

### ✓ **Isomers and types of isomers**

#### ➤ **Constitutional Isomers**

- **Functional Group Isomers**
- **Positional Isomers**
- **Geometric Isomers**

#### ➤ **Stereoisomers**

- **Enantiomers**
- **Diastereomers**
- **Meso Compounds**

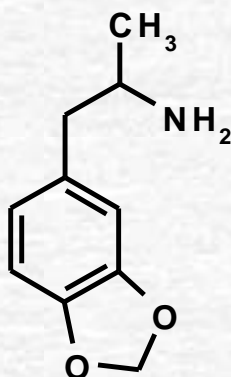
#### ➤ **Conformational Isomers**

- **Eclipsed, gauche, staggered, syn-clinal, anti-clinal forms**
- **Chair, boat, pseudo-chair, skew-boat**

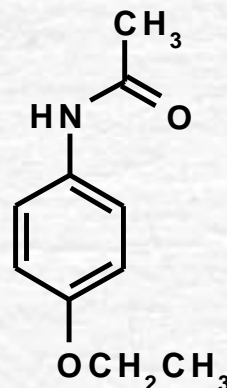
## Stereochemistry and Drug Action

### ✓ Functional Group Isomers

Same molecular formula, but different functional groups, e.g., n-propanol and methyl ethyl ether



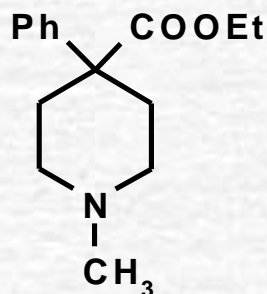
**3,4-MDA**  
(Ecstasy)



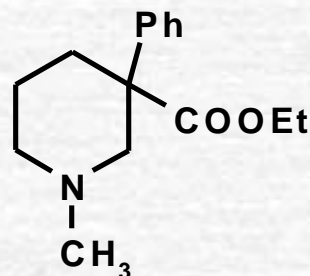
**phenacetin**  
(analgesic)

### ✓ Positional Isomers

Same molecular formula, same functional groups, but different positions of functional groups, e.g., n-propanol and i-propanol



**Mepiridine**  
(Analgesic)



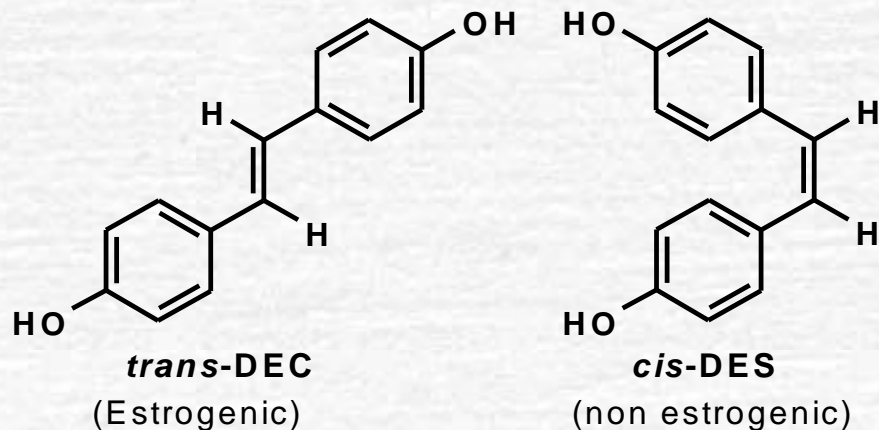
(not analgesic)

## Stereochemistry and Drug Action

### ✓ Geometric Isomers (cis/trans)

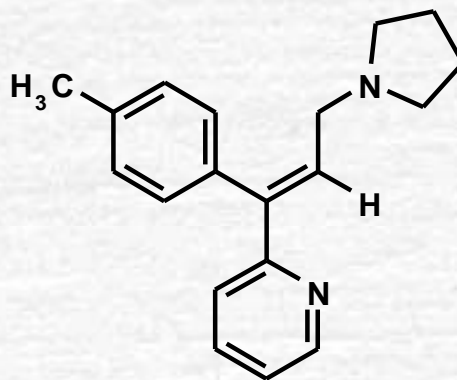
Same molecular formula, same functional groups, same positions, but different orientation around a double bond or on a ring.

