

Synthesis of Antitubercular Drugs

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1- Stereocontrolled Synthesis Of Lincomycin and clindomycin

2- Synthesis Of Ethambutol.

3- Synthesis Of Isoniazid.

4- Synthesis Of Pyrazinamide.

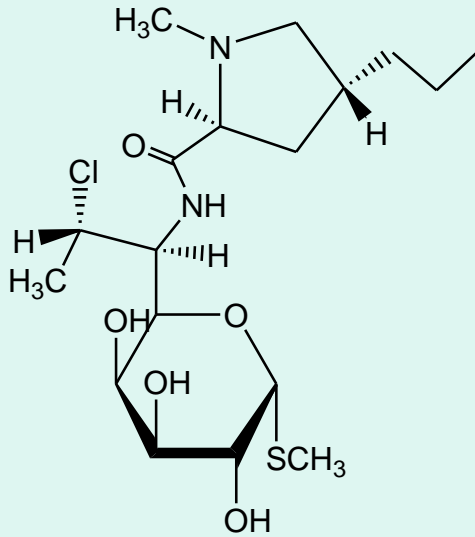
5- Synthesis of Nitroimidazofuran and nitroimidazopyran derivatives.

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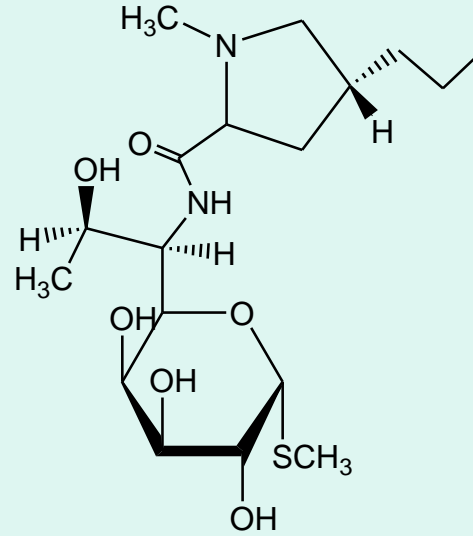
7- Synthesis Of Thiolactomycin.

8- Synthesis of Oxazolidinones Analogs.

Two simple but important aminoglycosides



Clindomycin

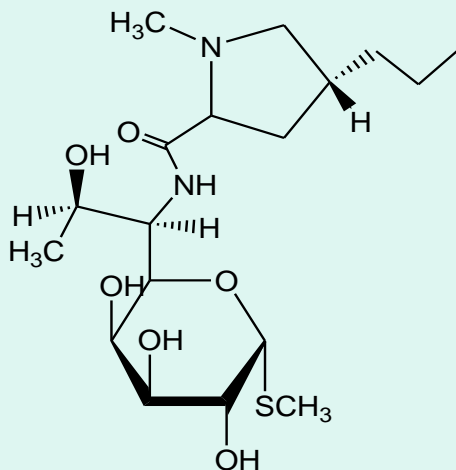


Lincomycin

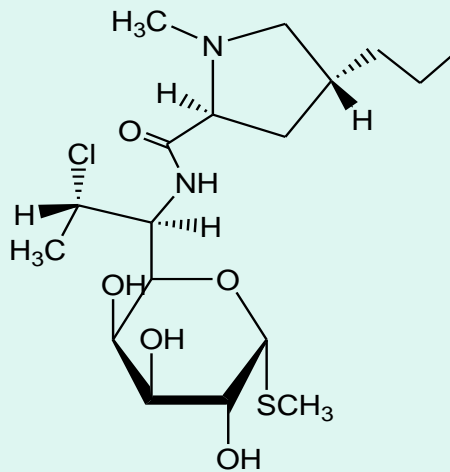
7(*S*)-Chloro-7-deoxylincomycin; Cleocin, or 7-deoxy-7(*S*)-Chlorolincomycin or (2*S-trans*)methyl-7-chloro-6,7,8-trideoxy-6-[[[1-Methyl-4-propyl-2-pyrrolidiny]carbonyl]amino]-1-thio-β-threo-α-D-galacto-octopyranoside]

- Lincomycin was first isolated in 1964 from cultures of *Streptomyces lincolensis*.
- Clindamycin is a semisynthetic analogue of natural antibiotic lincomycin and is prepared by chloro substitution of 7-OH of lincomycin.
- Hydrochloride salt of Clindamycin is used in the treatment of serious infections caused by gram-(+) bacteria.
- It is also helpful against protozoans such as *Toxoplasma* and *P. falciparum*.
- Clindamycin has 4-8 times more activity than lincomycin.
- Its mode of action involves inhibition of bacterial protein synthesis by binding the 50s ribosomal subunit.
- Side effects: Stomach upset and vomiting.

Stereocontrolled Synthesis Of Lincomycin



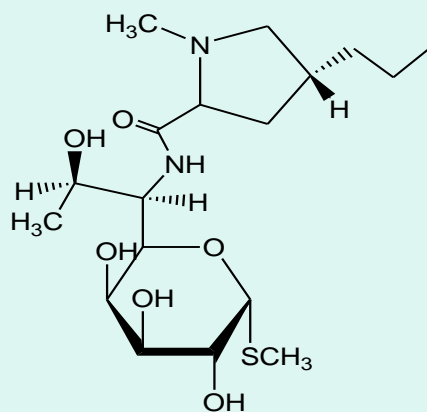
Lincomycin



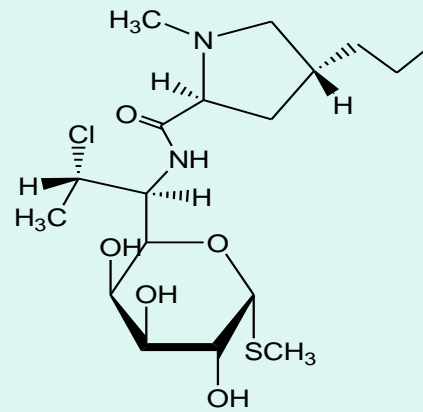
Clindomycin

- 1. Synthesis of Lincosamine
- 2. Synthesis of Thiomethyl lincosaminide
- 3. Synthesis of L-trans-n-propylhygric acid

