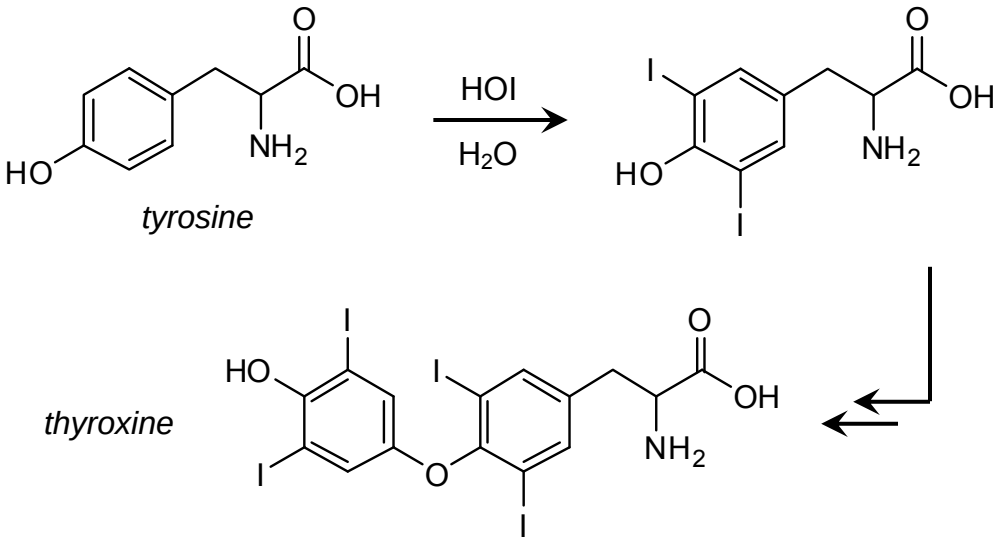
Chemistry 2302

Workshop 8
Electrophilic Aromatic Substitution in the Thyroid

Iodide (I^-) is an essential nutrient, and since the 1930's most of Americans' dietary iodide has been supplied by iodized salt. Before then, goiter—enlargement of the thyroid caused by iodide deficiency—was a particular problem in Midwestern states, including Minnesota, because of our iodine-poor soil and waters. The primary chemical function of the thyroid is to synthesize the metabolic hormone thyroxine. To do this, an enzyme called thyroid peroxidase (TP) oxidizes dietary I^- to form hypoiodous acid (HOI), which reacts with the amino acid tyrosine via electrophilic aromatic substitution:

A woman with goiter.



tyrosine

thyroxine

(No Lewis acid activator is needed in this reaction; tyrosine is a strong enough electron donor to add directly to HOI.) Without dietary iodide, the thyroid cannot carry out this function. In response, thyroid cells begin to proliferate, and the gland grows (as shown in the picture above).

1. Draw an electrophilic aromatic substitution mechanism for the first reaction above.

2. Explain why iodine atoms are added specifically to the carbons adjacent to the alcohol carbon.

3. Two iodine atoms are added to the aromatic ring. Is the second iodine added more or less easily than the first? Why?