

Antihypertensive agents: Classification and Synthesis

SUBJECT- PHARMACEUTICAL CHEMISTRY-VII (4T2)

JAGDEESH AHIRWAR

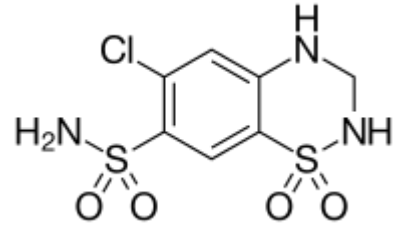
ASST. PROF. (CONTRACT)

**SOS in Pharmaceutical Sciences, Jiwaji University,
Gwalior**

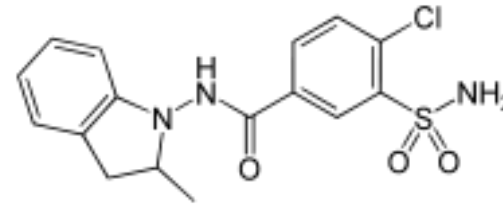
Classification

1. Diuretics-

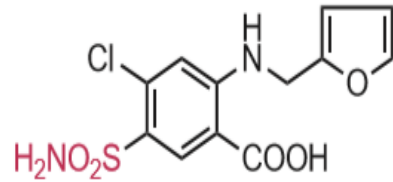
Thiazides: Hydrochlorothiazide



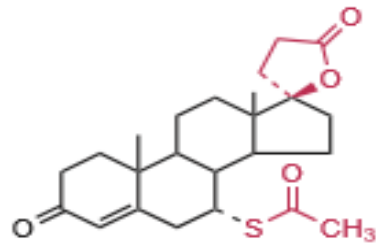
Indapamide



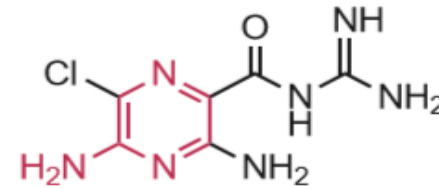
High ceiling: Furosemide.