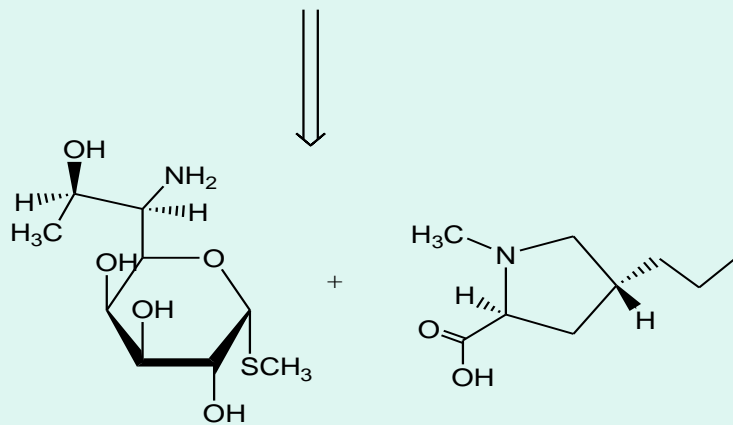
Retrosynthesis of Lincomycin



Lincomycin



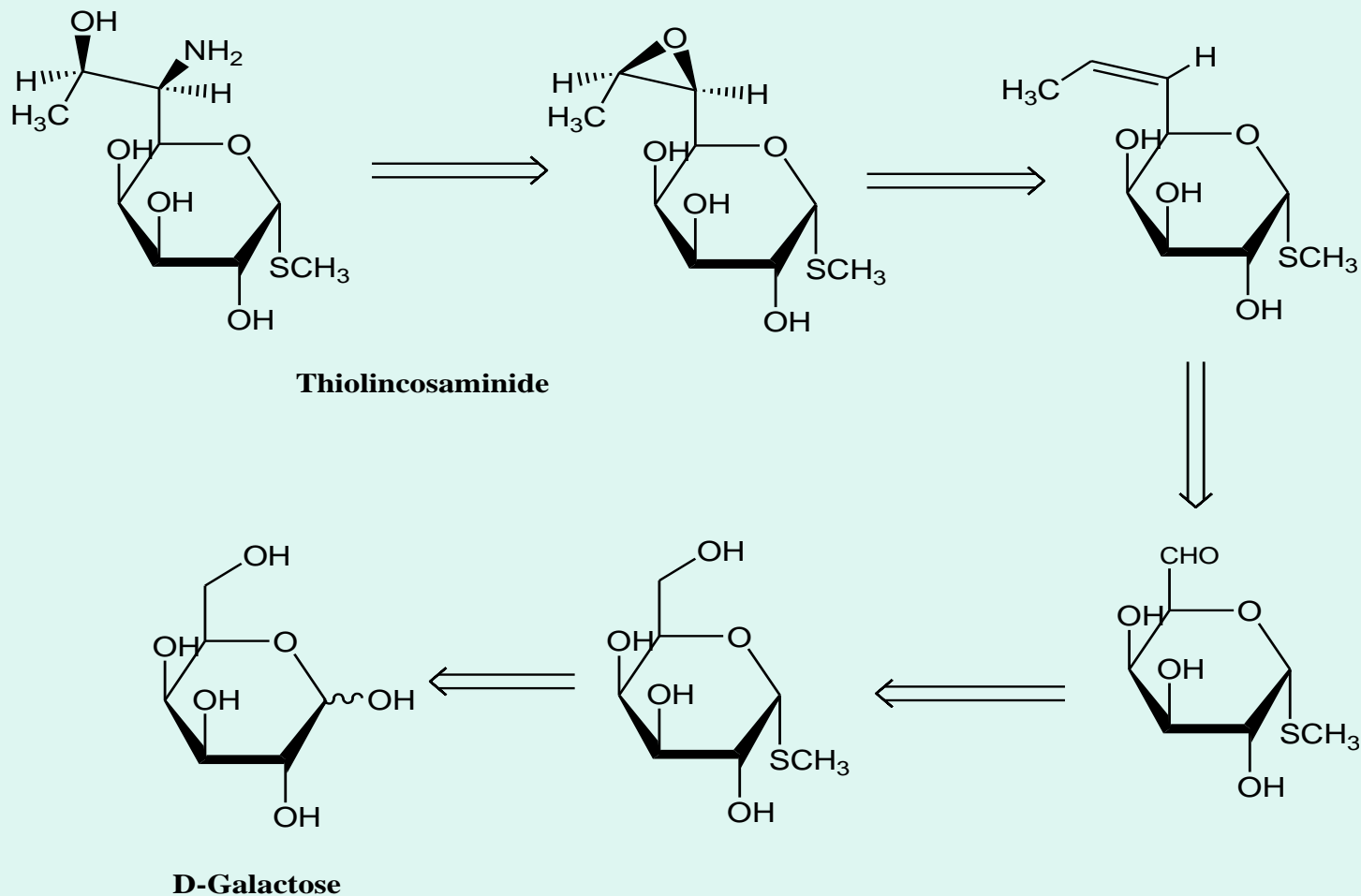
Clindomycin



Thiolincosaminide

L-Trans-*n*-propylhygric acid

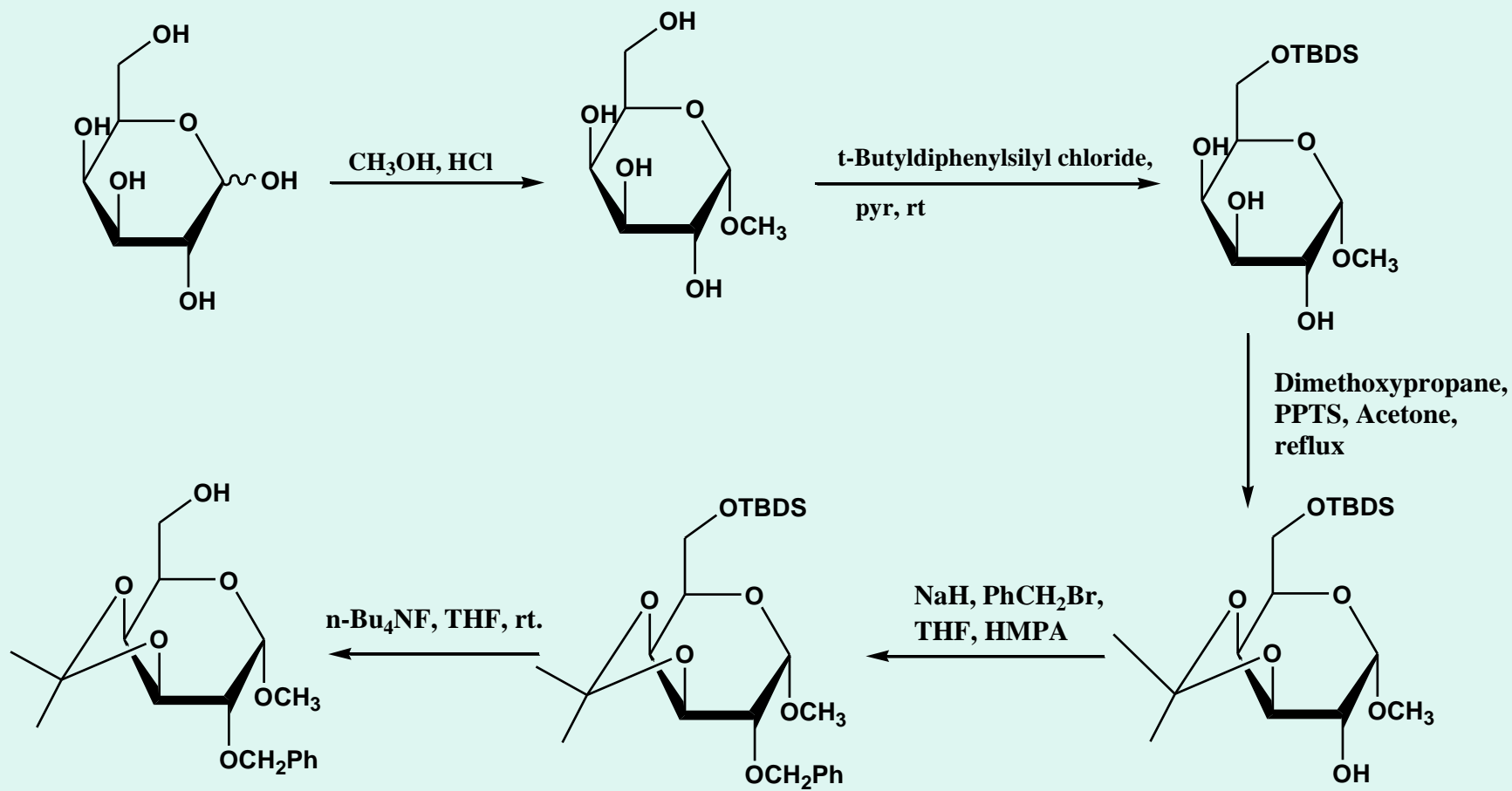
Retro-Synthesis of thiolincosaminide

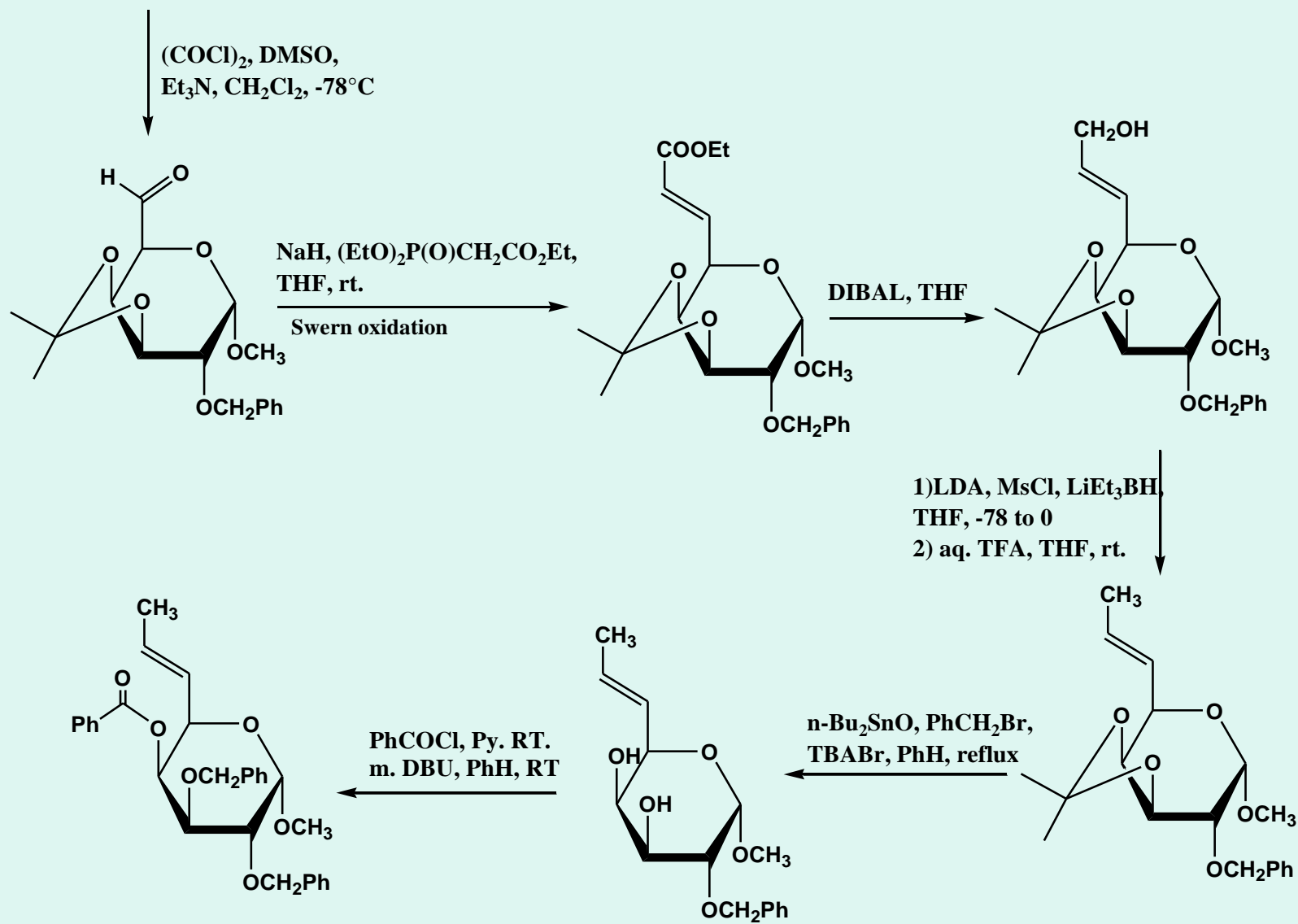


