

Phase-II reactions

Conjugation reactions and reagents

Reaction	Reagent	Group in substrate
Glucuronidation	UDP-glucuronate	-OH, -COOH, -NH ₂
Sulfation	PAPS	-OH, -NH ₂ , -SH
Methylation	SAM	-OH, -NH ₂
Acetylation	acetyl-CoA	-OH, -NH ₂
Sulfide formation	glutathione	Ar-halogen, Ar-epoxide
Amide formation	glycine, taurine	-COOH

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Glucuronidation

1. CONJUGATION WITH GLUCURONIC ACID

- ▶ UDP glucuronyl transferases
- ▶ Conjugates with OH & COOH are conjugated with glucuronic acid derived from glucose



Drug glucuronide + UDP

- ▶ Drugs - Aspirin, Paracetamol, PABA, Metronidazole, Morphine, Diazepam

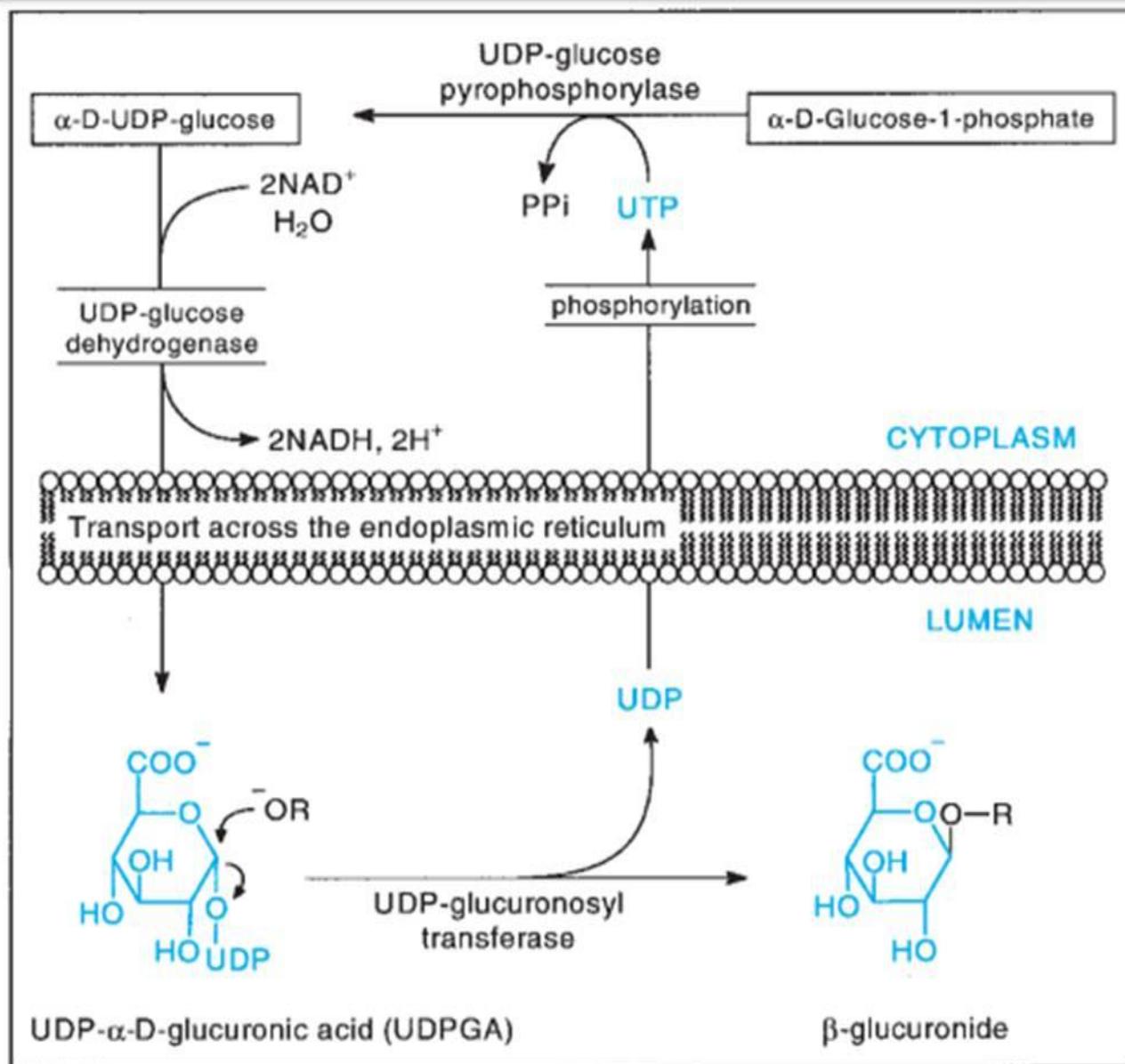
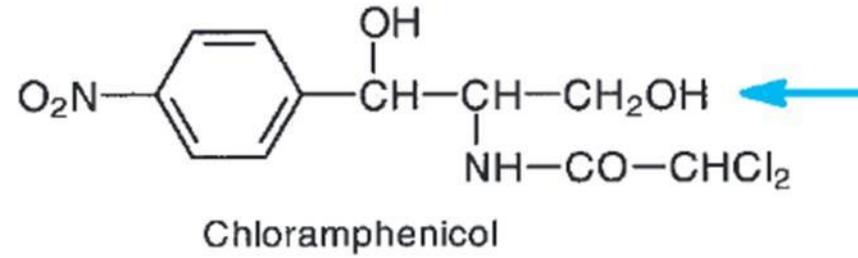
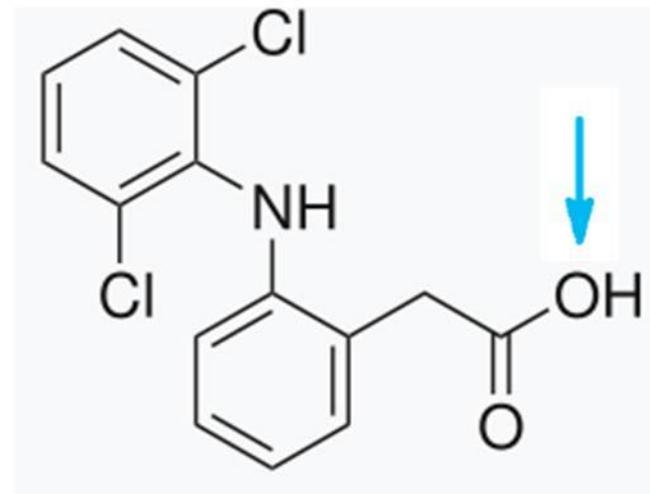


