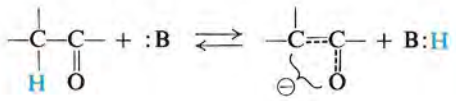
Carbanions I

Acidity of α-hydrogens

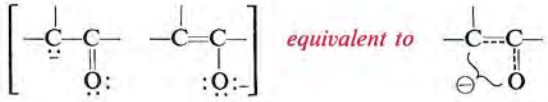
In our introduction to aldehydes and ketones, we learned that it is the carbonyl group that largely determines the chemistry of aldehydes and ketones. At that time, we saw in part how the carbonyl group does this: by providing a site at which nucleophilic addition can take place. But, like the carbon–carbon double bond and the benzene ring, the carbonyl can play another role, not as a functional group, but as a *substituent*. Now we are ready to learn the other part of the story: how the carbonyl group strengthens the acidity of the hydrogen atoms attached to the α-carbon and, by doing this, gives rise to a whole set of chemical reactions.

Ionization of an α-hydrogen,



I

yields a carbanion I that is a resonance hybrid of two structures, II and III,



II III I

resonance that is possible only through participation by the carbonyl group. Resonance of this kind is *not* possible for carbanions formed by ionization of β-hydrogens, γ-hydrogens, etc., from saturated carbonyl compounds.

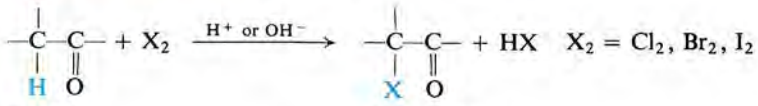
Problem 21.1 Which structure, II or III, would you expect to make the larger contribution to the carbanion I? Why?

Problem 21.2 Account for the fact that the diketone 2,4-pentanedione is about as acidic as phenol, and much more acidic than, say, acetone. Which hydrogens are the most acidic?

Problem 21.3 How do you account for the following order of acidity?

$$(C_6H_5)_3CH > (C_6H_5)_2CH_2 > C_6H_5CH_3 > CH_4$$

1. Halogenation of ketones. Discussed in Secs. 21.3–21.4.



Ketone — α-Halo ketone

Examples:

$$CH_3COCH_3 + Br_2 + :B^- \longrightarrow CH_3COCH_2Br + Br^- + H{:}B$$

Acetone — Bromoacetone

the rate expression

$$\text{rate} = k\,[\text{acetone}][:B]$$

mechanism

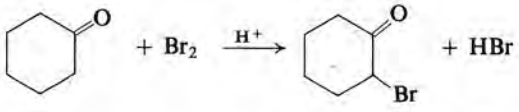
(1) $CH_3CCH_3 + :B^- \rightleftharpoons H{:}B + CH_3C{=}CH_2$ (O, O⊖) — **Slow:** *rate-determining*

I

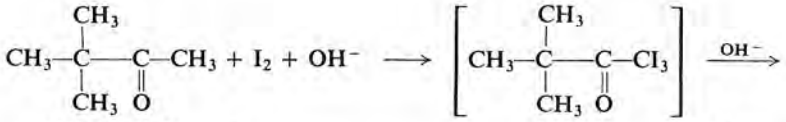
(2) $CH_3C{=}CH_2 + Br_2 \longrightarrow CH_3CCH_2Br + Br^-$ (O, O⊖) — **Fast**

I

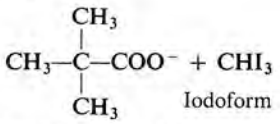
Examples:



Cyclohexanone — 2-Bromocyclohexanone



tert-Butyl methyl ketone
(3,3-Dimethyl-2-butanone)



Iodoform

Trimethylacetate ion

Acid-catalyzed halogenation of ketones. Enolization

$$\underset{\text{Acetone}}{CH_3COCH_3} + Br_2 \xrightarrow{\text{acid}} \underset{\text{Bromoacetone}}{CH_3COCH_2Br} + HBr$$

(1) $$CH_3-\overset{\overset{O}{\|}}{C}-CH_3 + H{:}B^+ \rightleftharpoons CH_3-\overset{\overset{{}^+OH}{|}}{C}-CH_3 + {:}B$$ **Fast**

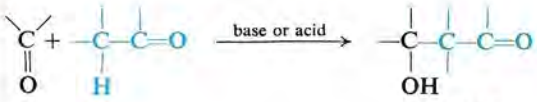
(2) $$CH_3-\overset{\overset{{}^+OH}{|}}{C}-CH_3 + {:}B \longrightarrow \underset{\text{Enol}}{CH_3-\overset{\overset{OH}{|}}{C}=CH_2} + H{:}B^+$$ **Slow**

(3) $$CH_3-\overset{\overset{OH}{|}}{C}=CH_2 + X_2 \longrightarrow \underset{\text{I}}{CH_3-\overset{\overset{{}^+OH}{\|}}{C}-CH_2X} + X^-$$ **Fast**

(4) $$CH_3-\overset{\overset{{}^+OH}{\|}}{C}-CH_2X + {:}B \rightleftharpoons CH_3-\overset{\overset{O}{\|}}{C}-CH_2X + H{:}B^+$$ **Fast**

2. Nucleophilic addition to carbonyl compounds.

(a) Aldol condensation. Discussed in Secs. 21.5–21.8.



An aldol
(A β-hydroxy carbonyl compound)

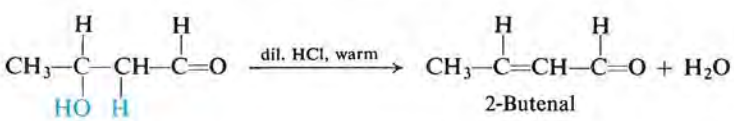
(1) $CH_3CHO + OH^- \rightleftharpoons H_2O + [CH_2CHO]^-$
Basic catalyst — I

(2) $CH_3-\underset{H}{\underset{|}{C}}=O + [CH_2CHO]^- \rightleftharpoons CH_3-\underset{H}{\underset{|}{C}}-CH_2CHO$
I — *Nucleophilic reagent* — II

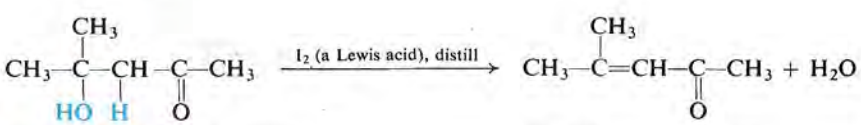
(3) $CH_3-\underset{H}{\underset{|}{C}}-CH_2CHO + H_2O \rightleftharpoons CH_3-\underset{H}{\underset{|}{C}}-CH_2CHO + OH^-$
II — III

