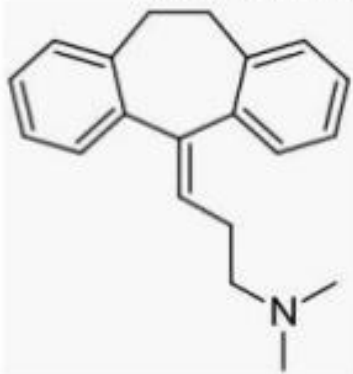


**TOPIC:TCA ANTIDEPRESSANTS**  
**SUBJECT: MEDICINAL CHEMISTRY**  
**NAME OF TEACHER : ZERAH SONU**  
**YEAR : 2019 BATCH**

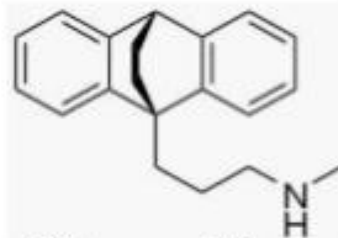
## SAR of TCA's

- 1) It consist of 3 ring in 6-7-6 or 6-6-6 format, with two phenyl rings fused by a central 6 or 7 membered ring that can be homocyclic or heterocyclic. The central ring can be bridged to form a tetracyclic rings

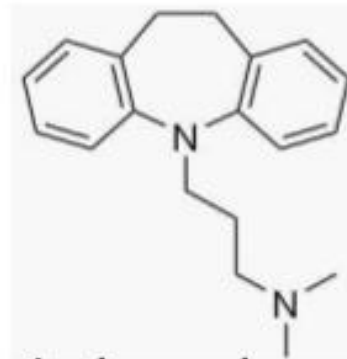


**Amitriptyline**

Homocyclic (contains only carbon in central ring)



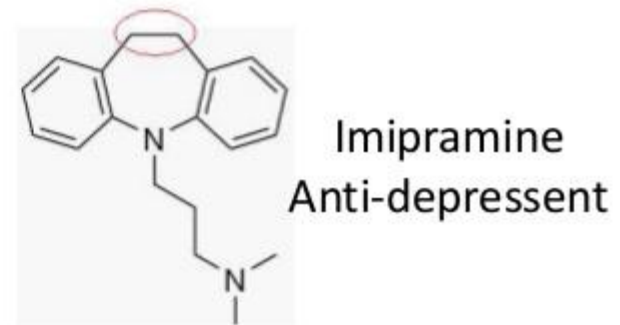
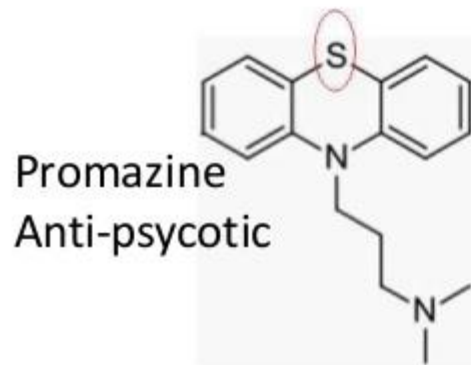
**Maprotiline**



**Imipramine**

Heterocyclic (contains other atoms than carbon like N/O/S in central ring)

- They differ from antipsychotics in that instead of a sulphur, the rings are connected by two carbon units



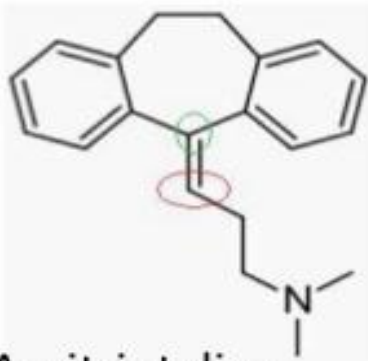
- The three rings do not contribute to receptor binding but are responsible for various CNS side effects due to high lipophilicity. (Thus this feature is absent in later inhibitors)

2) The methylene linker to the terminal amine must be 3 carbon units and can side chain can be attached by **any** carbon on the central ring

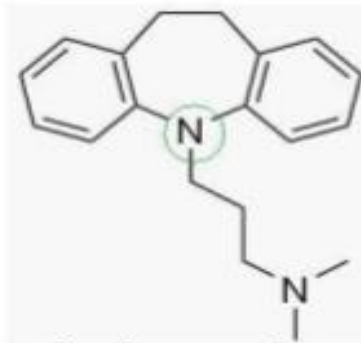
It can be saturated or unsaturated.

It should not be branched

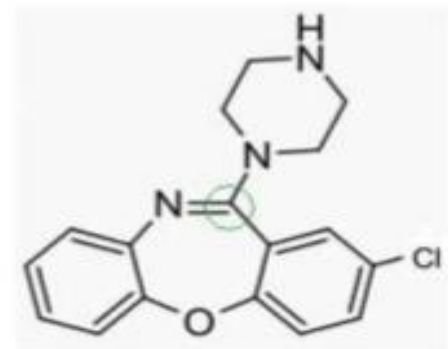
Cis form is potent than trans form



Amitriptyline  
**Unsaturated** (has Double bond) 3 carbon linker

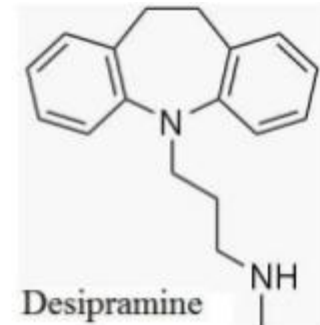
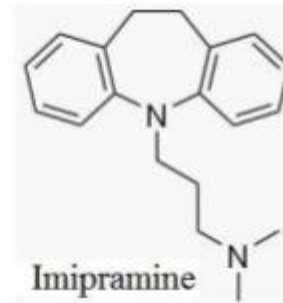


