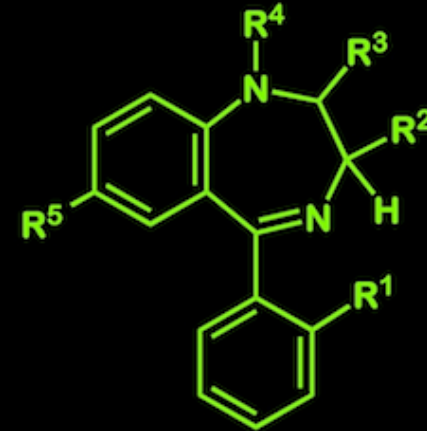


# ANXIOLYTICS, SEDATIVES & HYPNOTICS

## Part 2

### Dr. Aisyah Saad FAR 344/4

So, the world was looking for a safer and effective sedative... and they discovered...

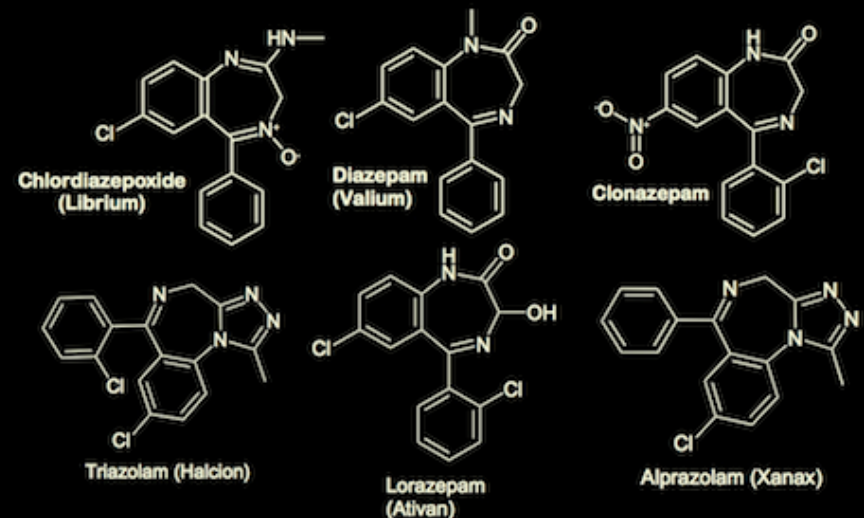


## benzodiazepines...

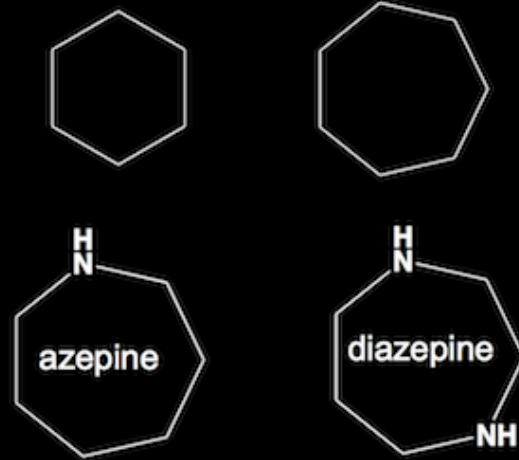
- **Leo Sternbach**
- **The chemist who invented BZDs**
- **Almost threw away some compounds during lab clean up, but submitted it for clinical studies and the rest is history...**
- **Librium introduced in 1960's**
- **Supersede barbiturates**



