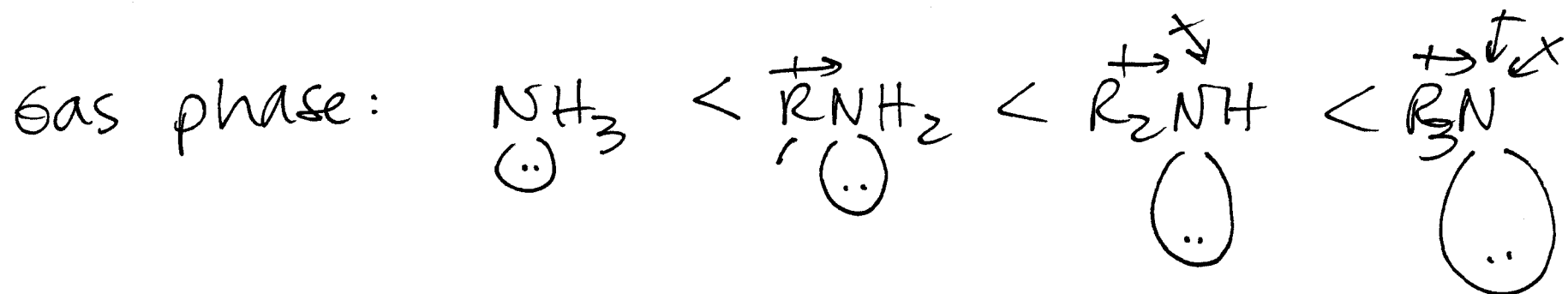
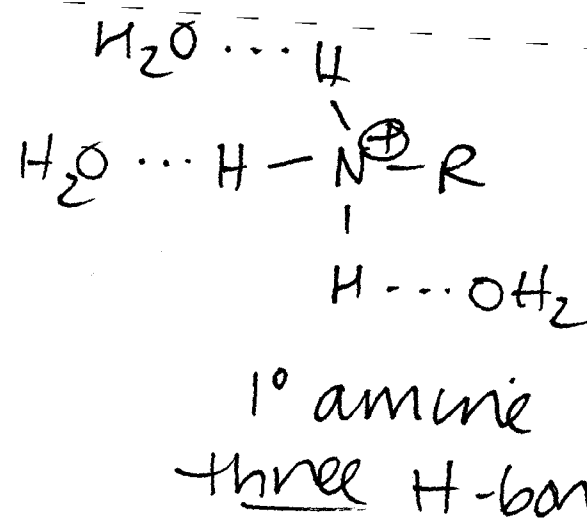
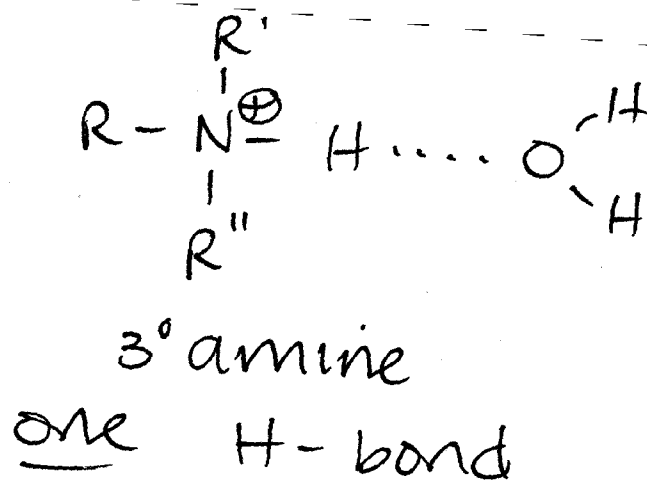


# Basicity of Amines - gas phase vs. sol'n



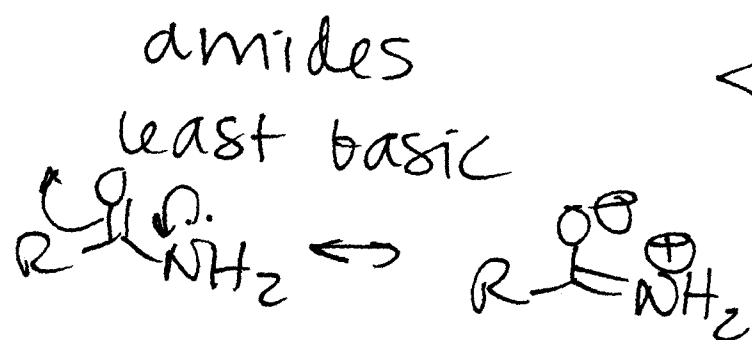
What's going on? Basicity is a function of the availability of the lone pair

1. Alkyl groups increase basicity by e<sup>-</sup> donation via induction
2. Solvation - stabilization of the ammonium ion by H-bonding.



tradeoff - the more R groups you have,  
the fewer H-bonds can be formed.

2° amines have the best combination -  
2 R groups donating e's  
2 H's for H-bonding.