Imipramine  
Saturated (no double bond) 3 carbon linker



Amoxepine has terminal amine attached to a **different carbon**

# Imipramine

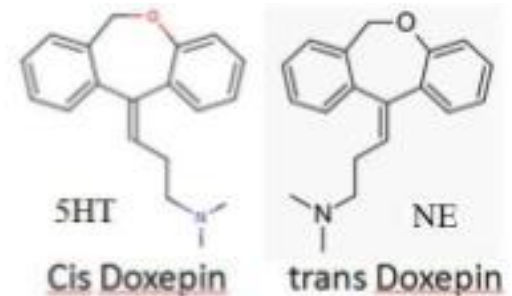


It is a tricyclic antidepressant (TCA) of the di-benzazepine group. It was the first compound of its type.

It is used in the treatment of

- Depression
- Bedwetting
- Within the body, Imipramine is demethylated to desipramine, another TCA.
- MOA: It blocks transporters of 5HT and NE which prevents their reuptake from the synapse and thus prevents depression in agreement to monoamine hypothesis

# Doxepin



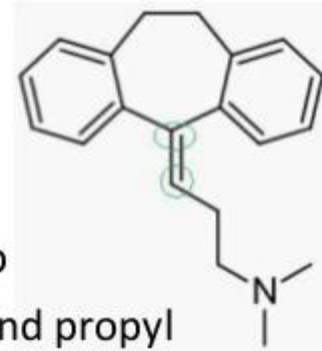
- It is a TCS of dibenzoxepine group with an unsaturated heterocyclic central ring containing oxygen
- Two isomers are possible and is marketed in 85:15 mixture of Trans : Cis
- Cis form inhibits reuptake of 5HT and Trans form inhibits reuptake of NE
- The isomers do not differ in bioavailability but the Trans is metabolized to a larger degree such that the demethylated (3<sup>o</sup> amine converts to 2<sup>o</sup> amine by loss of a methyl group) metabolite of both trans and cis exist in 1:1 ratio

It is used in the treatment of Depression and also Itch and insomnia

MOA: It blocks transporters of 5HT and NE which prevents their reuptake from the synapse and thus prevents depression in agreement to monoamine hypothesis



# Amitriptyline



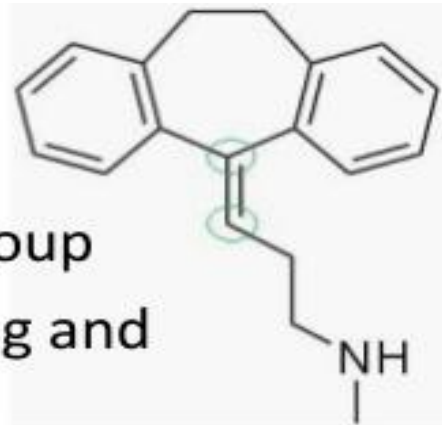
- It is a TCA of the dibenzocycloheptene group and has unsaturation in both the central ring and propyl linker
- It is metabolized into Nortriptyline by demethylation and it also is a TCA
- It is used in
  - Major Depression

MOA: It blocks transporters of 5HT and NE which prevents their reuptake from the synapse and thus prevents depression in agreement to monoamine hypothesis

# Nortriptyline

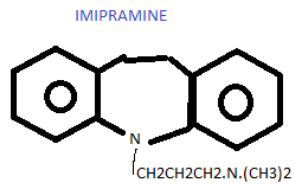
- It is a TCA of the dibenzocycloheptene group and has unsaturation in both the central ring and propyl linker
- It is a major demethylated metabolite of Amitriptyline
- It is used in
  - Depression
  - bedwetting and neuropathic pain

MOA: It blocks transporters of 5HT and NE which prevents their reuptake from the synapse and thus prevents depression in agreement to monoamine hypothesis

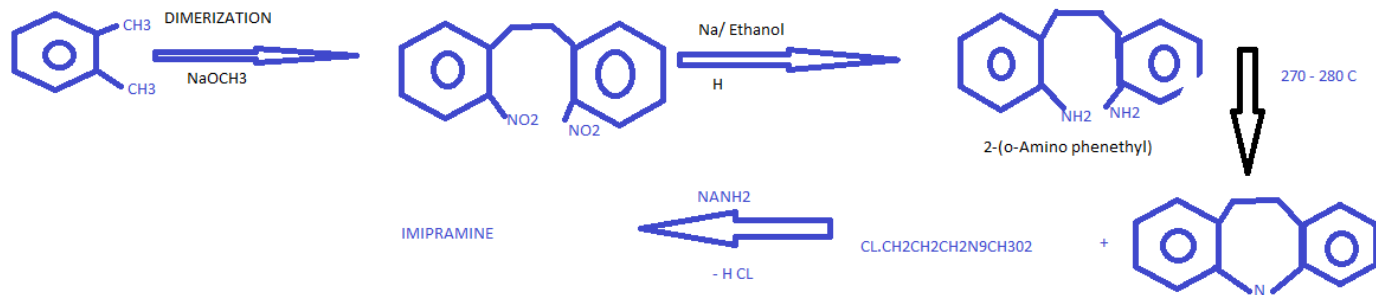




# Imipramine



5-[3-(DIMETHYL AMINO) PROPYL]- 10, 11 DIHYDRO 5H- DIBENZ [B,F] AZEPINE





**THANK  
YOU**