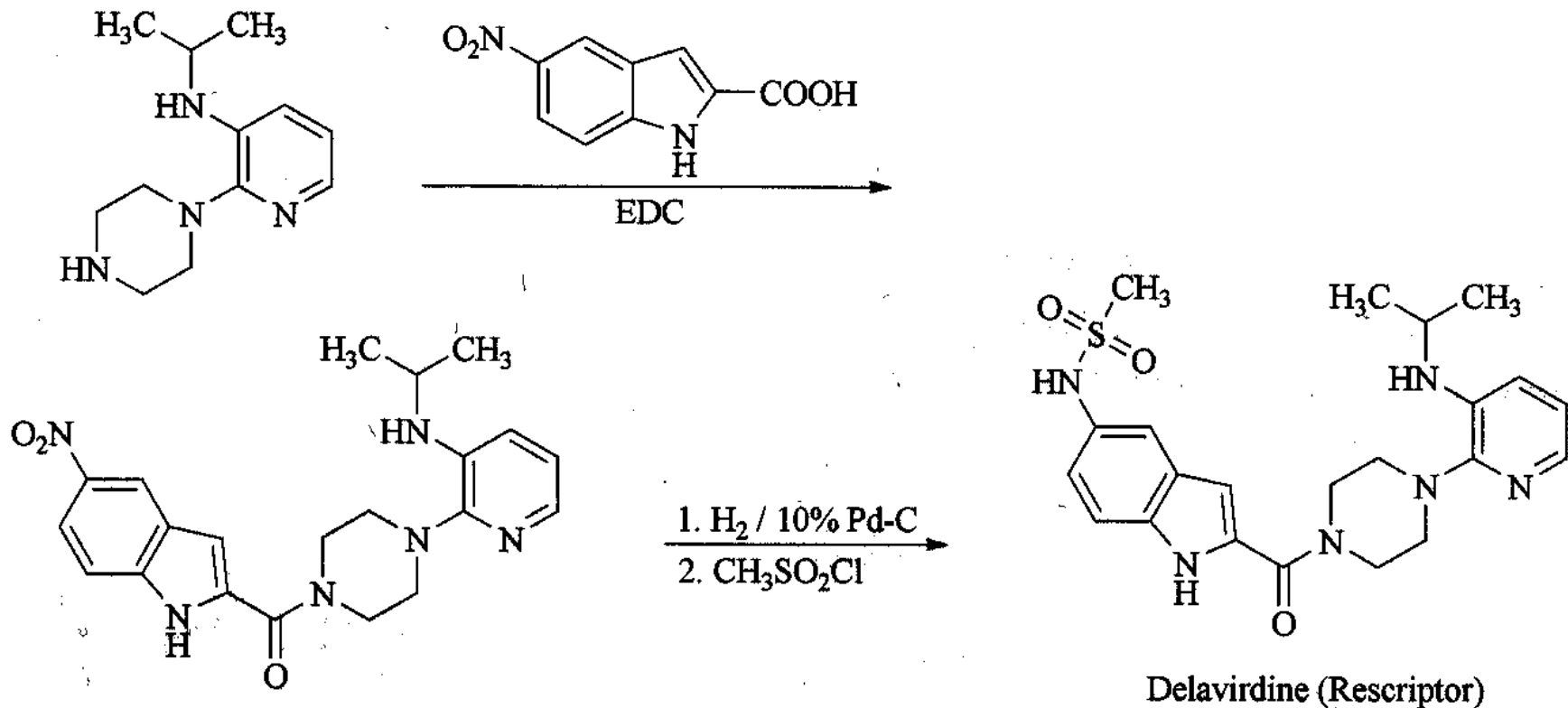


Trade name: Viramune (Boehringer Ingelheim).