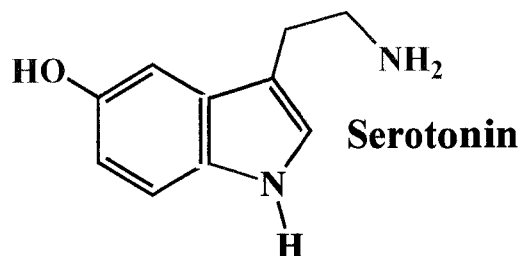
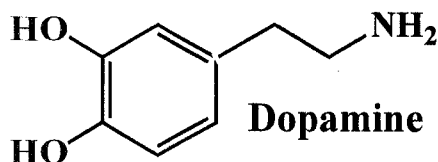
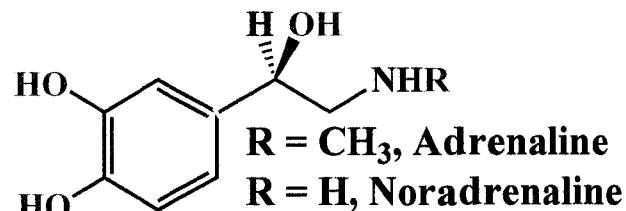
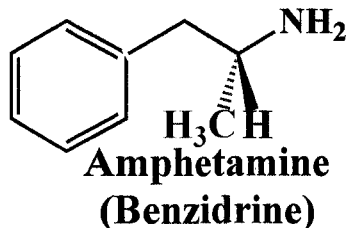
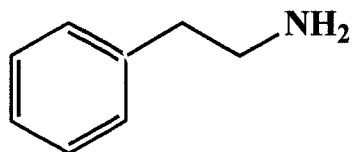


< alkylamines  
(as above)

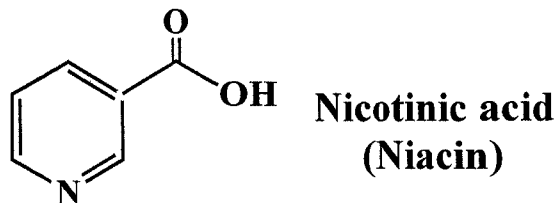
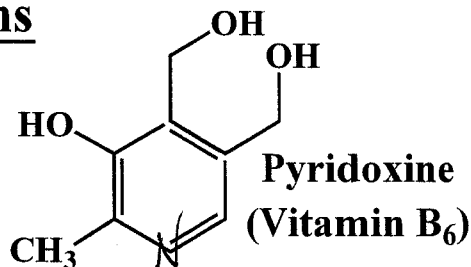
# Some Biologically Important Amines

Amines are widely encountered in biological and pharmacological studies. Some important examples are the 2-phenylethylamines, some vitamins, antihistamines, tranquilizers, and neurotransmitters.

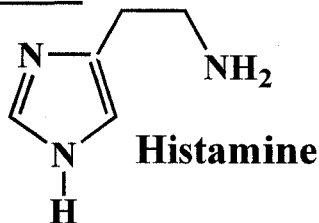
## 2-Phenylethylamines



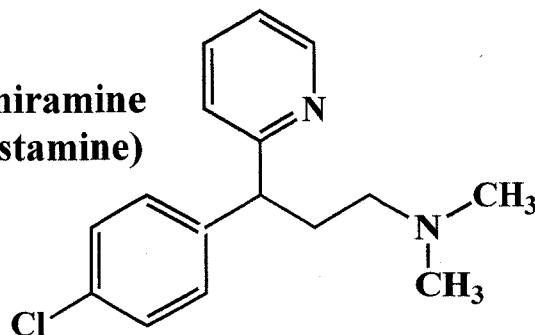
## Vitamins



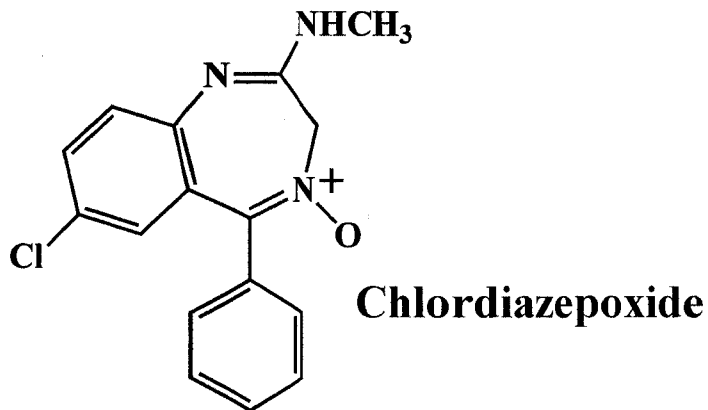
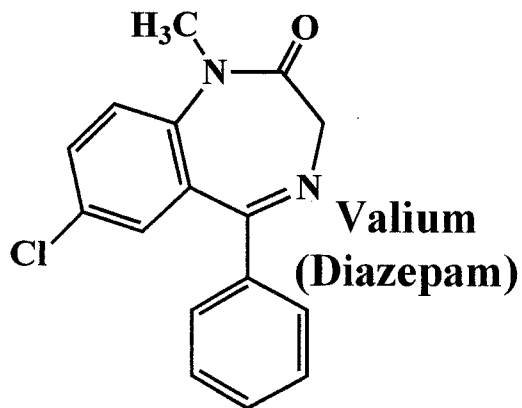
## Antihistamines