Figure 6-46. Synthesis of UDP-glucuronic acid and inversion of configuration ($\alpha \rightarrow \beta$) during glucuronidation of a phenolic xenobiotic (designated RO⁻).

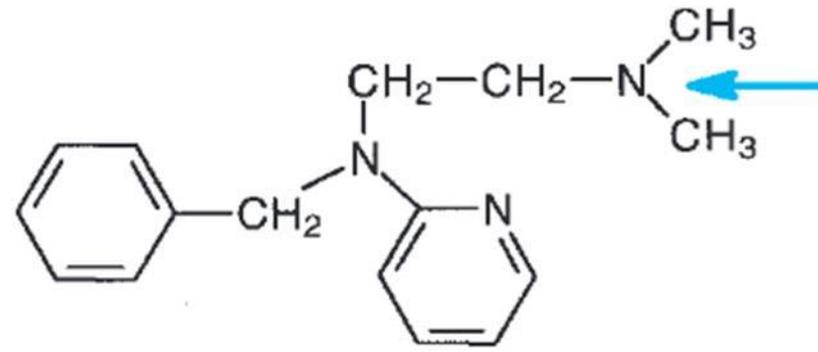
O-glucuronides (ethers)



O-glucuronides (esters)

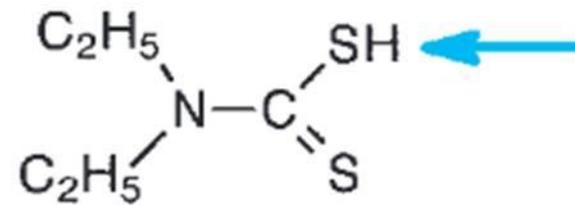


N-glucuronides



Tripeleminamine

S-glucuronides

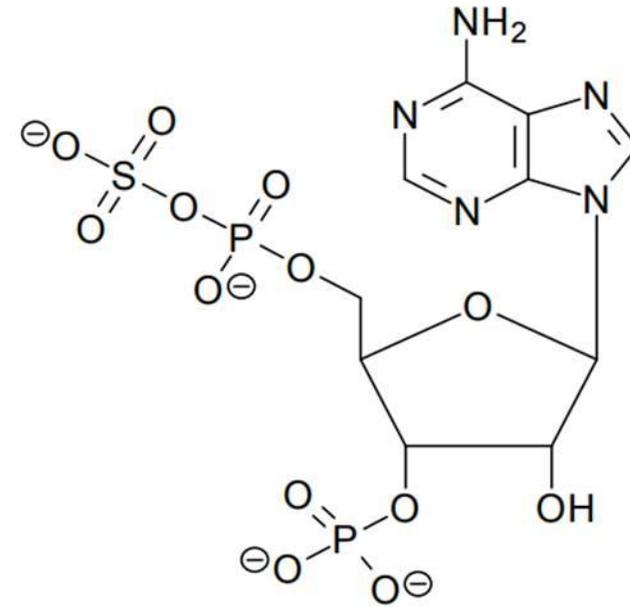