An important criteria to exhibit geometric isomerism is that the isomers cannot be interconverted through mere rotation around a single bond.



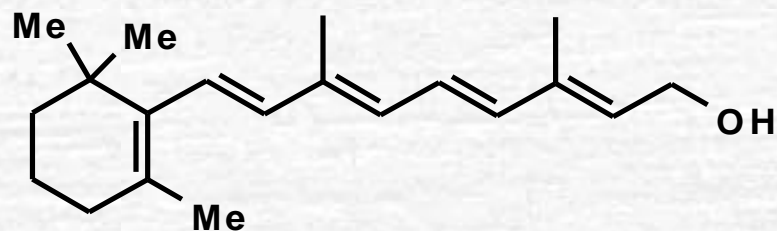
## Stereochemistry and Drug Action

### ✓ Geometric Isomers (cis/trans) ... other examples



Triprolidine (E)

Trans isomer, i.e., E, is 1000-times more histaminic than cis, Z

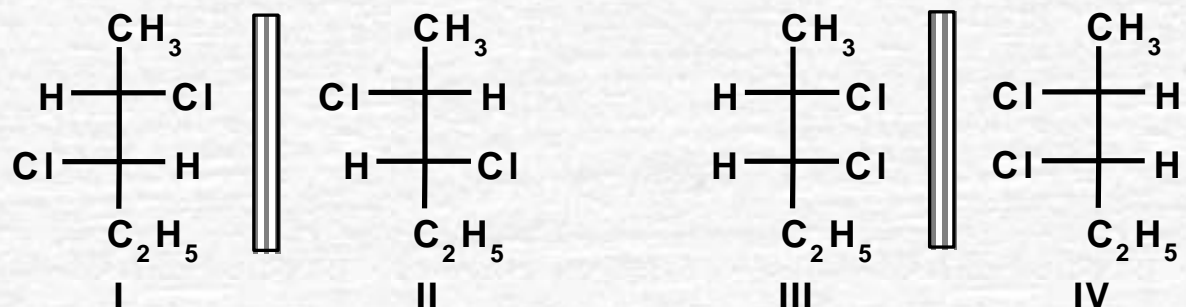


Vitamin A has all E double bonds, any Z would make it inactive!

## Stereochemistry and Drug Action

### ✓ Stereoisomers

- Enantiomers .... pair of stereoisomers that are related to each other as non-super-imposable mirror image isomers
- Meso compounds ... stereoisomers that have more than one chiral center and are super-imposable on their mirror images
- Diastereomers .... pair of stereoisomers containing more than one chiral center and are not mirror images of each other

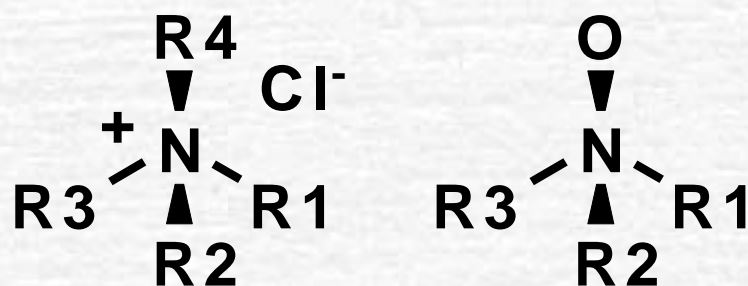


- What will be the effect of changing the -Et group to -Me?

