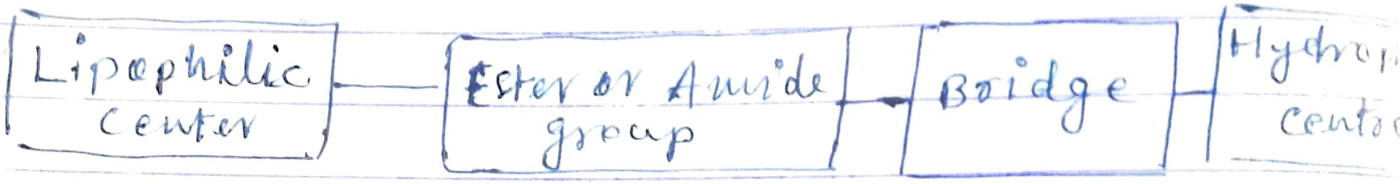
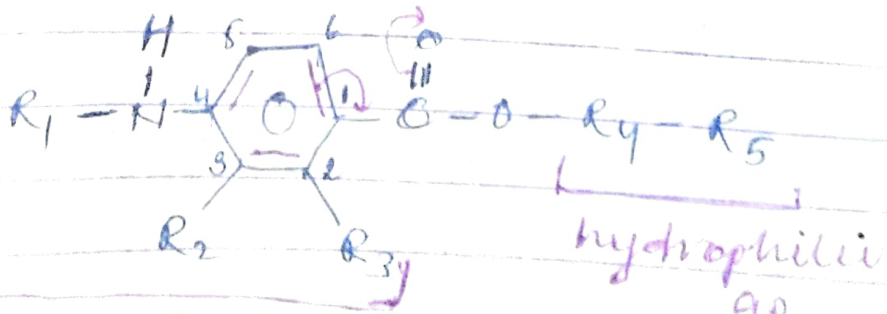
Local Anesthetic

The General st



- Lipophilic centre is responsible for to Penetrate the cell membrane of axon
- Hydrophilic centre is responsible for to transporting the drug to the membrane
- For best local anesthetic action the lipophilic centre and hydrophobic centre should be balence. and PKa value Range 7.5 – 9.5
  PKa > 9.5 ⇒ fully ionize ⇒ less effective
- The lipophilic centre is usually either a aron or heterocyclic ring system
- Hydrophilic centre is normally a 2° & 3° amine.

Ester derivatives

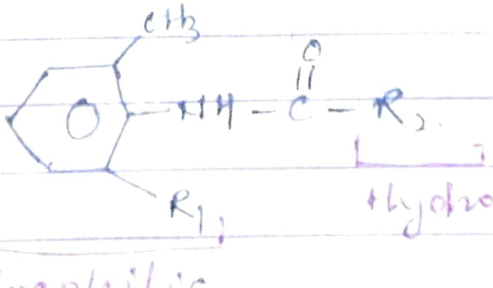


- chloroprocaine has a chloro substituent in o° position. The e^- withdrawing cl atom destabilizes the ester gp to hydrolysis. chloroprocaine is hydrolysed 4 time faster than procaine so onset of action ↑ is more than procaine
- The presence of n-butyl gp on the aromatic nitrogen atom increases the lipid solubility of tetracaine. Rapid of onset of action

- conjugation of the aromatic moiety with carbamyl gp enhance the act
- If aromatic moiety is substituted with the gp that increases the e^- density of the carbamyl oxygen then Act↑

- Amide are most resistant to metabolic hydrolysis than ester long duration of action
  Procainamide > procaine
- 3° Amines are more useful since they are less irritating.

Anilide derivatives -



- If R_1 substituted by the methyl gp as in lignocaine Act↑
- Amide bond is more stable to hydrolysis than the ester bond. long duration of action