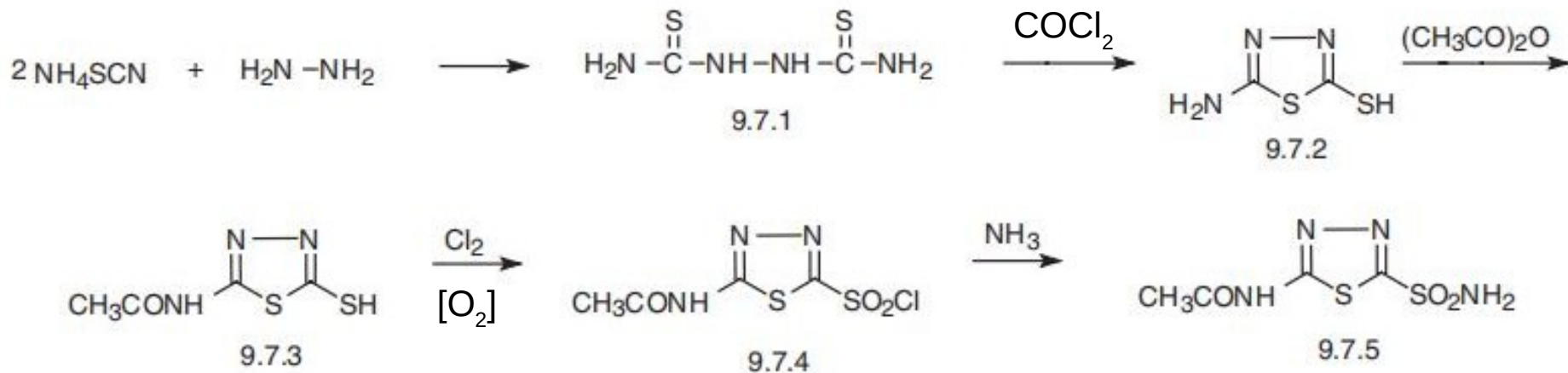


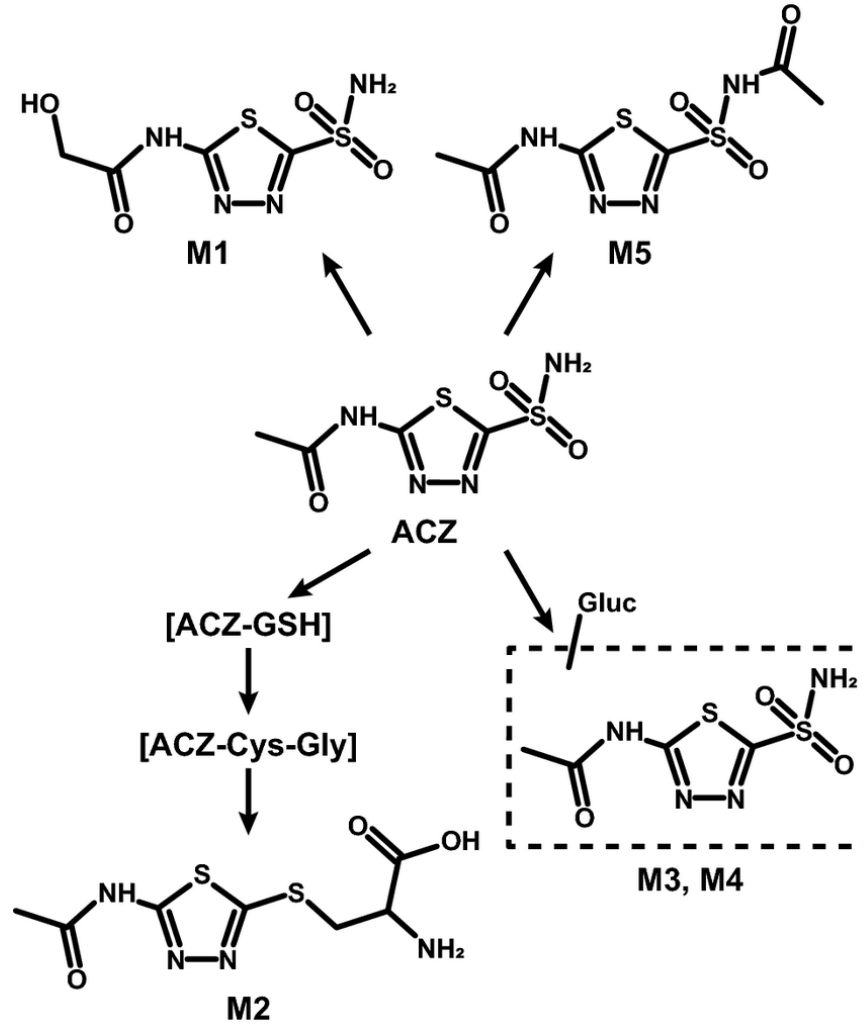
# Synteses and metabolism of selected diuretics

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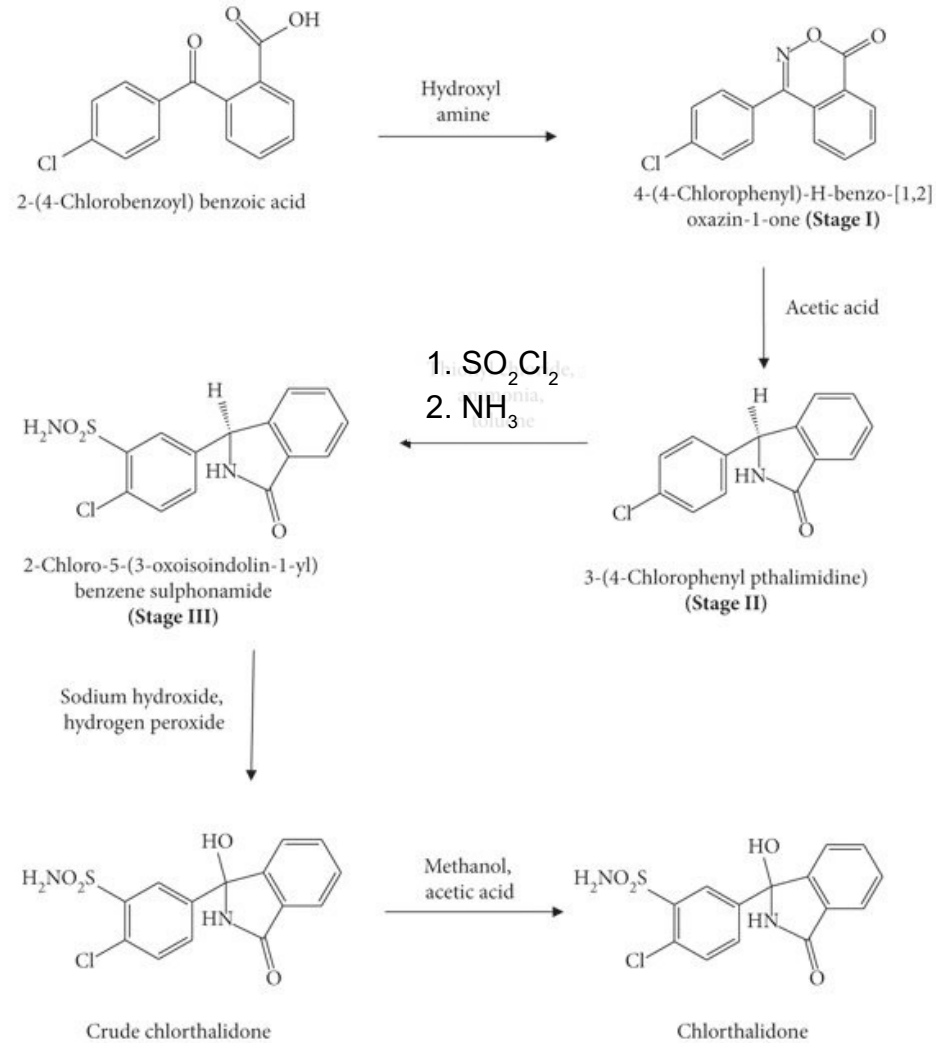
## Synthesis of acetazolamide