Chlorpheniramine  
(an antihistamine)

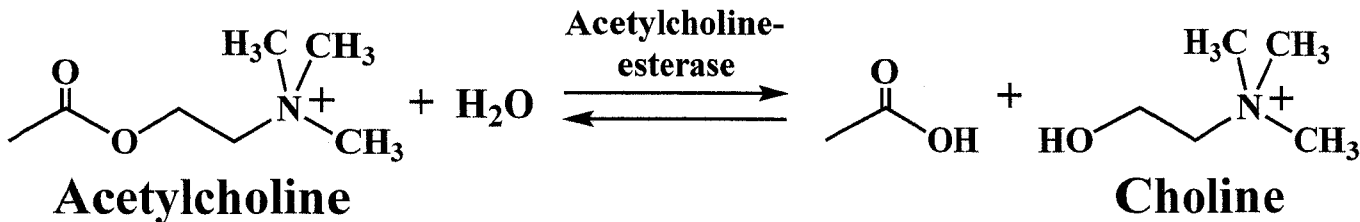


**Tranquilizers**    These examples are both 1,4-benzodiazepine anxiolytics.



## **Neurotransmitters**

Besides 2-phenylethylamines like noradrenaline, dopamine, and serotonin, the simpler amine-family compound acetylcholine is a neurotransmitter, one of great importance that acts at neuromuscular synapses.



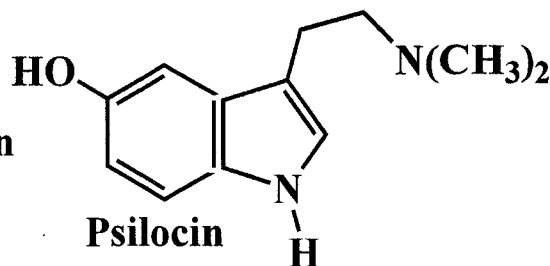
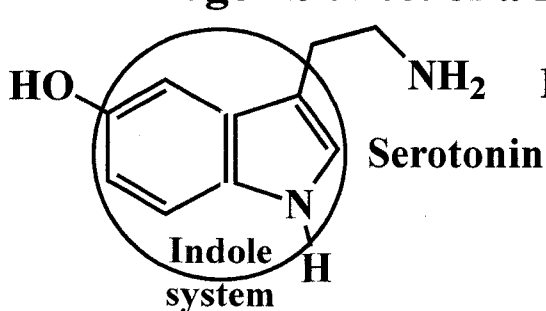
An essential feature of this system is that the esterase can almost immediately hydrolyze the neurotransmitter that has been received at the receptor site, freeing it to receive a later nerve impulse.

# Structure-Reactivity Relationships

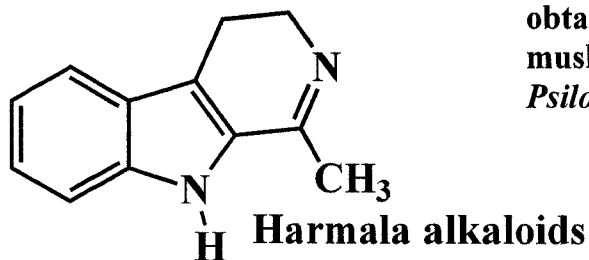
Medicinal chemists have long used structural features as a key to drug design. The structural similarity between the amphetamines and the natural brain hormones (like adrenaline, noradrenaline, and dopamine) is an example.

## Serotonin Mimics

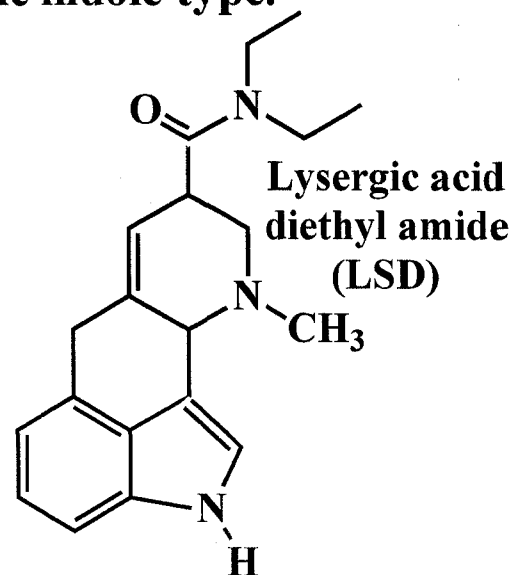
Another example of structure-reactivity relationships appears to be the hallucinogenic effect of a number of compounds of the indole type.