K⁺ Sparing: Spironolactone

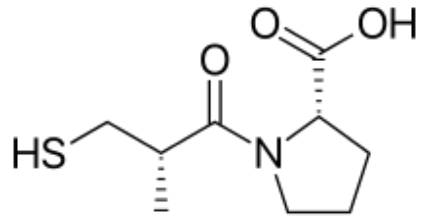


Amiloride

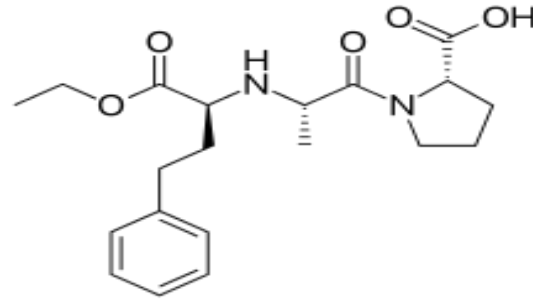


2. ACE inhibitors-

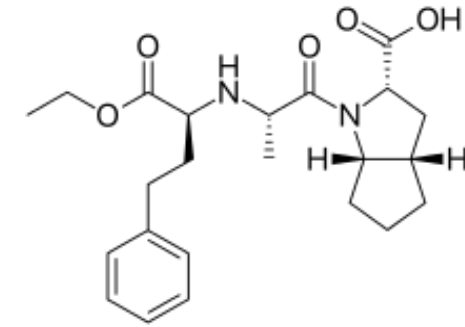
Captopril



Enalapril

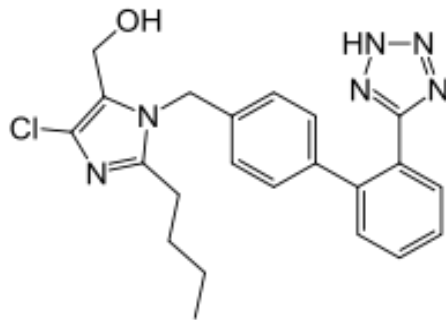


Ramipril

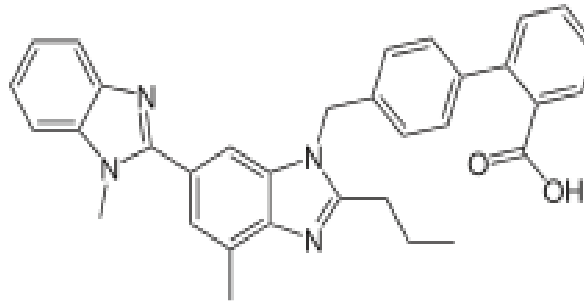


3. Angiotensin (AT1 receptor) blockers-

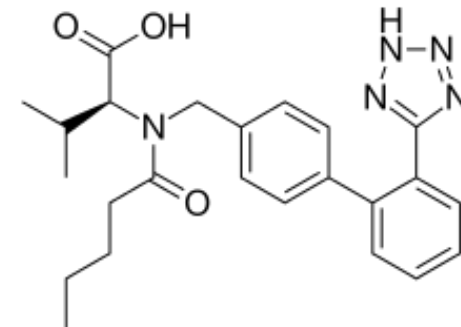
Losartan



Telmisartan

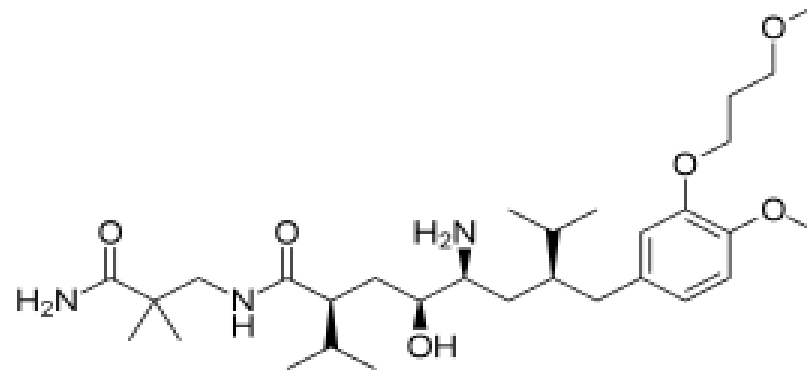


Valsartan



