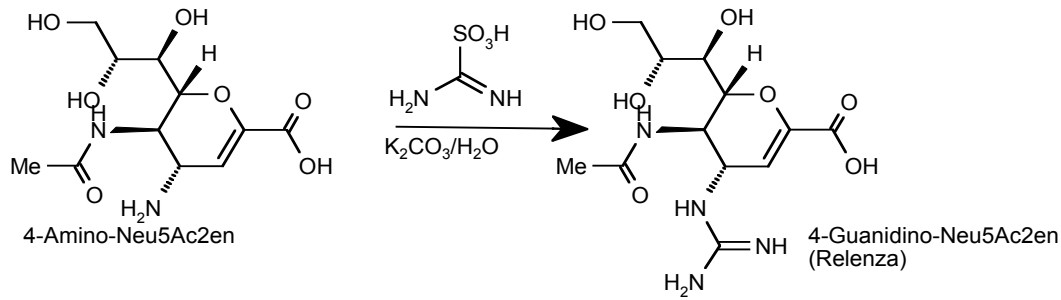
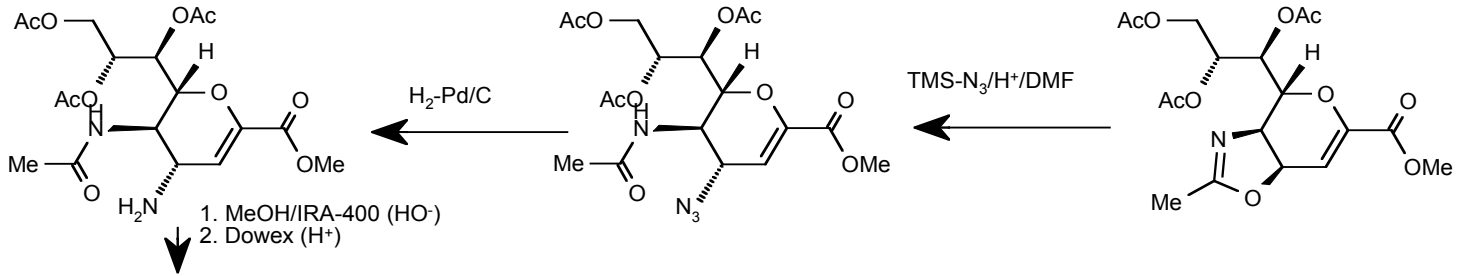
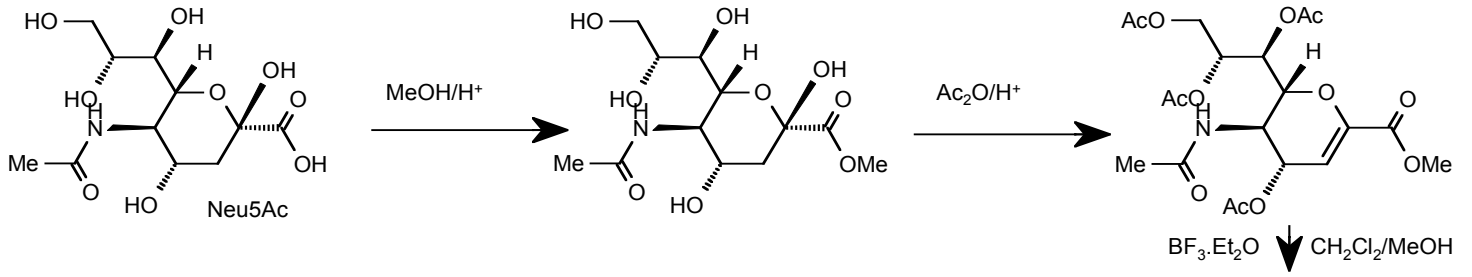
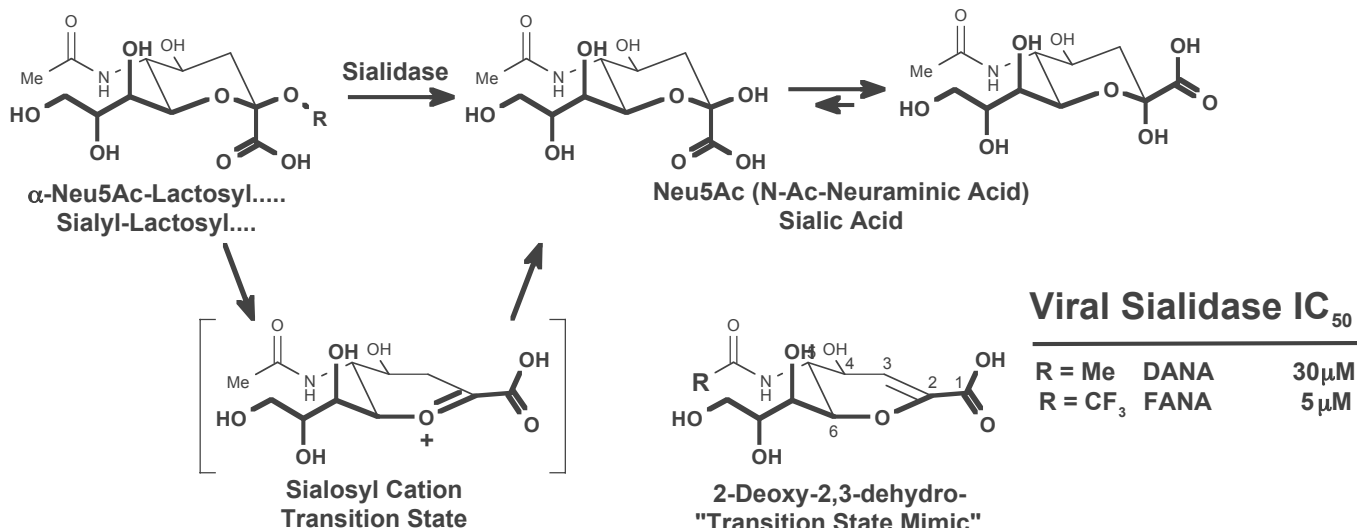