Dehydration of aldol products

The β-hydroxy aldehydes and β-hydroxy ketones obtained from aldol condensations are very easily dehydrated; the major products have the carbon–carbon double bond between the α- and β-carbon atoms. For example:

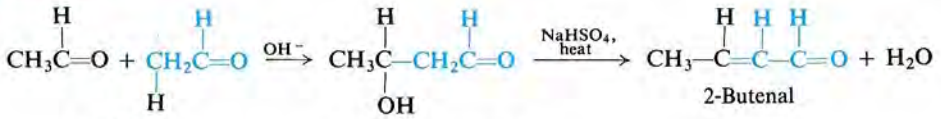


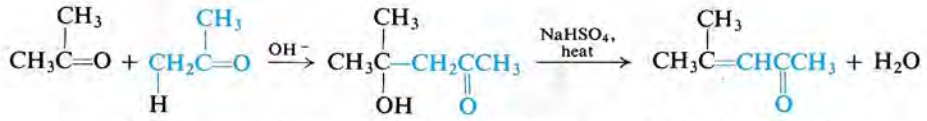
Aldol — 2-Butenal

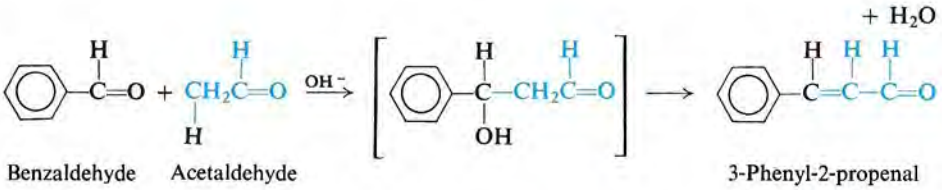


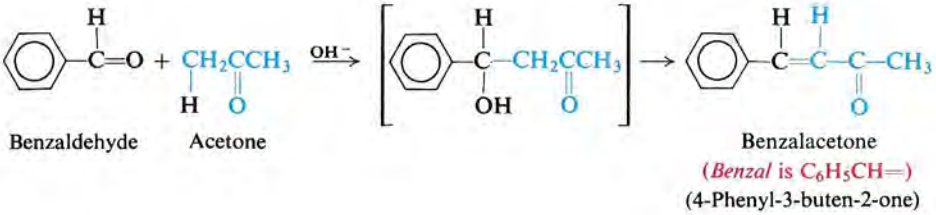
4-Hydroxy-4-methyl-2-pentanone — 4-Methyl-3-penten-2-one

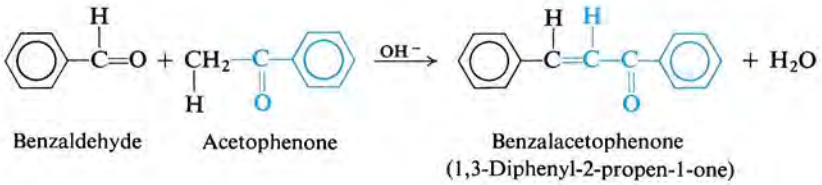
Examples:



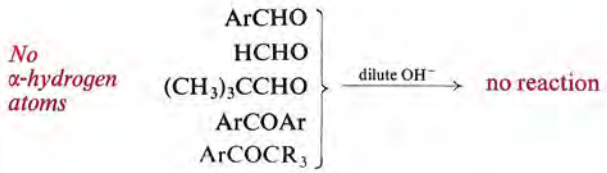






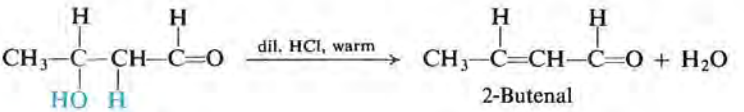


If the aldehyde or ketone does not contain an α-hydrogen, a simple aldol condensation cannot take place. For example:

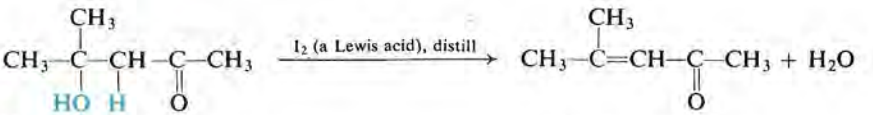


Dehydration of aldol products

The β-hydroxy aldehydes and β-hydroxy ketones obtained from aldol condensations are very easily dehydrated; the major products have the carbon–carbon double bond between the α- and β-carbon atoms. For example:

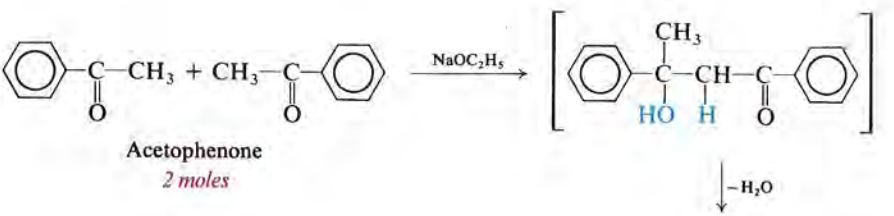


Aldol — 2-Butenal



4-Hydroxy-4-methyl-2-pentanone — 4-Methyl-3-penten-2-one

EXAMPLE

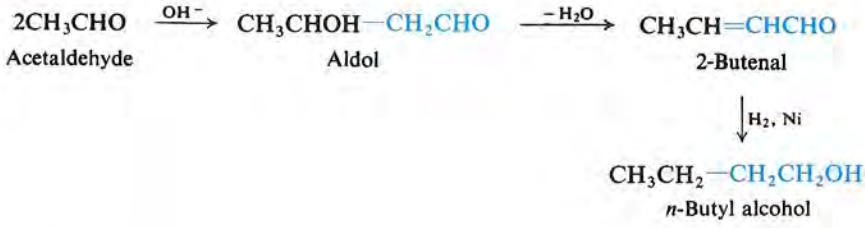


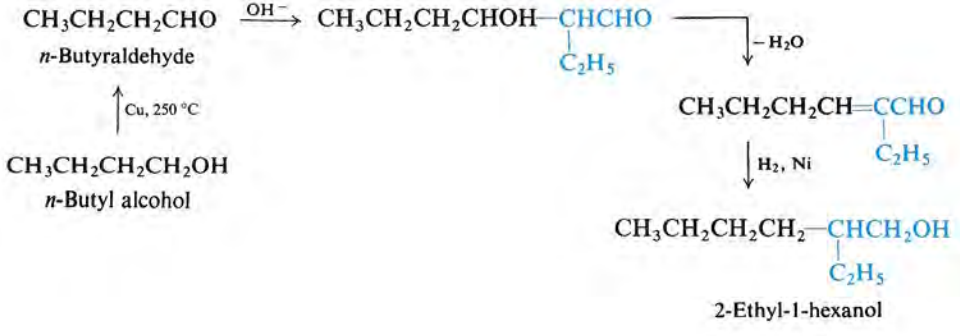
Acetophenone
2 moles

1,3-Diphenyl-2-buten-1-one

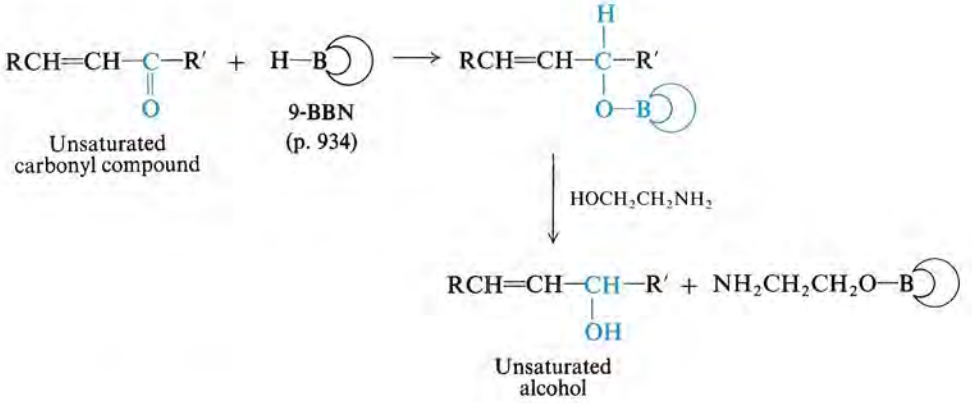
Use of aldol condensation in synthesis

EXAPLES





To prepare an unsaturated alcohol from an α,β-unsaturated aldehyde or ketone, we need a reagent that reduces only the carbonyl group and leaves the carbon–carbon double bond intact. A reagent that, in performing its particular job, selectively attacks one of several different functional groups is called a *chemoselective* reagent. It is a major aim of synthetic chemistry today to find highly selective reagents—regioselective, stereoselective, chemoselective—and nowhere is that aim more evident than in the development of oxidizing and reducing agents. The particular job facing us here can be done by the hydroborane known



as 9-BBN. Just as boranes add to carbon–carbon double bonds (Sec. 9.18), so this one adds to the carbonyl double bond; and, evidently because of the bulky organic group attached to boron, it does this very much faster than it adds to the carbon–carbon double bond. The result is an extraordinarily high degree of selectivity. (We shall encounter 9-BBN again, in Sec. 25.7.)

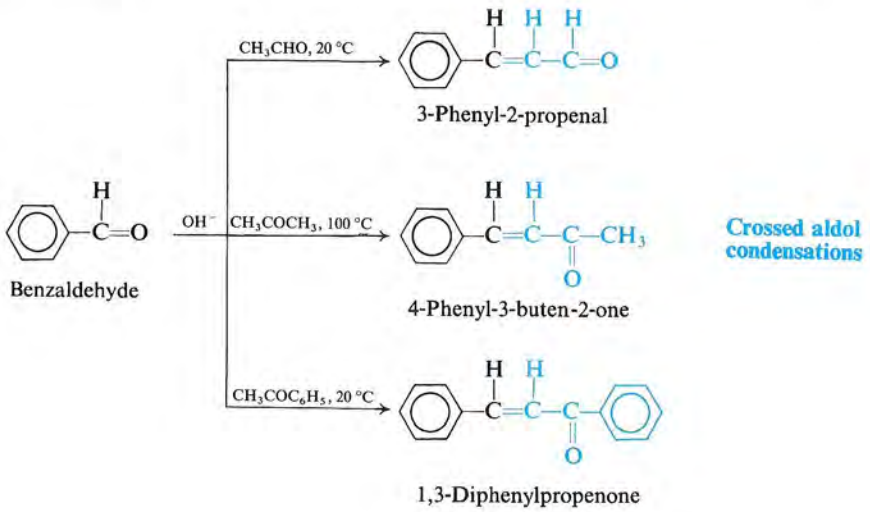
Problem 21.14 Outline the synthesis of the following alcohols starting from alcohols of smaller carbon number:

(a) 2-methyl-1-pentanol
(b) 4-methyl-2-pentanol
(c) 2-cyclohexylcyclohexanol
(d) 2,4-diphenyl-1-butanol
(e) 4-methyl-3-penten-2-ol

21.8 Crossed aldol condensation

An aldol condensation between two different carbonyl compounds—a so-called **crossed aldol condensation**—is not always feasible in the laboratory, since a mixture of the four possible products may be obtained. On a commercial scale, however, such a synthesis may be worthwhile if the mixture can be separated and the components marketed.

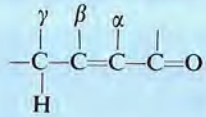
Under certain conditions, a good yield of a single product can be obtained from a crossed aldol condensation: (a) one reactant contains no α-hydrogens and therefore is incapable of condensing with itself (e.g., aromatic aldehydes or formaldehyde); (b) this reactant is mixed with the catalyst; and then (c) a carbonyl compound that contains α-hydrogens is added slowly to this mixture. There is thus present at any time only a very low concentration of the ionizable carbonyl compound, and the carbanion it forms reacts almost exclusively with the other carbonyl compound, which is present in large excess.



Problem 21.15 Outline the synthesis of each of the following from benzene or toluene and any readily available alcohols:

(a) 4-phenyl-2-butanol
(b) 1,3-diphenyl-1-propanol
(c) 1,3-diphenylpropane
(d) 2,3-diphenyl-1-propanol
(e) 1,5-diphenyl-1,4-pentadien-3-one

Problem 21.16 (a) What prediction can you make about the acidity of the γ-hydrogens of α,β-unsaturated carbonyl compounds,



as, for example, in 2-butenal? (b) In view of your answer to (a), suggest a way to synthesize 5-phenyl-2,4-pentadienal, $C_6H_5CH{=}CH{-}CH{=}CH{-}CHO$.

Reactions related to the aldol condensation

There are a large number of condensations that are closely related to the aldol condensation. Each of these reactions has its own name—*Perkin, Knoevenagel, Doebner, Claisen, Dieckmann*, for example—and at first glance each may seem quite different from the others. Closer examination shows, however, that like the aldol condensation each of these involves attack by a carbanion on a carbonyl group. In each case the carbanion is generated in very much the same way: the abstraction by base of a hydrogen ion *alpha* to a carbonyl group. Different bases may be used—sodium hydroxide, sodium ethoxide, sodium acetate, amines—and the carbonyl group to which the hydrogen is *alpha* may vary—aldehyde, ketone, anhydride, ester—but the chemistry is essentially the same as that of the aldol condensation. We shall take up a few of these condensations in the following problems and in following sections; in doing this, we must not lose sight of the fundamental resemblance of each of them to the aldol condensation.