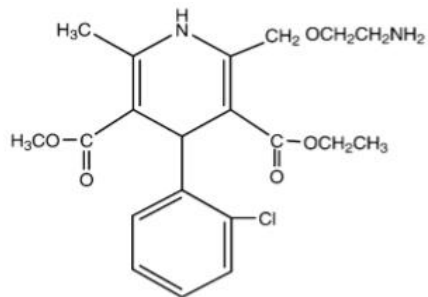
4. Direct renin inhibitor-

Aliskiren



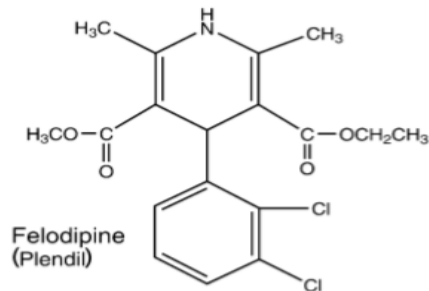
5. Calcium channel blockers-

Amlodipine



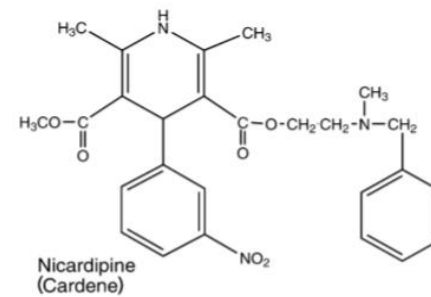
Amlodipine

Felodipine



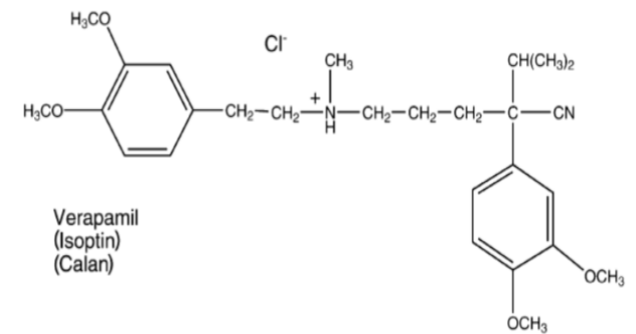
Felodipine
(Plendil)

Nicardipine



Nicardipine
(Cardene)

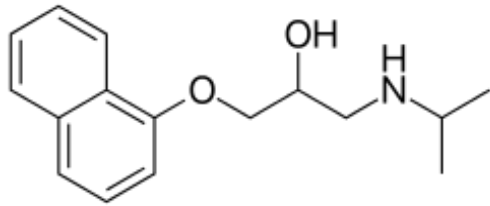
Verapamil



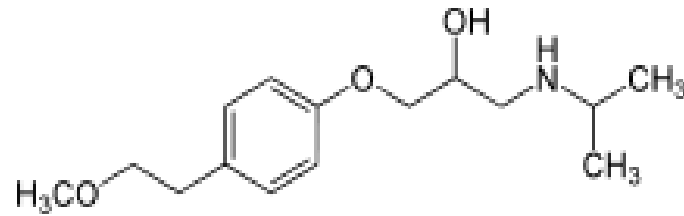
Verapamil
(Isoptin)
(Calan)