## Stereochemistry and Drug Action

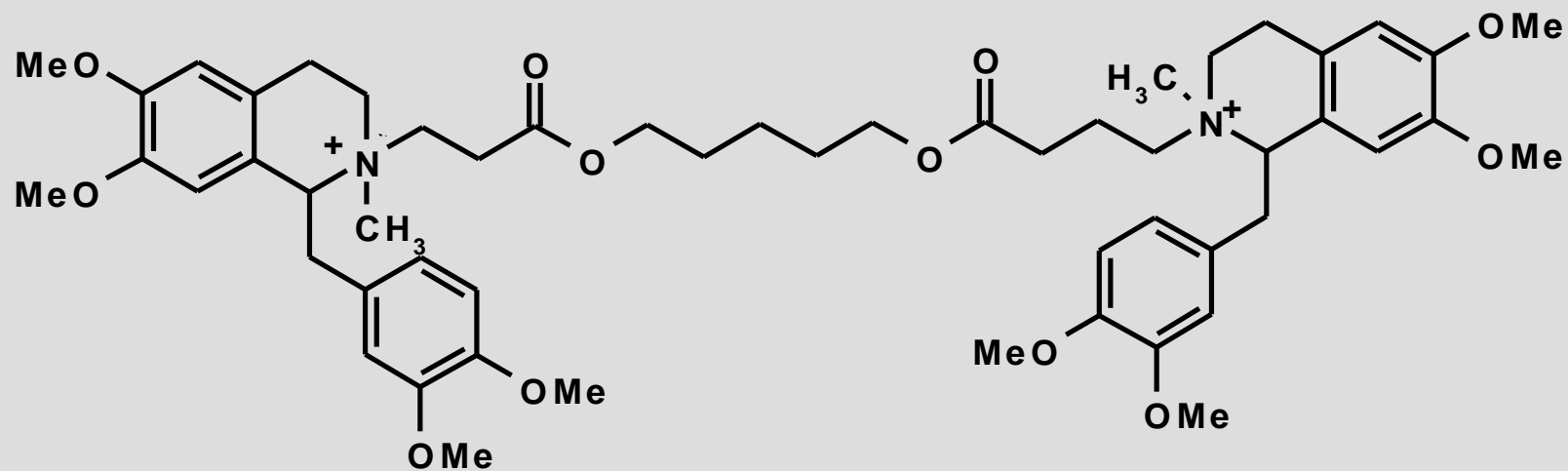
### ✓ Stereo Isomers

- Enantiomers .... arise ..... four different substituents on a tetrahedral carbon
- ..... can also come about because of a tetrahedral nitrogen or phosphorus
- ..... may also arise due to bridge nitrogens/phosphorus



## Stereochemistry and Drug Action

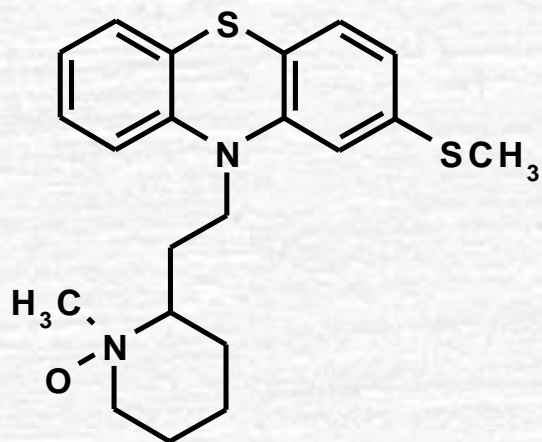
- ✓ Identify chiral centers (carbon, nitrogen, phosphorus)



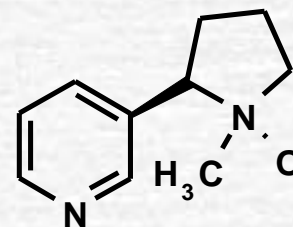
**Atracurium besylate (neuromuscular blocking agent)**

## Stereochemistry and Drug Action

- ✓ Identify chiral centers (carbon, nitrogen, phosphorus)