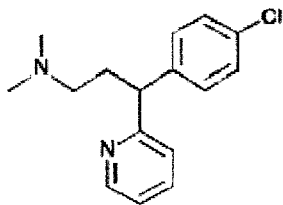
A hallucinogenic alkaloid obtained from the "sacred" mushrooms of Central America, *Psilocybe mexicana*.



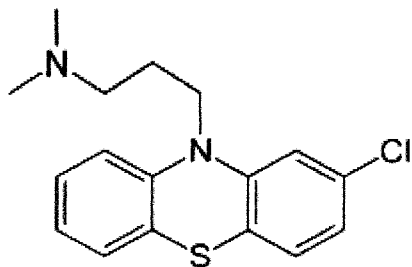
Found in plants in Peru, Ecuador, Columbia and Brazil. Used as a hallucinogen by native indians.



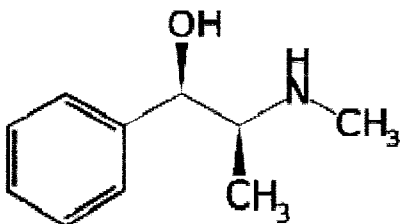
First synthesized by Albert Hofmann in 1938 at Sandoz Pharmaceutical Co. while working on derivatives of the hallucinogenic ergot alkaloids .



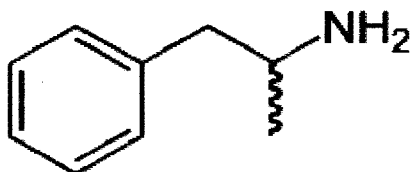
Chlorphenamine – an antihistamine



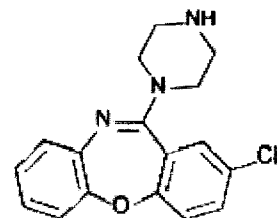
Chlorpromazine (Thorazine™) – an antipsychotic, used to treat schizophrenia



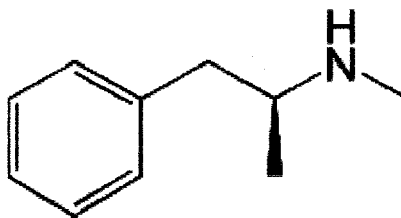
Ephedrine – a decongestant



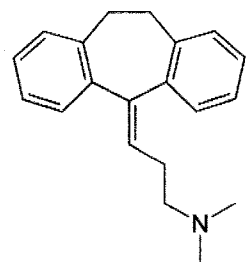
Amphetamine



Amoxapine – an antidepressant

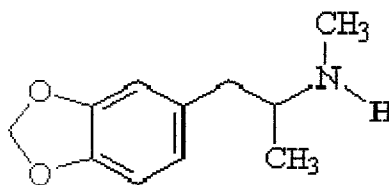


Methamphetamine

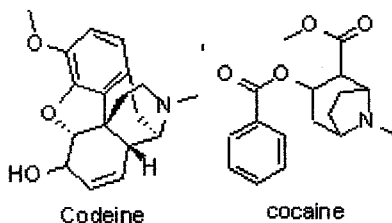
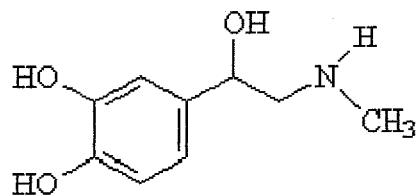


Amitriptyline - an antidepressant

MDMA (Ecstasy)



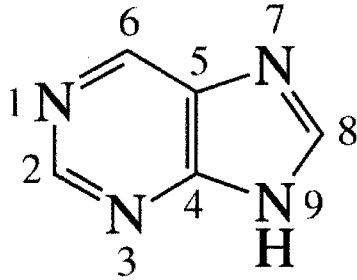
Adrenaline (epinephrine)