Problem 21.17 Esters can be condensed with aromatic aldehydes in the presence of alkoxides; thus benzaldehyde and ethyl acetate, in the presence of sodium ethoxide, give ethyl 3-phenylpropenoate, $C_6H_5CH{=}CHCOOC_2H_5$. Show all steps in the most likely mechanism for this condensation.

Problem 21.18 Account for the following reactions:

(a) $C_6H_5CHO + CH_3NO_2 \xrightarrow{KOH} C_6H_5CH{=}CHNO_2 + H_2O$

(b) $C_6H_5CHO + C_6H_5CH_2CN \xrightarrow{NaOC_2H_5} C_6H_5CH{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}CN + H_2O$

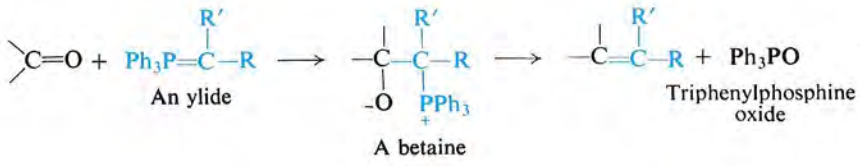
(c) $CH_3CHO + NaC{\equiv}CH \xrightarrow{NH_3(l)} \underset{\displaystyle ONa}{\underset{|}{CH_3CHC}}{\equiv}CH \xrightarrow{NH_4Cl} \underset{\displaystyle OH}{\underset{|}{CH_3CHC}}{\equiv}CH$

(d) **A Perkin condensation:**

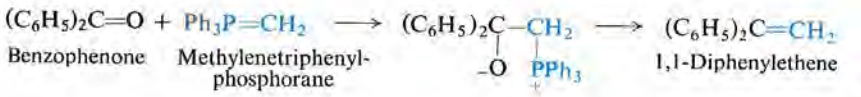
$$\underset{\text{Acetic anhydride}}{C_6H_5CHO + (CH_3CO)_2O} \xrightarrow{CH_3COONa} \underset{\text{3-Phenylpropenoic acid}}{C_6H_5CH{=}CHCOOH}$$

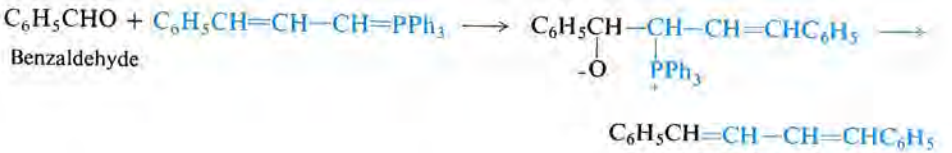
21.10 The Wittig reaction

In 1954, Georg Wittig (then at the University of Tübingen) reported a method of synthesizing alkenes from carbonyl compounds, which amounts to the replacement of carbonyl oxygen, =O, by the group =CRR′. The heart of the synthesis is the nucleophilic attack on carbonyl carbon by an *ylide* to form a *betaine* which—often spontaneously—undergoes elimination to yield the product.



For example:



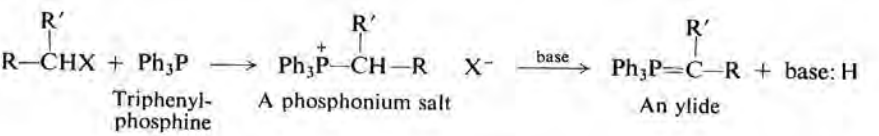


The reaction is carried out under mild conditions, and the position of the carbon–carbon double bond is not in doubt. Carbonyl compounds may contain a wide variety of substituents, and so may the ylide. (Indeed, in its broadest form, the Wittig reaction involves reactants other than carbonyl compounds, and may lead to products other than substituted alkenes.)

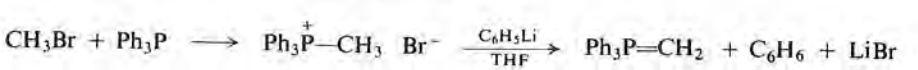
The phosphorus ylides have hybrid structures, and it is the negative charge on

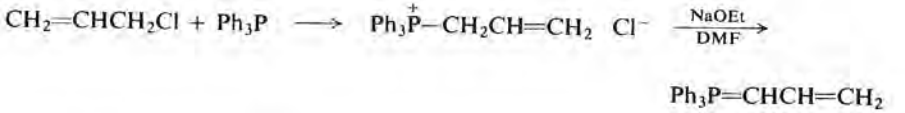
carbon—the carbanion character of ylides—that is responsible for their characteristic reactions: in this case, nucleophilic attack on carbonyl carbon.

The preparation of ylides is a two-stage process, each stage of which belongs to a familiar reaction type: nucleophilic attack on an alkyl halide, and abstraction of a proton by a base.



Many different bases have been used—chiefly alkoxides and organometallics—and in a variety of solvents. For example:



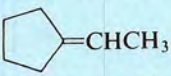


In 1979, the Nobel Prize was awarded to Georg Wittig and to H.C. Brown (p. 349), in recognition of their remarkable contributions to synthetic organic chemistry: Brown's centering about the element boron and Wittig's about phosphorus.

Problem 21.19 What side reactions would you expect to encounter in the preparation of an ylide like $Ph_3P{=}C(CH_3)CH_2CH_3$?

Problem 21.20 Give the structure of an ylide and a carbonyl compound from which each of the following could be made.

(a) $CH_3CH_2CH_2CH{=}C(CH_3)CH_2CH_3$
(b) $C_6H_5C(CH_3){=}CHCH_2C_6H_5$
(c) $C_6H_5CH{=}CHC_6H_5$

(d) 

(e) 1,4-diphenyl-1,3-butadiene (an alternative to the set of reagents used on p. 812)
(f) $CH_2{=}CHCH{=}C(CH_3)COOCH_3$

Problem 21.21 Outline all steps in a possible laboratory synthesis of each ylide and each carbonyl compound in the preceding problem, starting from benzene, toluene, alcohols of four carbons or fewer, acetic anhydride, triphenylphosphine, and cyclopentanol, and using any needed inorganic reagents.

Problem 21.22 Give the structures of compounds A–C.

$C_6H_5OCH_2Cl + Ph_3P$, then *t*-BuOK $\longrightarrow$ A ($C_{25}H_{21}OP$)
A + ethyl methyl ketone $\longrightarrow$ Ph_3PO + B ($C_{11}H_{14}O$)
B + dilute aqueous acid $\longrightarrow$ C ($C_5H_{10}O$)

The above sequence offers a general route to what class of compounds?

Problem 21.23 Give the structures of compounds D–F.