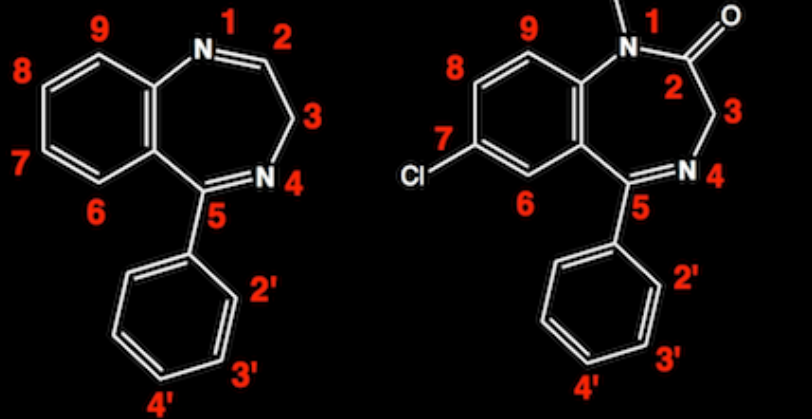
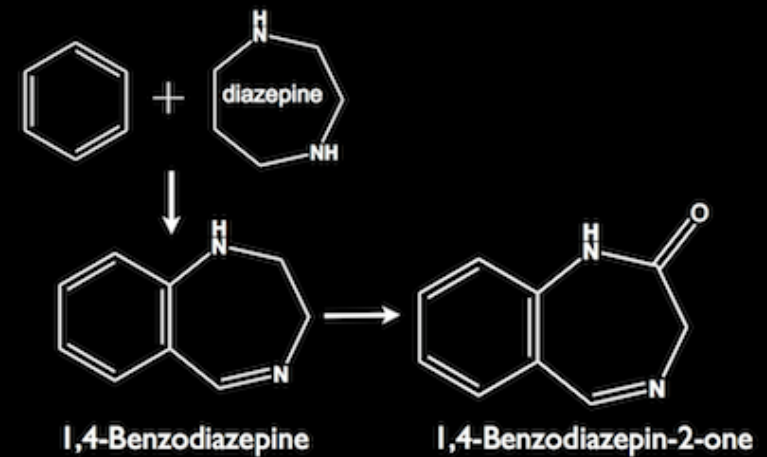
## Meet the superstars...



## how to name a BZD?



## how to name a BZD

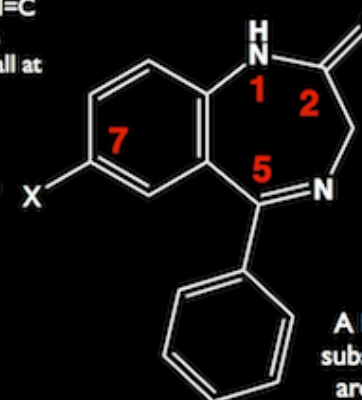


7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one

## SAR of BZDs

- plus,
- at C-6, -8 & -9 : no substituent
  - do not remove or reduce the N=C (4,5) : a must
  - Keep it Small at N-1.

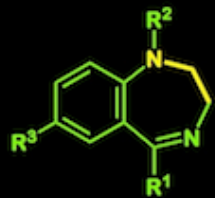
Electron-withdrawing group  
e.g. Cl, F, Br



- Also,
- The epoxide causes reduced activity.
  - Triazolo's e.g. Xanax requires no electronegative substituent at C-7 for activity

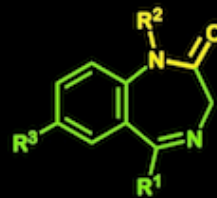
A bulky organic substituent e.g. an aromatic group