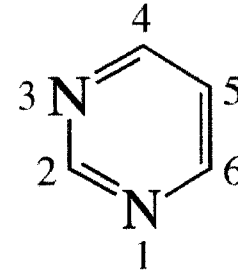
Codeine

cocaine

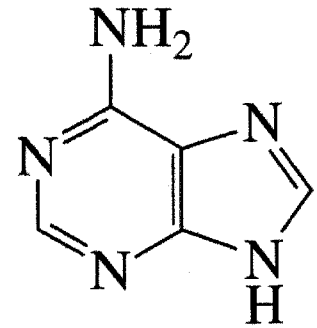
# Purine and Pyrimidine



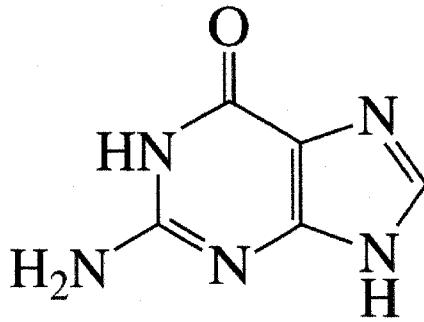
**purine**



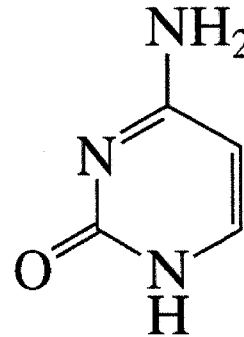
**pyrimidine**



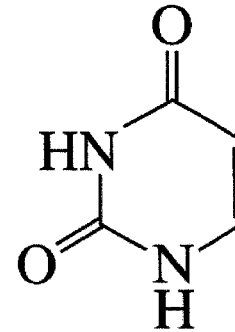
**adenine**



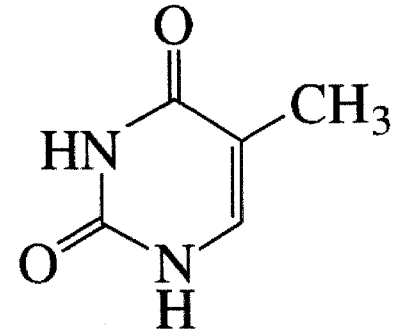