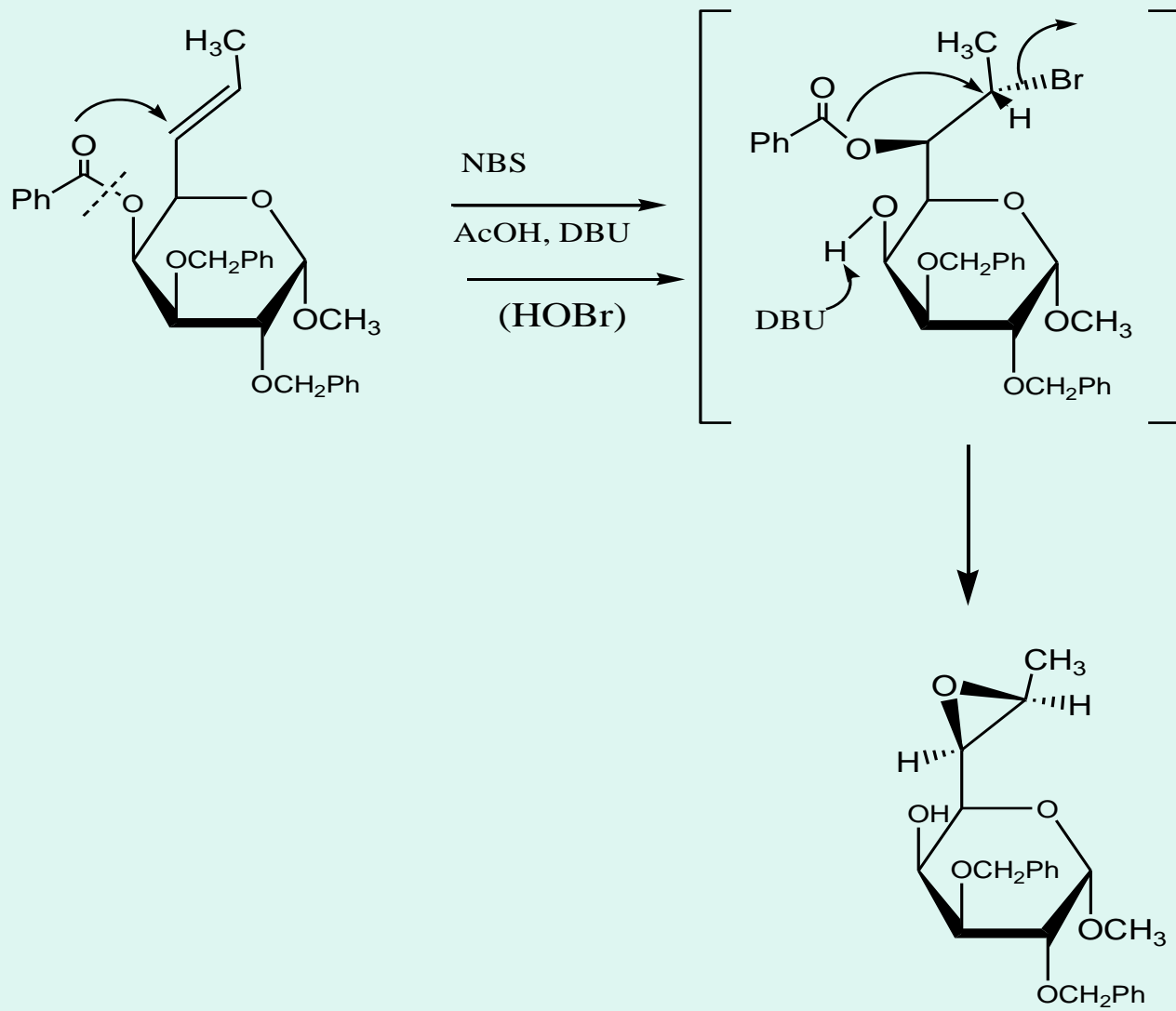
Synthesis of thiolincosaminide

- 1. Synthesis of Epoxy alcohol substrate
- 2. Intramolecular Nitrogen Delivery
- 3. Synthesis of lincosamine hexaacetate
- 4. Introduction of thiomethyl group
- 5. Conversion of Oxazoline derivative into thiomethyl lincosaminide