6. β - Adrenergic blockers-

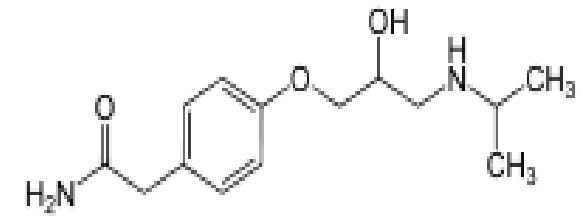
Propranolol



Metoprolol

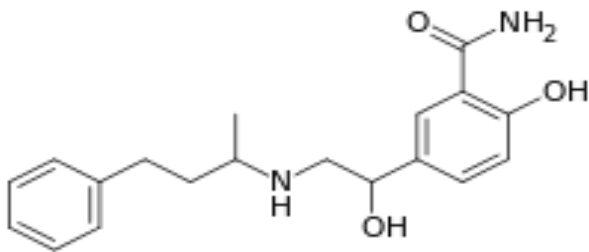


Atenolol

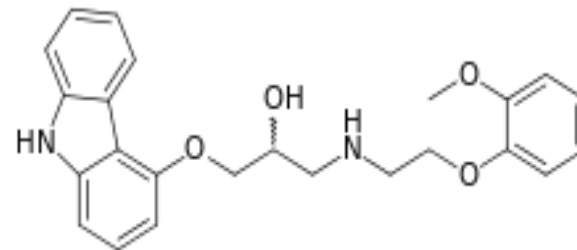


7. β + α - Adrenergic blockers-

Labetalol

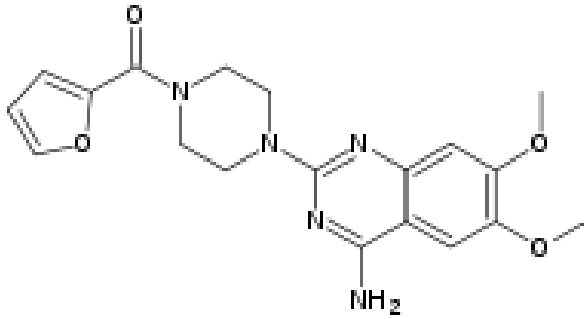


Carvedilol

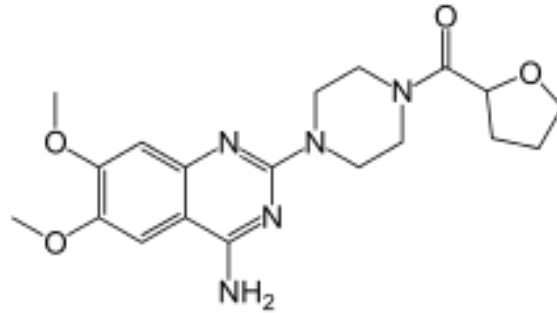


8. α -Adrenergic blockers-

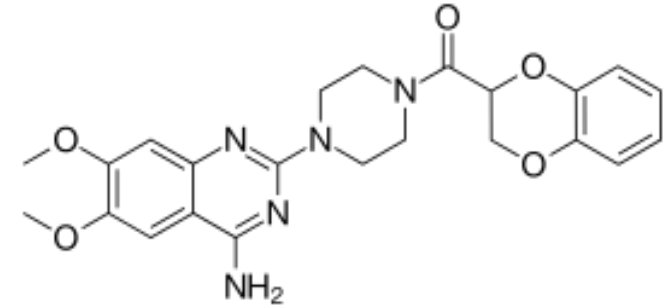
Prazosin



Terazosin

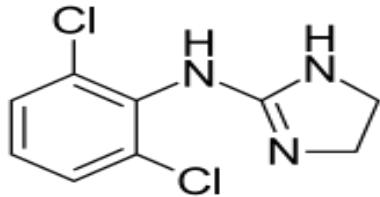