Thioridazine N-oxide

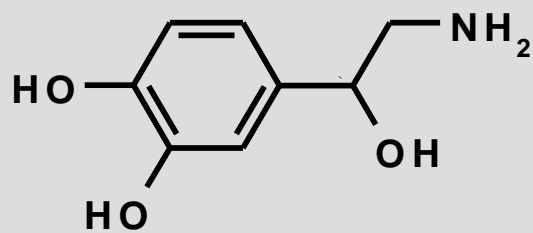


Nicotine N-oxide

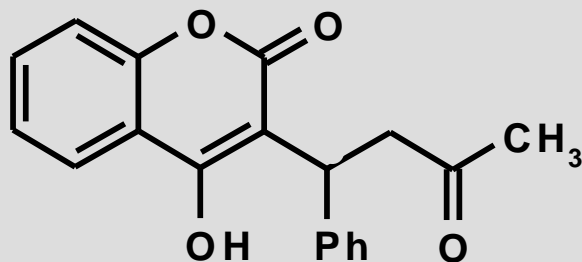


## Stereochemistry and Drug Action

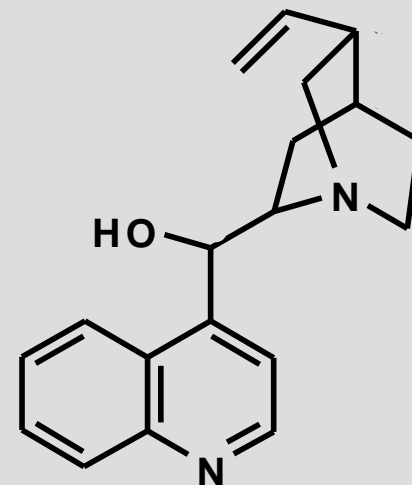
- ✓ Identify chiral centers (carbon, nitrogen, phosphorus)