**guanine**



**cytosine**

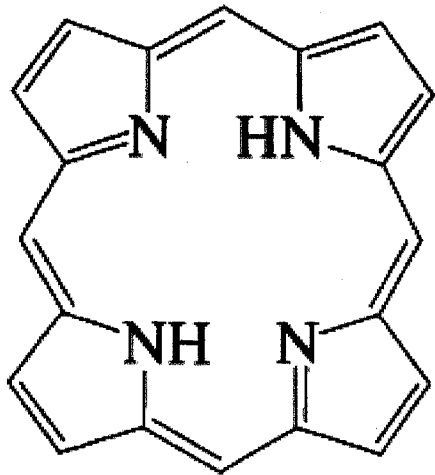


**uracil**

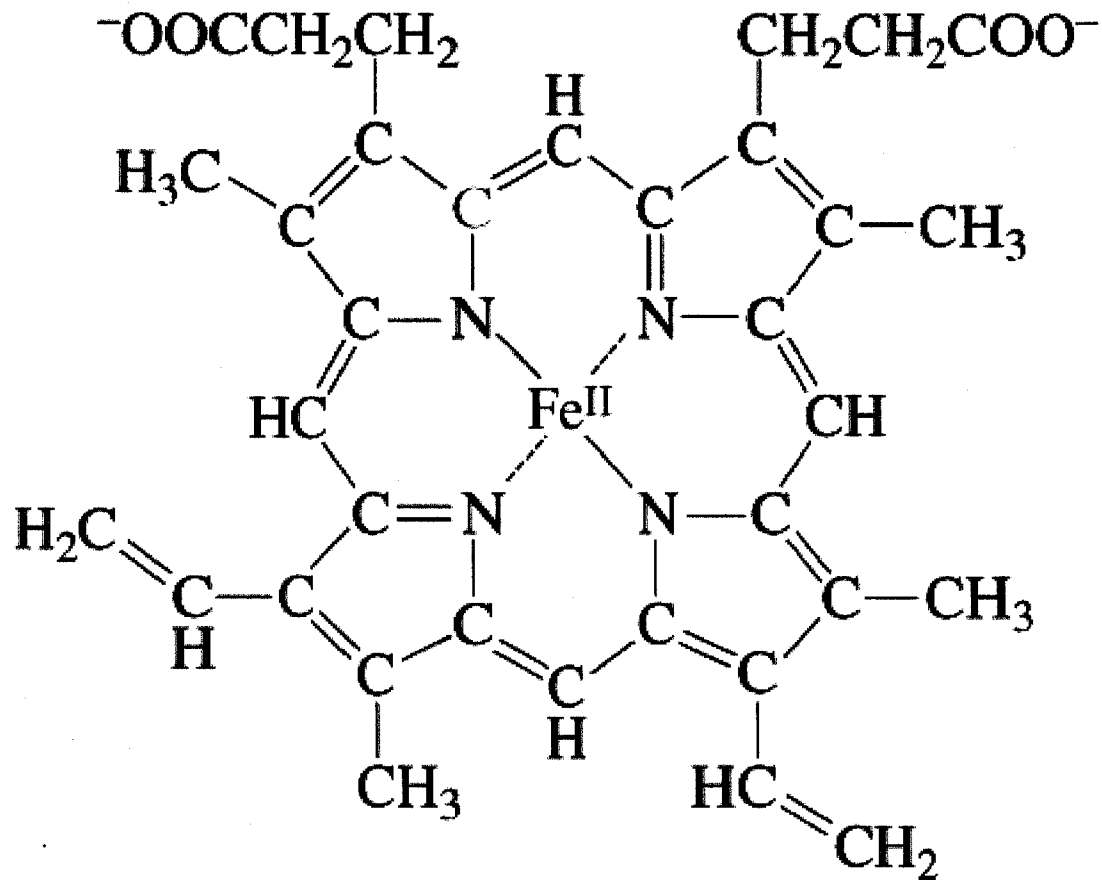


**thymine**

# Porphyrin



**a porphyrin ring system**

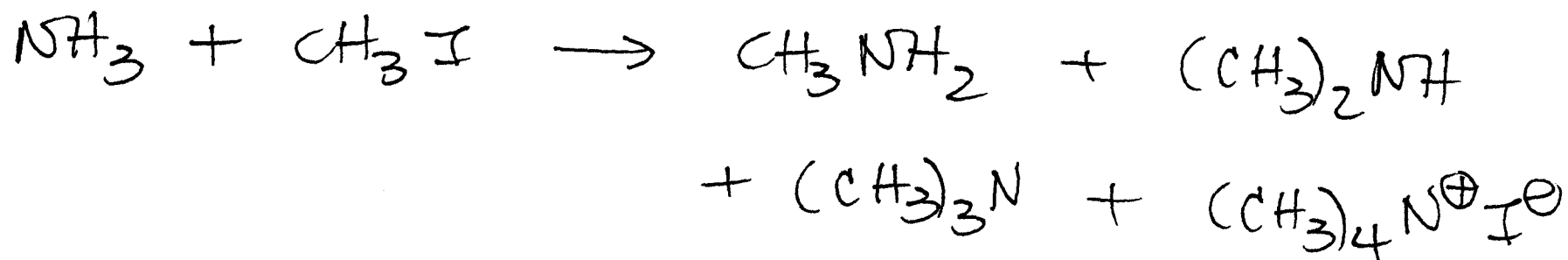


**iron protoporphyrin IX  
heme**

## SLIP 20.5 - Phase Transfer

### Syntheses of Amines

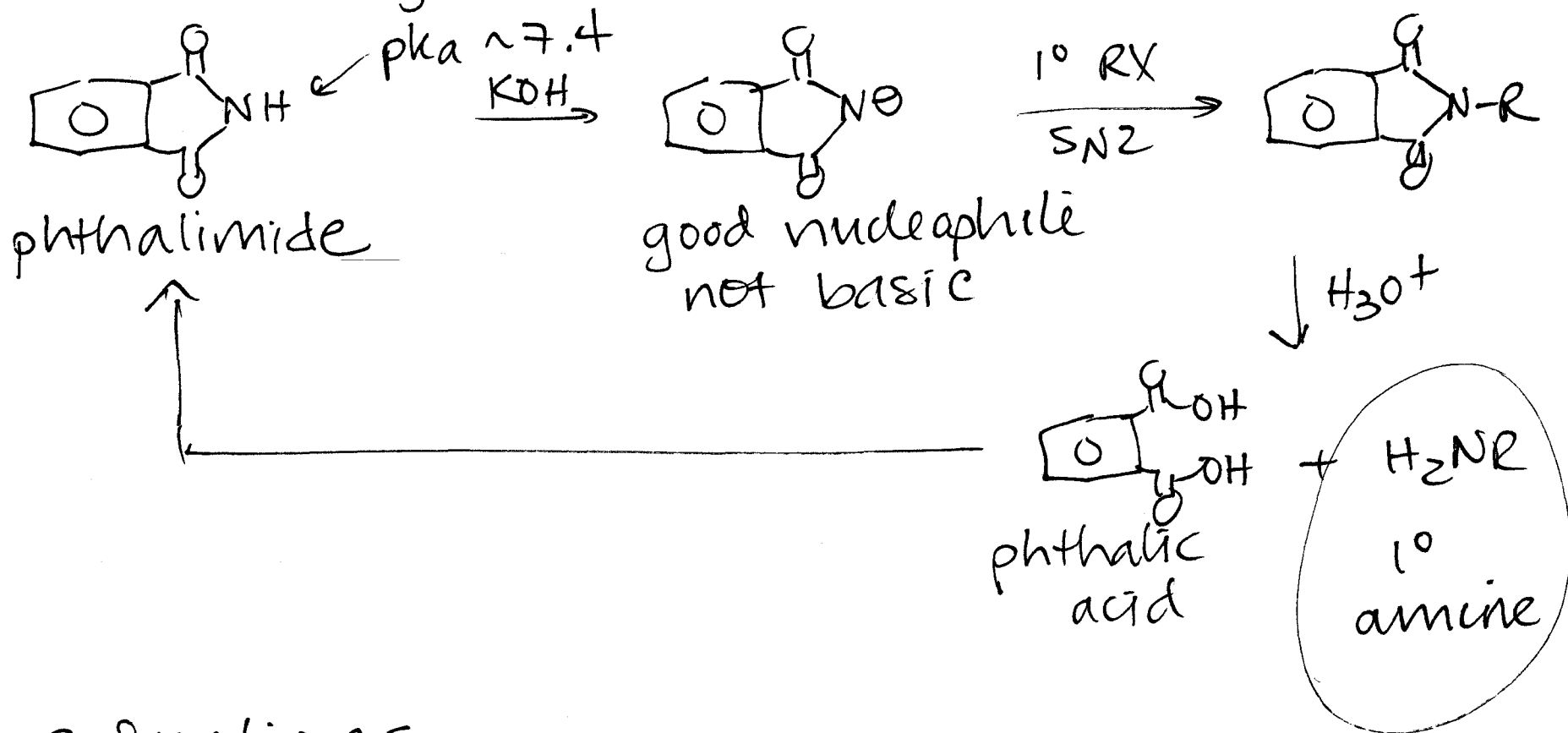
