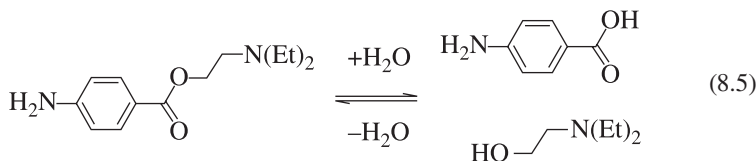


As a consequence, it is recommended to preserve aqueous atropine solutions buffered at around pH 3.5–4. If stored in lime glass, the stability is reduced as a result of the alkalinity of the glass.

Another good example of hydrolysis reaction is the anesthetic procaine, which is prone to specific acid-catalyzed decomposition (of the protonated form) at a pH value less than 2.5, a specific base-catalyzed hydrolysis between pH 5.5 and 8.5, titration around pH 8.5–11.0, and, finally, the base-catalyzed hydrolysis of the free base at a pH value greater than 12.0. Maximum stability occurs at pH 3.5.



Commercial preparations of procaine are limited to injectable forms. As water is the solvent of choice for injectable drugs, procaine can be protected from hydrolysis by increasing the solubility of procaine in a nonaqueous environment and by protecting (shielding) the drug from hydrolysis by employing surfactants to micellize the drug.

Degradation by hydrolysis is affected by a number of factors, including solution pH, buffer salts, ionic strength, and so on. In addition, in the presence of cosolvents, complexing agent's surfactant can also affect this type of degradation. The most important factor is the solution pH, as the hydroxyl ions are stronger nucleophiles than water; thus, degradation reactions are usually faster in alkaline solution than in water. At low pH, protons can also catalyze hydrolysis reactions as a result of specific acid–base catalysis. Besides these two ions, buffer ions such as acetate and citric acid can also catalyze degradation, where the effect is known as general acid–base degradation. Therefore, pH adjustment should make the right choice of buffers and, where possible, in smallest quantities (strength).

8.2.4.2 Oxidation

The second most common way in which a compound can decompose in solution is via oxidation. Reduction–oxidation (redox) reactions involve either the transfer of oxygen or hydrogen atoms or the transfer of electrons. Oxidation is promoted by the presence of oxygen, and the reaction can be initiated by the action of heat, light, or trace metal ions that produce organic free radicals. These radicals propagate the oxidation reaction, which proceeds until inhibitors destroy the radicals or until side reactions eventually break the chain. A simple test to see if a drug substance is prone to oxidation is to bubble air or oxygen or treat with hydrogen peroxide and estimate the level of degradation.

The sensitivity of each new drug entity to atmospheric oxygen must be evaluated to establish if the final product should be packaged under inert atmospheric conditions and if it should contain an antioxidant. Sensitivity to oxidation of a solid drug can be ascertained by investigating its stability in an atmosphere of high oxygen tension.