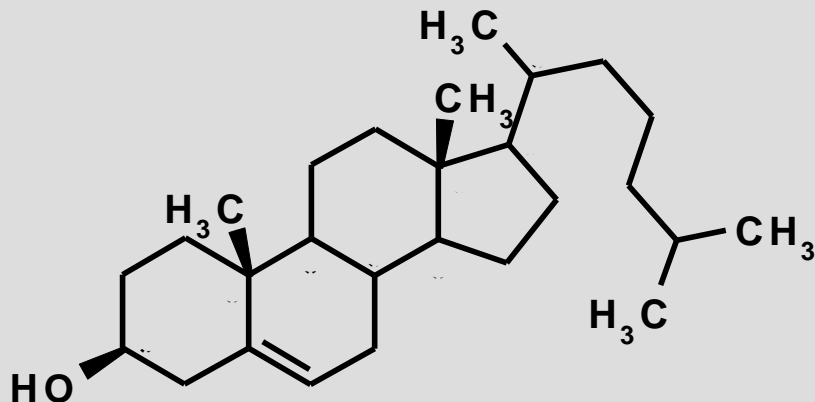
Nor-epinephrine



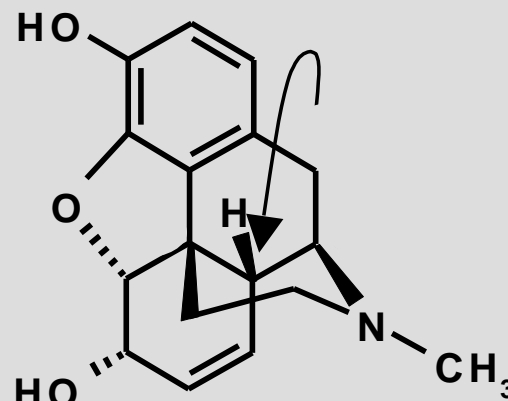
warfarin



quinine



cholesterol

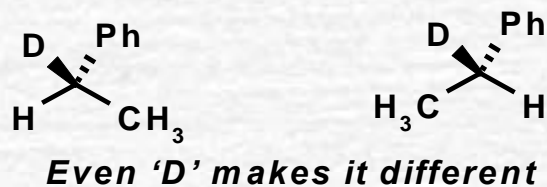


morphine

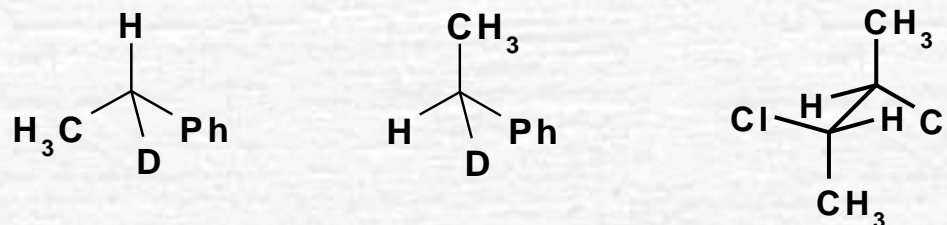
# Stereochemistry and Drug Action

## ✓ Enantiomers and projections

### Standard Projection



### Saw Horse Projection



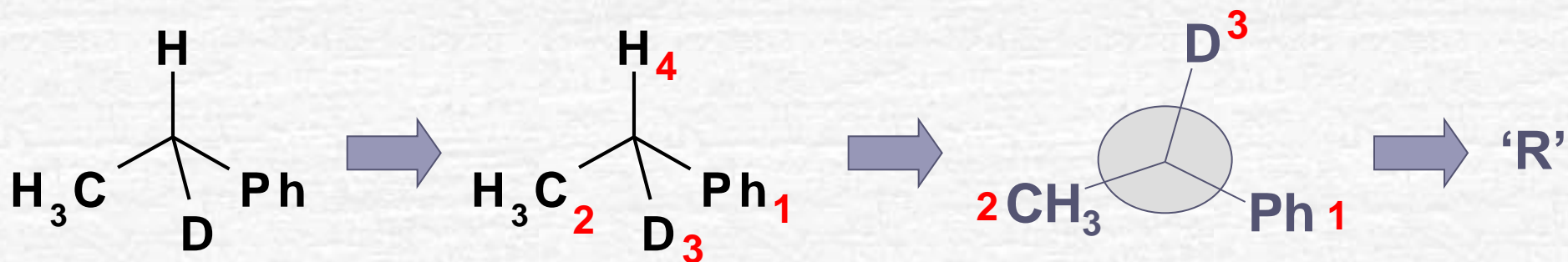
### Fischer Projection



## Stereochemistry and Drug Action

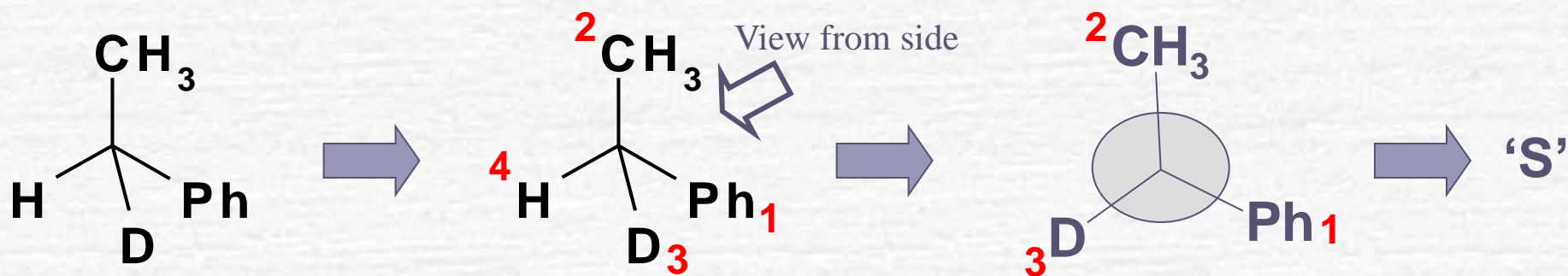
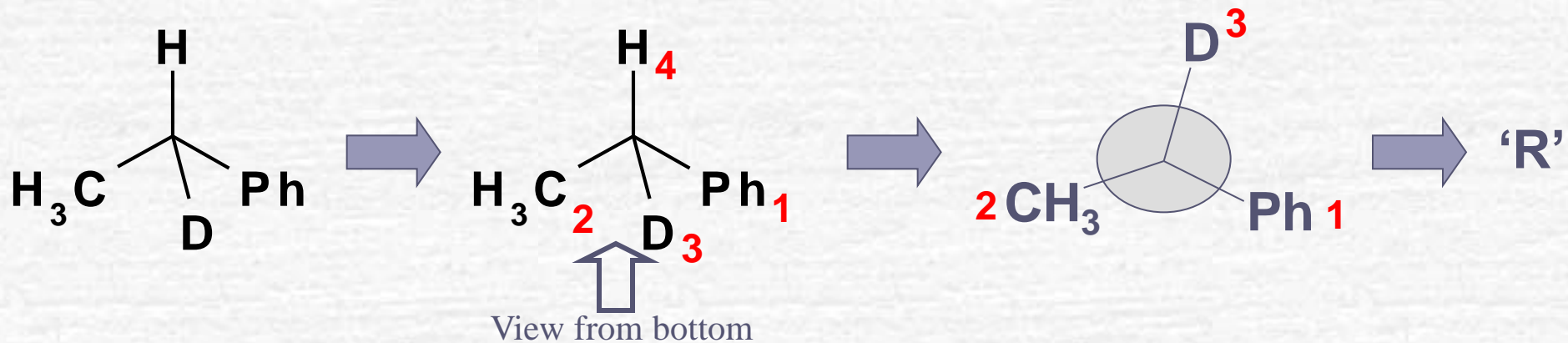
### ✓ Identification of Enantiomers or Chiral Centers

- Step 1 identify chiral center
- Step 2 assign priority
  - ... higher the atomic number, higher the priority
