

Fig. 48.13 • All-trans-retinol (a) undergoes thermal degradation to give 13-cis-retinol (b) and undergoes photodegradation to form 9-cis-retinol (c).

also enables the molecule to undergo geometrical isomerization. The double bonds in the chain are all in the *trans* configuration. On storage of all-trans-retinol or on subjecting it to heat, the molecule changes configuration at the double bond at the 13-position of the molecule, to form 13-cis-retinol (Fig. 48.13), which has no activity as a vitamin.

Structural isomers are sometimes formed as a result of drug degradation. The best known example of this is betamethasone-17-valerate, a potent corticosteroid. A major route of degradation of this drug is by migration of the valerate ester substituent to the side chain, forming betamethasone-21-valerate (Fig. 48.14). The mechanism is promoted by the close proximity of the hydroxyl group in the side chain to the ester substituent. This reaction is of concern where topical formulations of betamethasone-17-valerate are diluted with an inappropriate diluent.

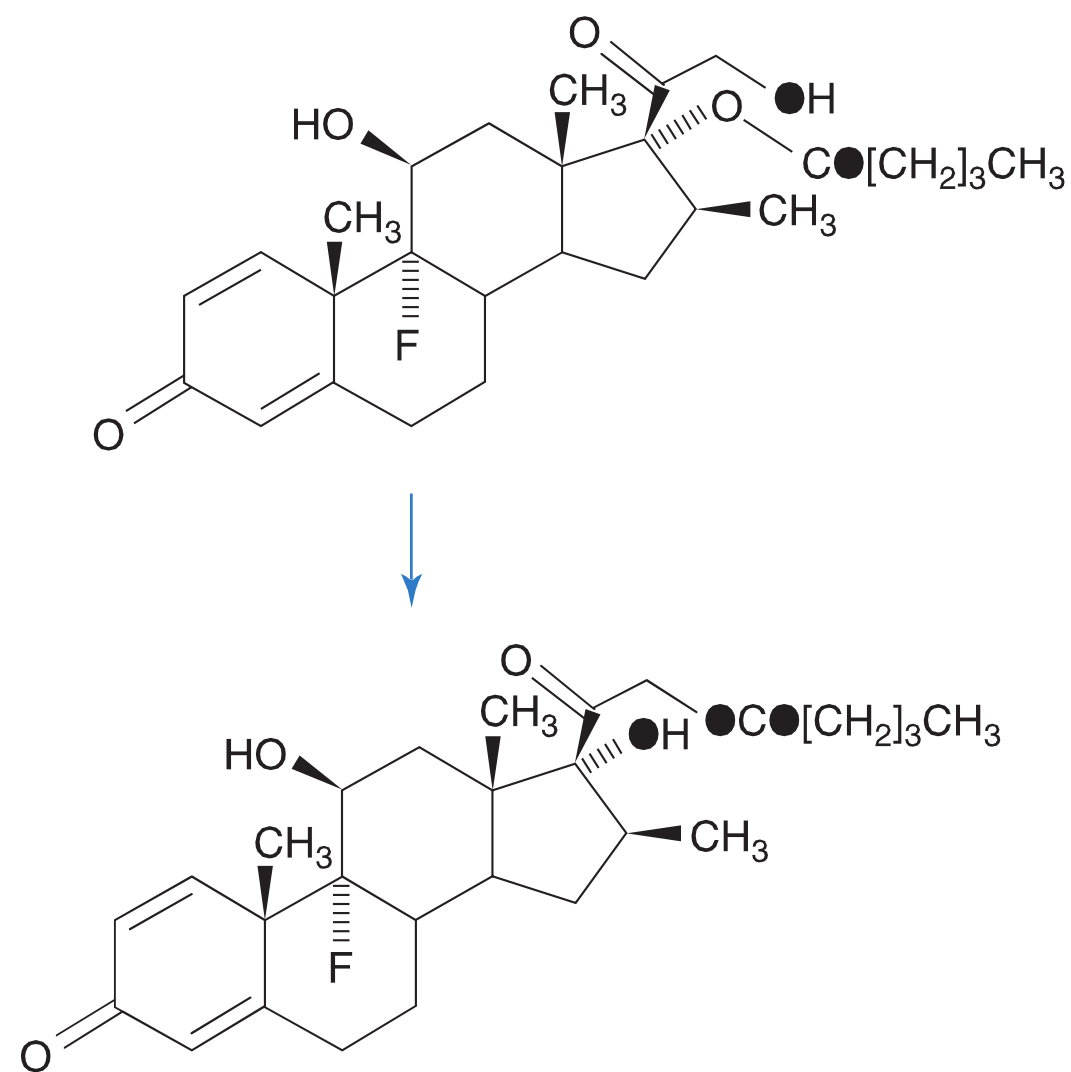


Fig. 48.14 • Degradation of betamethasone-17-valerate to betamethasone-21-valerate.

Photodegradation

Molecules that absorb the wavelengths of light associated with sunlight or artificial light may be susceptible to light-induced degradation (*photolysis*). The 300–400 nm wavelengths tend to be most damaging. Shorter wavelengths are also damaging but are

not of practical concern because they are not present in sunlight or artificial light.

Carbonyl, nitro, alkene, aryl chloride and phenolic compounds are most susceptible to photodegradation. Many photolysis reactions involve oxidation