## Types of pharmaceutically-relevant benzodiazepines



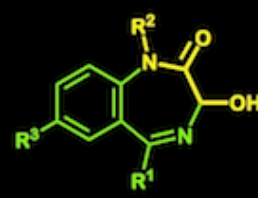
Oxygen-free BZD

Medazepam



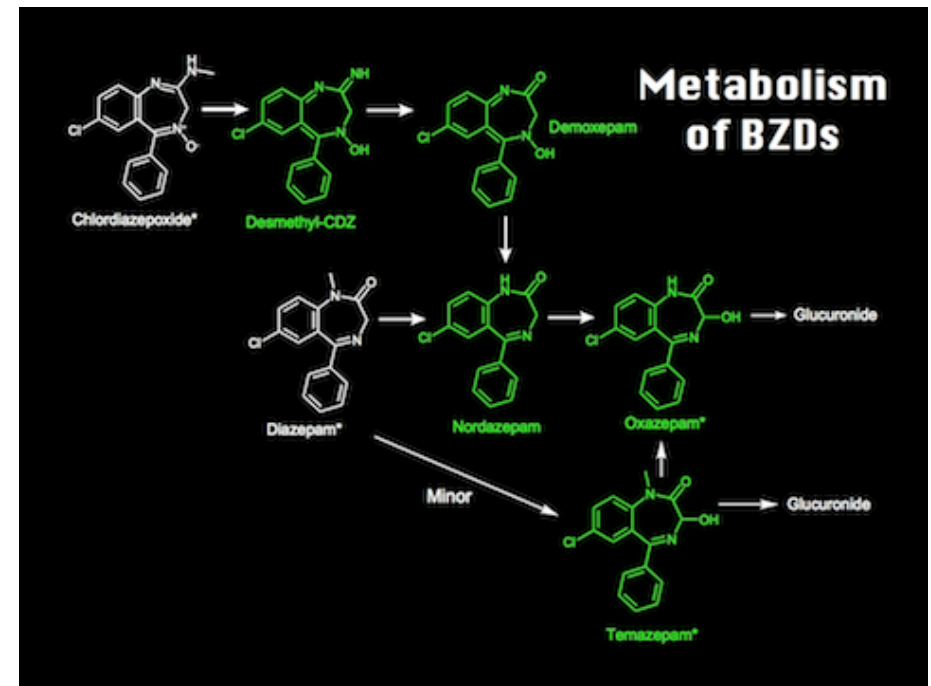
Lactam partial structure

Diazepam  
Nitrazepam



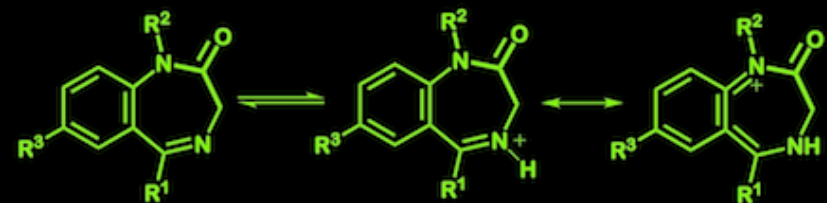
Hydroxylactam substructure

Lorazepam  
Oxazepam



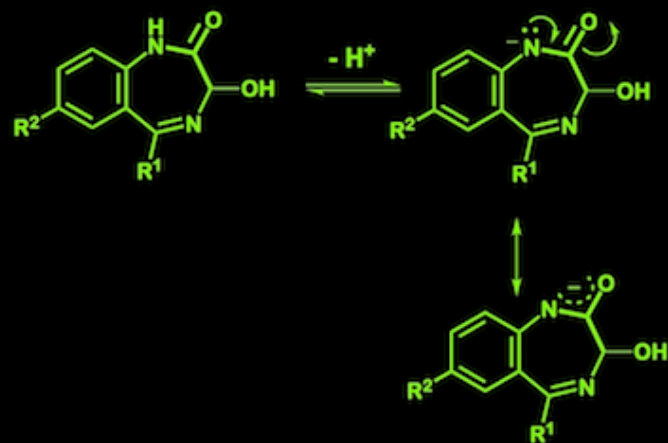
Let's see how some benzodiazepines behave when they're exposed to light, heat, acid & alkali

## Weak acid properties of BZD with lactam substructure



Protonation occurs at N-4 which generates a phenylogous amidinium cation

## Weak acid properties of BZD with hydrolactam substructure



## Hydrolysis of BZD with lactam/ hydrolactam structure



## Stability of Chlordiazepoxide to Light



## Acid Hydrolysis of Chlordiazepoxide

