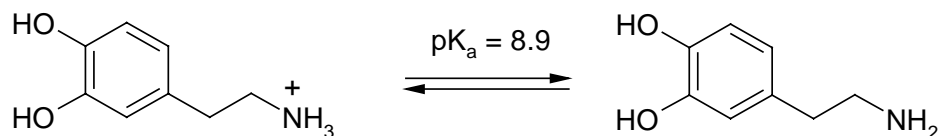


Drug Metabolism, Prodrugs

Please answer Q1 and either Q2 or Q3.

1. Parkinson's disease is characterized by a progressive loss of neurotransmitter dopamine. The equilibrium between the protonated and the neutral form is shown below.



- Why the oral administration of dopamine is not an effective treatment of Parkinson's disease?
- Propose a prodrug approach to overcome the limited efficacy of oral dopamine?
- How could you ensure that the formation of dopamine from your prodrug occurs mainly in the nervous tissue?
- Propose a major metabolic reaction that leads to the inactivation of dopamine in the brain
- Propose a major metabolic reaction that leads to inactivation of the prodrug outside the brain
- Propose approaches to protect the prodrug or dopamine from degradation, thus prolonging their action.

2. Assuming that cytochrome P450 is responsible for the metabolism of the following compounds, show the structure of the major primary oxidation product or the final metabolite from each of the molecules below:

