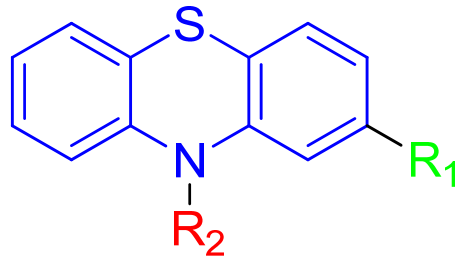


SAR of phenothiazines



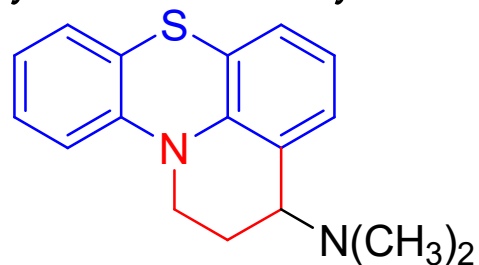
The antipsychotic activity of phenothiazine is affected by following substituents

- **Alkyl side chain**

- for maximum activity the phenothiazine ring and nitrogen atom must be connected by three carbon chain

- Branching of carbon chain at β position by small alkyl groups decreases activity.

- bridging of position 3 of the side chain to 1 of phenothiazine significantly reduces antipsychotic activity.



Amino group

For maximum activity the amino function must be tertiary in nature.

Primary and secondary amino groups are less potent

- Alkylation of the amino group with groups larger than methyl decreases antipsychotic activity.
- Compound containing piperazine / piperidine ring are less potent than dimethylamino derivatives but substitution at 4th position of piperazine / piperidine by hydroxyethyl group substantially increases the activity.

Phenothiazine ring substituents

- The location and nature of substituent on the phenothiazine ring critically affect the antipsychotic activity.
- Potency increases in the following order of position of ring substituents $1 < 4 < 3 < 2$
- 2nd substituents of phenothiazine increases the potency in following order $\text{OH} < \text{H} < \text{CH}_3 < \text{C}_3\text{H}_7\text{CO} < \text{CH}_3\text{CO} < \text{SCH}_3 < \text{CF}_3$
- Oxidation of sulphur atom of phenothiazine decreases activity.