# Synthesis of Relenza

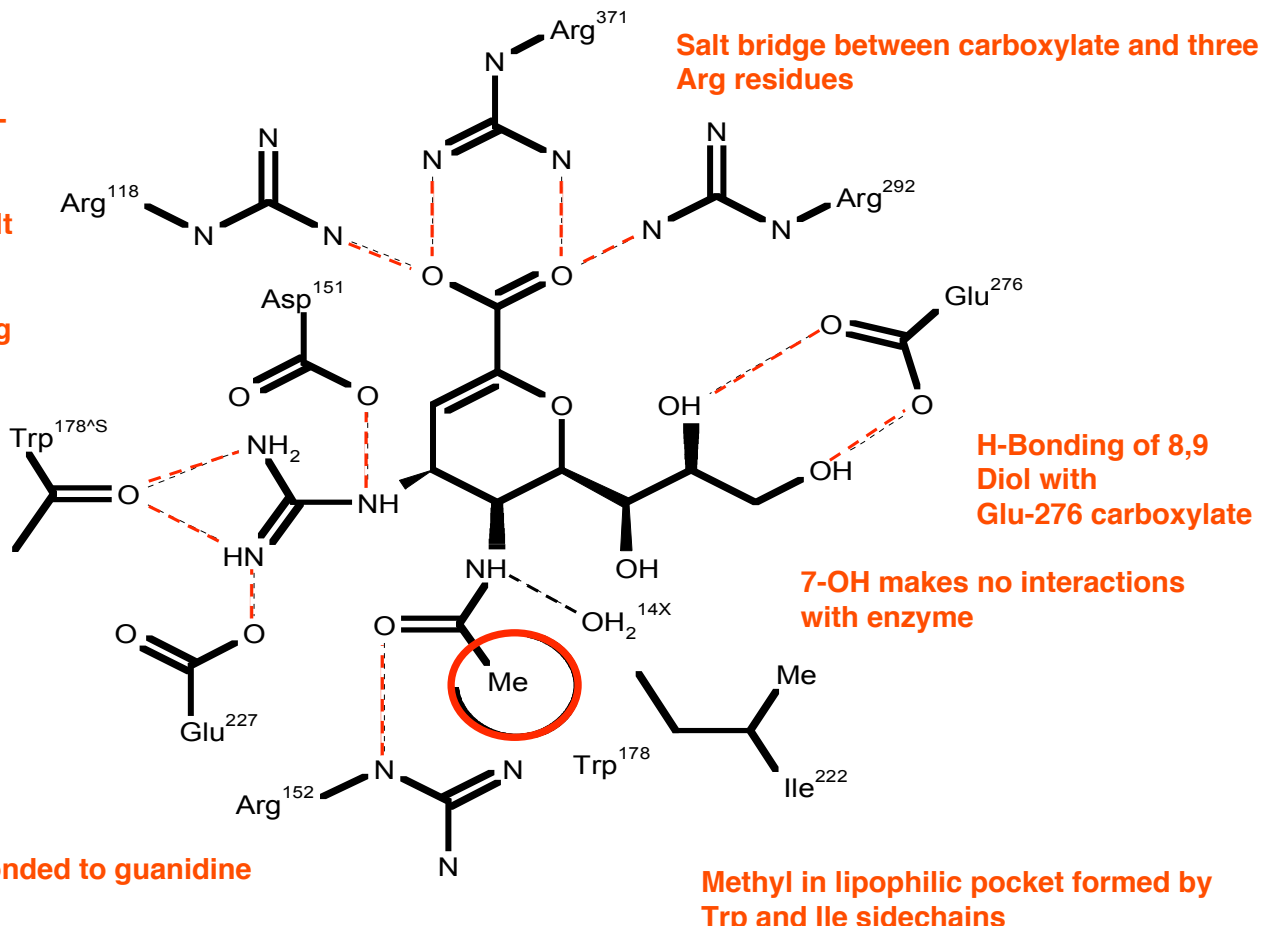


## Early Inhibitors - Transition State Mimics



## Relenza Interactions with sialidase

Guanidine H-bonded to backbone C=O, and salt bridged with neighbouring acidic sidechains



