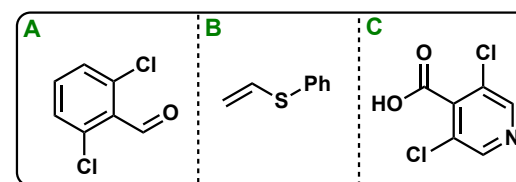


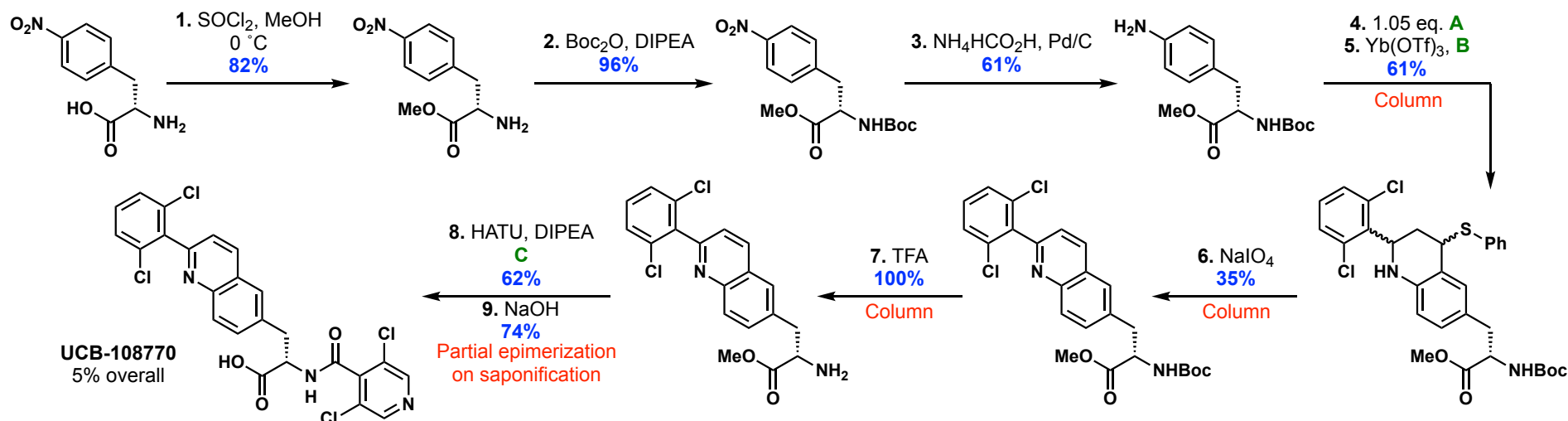


- A VLA-4 antagonist as a potential treatment for multiple sclerosis
- VLA-4 is produced by T and B cells and causes inflammation
- MS is caused by inflammation of the myelin sheath in the CNS when immune cells attack the myelin

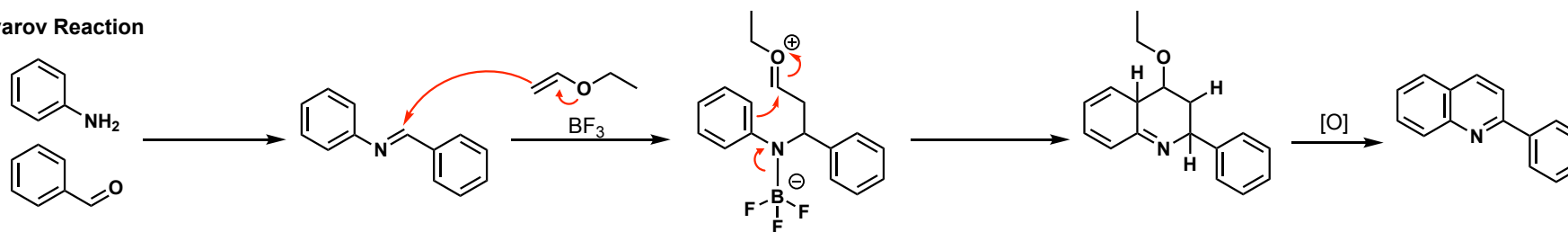
- Multikilogram synthesis meeting Good Manufacturing Practice (GMP) standards was required for toxicological studies



## Discovery

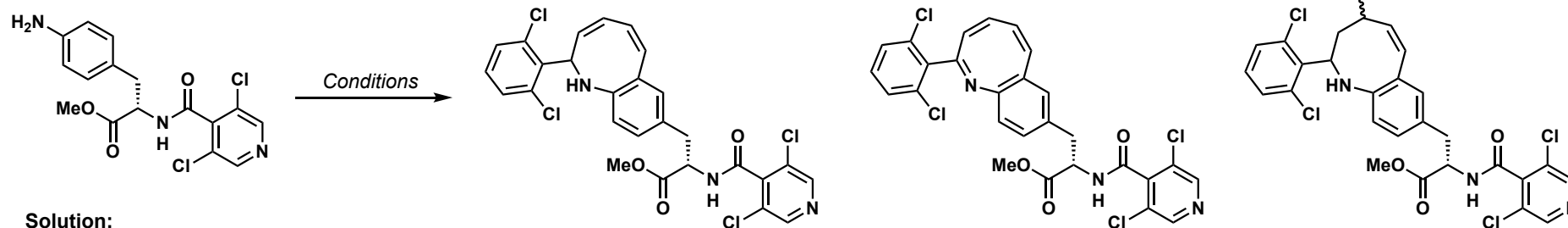


## Povarov Reaction



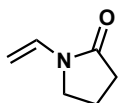
EP 1501801 A1, 2005;  
 EP 1501801 B1, 2008;  
 Org. Process Res. Dev. 2019 <https://doi.org/10.1021/acs.oprd.9b00421>

## Povarov Impurity Profile

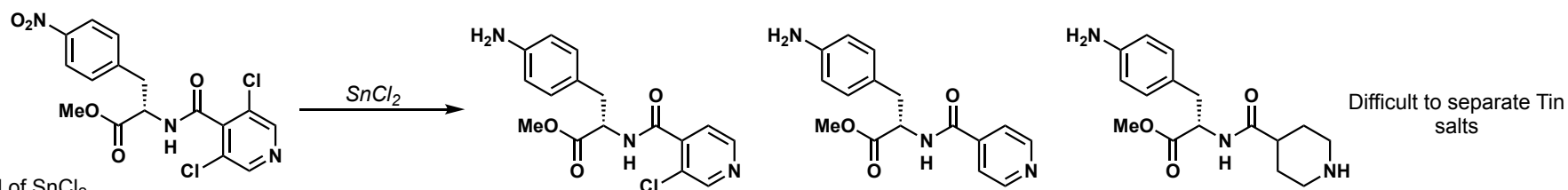


## Solution:

$\text{Ce}(\text{NH}_4)_2(\text{NO}_3)_6$  catalyst  
Different Dienophile:



## Reduction Impurity Profile



## Solution:

Pt/C instead of  $\text{SnCl}_2$   
MeOH/THF  
Low pressure  $\text{H}_2$

## GMP Route