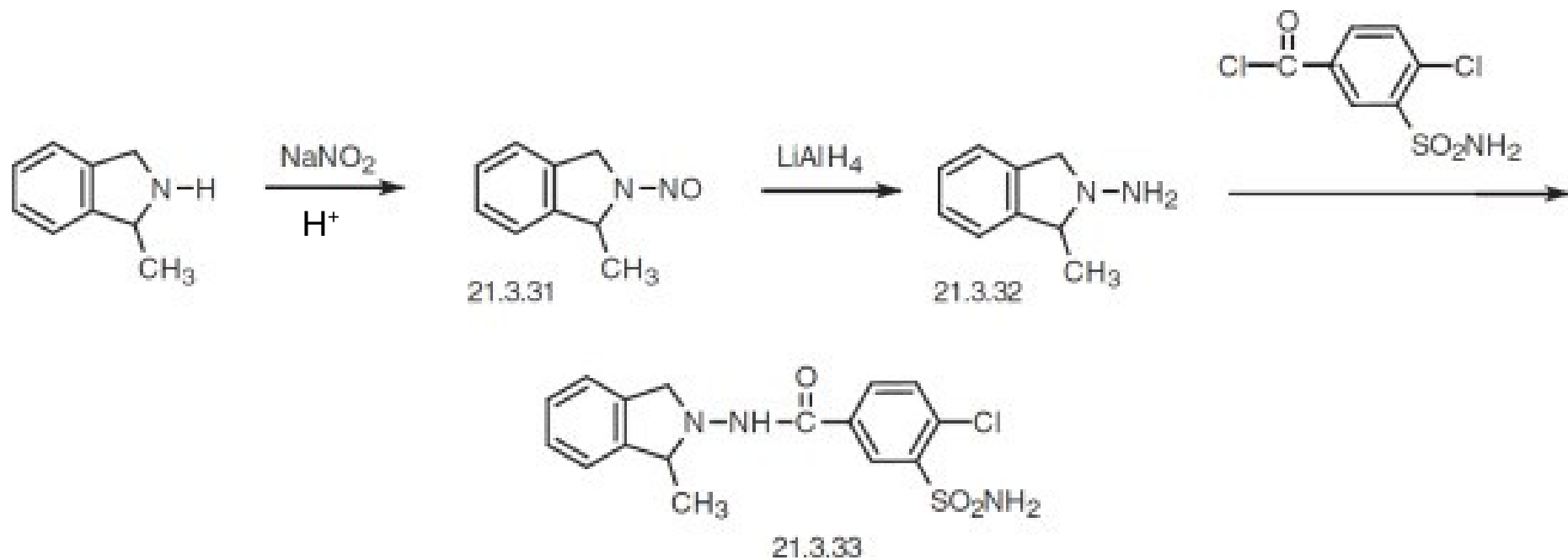
# Metabolism of acetazolamide



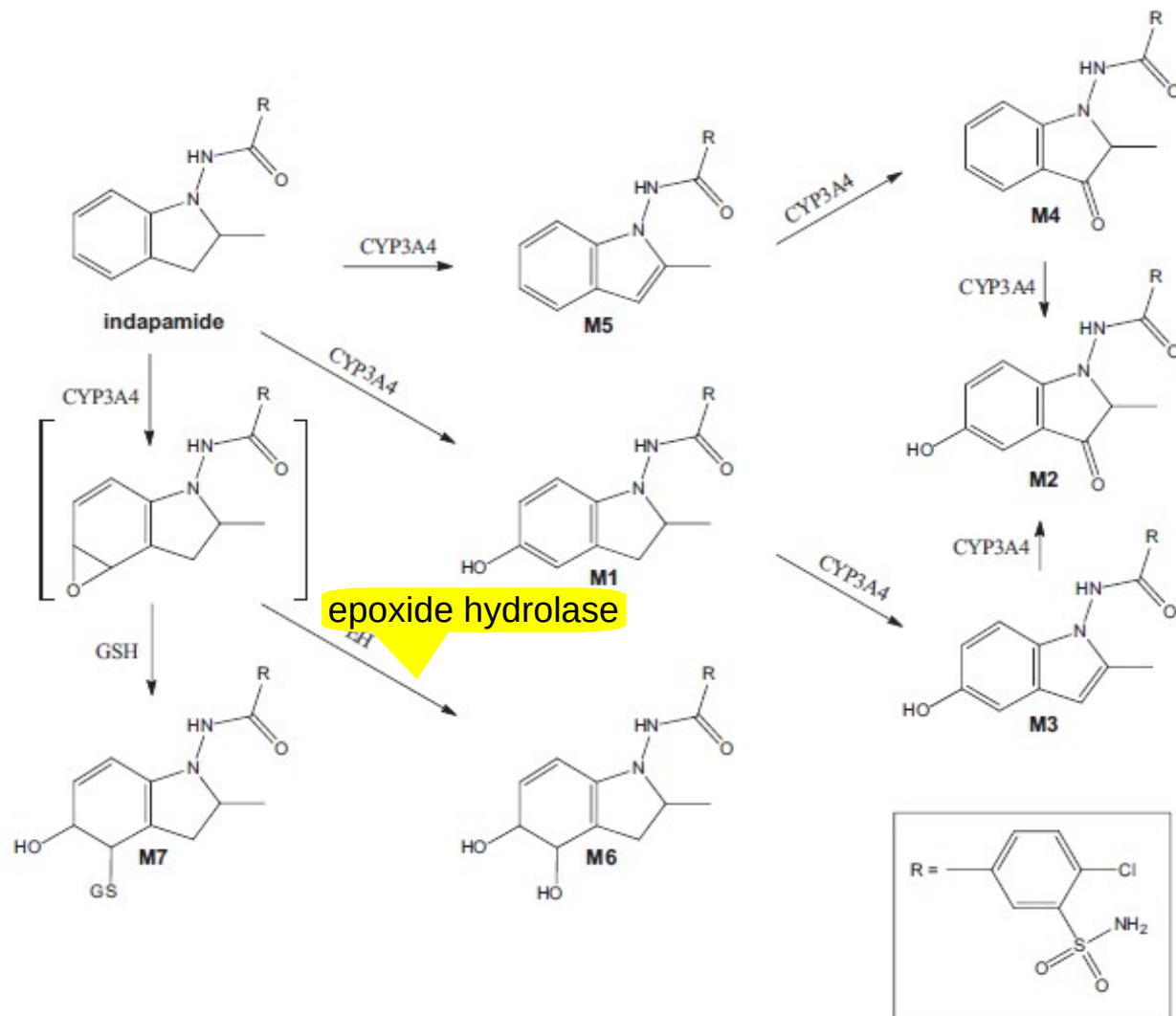
# Synthesis of chlorthalidone



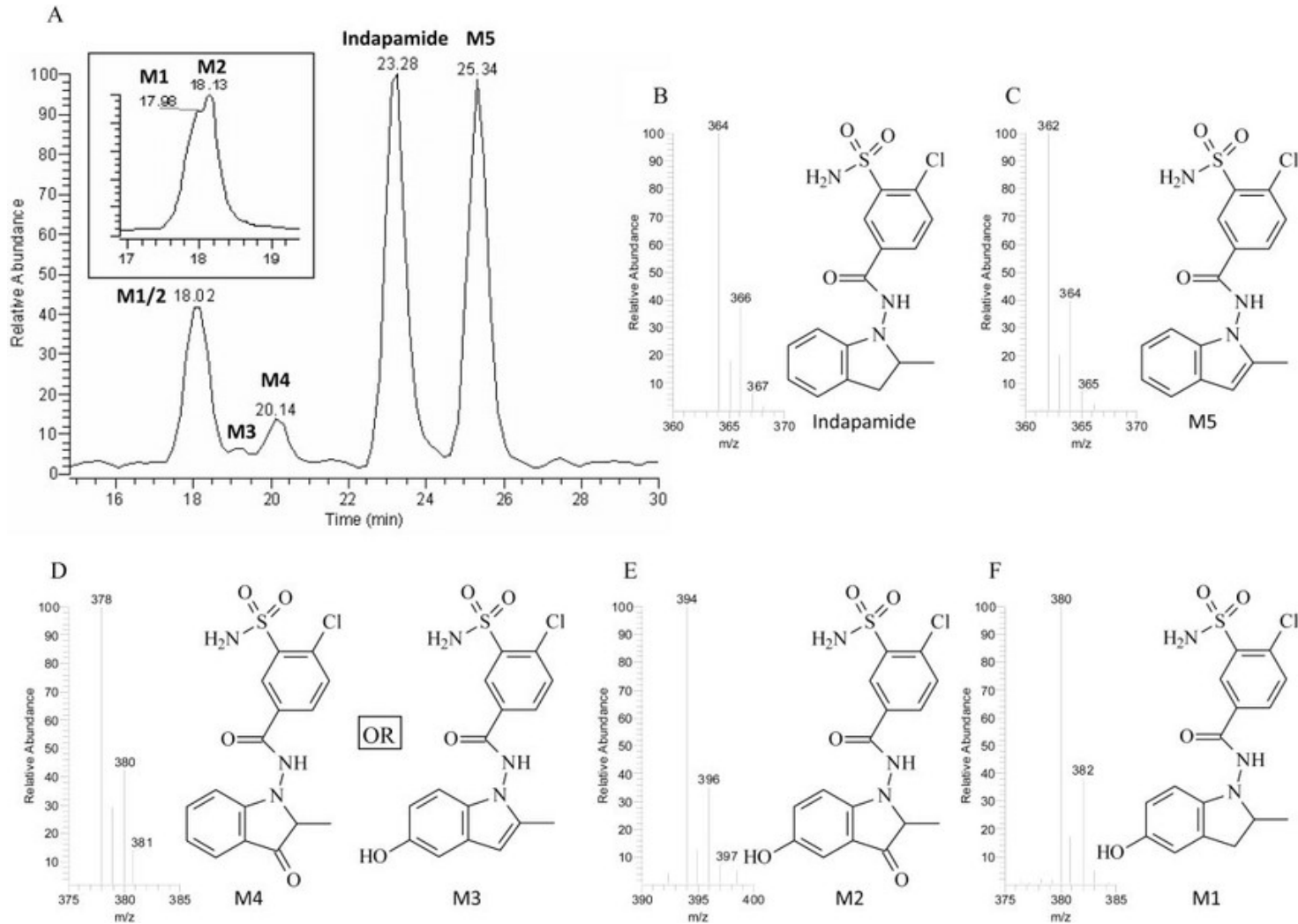