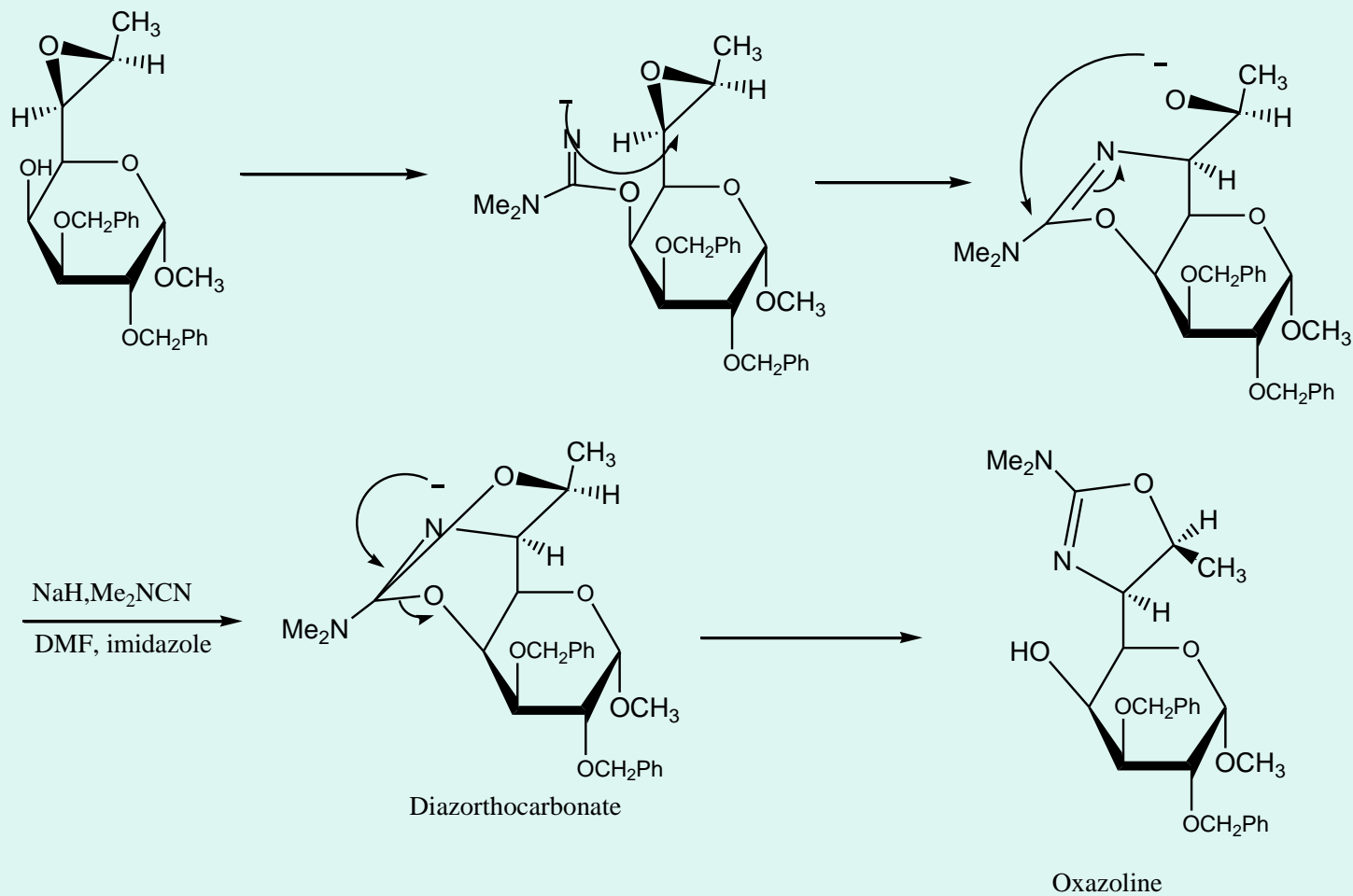
Synthesis of Epoxyalcohol

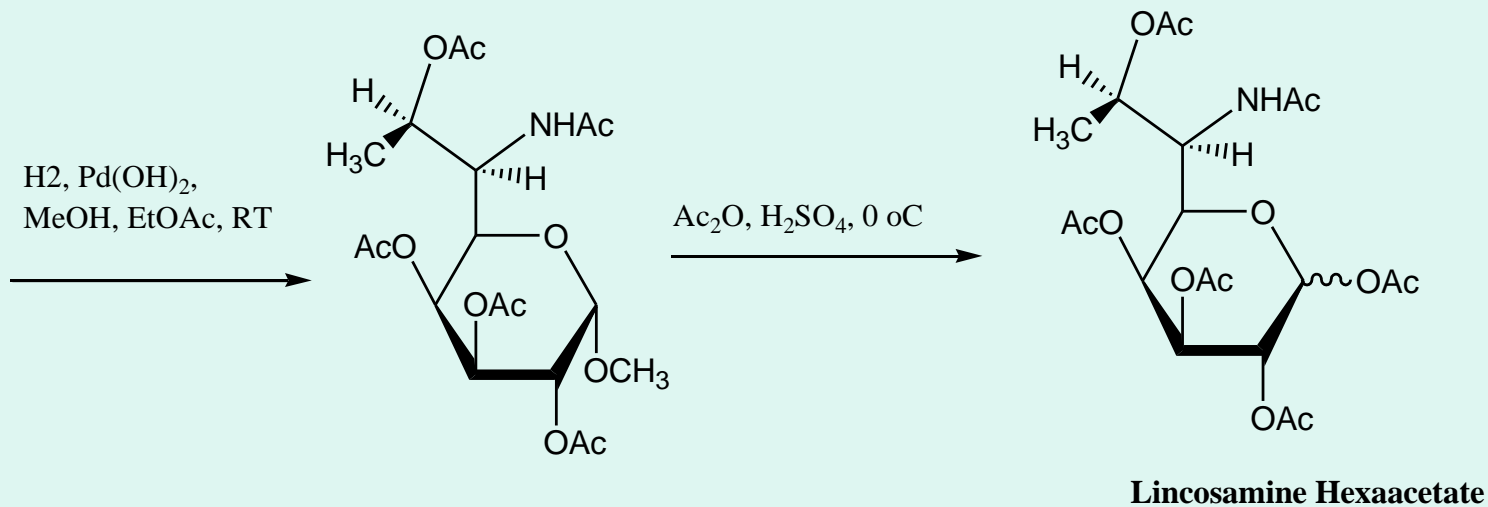
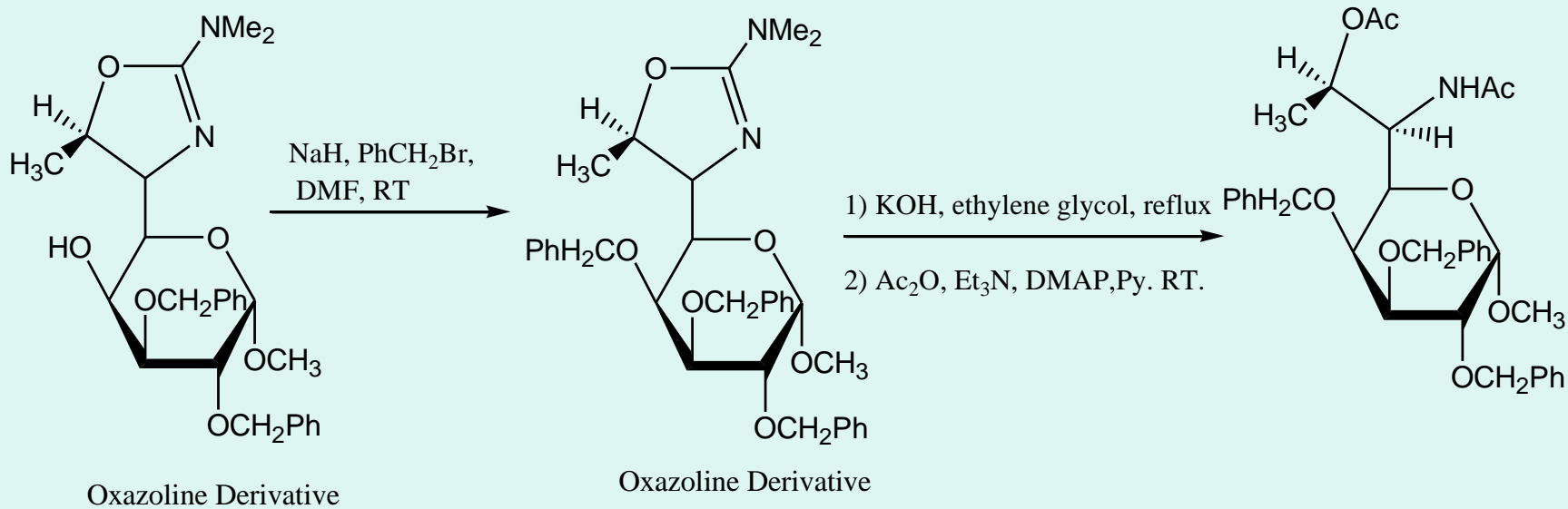




