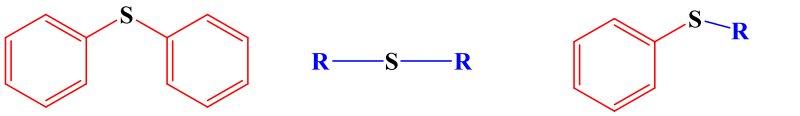
## THIOETHERS

The thioether is mentioned because it is found in a variety of drug molecules as a diaryl-, dialkyl-, or aryl alkyl thioether




**Diaryl thio-ether** **Dialkyl thio-ether** **Aryl Alkyl thio-ether**

***General structures of thioethers***

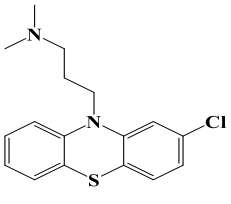
## SOME DRUG CLASSES CONTAINING THIOETHERS

**a.** Slight structural changes in which the sulphur is removed can alter the biological activity of a drug as in chlorpromazine **(1)** which has antipsychotic while imipramine **(2)** is antidepressant.

**b.** In diuretics; Substitution with a lipophilic group such as thioether at position 3 gives an increase in the diuretic potency and duration of action as in benzthiazide **(3)**

**c.** In $H_2$-receptor antagonist for example cimetidine **(4)**; thioether has important role, can you mention it??

**d.** The largest series of compounds containing a thioether group are β-lactam antibiotics **(5)**, **(6)**, **(7)**.

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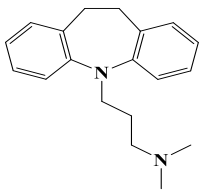


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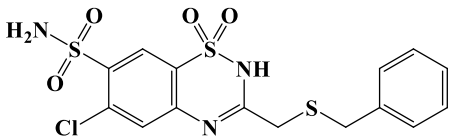


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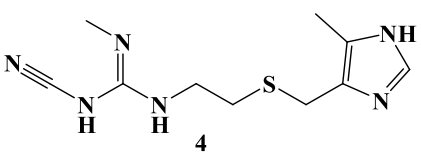


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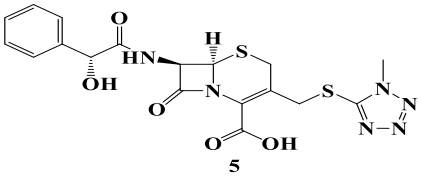


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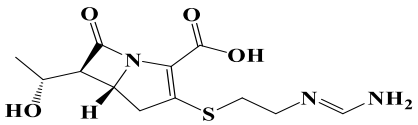

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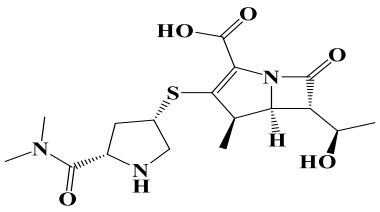

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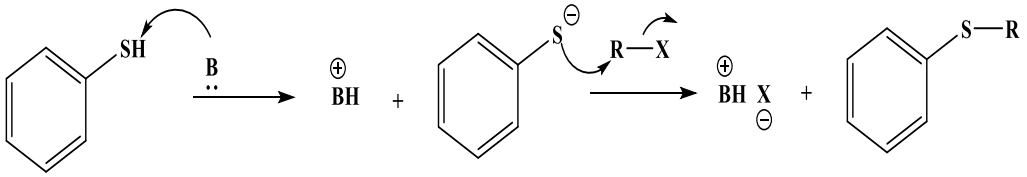
## CHEMISTRY OF THIOETHER

*Reaction between an nucleophilic species [thiol containing compounds] with an alkyl or aryl halide in the presence of base, the product will be called thioether* **.**



***Mechanism of thioether synthesis by*** **SN$^2$** ***mechanism.***

## PROCEDURE of S-Alkylation

### *Objectives*

- ***To make Students Familiar with S-Alkylation Procedure in Drug Design***
- ***SAR study to evaluate the effect of (R) group on activity of the new derivative; see details in O-alkylation lab.***

### PROCEDURE

**1)** Put **0.4g** of thiol containing compound (comp. A) in round bottomed flask and add **3ml** of **96%** ethanol.

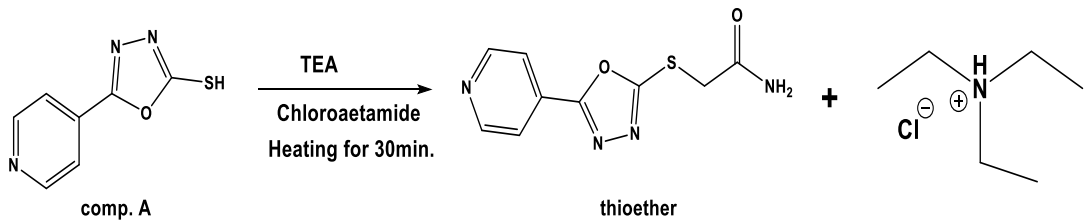
**2)** Add **0.36ml** of Triethylamine (base) [what are its roles?] with stirring until clear solution is obtained.

**3)** To this solution add **0.21g** of alkyl halide (in our experiment is chloroacetamide).

**4)** Heat gently for **30 minutes** and observe the changes.

**5)** Switch of the heat, add DW (why?) with shaking for **30-60** seconds

**6)** Filter, dry, and weigh.




comp. A thioether

## QUESTIONS

**a.** How will SN$^1$ mechanism be operated?