# Synthesis of indapamide



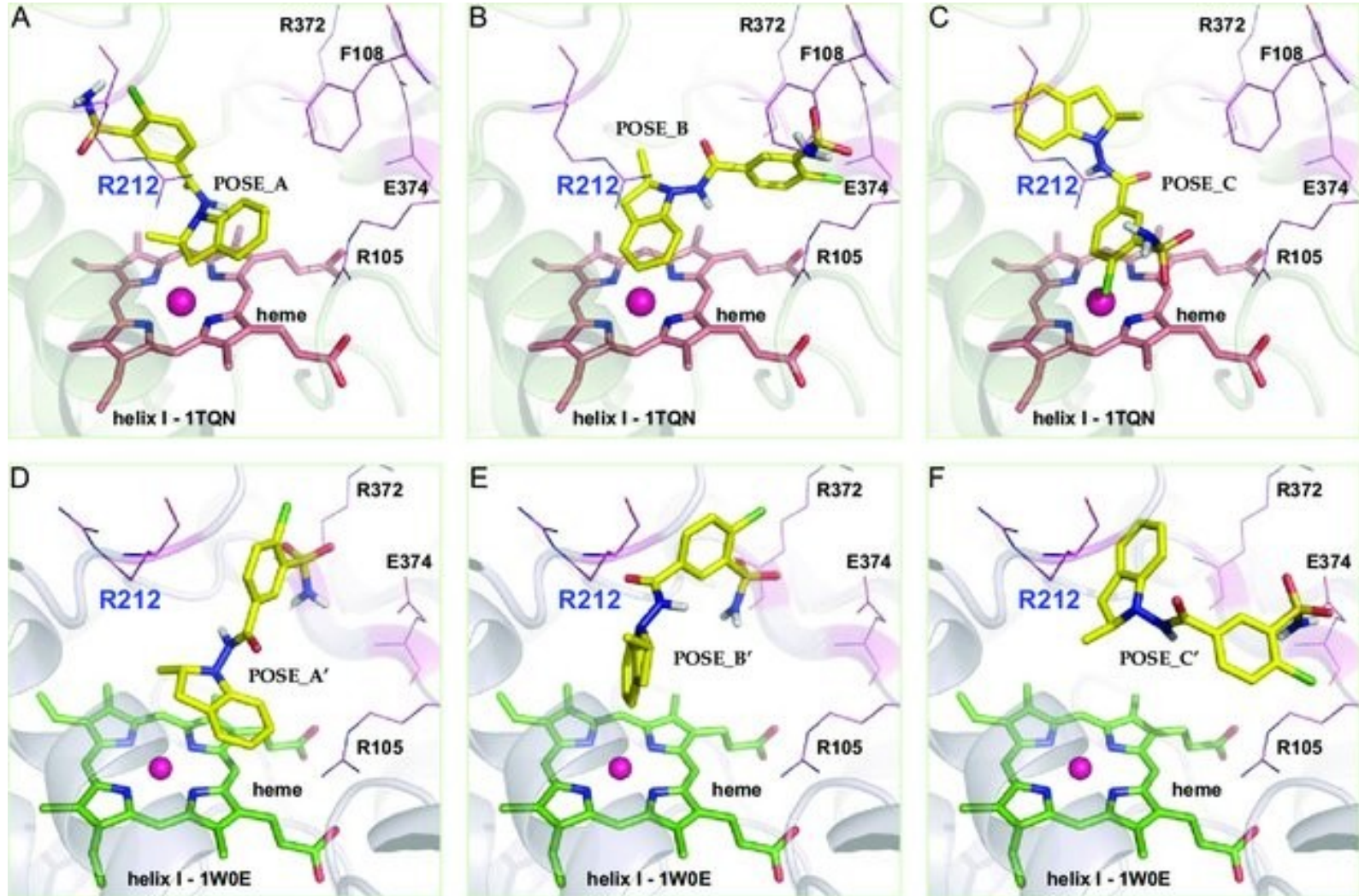
# Metabolism of indapamide



# Metabolites of indapamide formed at CYP3A4