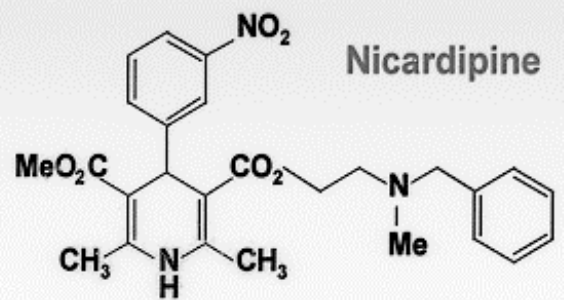
# The Road to Amlodipine...1. A Blind Alley

**Nifedipine**



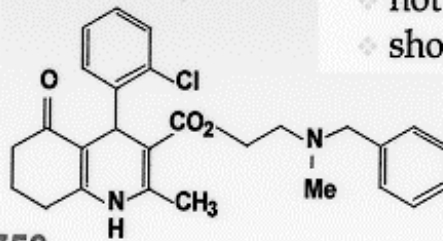
- ❖ insoluble
- ❖ photosensitive
- ❖ short  $t_{1/2}$
- ❖ low/variable absorption

**Nicardipine**



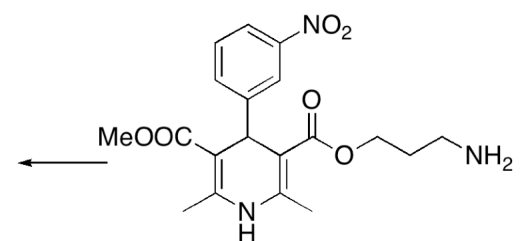
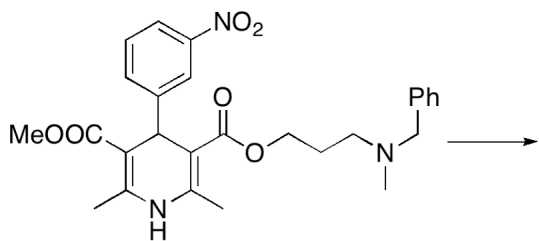
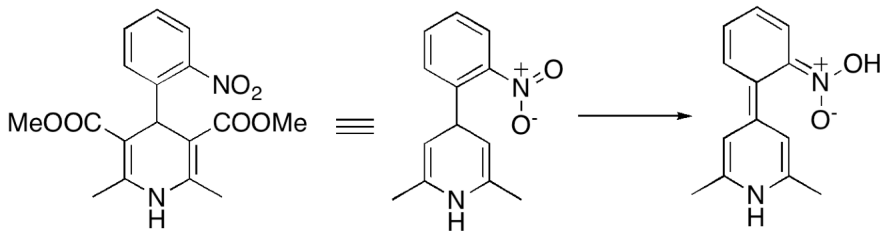
- ❖ soluble (polar side chain)
- ❖ not photosensitive
- ❖ short  $t_{1/2}$