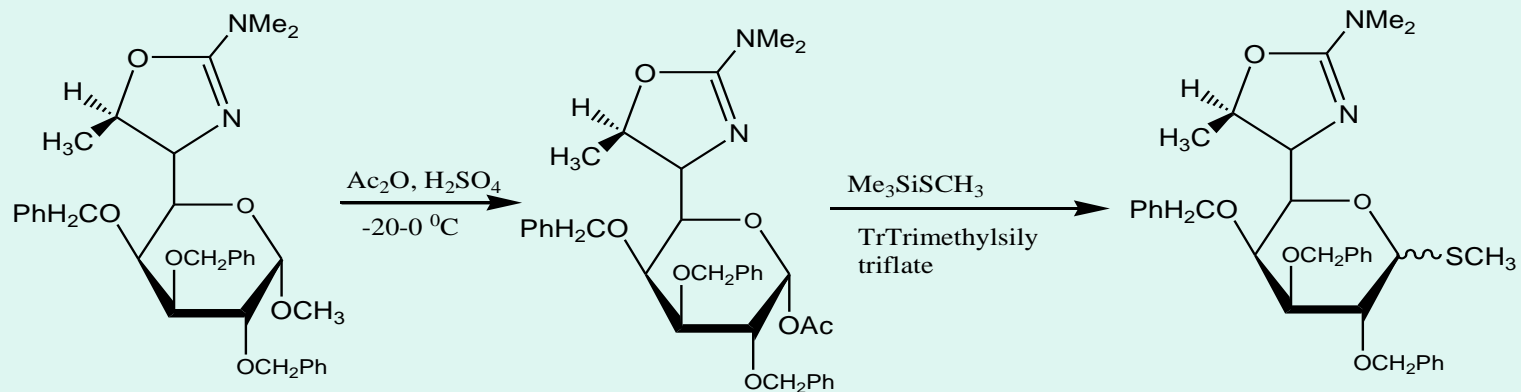


Synthesis of Oxazoline Derivative

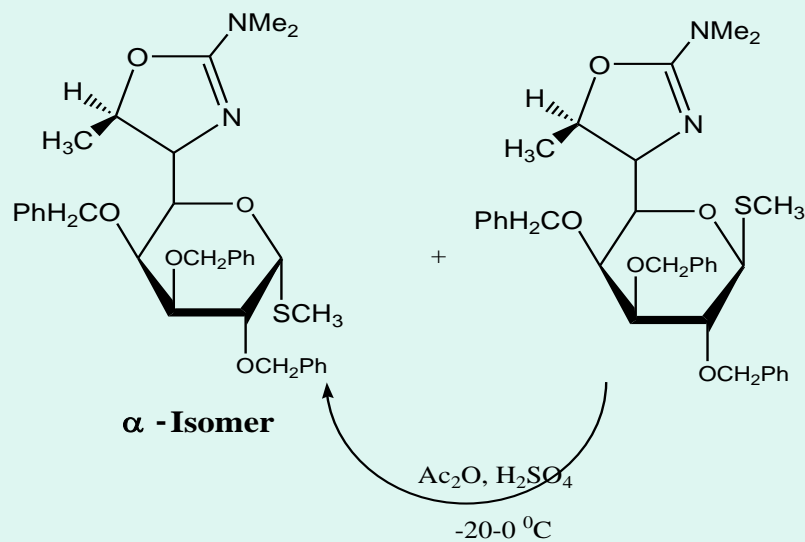




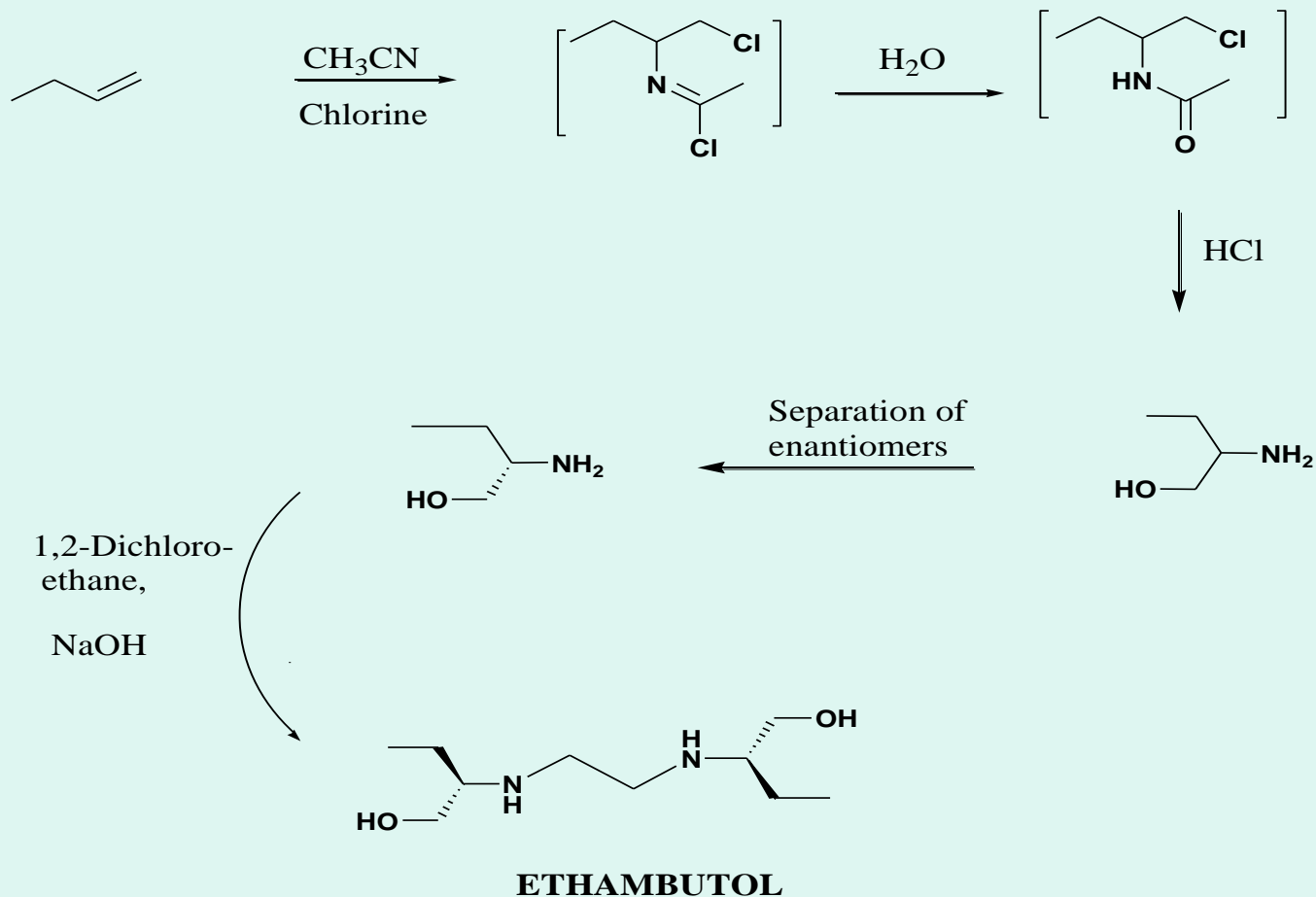