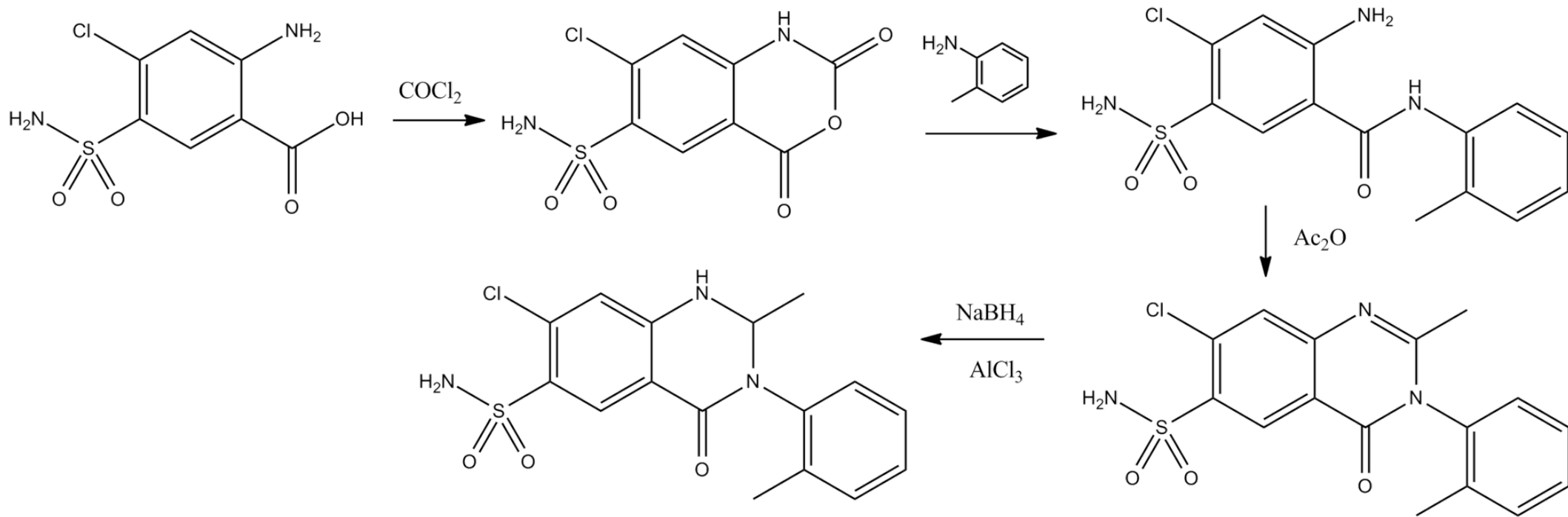


Possible different orientations of indapamide molecule to the active site of CYP3A4 resulting into different metabolites