Doxazosin

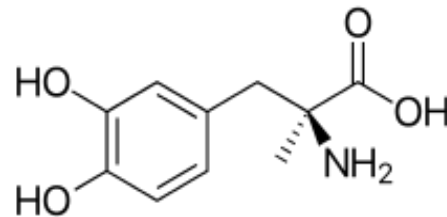


9. Central sympatholytic-

Clonidine

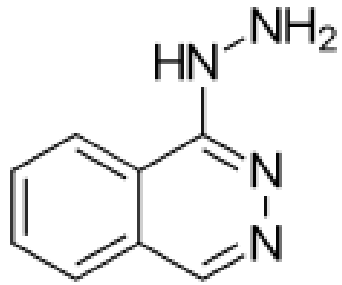


Methyldopa

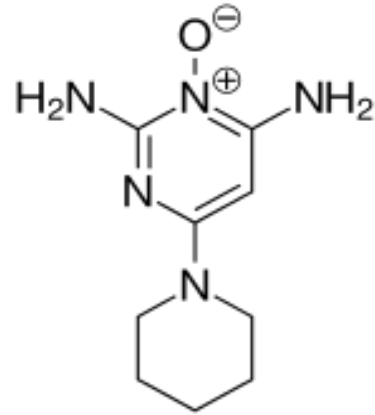


10. Vasodilators-

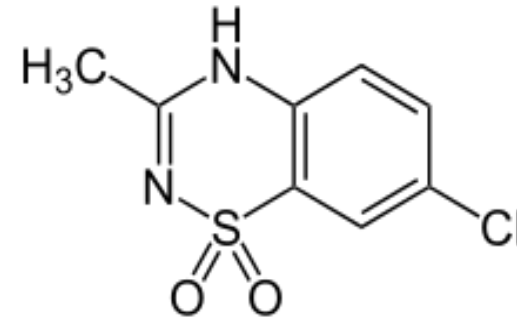
Hydralazine



Minoxidil

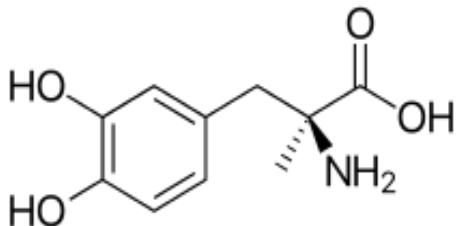


Diazoxide



Synthesis of Methyldopa

Structure-

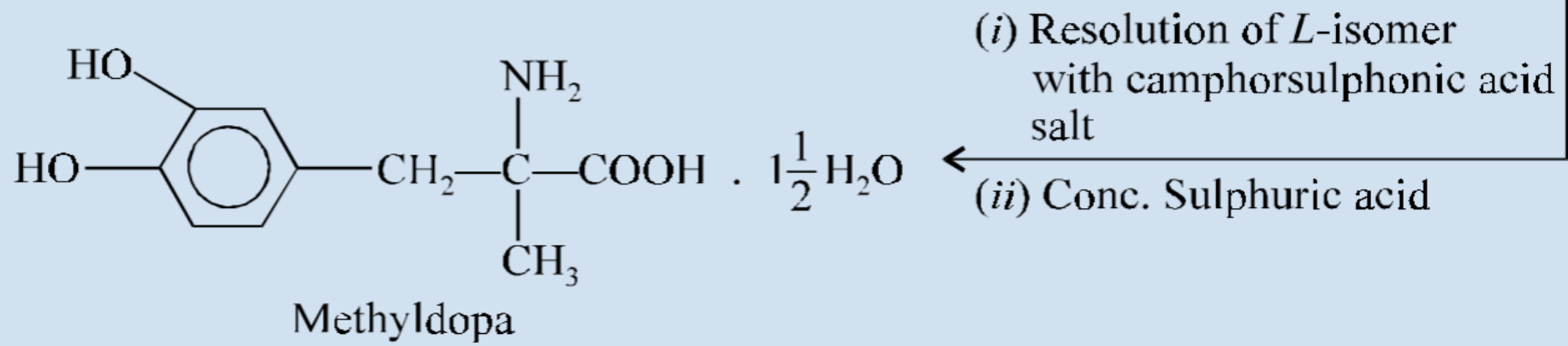
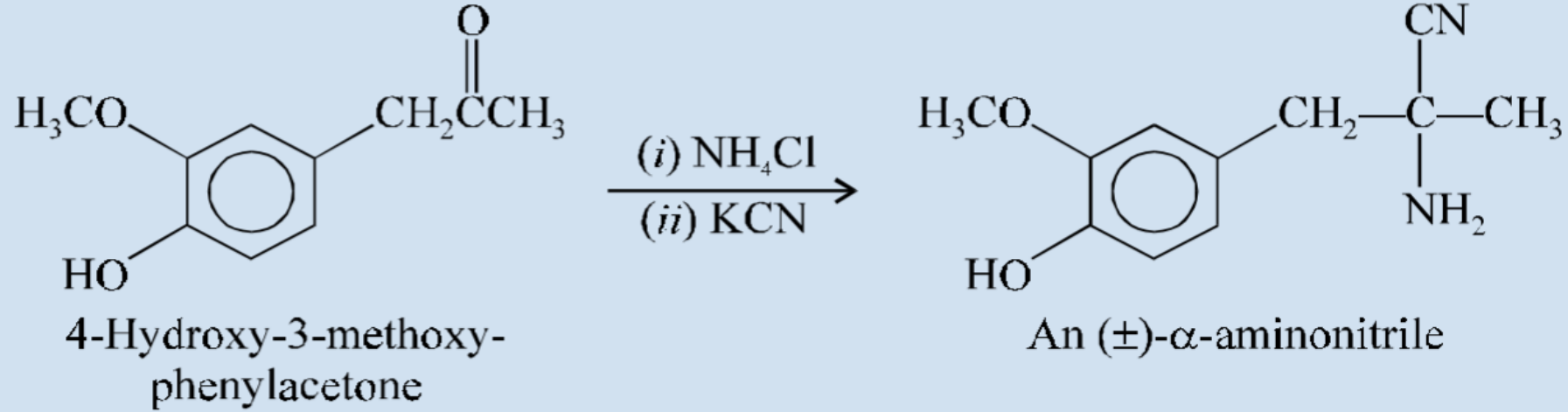


