PROBLEM 22-27

In the problem-solving feature above, methylcyclohexanone was seen to react at its *unsubstituted* α carbon. Try to write a mechanism for the same reaction at the methyl-substituted carbon atom, and explain why this regiochemistry is not observed.

PROBLEM 22-28

Predict the major products of the following base-catalyzed aldol condensations with dehydration.

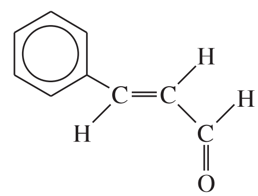
(a) benzophenone (PhCOPh) + propionaldehyde

(b) 2,2-dimethylpropanal + acetophenone

PROBLEM 22-29

(a) Cinnamaldehyde is used in artificial cinnamon flavoring. Show how cinnamaldehyde is synthesized by a crossed aldol condensation followed by dehydration.

cinnamaldehyde



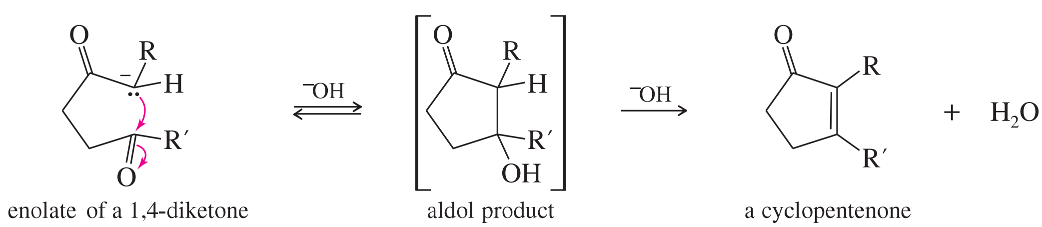
(b) Adding acetophenone slowly to a cold solution of LDA produces the enolate of acetophenone; but adding LDA slowly to a cold solution of acetophenone produces a condensation product. Show the reactions happening in each case, and explain why we observe such different results.

PROBLEM-SOLVING HINT

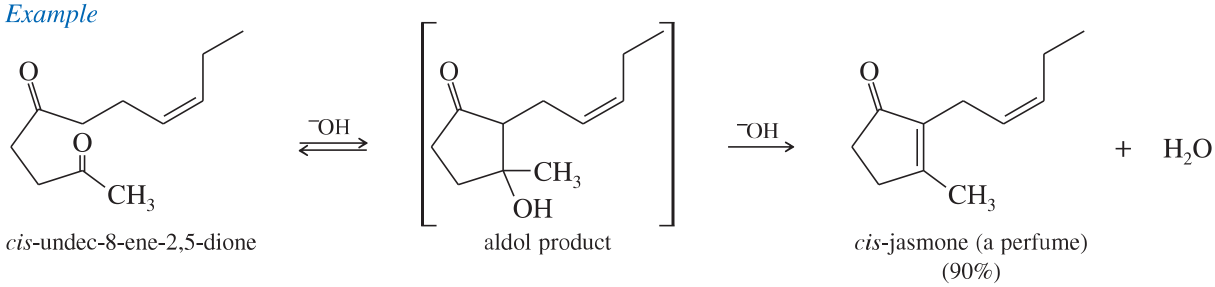
Practice predicting the structures of aldol products (before and after dehydration) and drawing the mechanisms. These reactions are among the most important in this chapter.

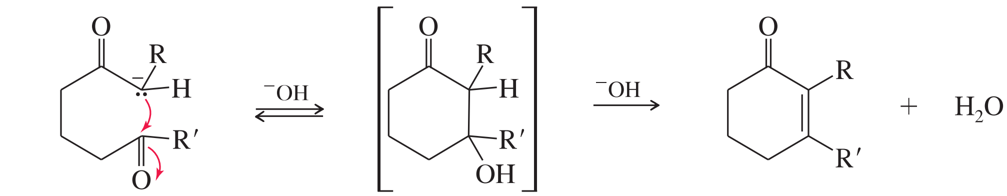
22-10 Aldol Cyclizations

Intramolecular aldol reactions of diketones are often useful for making five- and six-membered rings. Aldol cyclizations of rings larger than six and smaller than five are less common because larger and smaller rings are less favored by their energy and entropy. The following reactions show how a 1,4-diketone can condense and dehydrate to give a cyclopentenone and how a 1,5-diketone gives a cyclohexenone.