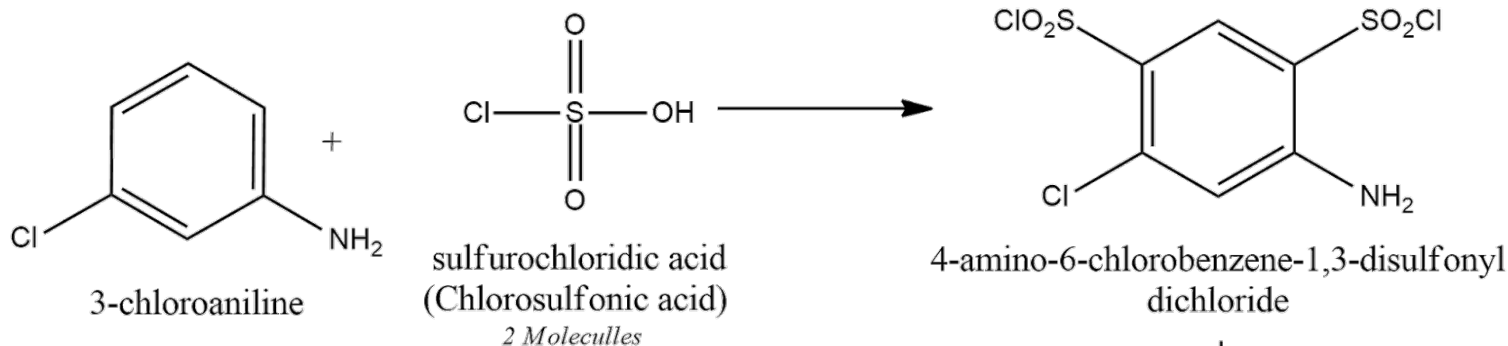




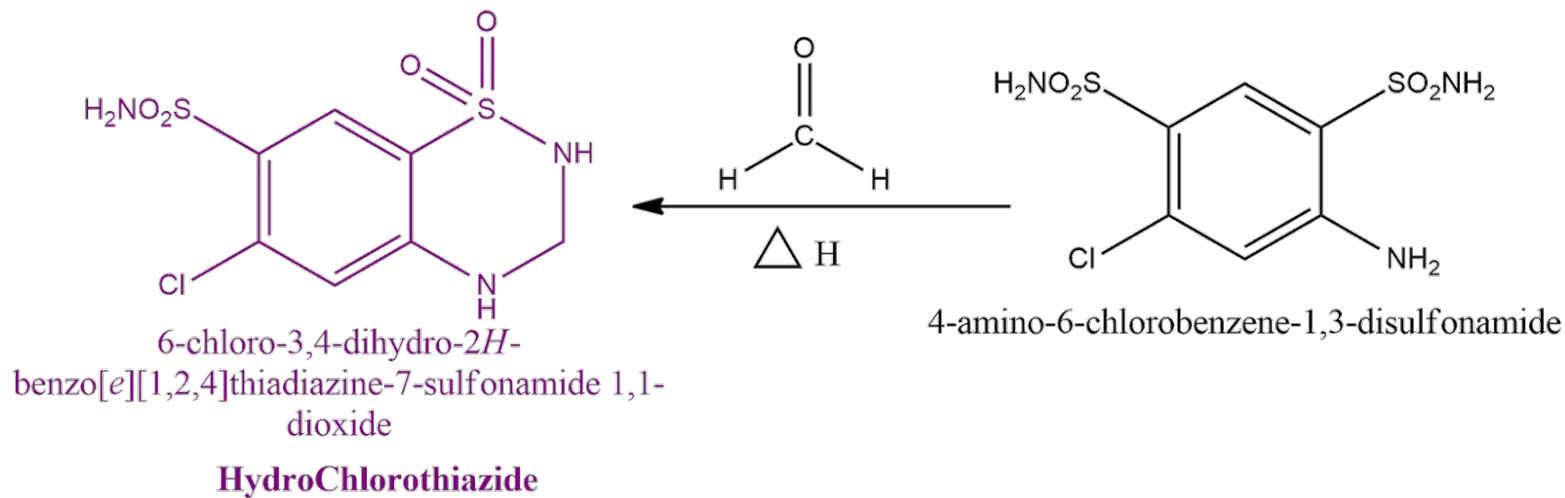
# Synthesis of metolazone



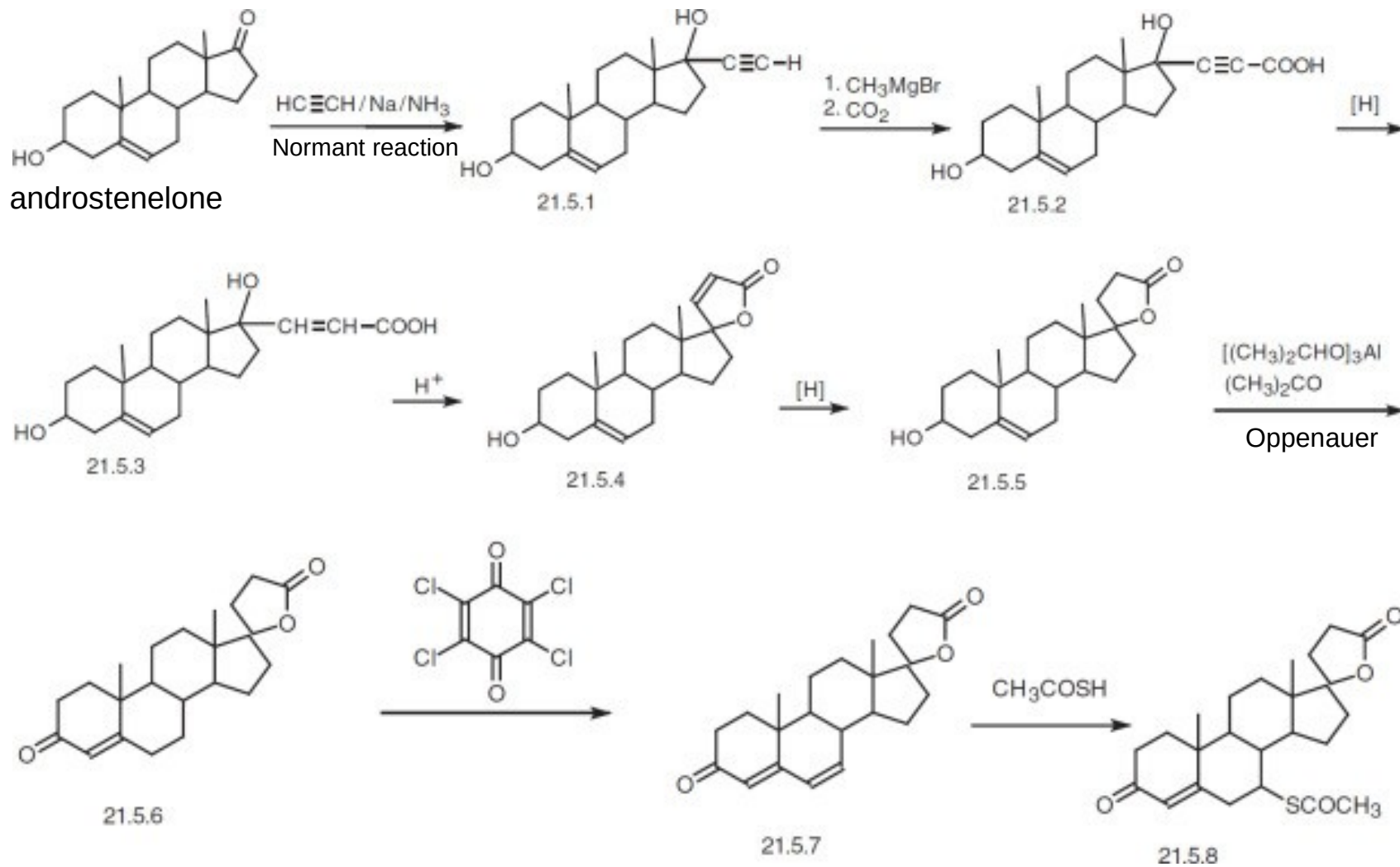
# Synthesis of hydrochlorothiazide



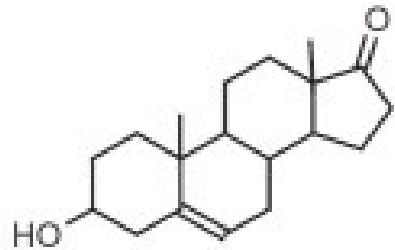
[www.medicinal-chemistry-notes.blogspot.com](http://www.medicinal-chemistry-notes.blogspot.com)  
Post written by  