Introduction of thiomethyl group



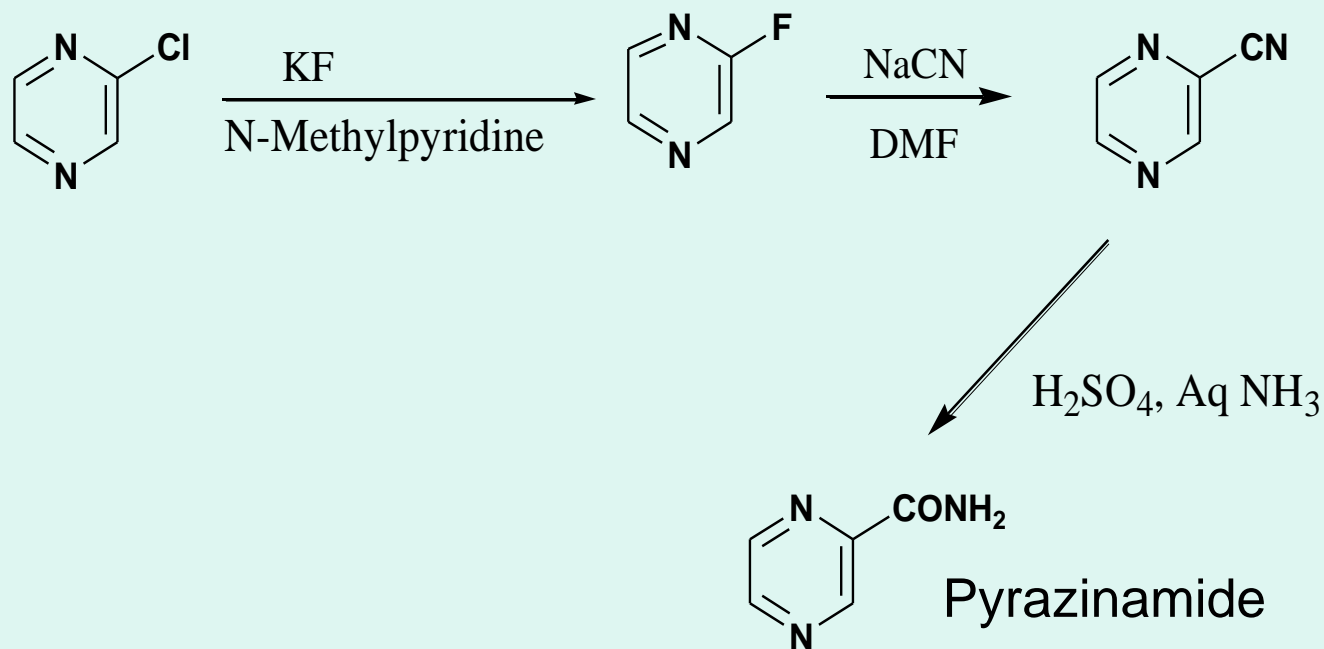
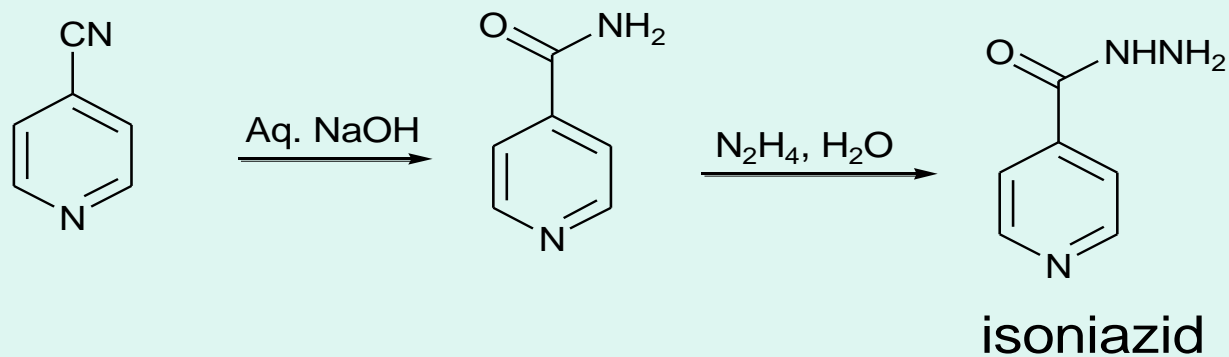
↻ **α - Isomer**
↻ **β - Isomer**