#### 1. $S_N2$ - alkylation of ammonia



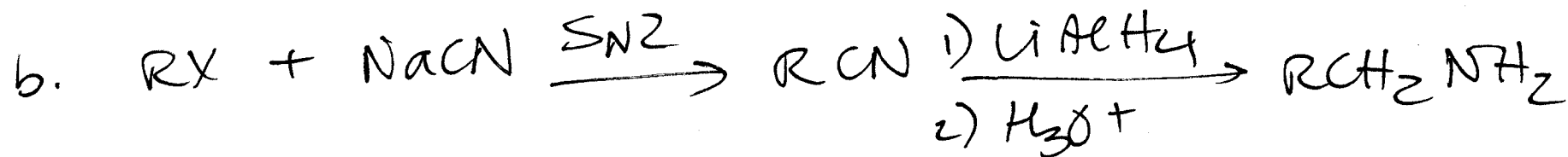
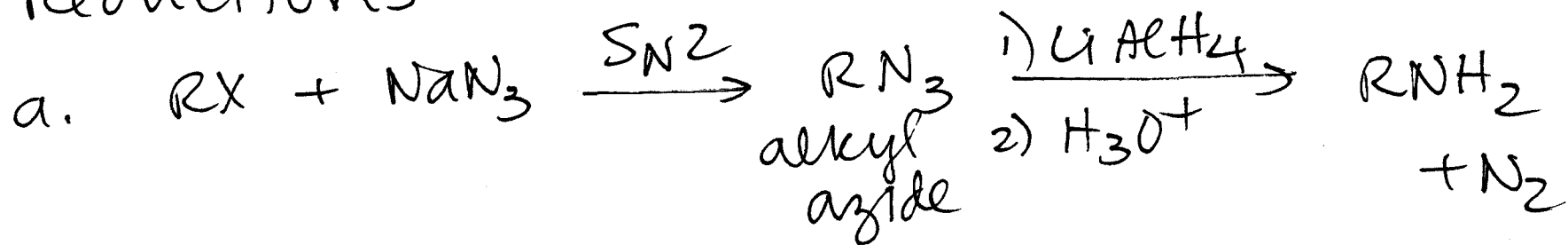
The only way to make this work is  
to use excess  $\text{NH}_3 \rightarrow 1^\circ$  amine

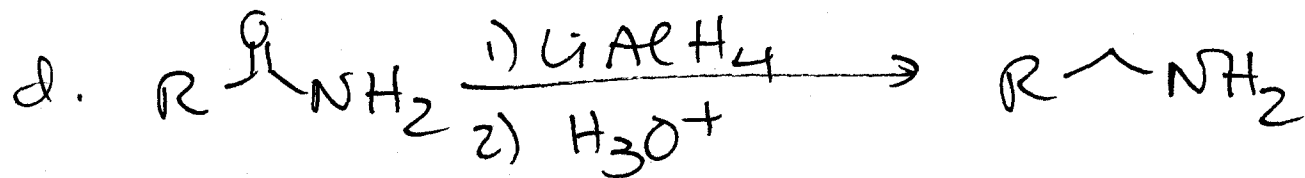
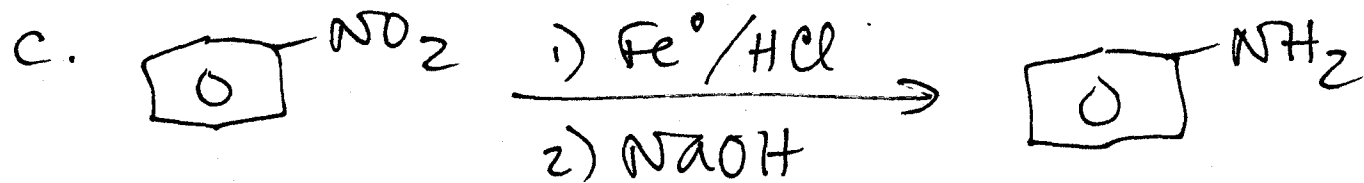
Also use xs  $\text{CH}_3\text{I}$  (exhaustive methylation)  
 $\rightarrow 4^\circ$  ammonium iodide