Dr. Aqeel Nasim



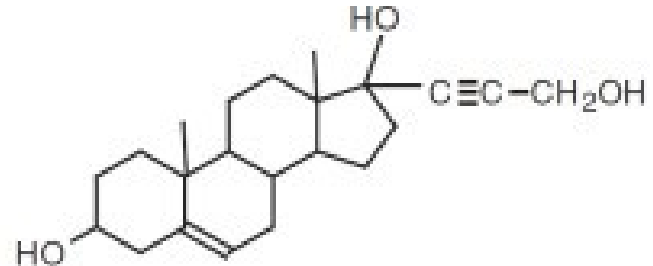
# Synthesis of spironolactone



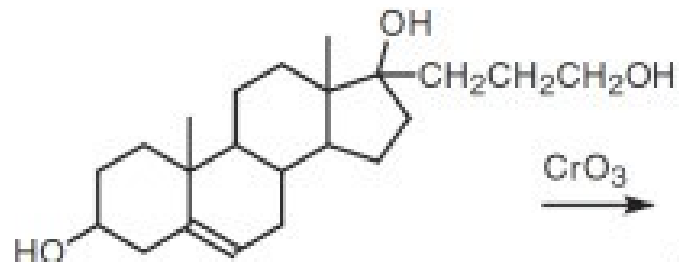
## An alternative synthesis of spironolactone



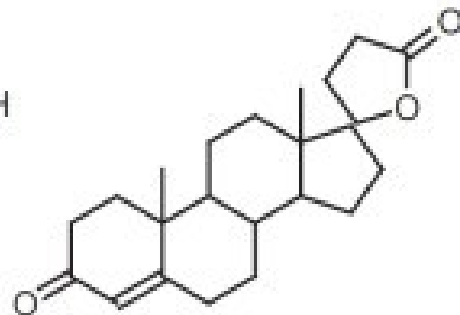
androst-4-en-3-one



21.5.9

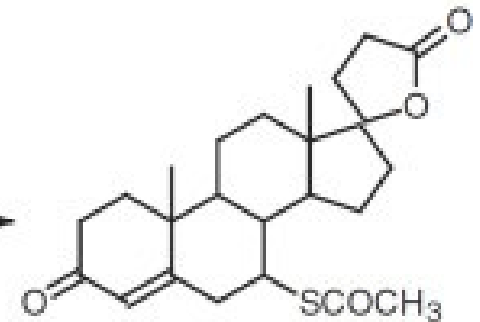
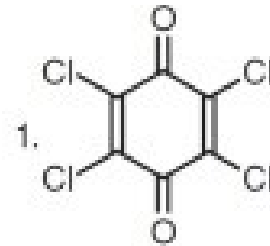


