## QUESTIONS FOR DISCUSSION

1. Monoamine oxidase has a pH activity profile with a maximum at approximately pH 9.5, a midpoint for the ascending branch at approximately pH 7.5, and a midpoint for the descending branch at approximately pH 10.3. Suggest possible active-site residues for this enzyme. Use Table 6-1 to justify your choices.
2. Lysozyme acts to cleave glycosidic bonds in polysaccharides. A proposed mechanism is shown in **Figure 6-23**, emphasizing the catalytic roles of two acidic residues in the active site. The rate of polysaccharide hydrolysis as a function of pH shows a maximum at approximately pH 5.2, with a midpoint for the ascending branch at approximately pH 3.9 and a midpoint for the descending branch at approximately pH 6.7. Describe the state of titration (ionized or not) of Asp 52 and Glu 35 at pH 3.0, on the ascending branch at pH 3.9, at the maximum at pH 5.2, on the descending branch at pH 6.7, and at pH 8.0.
3. For the following enzymes, decide whether the suggested amino acid could replace the indicated active-site residue, to maintain activity. Explain your choice in each case.
   a. Chymotrypsin: Replace serine 195 with (A) threonine; (B) cysteine; (C) alanine.
   b. Ribonuclease A: Replace histidine 12 with (A) lysine; (B) tyrosine; (C) cysteine.
   c. Carbonic anhydrase: Replace glutamate 106 with (A) lysine; (B) aspartate; (C) tyrosine.
4. The Zn(II) cofactor in human carbonic anhydrase isozymes I and II can be replaced by Co(II) with nearly complete restoration of enzymatic activity. $Mg^{2+}$ and $Ca^{2+}$ are both divalent cations present in biological systems at much higher concentrations than either zinc or cobalt. Why can't magnesium or calcium replace zinc (or cobalt) as a cofactor for carbonic anhydrase?
5. Interestingly, carbonic anhydrase can also act as an esterase, hydrolyzing *p*-nitrophenyl acetate, for example. Suggest a possible mechanism for this esterase action.
6. Figure 6-14 shows three inhibitors of carbonic anhydrase. Which structural features do they have in common?
7. A bacterial proline racemase interconverts the two stereoisomers of proline. It is strongly inhibited by pyrrole-2-carboxylic acid. However, tetrahydrofuran-2-carboxylic acid is not an inhibitor. Draw the structures of all four compounds. What does this suggest

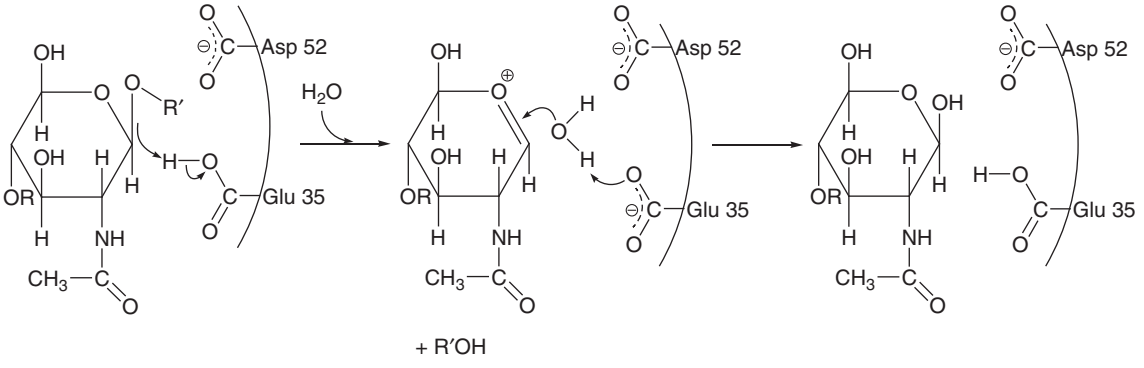


**Figure 6-23** Mechanism for action of lysozyme, emphasizing acid–base catalysis by the side chains of Glu 36 and Asp 52.

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