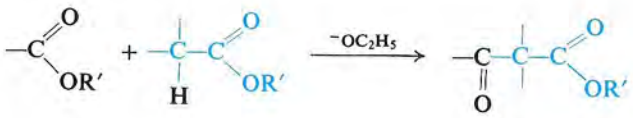
(a) $C_6H_5COCH_2CH_2CH_2CH_2Br + Ph_3P$, then NaOEt $\longrightarrow$ D ($C_{11}H_{12}$)
(b) $BrCH_2CH_2CH_2Br + Ph_3P$, then base $\longrightarrow$ E ($C_{39}H_{34}P_2$)
E + *o*-$C_6H_4(CHO)_2$ $\longrightarrow$ F ($C_{11}H_{10}$)

Problem 21.24 Give the structures of compounds G and H, and account for the stereochemistry of each step.

trans-2-octene + $C_6H_5CO_2OH$ $\longrightarrow$ G ($C_8H_{16}O$)
G + Ph_2PLi, then CH_3I $\longrightarrow$ H ($C_{21}H_{29}OP$)
H $\longrightarrow$ *cis*-2-octene

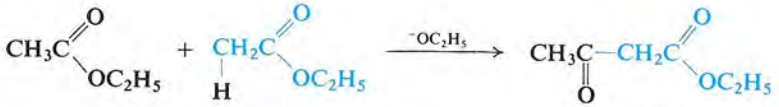
3. Nucleophilic acyl substitution.

(a) Claisen condensation. Discussed in Secs. 21.11–21.12.



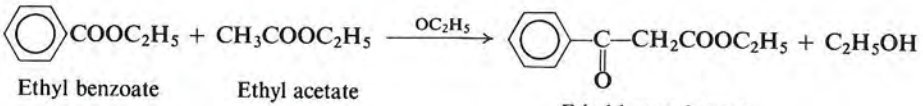
A β-keto ester

Examples:



Ethyl acetate
2 moles

Ethyl acetoacetate



Ethyl benzoate Ethyl acetate

Ethyl benzoylacetate

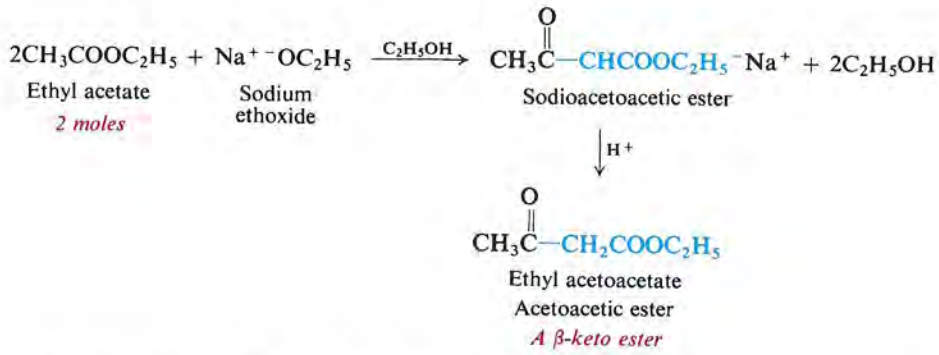
(b) Acylation of organocopper compounds. Discussed in Sec. 18.6.

4. Nucleophilic aliphatic substitution.

(a) Coupling of alkyl halides with organometallic compounds. Discussed in Sec. 3.17.
(b) Synthesis of acetylides. Discussed in Sec. 12.13.
(c) Alkylation of malonic ester and acetoacetic ester. Discussed in Secs. 25.2–25.3.

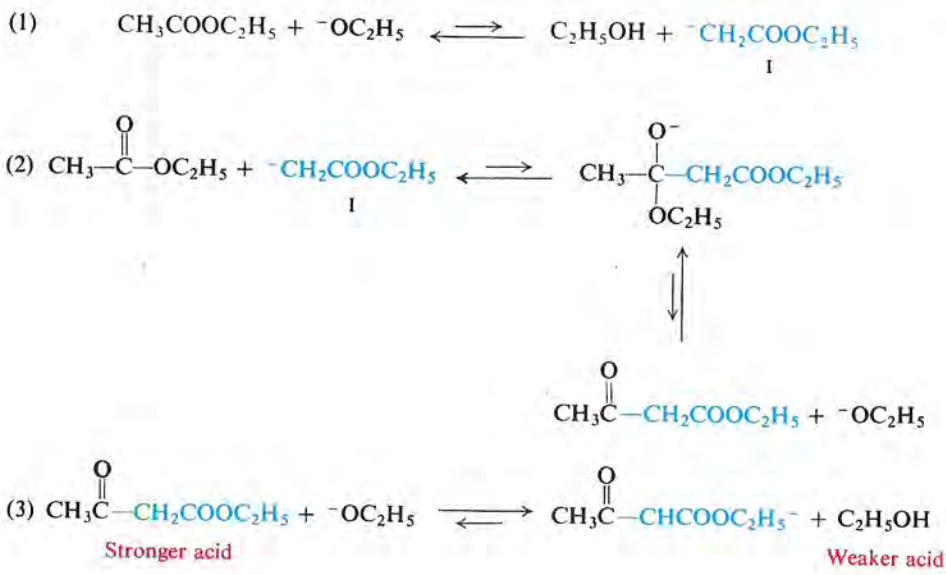
5. Addition to α,β-unsaturated carbonyl compounds. Michael addition. Discussed in Sec. 27.7. ■

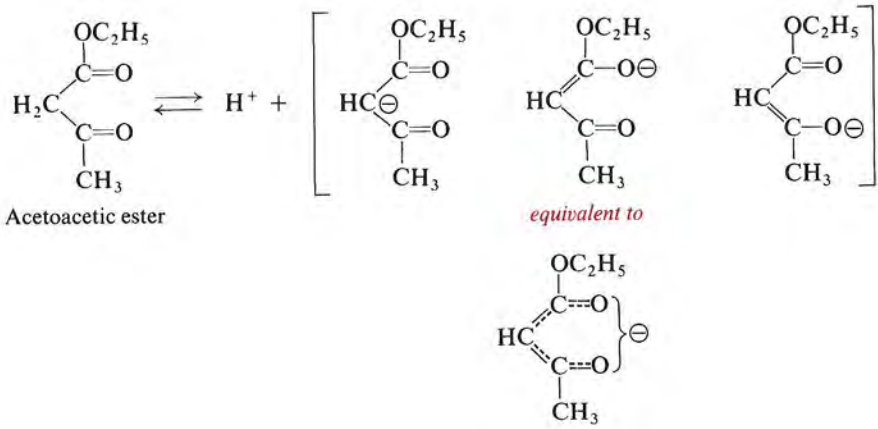
Claisen condensation. Formation of β-keto esters