# Delavirdine

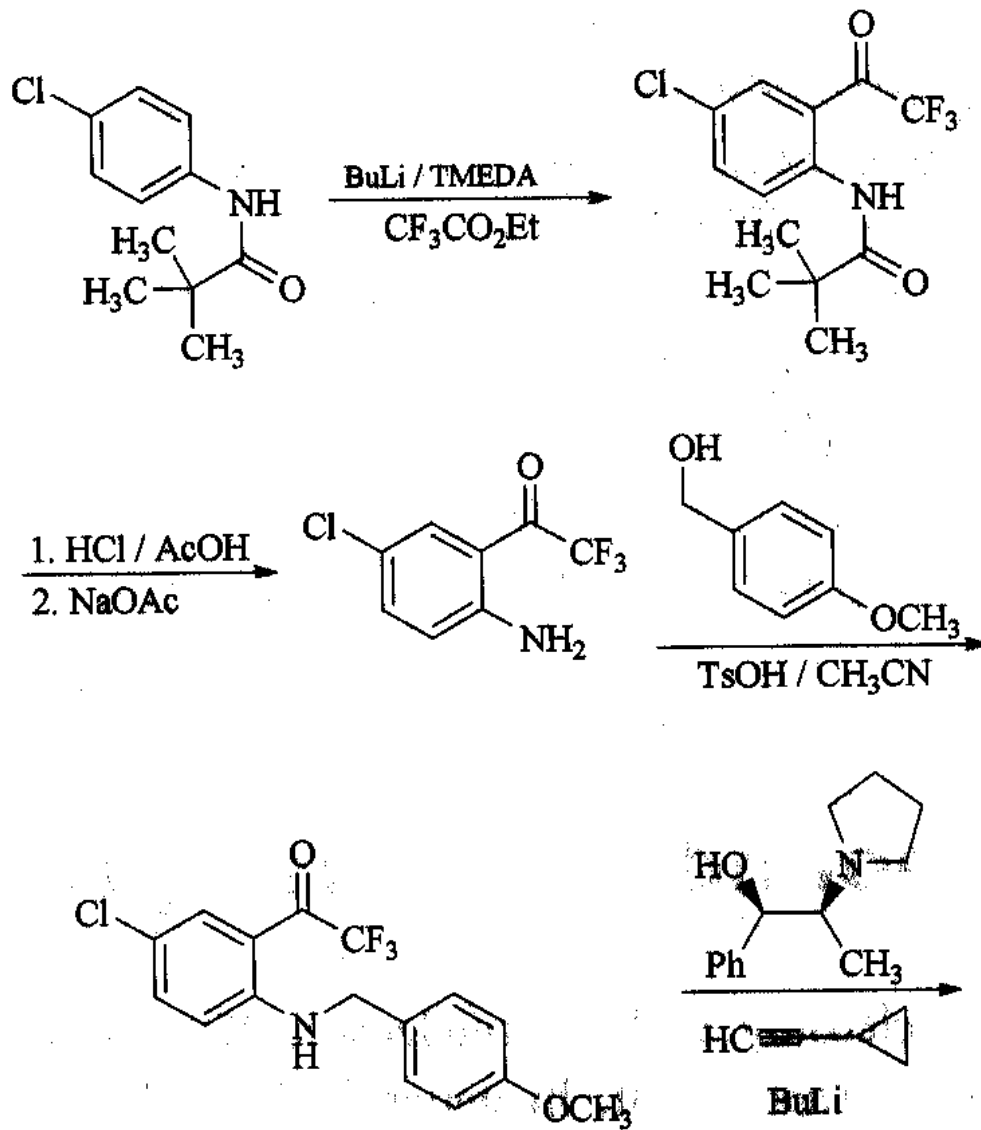


# Delavirdine

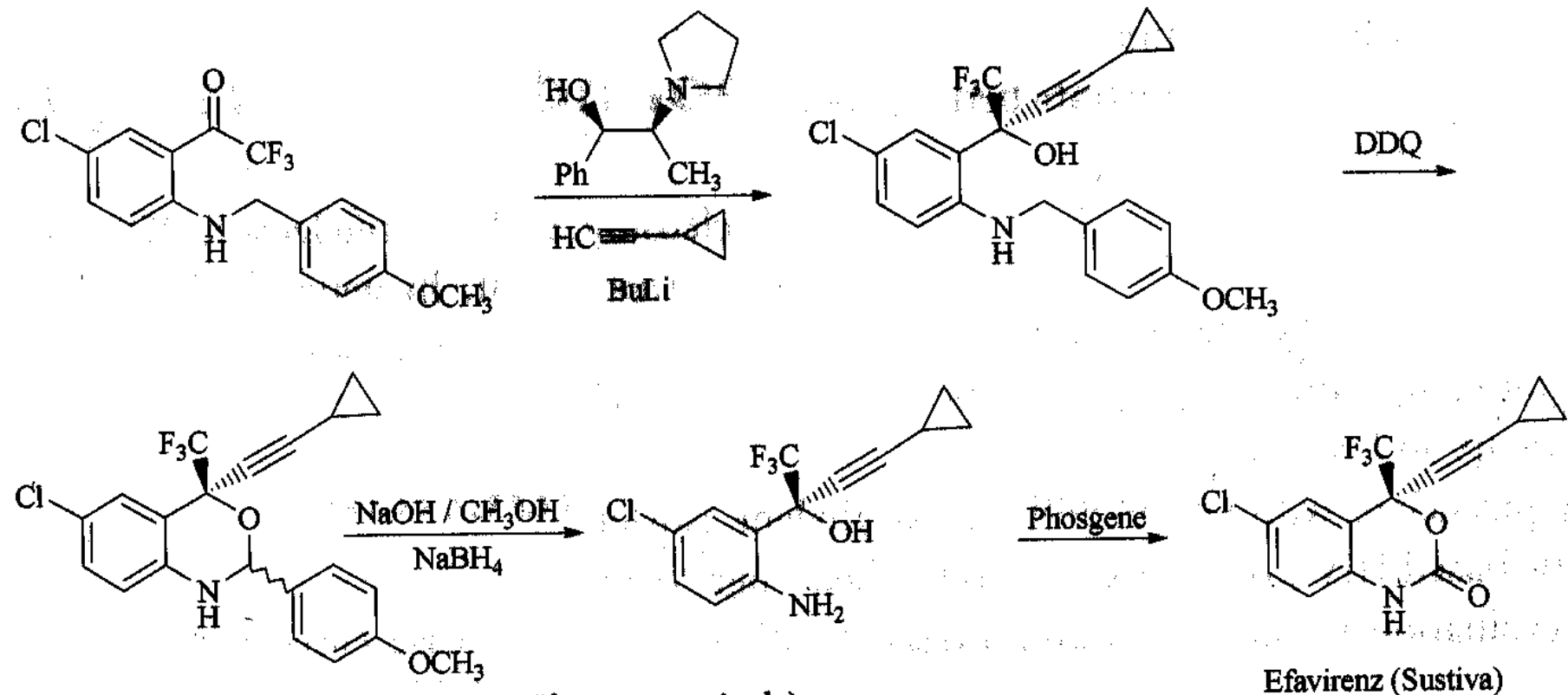


*Trade name:* Rescriptor (Pharmacia & Upjohn).

# Efavirenz



# Efavirenz

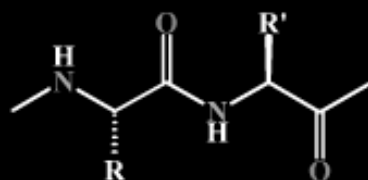


Trade name: Sustiva (DuPont Pharmaceuticals).

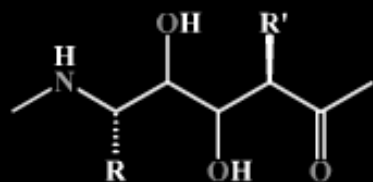
Efavirenz (Sustiva)

## D2.2.2 Mimicking the Peptidic Bond

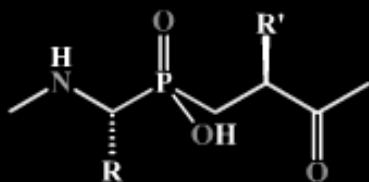
Some atoms or groups of atoms of the backbone of the peptide can be replaced by equivalent