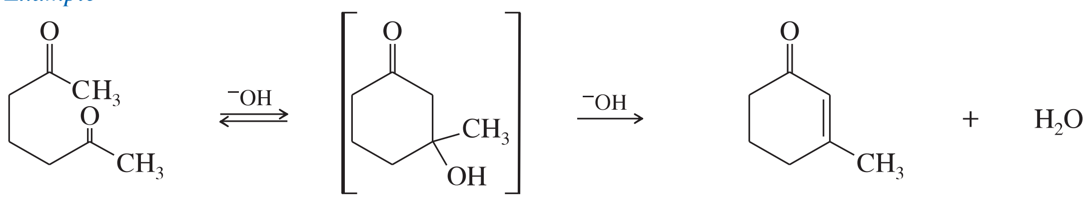
Example





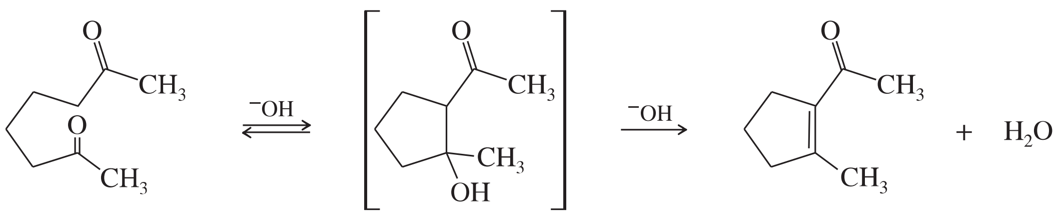
enolate of a 1,5-diketone — aldol product — a cyclohexenone

Example



heptane-2,6-dione (a 1,5-diketone) — aldol product — 3-methylcyclohex-2-enone

The following example shows how the carbonyl group of the product may be outside the ring in some cases.



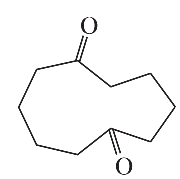
octane-2,7-dione — aldol product — 1-acetyl-2-methylcyclopentene

PROBLEM 22-30

Show how octane-2,7-dione might cyclize to a cycloheptenone. Explain why ring closure to the cycloheptenone is not favored.

PROBLEM 22-31

When cyclodecane-1,6-dione is treated with sodium carbonate, the product gives a UV spectrum similar to that of 1-acetyl-2-methylcyclopentene. Propose a structure for the product, and give a mechanism for its formation.