IUPAC Name- α-methyl-3-hydroxy-L-tyrosine

Properties-

- Methyldopa appears as colourless or almost colourless crystals or white to yellowish-white fine powder.
- It is soluble in water Isopropanol, ethanol, it is hygroscopic in nature and decomposed by oxidizing agents.
- Absorption from the gastrointestinal tract is variable but averages approximately 50%.
- Methyldopa is extensively metabolized. Approximately 70 percent of the drug which is absorbed is excreted in the urine as methyldopa and their conjugates.
- Antihypertensive effect develops over 4–6 hours and lasts for 12–24 hours.

Synthesis



Mechanism of action

Methyldopa is a prodrug and is metabolized in the central nervous system. The antihypertensive action of methyldopa seems to be attributable to its conversion into alpha methyl norepinephrine, which is a potent alpha-2 adrenergic agonist that binds to and stimulates potent central **inhibitory alpha-2 adrenergic receptors**. This results in a decrease in sympathetic outflow and decreased blood pressure.

Uses-

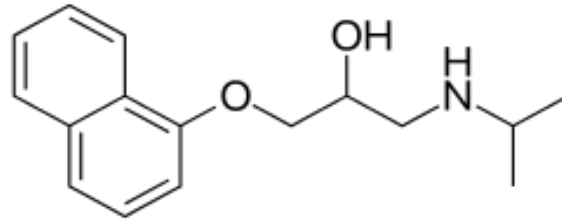
- Adrenergic alpha-Agonists; Antihypertensive Agents; Sympatholytic
- Methyldopa is indicated in the treatment of moderate to severe hypertension, including that complicated by renal disease.
- Methyldopa is an effective antihypertensive agent when given in conjunction with a diuretic.
- Methyldopa is contraindicated in patients with active hepatic disease, such as acute hepatitis and active cirrhosis.

Dose-

- The usual initial of methyldopa is dose is 250-500 mg twice daily.