21.5.10



21.5.6

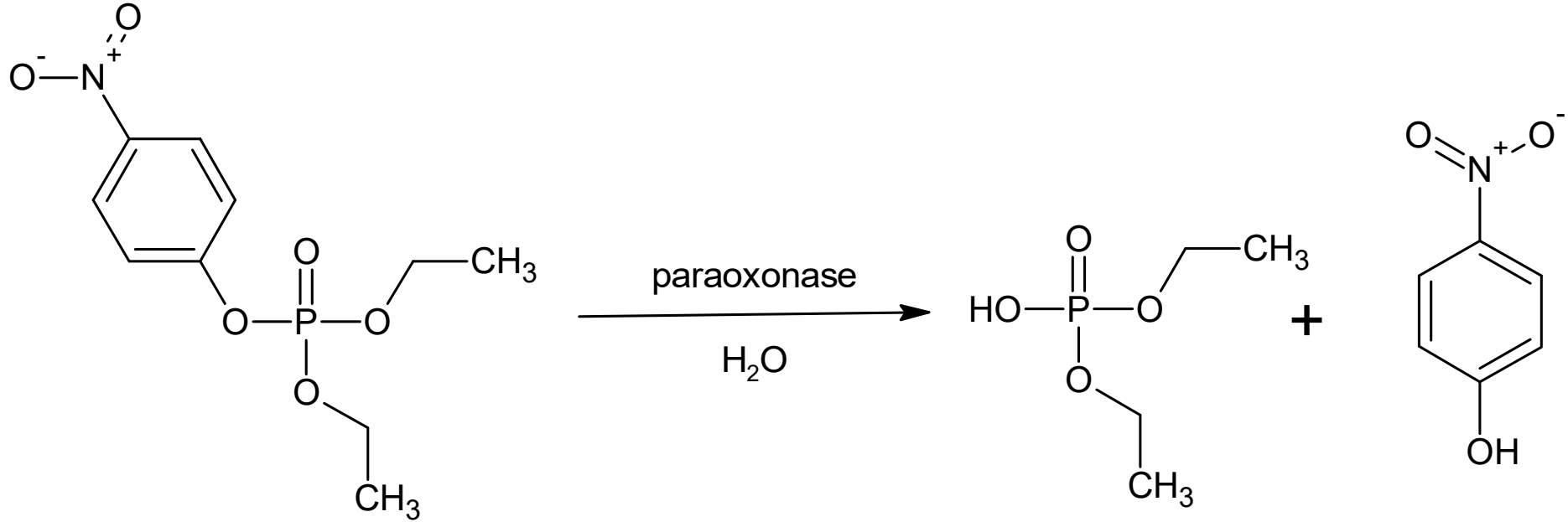
androst-4-en-3,17-dione



21.5.8

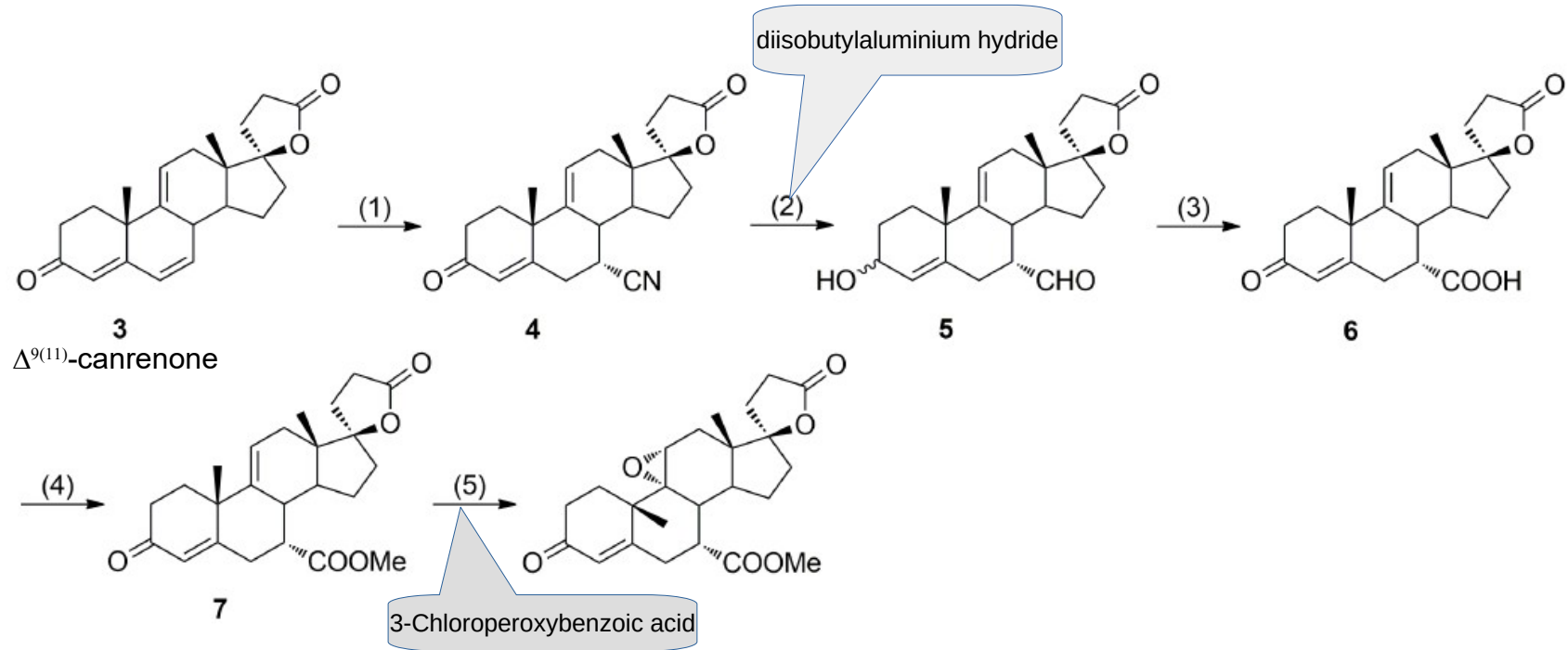


Where paraoxonase took its name?



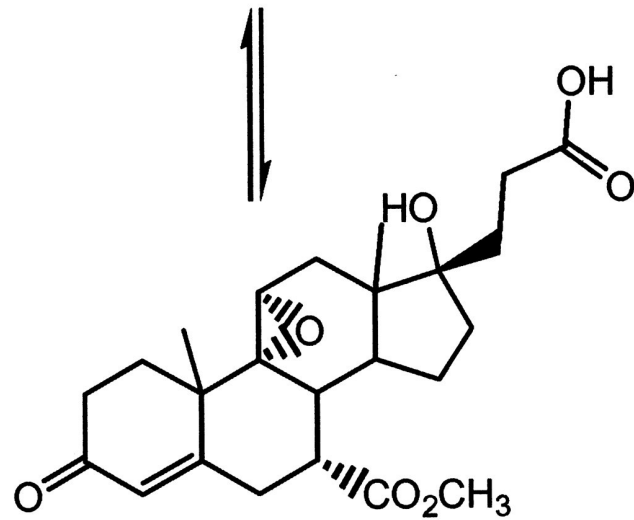
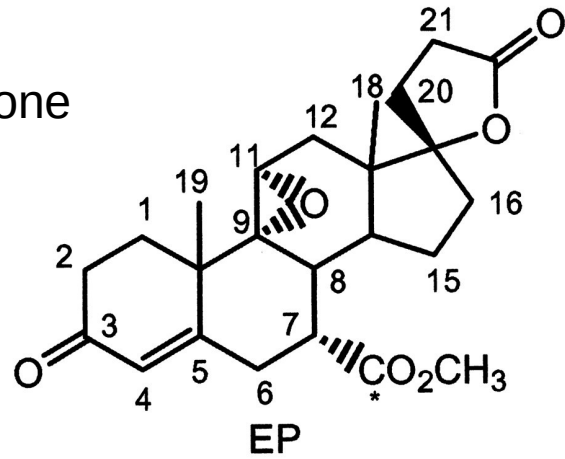
paraoxon

# Synthesis of eplerenone



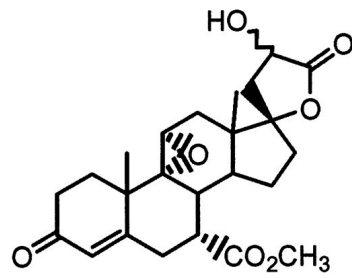
**Scheme 1.** The original eplerenone synthesis from Ciba-Geigy AG (Basel, Switzerland) [17,18]. *Reagents and Conditions:* (1)  $\text{Et}_2\text{AlCN}$ , THF; (2) DIBAL-H, benzene; (3)  $\text{CrO}_3$ ,  $\text{H}_2\text{SO}_4$ , acetone; (4)  $\text{CH}_2\text{N}_2$ ,  $\text{CH}_2\text{Cl}_2$ ; (5) m-CPBA,  $\text{CH}_2\text{Cl}_2$  or  $\text{H}_2\text{O}_2$ ,  $\text{Cl}_3\text{CCN}$ ,  $\text{K}_2\text{HPO}_4$ ,  $\text{CH}_2\text{Cl}_2$ .