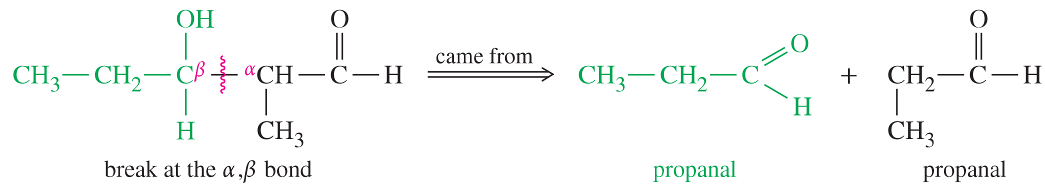


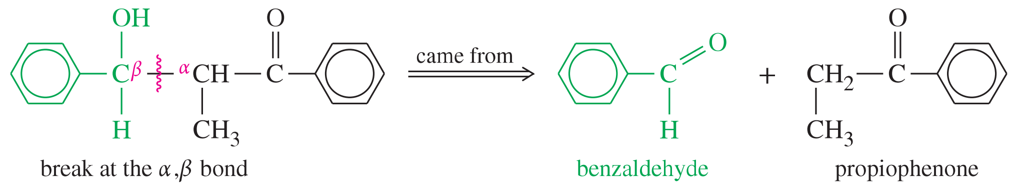
cyclodecane-1,6-dione

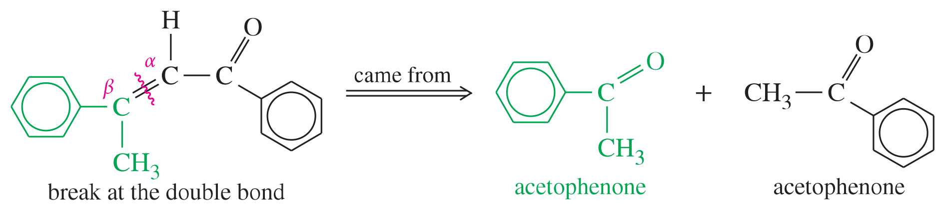
22-11 Planning Syntheses Using Aldol Condensations

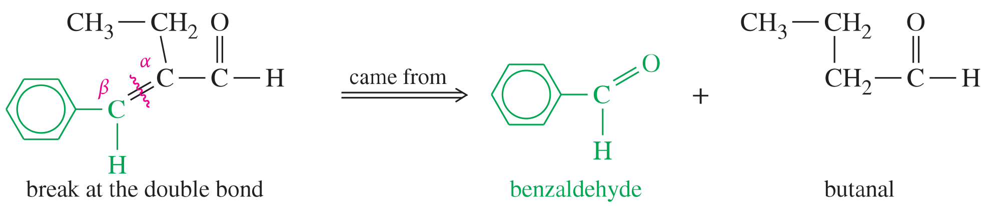
As long as we remember their limitations, aldol condensations can serve as useful synthetic reactions for making a variety of organic compounds. In particular, aldol condensations (with dehydration) form new carbon–carbon double bonds. We can use some general principles to decide whether a compound might be an aldol product and which reagents to use as starting materials.

Aldol condensations produce β-hydroxy aldehydes and ketones (aldols) and α,β-unsaturated aldehydes and ketones. If a target molecule has one of these functionalities, an aldol should be considered. To determine the starting materials, divide the structure at the α,β bond. In the case of the dehydrated product, the α,β bond is the double bond. The following analyses show the division of some aldol products into their starting materials.





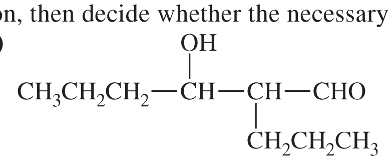




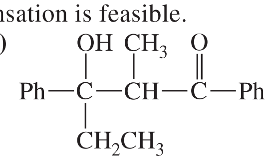
PROBLEM 22-32

Show how each compound can be dissected into reagents joined by an aldol condensation, then decide whether the necessary aldol condensation is feasible.

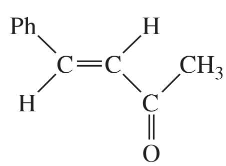
(a)



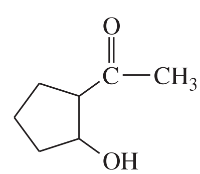
(b)



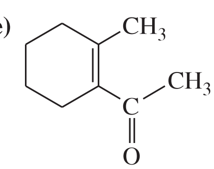
(c)



(d)

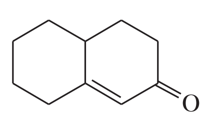


(e)



PROBLEM 22-33

The following compound results from base-catalyzed aldol cyclization of a 2-substituted cyclohexanone.



(a) Show the diketone that would cyclize to give this product.
(b) Propose a mechanism for the cyclization.