  - ... atoms with same atomic number → heavier isotope, higher priority
  - ... if same priority for immediate atoms, continue down the second atom
  - ... double bonds are duplicated; triple bonds are triplicated
- Step 3 visualize molecule so that the group of lowest priority is directed away
- Step 4 draw (or visualize) Newmann projection of the remaining three groups
- Step 5 write the priority order 1, 2 and 3; draw (or visualize) an arrow traveling from 1→2→3
- Step 6 if the arrow travels clockwise, the chiral center is 'R'; otherwise it is 'S'



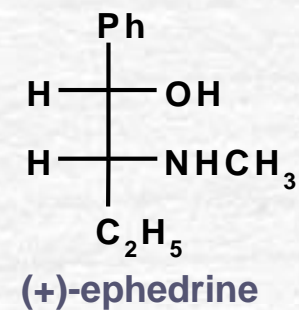
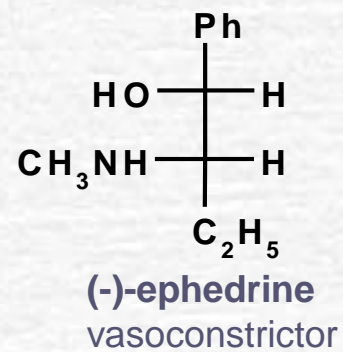
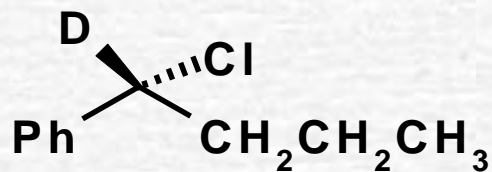
## Stereochemistry and Drug Action