# Metabolic activation of eplerenone

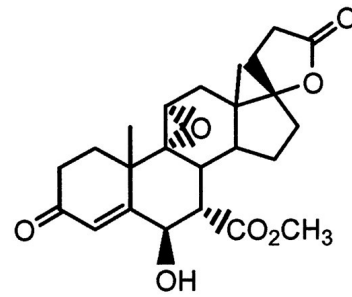




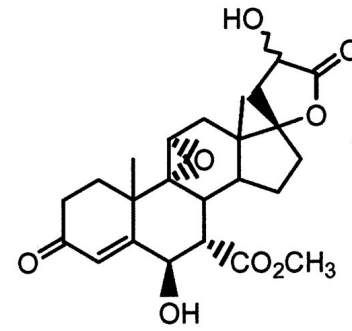
Metabolites of eplerenon  
identified in human  
plasma, urine, and feces



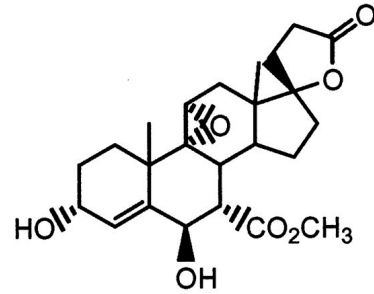
21-OHEP



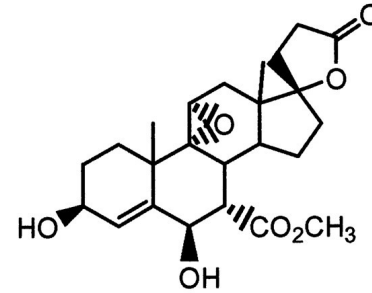
6β-OHEP



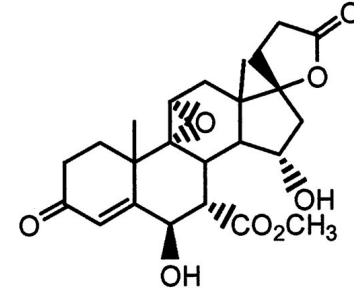
6β, 21-OHEP



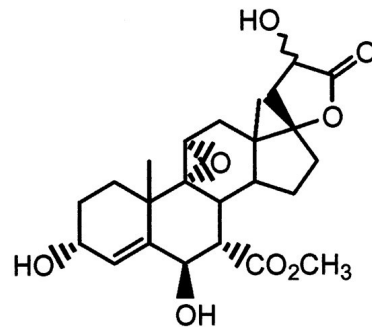
3α, 6β-OHEP



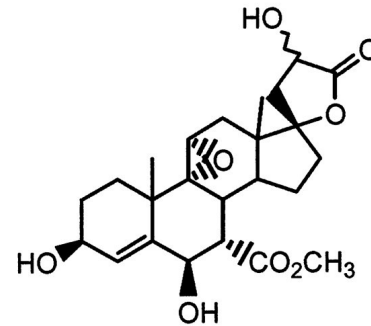
3β, 6β-OHEP



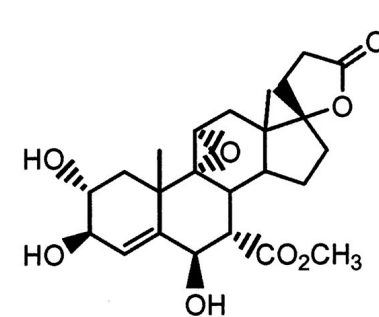
6β, 15α-OHEP



3α, 6β, 21-OHEP

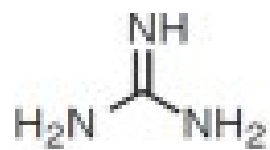


3β, 6β, 21-OHEP

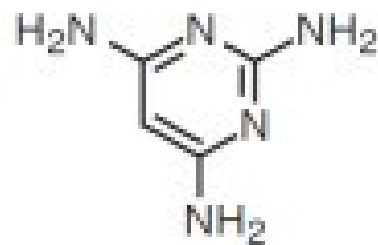


2α, 3β, 6β-OHEP

## Synthesis of triamterene

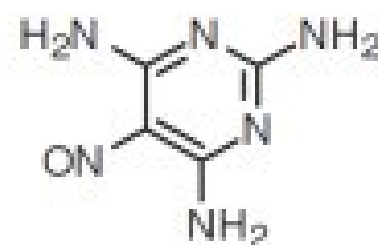


$\text{CH}_3\text{ONa}$



21.5.11

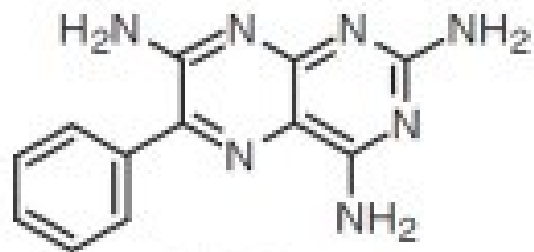
$\text{HNO}_2$



21.5.12

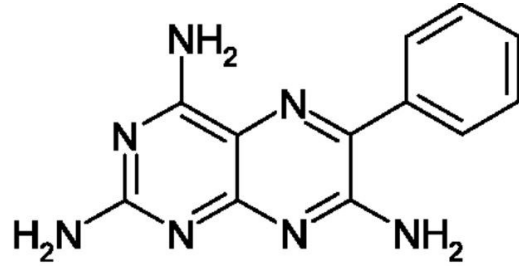


2.  $\text{CH}_3\text{ONa}$



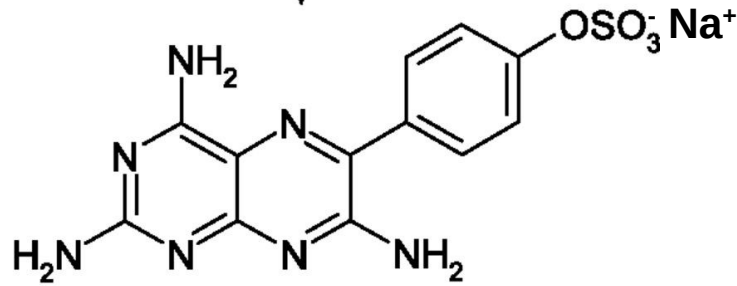
21.5.13

## Triamterene metabolism



**triamterene**

**Na<sup>+</sup> channel potency: ~5600 nM**



**4-hydroxytriamterene sulfate**

**Na<sup>+</sup> channel potency: ~19000 nM**