Diethyldithiocarbamate

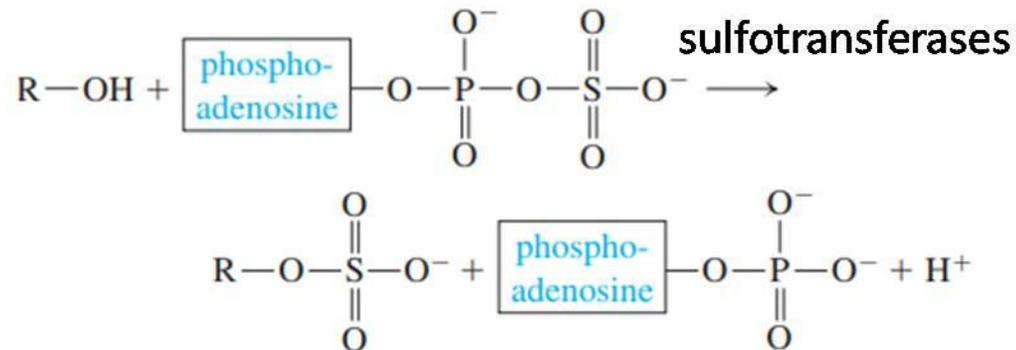
Sulfation

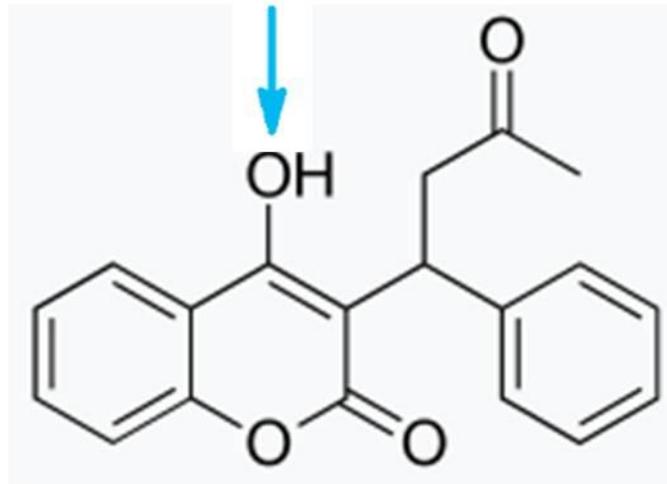
CONJUGATION WITH SULFATE

- ▶ Drug groups-Amino, Hydroxyl
- ▶ Cytoplasmic Enzymes - Sulfotransferases / Sulfokinases.
- ▶ Methyl dopa, Steroids, Chloramphenicol, Warfarin

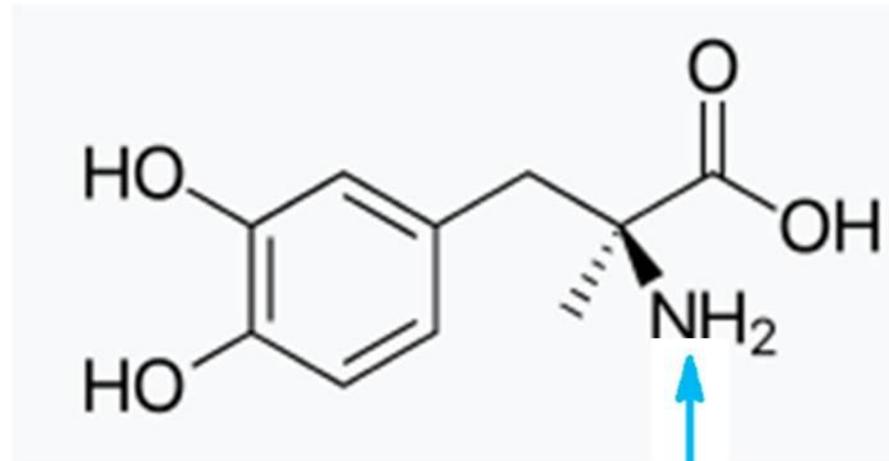


3'-phosphoadenosine 5'-phosphosulfate (PAPS)





Warfarin



Methyl-DOPA