groups. The following examples are some of the most common replacements considered in backbone mimicry.



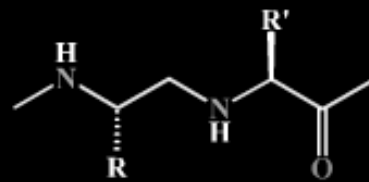
Peptide Bond



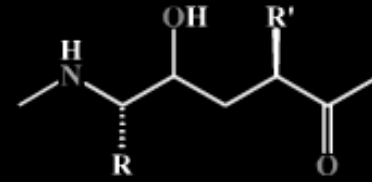
Dihydroxyethylene



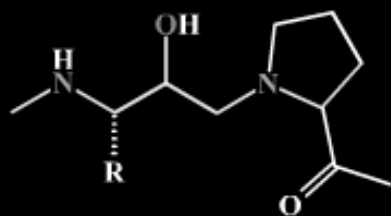
Phosphinate



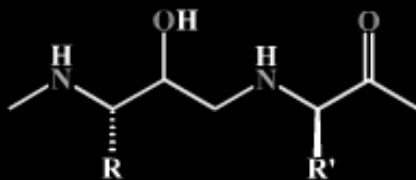
Reduced Amide



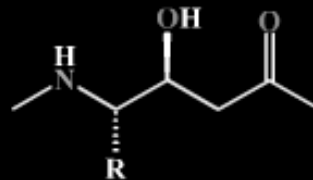
Hydroxyethylene



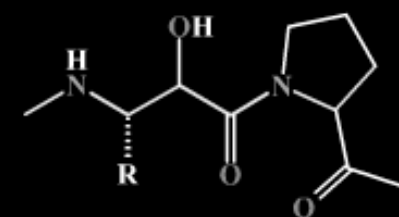
Hydroxyethylamine (R cyclic)



Hydroxyethylamine (R' acyclic)