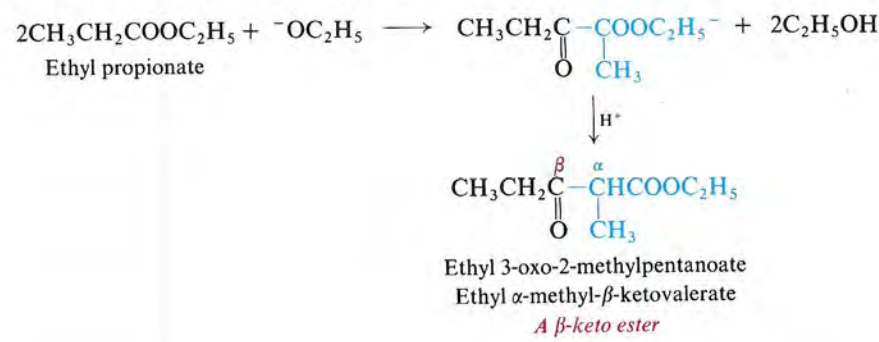
Ethyl acetoacetate is the ester of a *β-keto acid*; its preparation illustrates the reaction known as the **Claisen condensation**.

The generally accepted mechanism for the Claisen condensation (shown here for ethyl acetate) is:

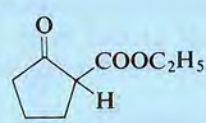




As we might expect, the Claisen condensation of more complicated esters yields the products resulting from ionization of an α-hydrogen of the ester; as a result, it is always the α-carbon of one molecule that becomes attached to the carbonyl carbon of another. For example:



Problem 21.25 Sodium ethoxide converts ethyl adipate into 2-carbethoxycyclopentanone (II). This is an example of the **Dieckmann condensation**.

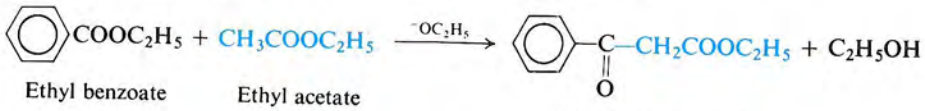


II

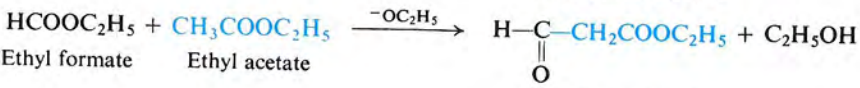
(a) How do you account for formation of II? (b) What product would you expect from the action of sodium ethoxide on ethyl pimelate (ethyl heptanedioate)? (c) Would you expect similar behavior from ethyl glutarate or ethyl succinate? Actually, ethyl succinate reacts with sodium ethoxide to yield a compound of formula $C_{12}H_{16}O_6$ containing a six-membered ring. What is the likely structure for this last product?

Crossed Claisen condensation

Like a crossed aldol condensation (Sec. 21.8), a **crossed Claisen condensation** is generally feasible only when one of the reactants has no α-hydrogens and thus is incapable of undergoing self-condensation. For example:

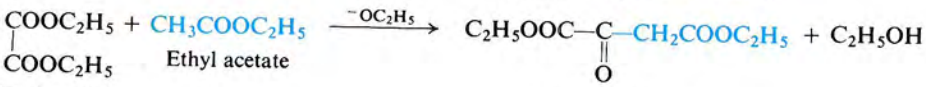


Ethyl benzoate + Ethyl acetate → Ethyl benzoylacetate + C_2H_5OH

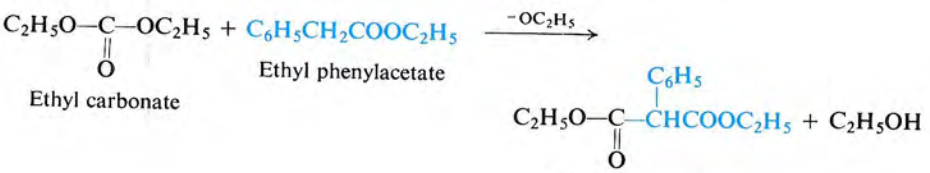


Ethyl formate + Ethyl acetate → Ethyl formylacetate + C_2H_5OH

(known only as the Na salt)



Ethyl oxalate + Ethyl acetate → Ethyl oxaloacetate + C_2H_5OH

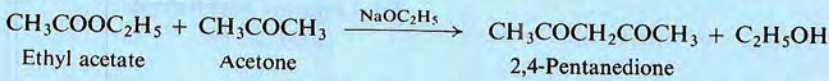


Ethyl carbonate + Ethyl phenylacetate → Ethyl phenylmalonate + C_2H_5OH

Phenylmalonic ester

Problem 21.26 In what order should the reactants be mixed in each of the above crossed Claisen condensations? (*Hint*: See Sec. 21.8.)

Problem 21.27 Ketones (but not aldehydes) undergo a crossed Claisen condensation with esters. For example:



Ethyl acetate + Acetone → 2,4-Pentanedione + C_2H_5OH

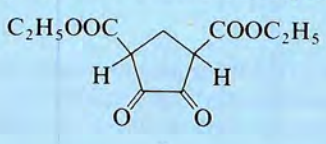
(a) Outline all steps in the most likely mechanism for this reaction. (b) Predict the principal products expected from the reaction in the presence of sodium ethoxide of ethyl propionate and acetone; (c) of ethyl benzoate and acetophenone; (d) of ethyl oxalate and cyclohexanone.

Problem 21.28 Outline the synthesis from simple esters of:

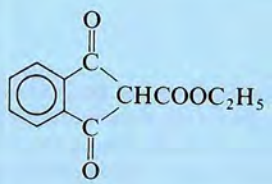
(a) ethyl α-phenylbenzoylacetate, $C_6H_5COCH(C_6H_5)COOC_2H_5$

(b) ethyl 2,3-dioxo-1,4-cyclopentanedicarboxylate (I). (*Hint*: Use ethyl oxalate as one ester.)