**UK-41,753**

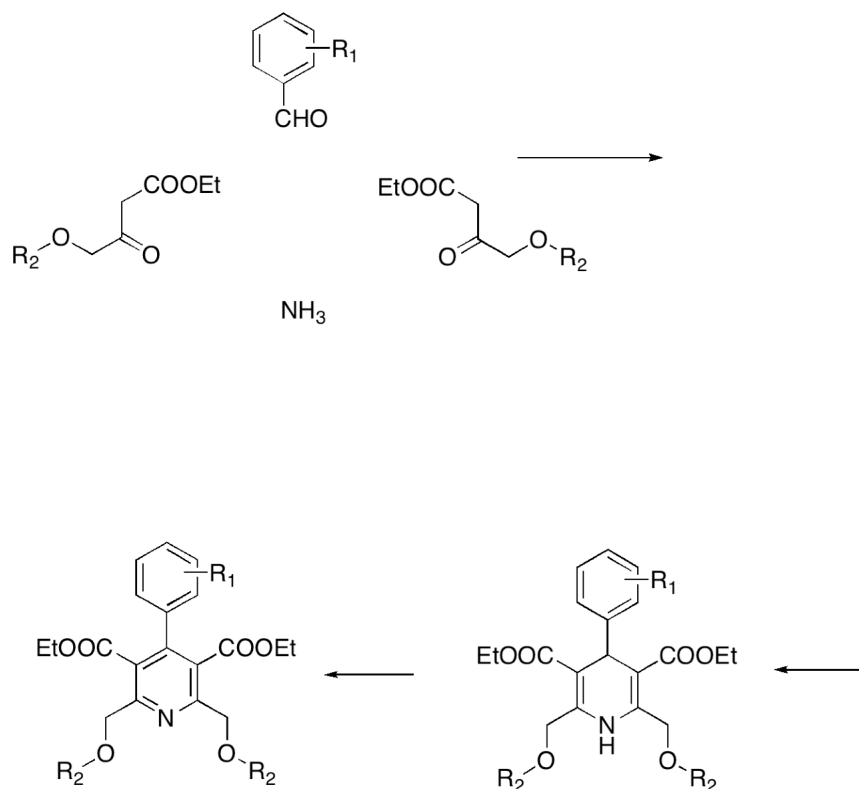


- ❖ novel, patentable
- ❖ soluble
- ❖ rapidly metabolised

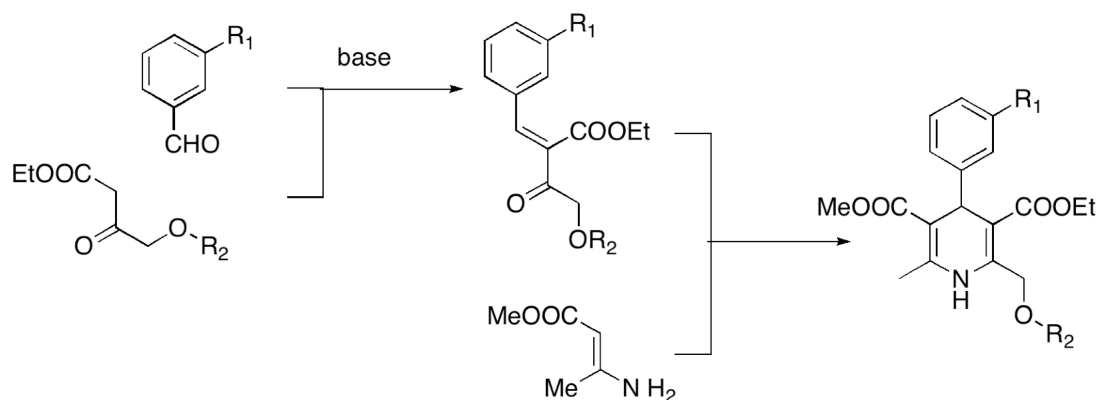
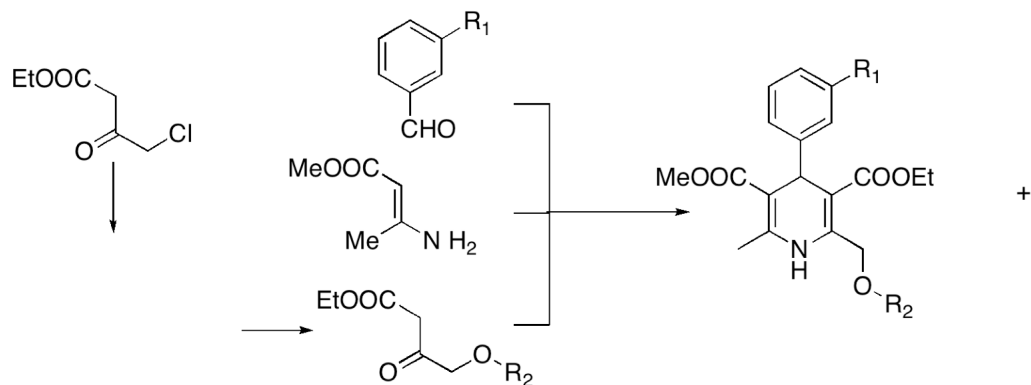
## Reasons for the Problems....



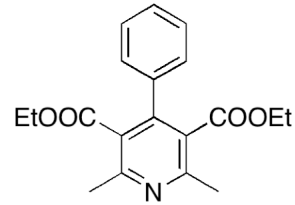
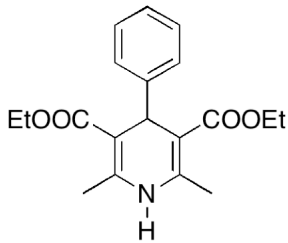
# Accessing Analogues: I've a Hunch it's a Hantsch



## Unsymmetrical Stepwise Hantsch



# DHP Oxidation Stabilization



## Amlodipine - Structural Features

*isomer activity ratio >1000*

*photostable*