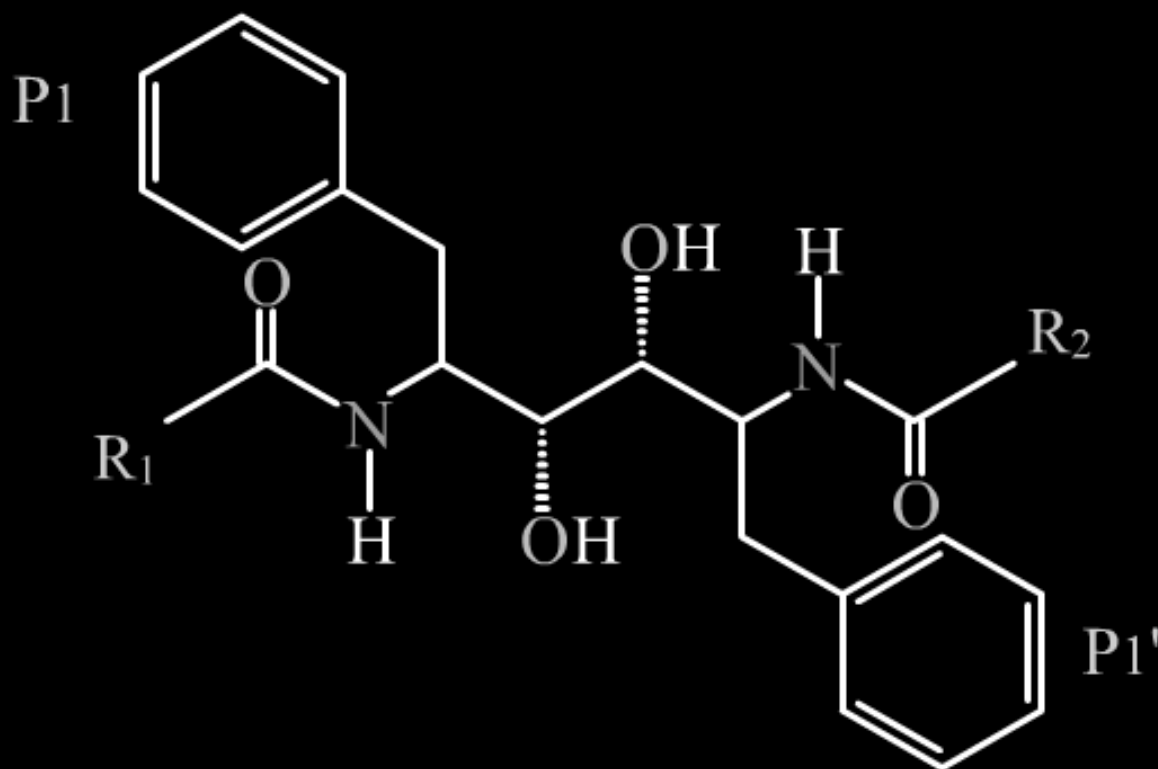
Statine



Norstatine

## D2.10.2 The Peptide Problem

Using the transition-state inhibitor approach, peptide inhibitors were conceived by replacing the scissile bond of the peptide substrate by a isostere that is not cleaved; A-77703 is an example of inhibitor containing the "dihydroxyethylene" moiety. Since these inhibitors showed low oral activity, new inhibitors with good bioavailability were designed based on a peptidomimicry approach.

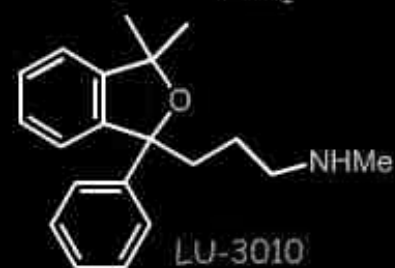
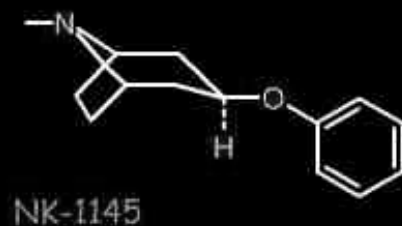
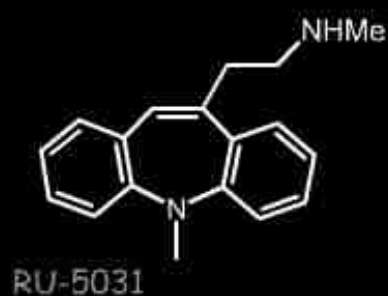


Diol Inhibitor A-77703



## C4.3.2 Reference Set of Antidepressant Molecules

The following known active structures were considered for the development of a pharmacophore model based on the discovery of novel antidepressant agents.



**Ende**