Phase I metabolism covers oxidations, reductions, and hydrolytic reactions. In this section we are focusing on oxidations, but many oxidations are coupled with a hydrolysis. We will treat the downplay the hydrolysis stage and emphasize on the oxidation step. The cytochrome P-450 (CYP-450) family of enzymes performs many of the oxidations in the body.

Oxidations are often divided into three categories:

- sp\(^3\) hybridized carbons
- sp\(^2\) hybridized carbons
- heteroatoms

These few reactions do not cover the entire spectrum of possible drug metabolisms, but they do indeed include a surprisingly high percentage of the commonly encountered metabolic reactions in drugs.

**sp\(^3\) hybridized carbon oxidations**

Oxidations of sp\(^3\) hybridized carbons are often observed as dealkylations, especially demethylations of amines and ethers. Amines that lose an N-methyl group often take on the prefix “nor”. Ethers that lose an O-methyl group take on the prefix “desmethyl”.

![Chemical structures](image)

Alcohol oxidations are also common. Secondary alcohols tend to be oxidized to ketones. Primary alcohols initially are oxidized to aldehydes, when tend to rapidly oxidized to carboxylic acids. In the example of losartan, the acid is considered the only metabolite since the aldehyde is so short-lived.
**sp² hybridized carbon oxidations**

Oxidations of sp² hybridized carbons normally involve aromatic rings. The aromatic ring is initially epoxized, and the epoxide rearranges to restore aromaticity and form a phenol. The rearrangement is frequently not regioselective, and isomeric metabolites may be observed.

**heteroatom oxidations**

Heteroatom oxidations occur on sulfur atoms and nitrogens, especially sp² hybridized nitrogens.