(c) ethyl 1,3-dioxo-2-indanecarboxylate (II)

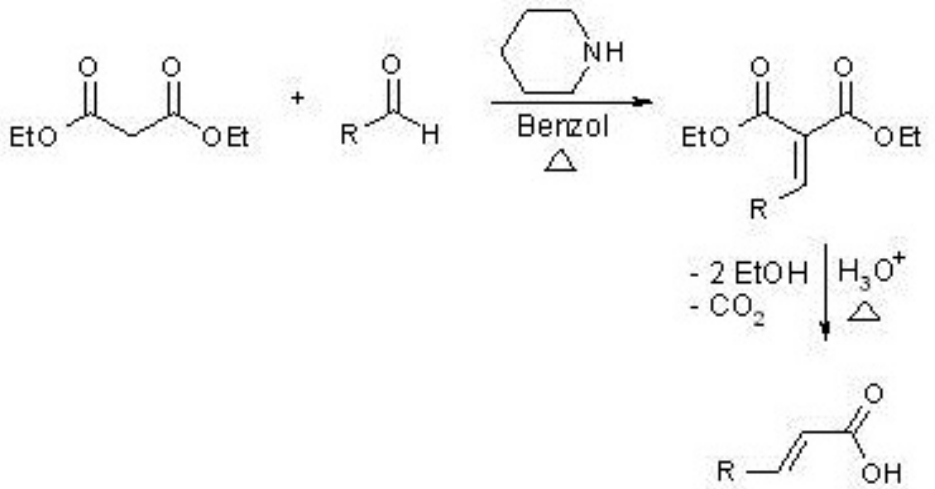


I



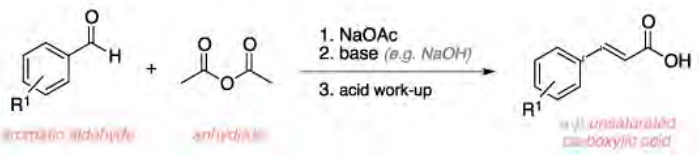
II

Knoevenagel Condensation

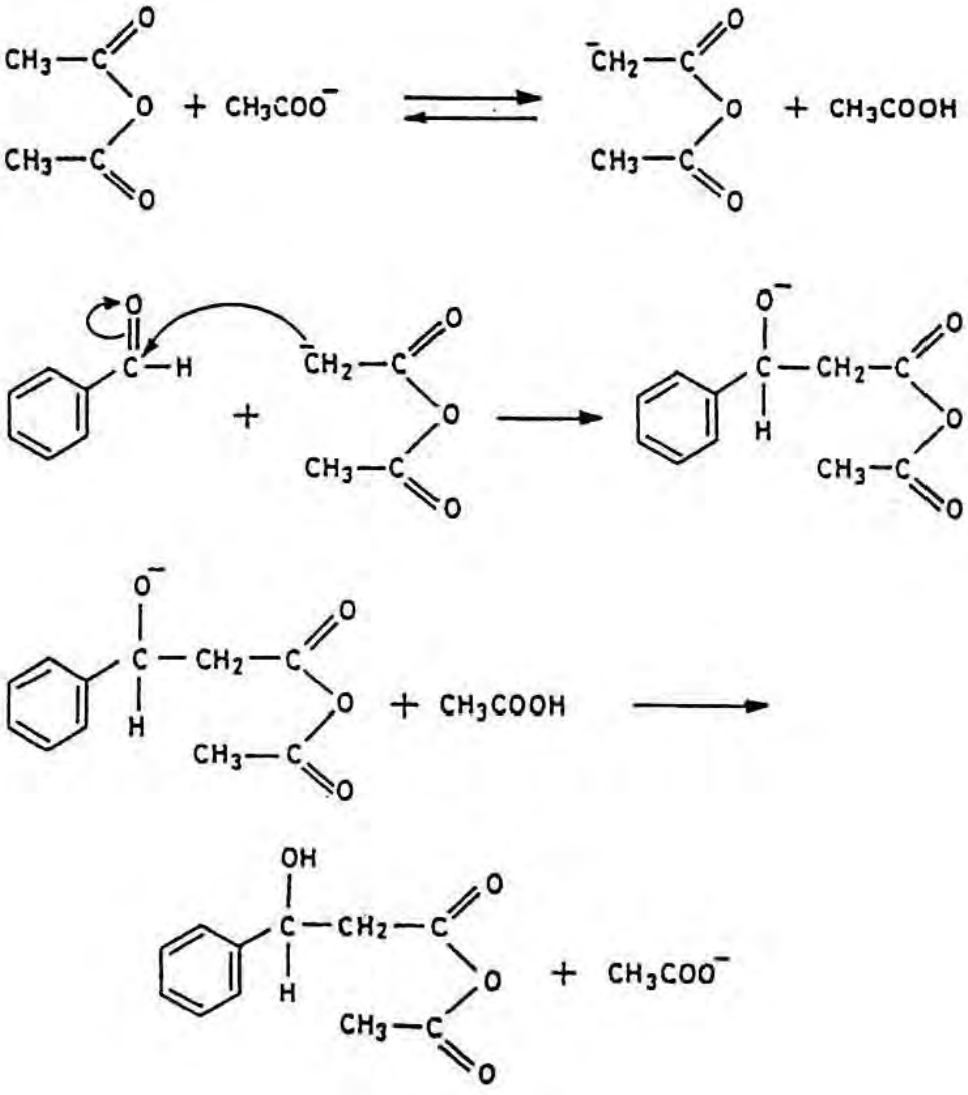


The condensation of carbon acid compounds with aldehydes to afford α,β-unsaturated compounds.

Perkin Condensation

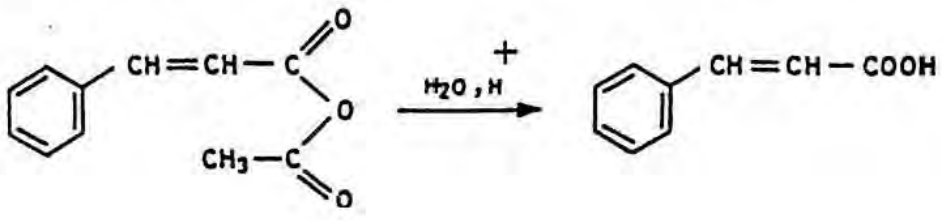


Mechanism



Scheme 5.12

Water is eliminated in the presence of the anhydride under the temperature of the reaction. The acid is finally obtained by hydrolysis.



PROBLEMS

1. Write balanced equations, naming all organic products, for the reaction (if any) of phenylacetaldehyde with:

(a) dilute NaOH
(b) dilute HCl
(c) aqueous Na_2CO_3
(d) Br_2/CCl_4
(e) $Ph_3P{=}CH_2$

2. Answer Problem 1 for cyclohexanone.

3. Write balanced equations, naming all organic products, for the reaction (if any) of benzaldehyde with:

(a) dilute NaOH
(b) conc. NaOH
(c) acetaldehyde, dilute NaOH
(d) propionaldehyde, dilute NaOH
(e) acetone, dilute NaOH
(f) product (e), dilute NaOH
(g) acetophenone, NaOH
(h) acetic anhydride, sodium acetate, heat
(i) ethyl acetate, sodium ethoxide
(j) ethyl phenylacetate, sodium ethoxide
(k) formaldehyde, conc. NaOH
(l) 2-butenal, NaOH
(m) $Ph_3P{=}CHCH{=}CH_2$
(n) $Ph_3P{=}CH(OC_6H_5)$
(o) product (n), dilute acid

4. Write equations for all steps in the synthesis of the following from propionaldehyde, using any other needed reagents:

(a) β-hydroxy-α-methylvaleraldehyde
(b) 2-methyl-1-pentanol
(c) 2-methyl-2-pentenal
(d) 2-methyl-2-penten-1-ol
(e) 2-methyl-1,3-pentanediol
(f) α-methylvaleric acid
(g) 2-methyl-3-phenylpropenal
(h) CH_3CD_2CHO
(i) $CH_3CH_2CH^{18}O$
(j) 2-methyl-3-hexene

5. Write equations for all steps in the synthesis of the following from acetophenone, using any other needed reagents:

(a) benzoic acid
(b) 1,3-diphenyl-2-buten-1-one
(c) 1,3-diphenyl-1-butanol
(d) 1,3-diphenyl-2-buten-1-ol
(e) 1,3-diphenyl-2-propen-1-one
(f) α-phenylpropionaldehyde (*Hint*: See Problem 21.22.)