### ✓ Identification of Enantiomers or Chiral Centers



## Stereochemistry and Drug Action

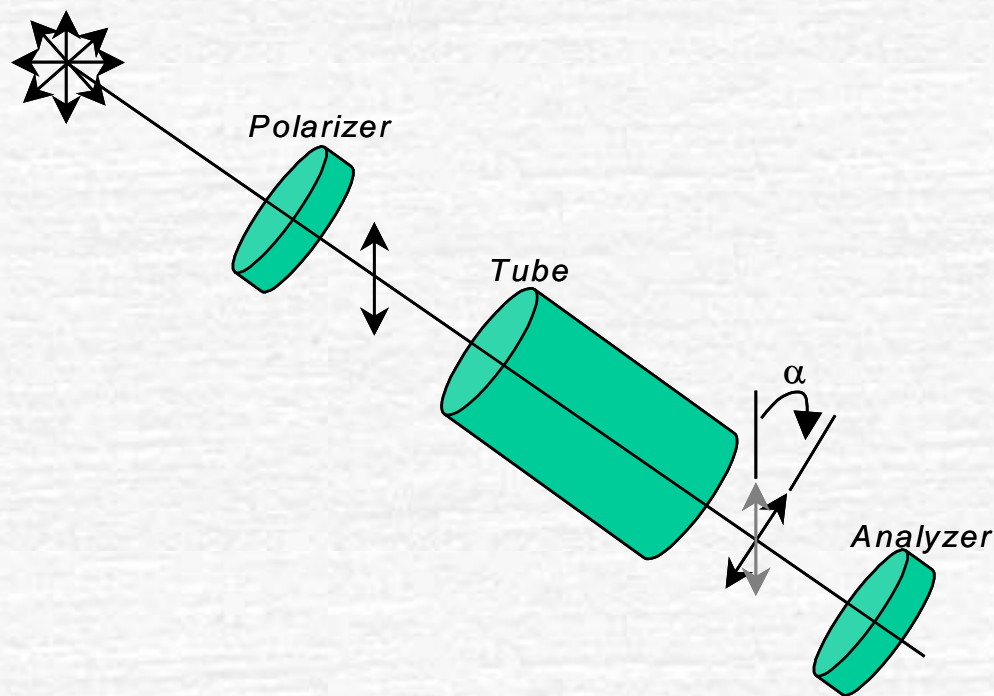
### ✓ Identification of Enantiomers or Chiral Centers