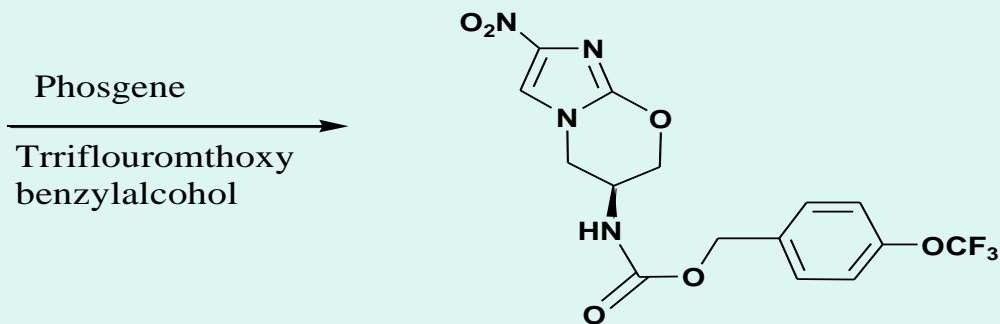
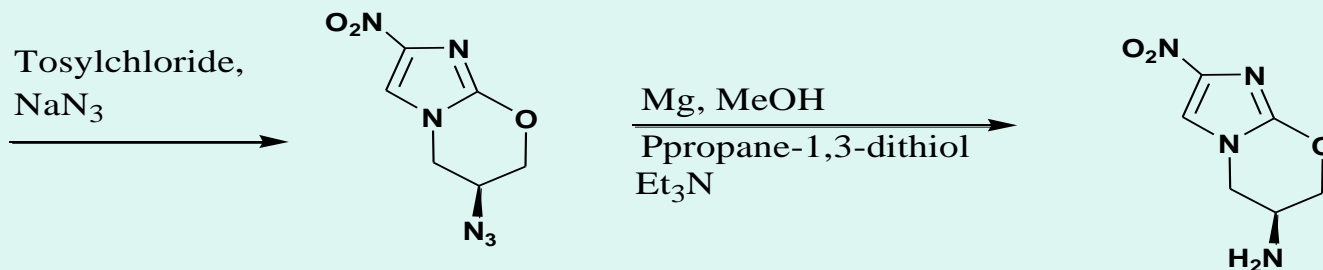
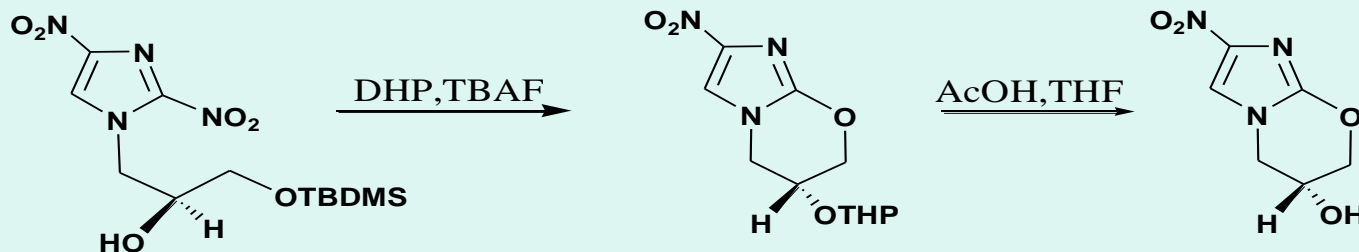
Synthesis Of Ethambutol



Synthesis of isoniazid and Pyrazinamide

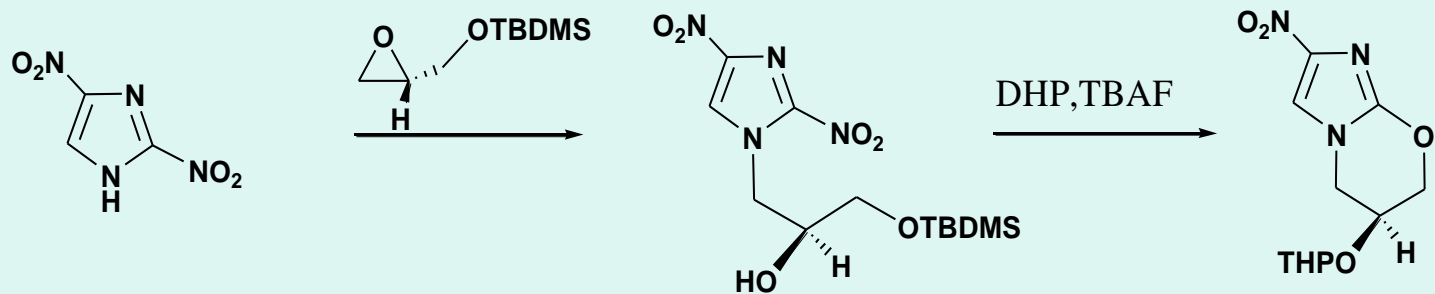


Synthesis of Nitroimidazofuran and nitroimidazopyran derivatives.

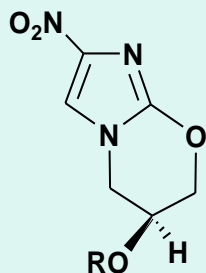


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Synthesis of Nitroimidazofuran and nitroimidazopyran derivatives