## 2. Gabriel Synthesis (section 16.18)



## 3. Reductions

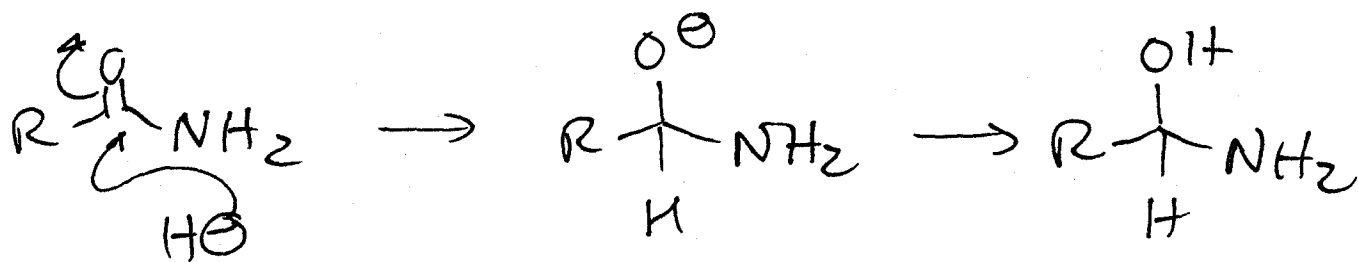




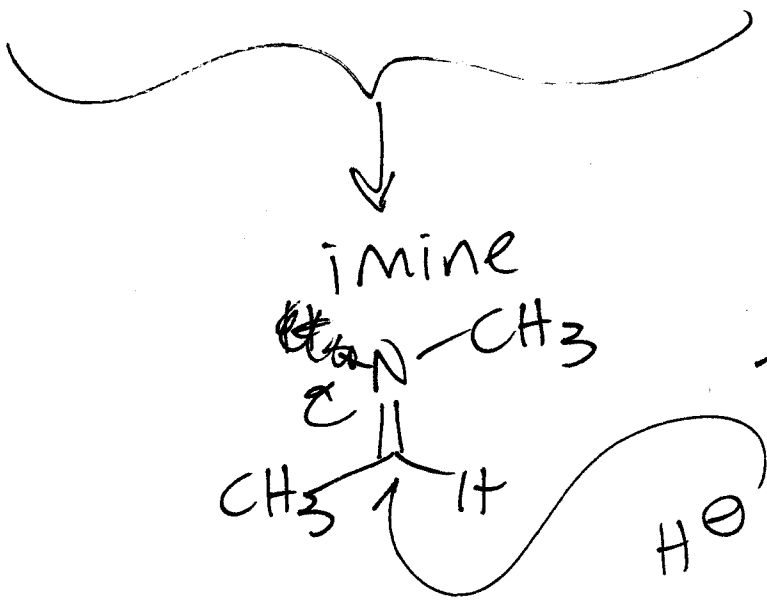
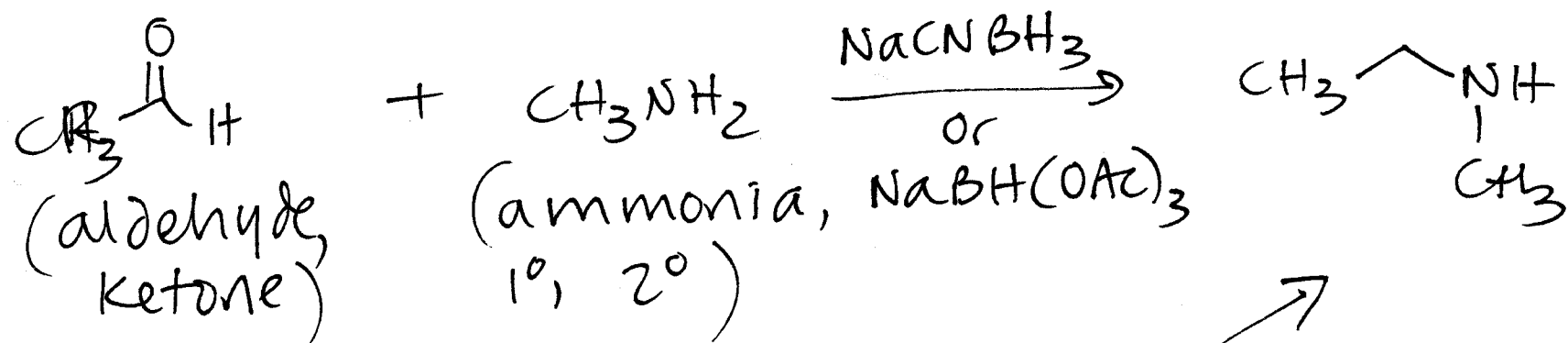
1° amide  $\rightarrow$  1° amine

2° amide  $\rightarrow$  2° amine

3° amide  $\rightarrow$  3° amine



# 4. Reductive Amination (Ch. 17)



$\text{NH}_3 \rightarrow 1^\circ \text{ amine}$   
 $1^\circ \text{ amine} \rightarrow 2^\circ \text{ amine}$   
 $2^\circ \text{ amine} \rightarrow 3^\circ \text{ amine}$

Always get  $\text{CH-N}$   
 ↑  
 hydride