Synthesis of Propranolol

Structure-



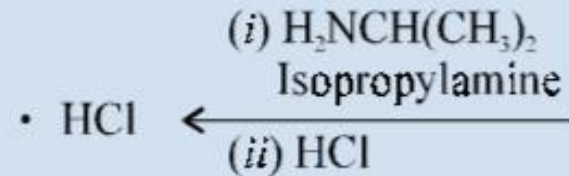
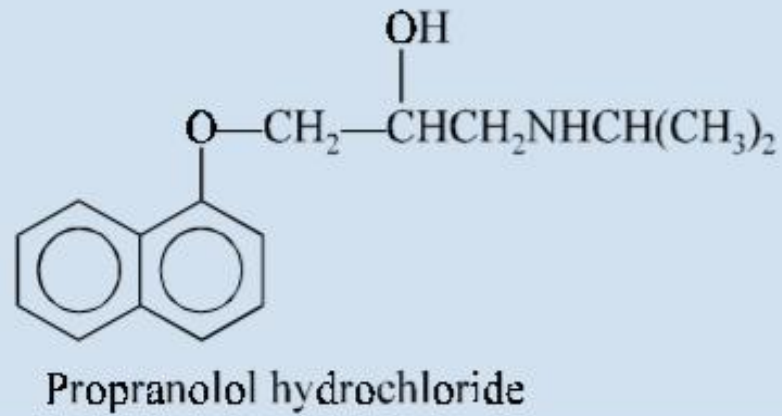
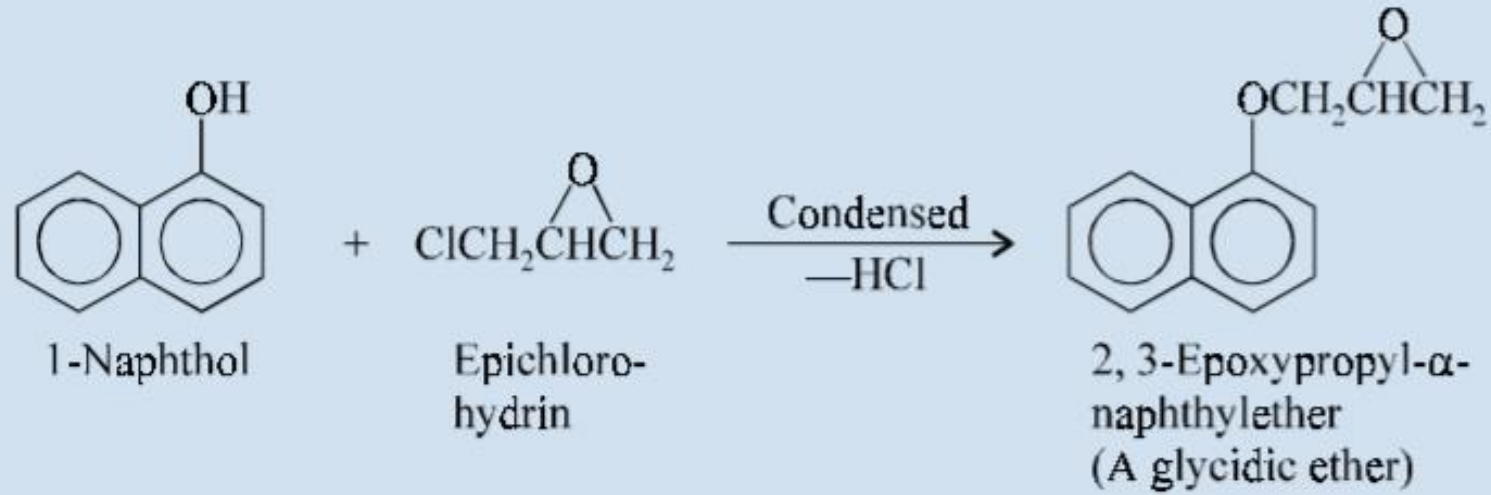
IUPAC Name- 1-(naphthalen-1-yloxy)-3-[(propan-2-yl)amino]propan-2-ol

Properties-

- Propranolol is well absorbed after oral administration, but has low bioavailability due to high first pass metabolism in liver. Bioavailability of propranolol is higher when it is taken with meals because food decreases its first pass metabolism.
- The plasma half-life of propranolol is 3 to 6 hours.
- Propranolol undergoes side chain oxidation to α -naphthoxylactic acid, ring oxidation to 4'-hydroxypropranolol, or glucuronidation to Propranolol glucuronide.
- 91% of an oral dose of propranolol is recovered as 12 metabolites in the urine.
- The elimination half life of propranolol is approximately 8 hours.

Synthesis

Synthesis



Mechanism of Action-

Propranolol inhibits adrenergic responses mediated through the β receptors. Propranolol is a synthetic, nonselective beta-adrenergic receptor blocker with antianginal, antiarrhythmic, antihypertensive properties. Propranolol competitively antagonizes beta-adrenergic receptors, blocking of these receptors leads to vasoconstriction, inhibition of angiogenic factors like vascular endothelial growth factor (VEGF) and basic growth factor of fibroblasts, induction of apoptosis of endothelial cells, as well as down regulation of the renin-angiotensin-aldosterone system, resulting to reduction in cardiac output.

Uses-

Adrenergic beta-antagonists are used for treatment of hypertension, cardiac arrhythmias, angina pectoris, glaucoma, migraine headaches, and anxiety.

Dose-

- ✓ Oral—10 mg BD to 160 mg QID (average 40–160 mg/ day). Start with a low dose and gradually increase according to need;
- ✓ i.v.—2 to 5 mg injected over 10 min with constant monitoring.
- ✓ It is not injected **s.c.** or **i.m.** because of irritant property

Thank You ...