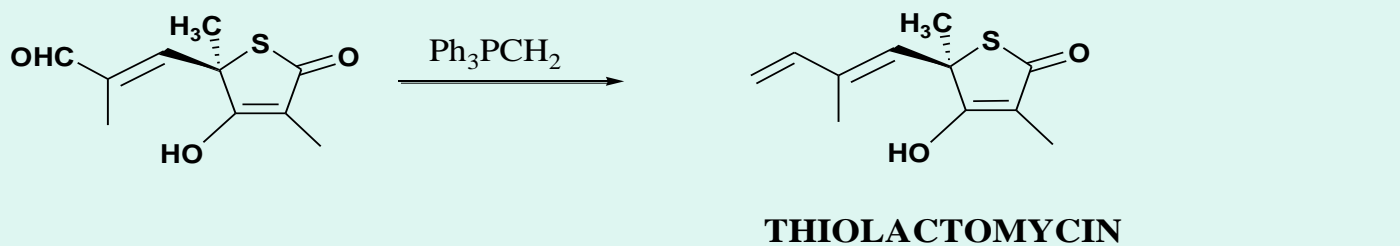
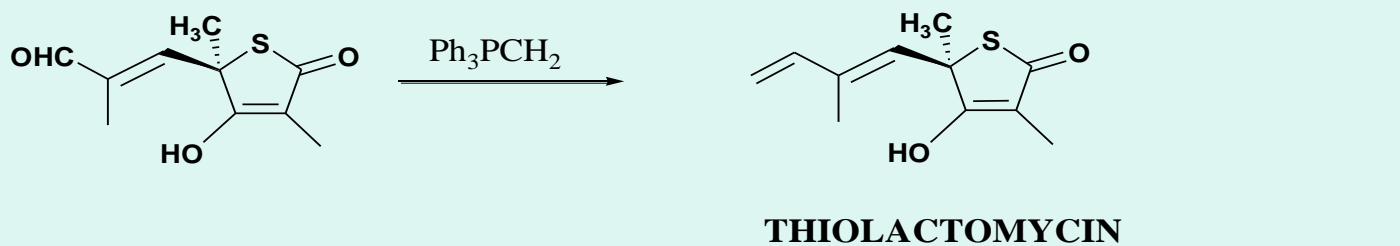
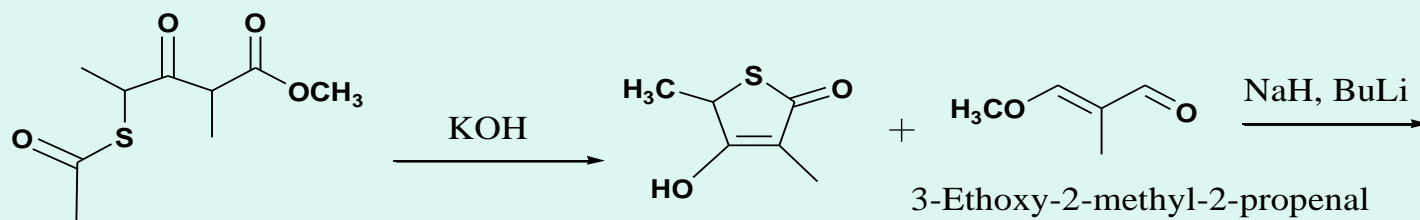
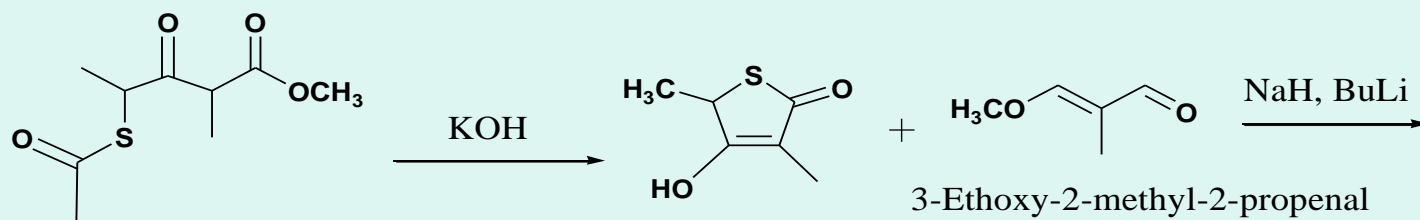
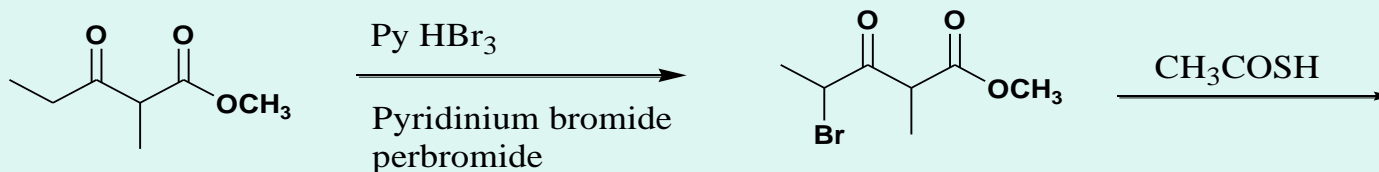


1. HCl,
2. Base, Alkylation



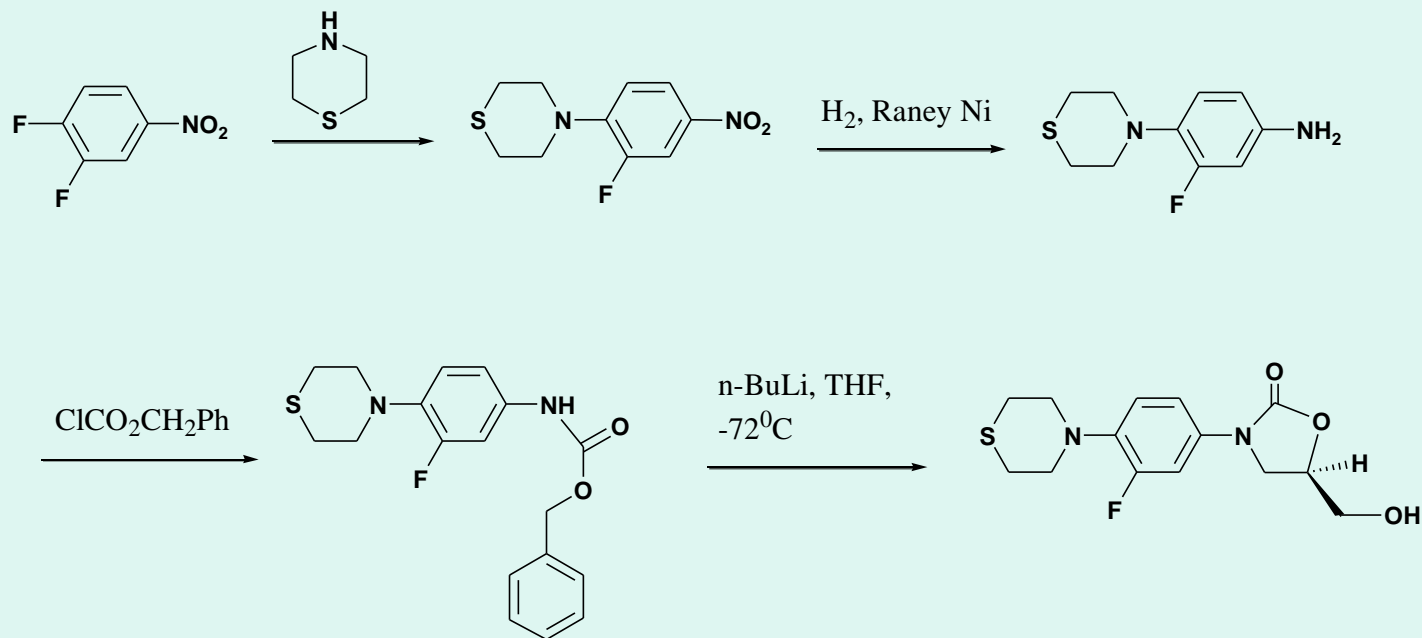
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 $R = \text{CH}_2\text{C}_6\text{H}_4\text{-OCF}_3$

Synthesis Of Thiolactomycin.

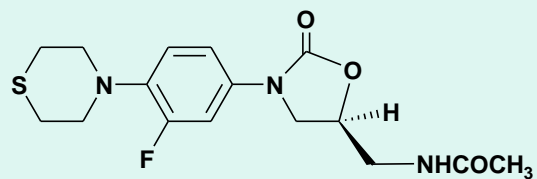


THIOLACTOMYCIN

Synthesis of Oxazolidinones Analogs.



1. Tosylchloride
2. NaN₃
3. Ph₃P
4. H₂O, Heat
5. Ac₂O, Pyridine



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