## Stereochemistry and Drug Action

### ✓ **Properties of Enantiomers**

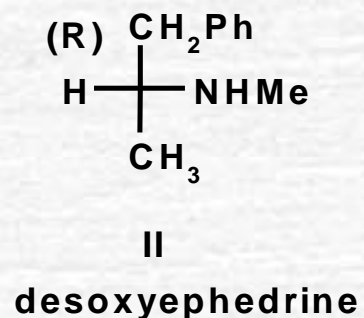
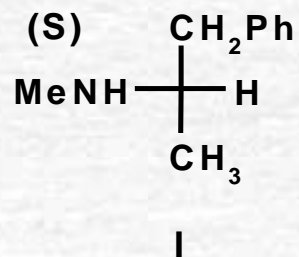
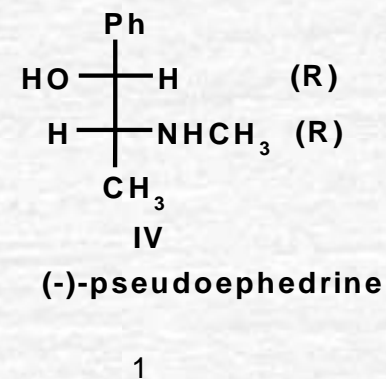
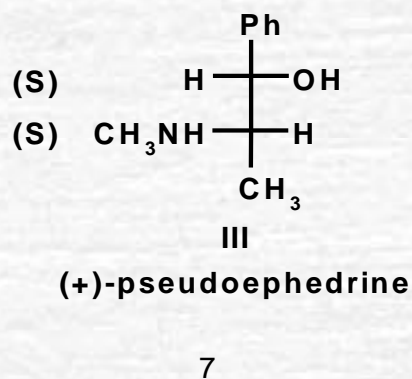
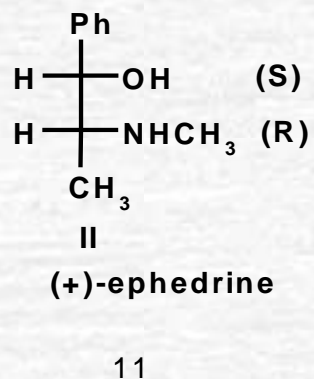
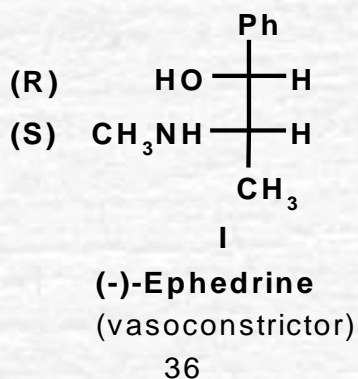
- **Physical properties ... bp, mp, solubility, pKa, pKb, thermal stability, etc. .... all identical**
- **Rotate the plane of polarization of plane polarized light ... the phenomenon of optical activity**



# Stereochemistry and Drug Action

## ✓ Properties of Enantiomers

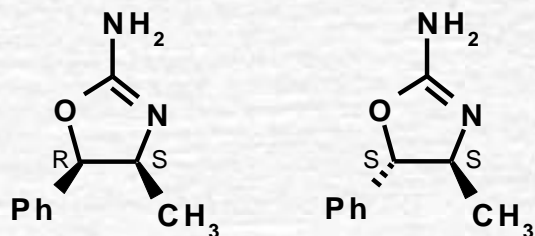
➤ Reactivity with chiral molecules .... e.g., enzymes, receptors, ..... drug action/metabolism



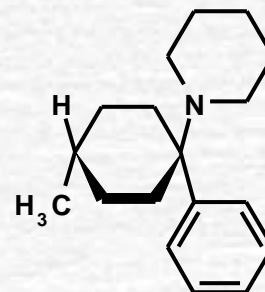
**Methamphetamine**  
10X more potent  
CNS stimulant  
Less cardiovascular

# Stereochemistry and Drug Action

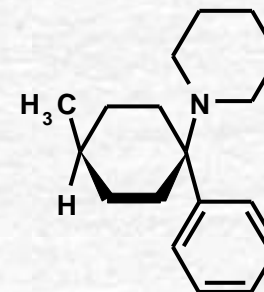
## ✓ Properties of Enantiomers



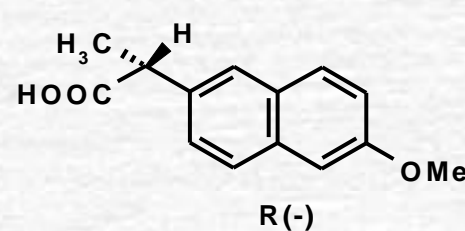
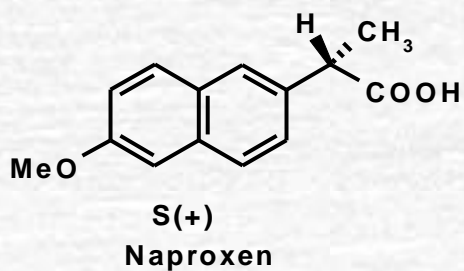
**Cis-4-methylaminorex**  
Potent amphetamine  
psychostimulant



*Effective dose*  
(5.5 mg/Kg)



(>150 mg/Kg)





## Stereochemistry and Drug Action

- ✓ Why do chiral molecules react differently with biological molecules?