6. Give the structures of the principal products expected from the reaction in the presence of sodium ethoxide of:

(a) ethyl *n*-butyrate
(b) ethyl phenylacetate
(c) ethyl isovalerate
(d) ethyl formate and ethyl propionate
(e) ethyl oxalate and ethyl succinate
(f) ethyl benzoate and ethyl phenylacetate
(g) ethyl propionate and cyclohexanone
(h) ethyl phenylacetate and acetophenone
(i) ethyl carbonate and acetophenone

7. Sodium ethoxide is added to a mixture of ethyl acetate and ethyl propionate. (a) Give the structures of the products expected. (b) Would this reaction be a good method of synthesizing any one of these?

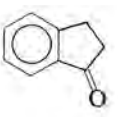
8. Outline all steps in a possible synthesis of each of the following via the Claisen condensation, using any needed reagents:

(a) $C_6H_5COCH(CH_3)COOC_2H_5$
(b) $C_6H_5CH_2COCH(C_6H_5)COOC_2H_5$
(c) $C_2H_5OOCCOCH(CH_3)COOC_2H_5$
(d) $C_6H_5CH(CHO)COOC_2H_5$
(e) $(CH_3)_2CHCOCH_2COCH_3$
(f) $C_6H_5COCH_2COCH_3$
(g) 2-benzoylcyclohexanone
(h) $C_2H_5OOCCH(CHO)CH_2COOC_2H_5$

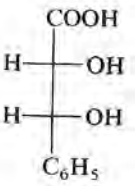
9. The 3-phenylpropenoic acid obtained by the Perkin condensation is the more stable *trans* isomer. Suggest a method of preparing the *cis* acid.

10. Outline all steps in a possible laboratory synthesis of each of the following from benzene, toluene, acetic anhydride, triphenylphosphine, and alcohols of four carbons or fewer, using any needed inorganic reagents:

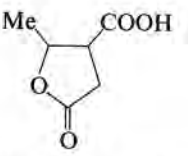
(a) 4-hydroxy-4-methyl-2-pentanone
(b) 4-methyl-2-pentanol
(c) 2-butenal
(d) 3-phenyl-2-propen-1-ol
(e) 3-(*p*-nitrophenyl)propenal
(f) 1,3-butanediol
(g) 3-methyl-2-butenoic acid (via aldol condensation)
(h) 3-methyl-1-pentyn-3-ol (*Oblivon*, a hypnotic)
(i) 1-phenyl-1,3,5-hexatriene
(j) 1,6-diphenyl-1,3,5-hexatriene
(k) 2,3-dimethyl-2-pentenoic acid
(l) indanone (I)
(m) racemic *erythro*-2,3-dihydroxy-3-phenylpropanoic acid (II and its enantiomer)



I



II



γ-Methylparaconic acid

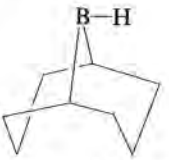
11. How do you account for the formation of γ-methylparaconic acid from the reaction of acetaldehyde with succinic acid?

12. The aldol condensation of unsymmetrical ketones (ethyl methyl ketone, for example) is usually of little value in synthesis. Why do you think this is so?

13. The compound *pentaerythritol*, $C(CH_2OH)_4$, used in making explosives, is obtained from the reaction of acetaldehyde and formaldehyde in the presence of calcium hydroxide. Outline the probable steps in this synthesis.

14. The labeled alkene, 1,3,3-trideuteriocyclohexene, needed for a particular stereochemical study, was prepared from cyclohexanone. Outline all steps in such a synthesis.

15. The reagent 9-BBN has the structure shown below. It is made by the reaction of diborane with a diene. Can you suggest a possible structure for this diene?



9-Borabicyclo[3.3.1]nonane
9-BBN

16. In *acid-catalyzed aldol condensations*, acid is believed to perform two functions: to catalyze conversion of carbonyl compound into the enol form, and to provide protonated carbonyl compound with which the enol can react. The reaction that then takes place can, depending upon one's point of view, be regarded either as acid-catalyzed nucleophilic addition to a carbonyl group, or as electrophilic addition to an alkene. On this basis, write all steps in the mechanism of acid-catalyzed aldol condensation of acetaldehyde. In the actual *condensation* step, identify the nucleophile and the electrophile.

17. In alkaline solution, 4-hydroxy-4-methyl-2-pentanone is partly converted into acetone. What does this reaction amount to? Show all steps in the most likely mechanism. (*Hint*: See Sec. 8.26.)

18. (a) The haloform test (Sec. 18.21) depends upon the fact that three hydrogens on the same carbon atom are successively replaced by halogen. Using acetone as an example, show why the carbon that suffers the initial substitution should be the preferred site of further substitution. (*Hint*: See Sec. 19.14.)

(b) The haloform test also depends upon the ease with which the trihalomethyl ketone produced in (a) is cleaved by base. What is the most likely mechanism for this cleavage? What factor makes such a reaction possible in this particular case?

19. Upon treatment with dilute NaOH, 3-methyl-2-butenal, $(CH_3)_2C{=}CHCHO$, yields a product of formula $C_{10}H_{14}O$, called *dehydrocitral*. What is a likely structure for this product, and how is it formed? (*Hint*: See *citral*, Problem 24, p. 705.)

20. Meanwhile, back at the laboratory, our naïve graduate student (Problem 19, p. 704) had need of the hydroxy ester $(CH_3)_2C(OH)CH_2COOC_2H_5$. Turning once again to the Grignard reaction, he prepared methylmagnesium iodide and to it he added acetoacetic ester. Everything went well; indeed, even without the application of heat, the reaction mixture bubbled merrily. Working carefully and with great skill, he isolated an excellent yield of the starting material, acetoacetic ester. He poured this down the sink and fled, sobbing, to his research director's office, where he begged for a new research problem.

What reaction had taken place? What was the bubbling due to? (In Problem 15, p. 989, we shall see how he made out with his new research problem.)

21. (a) The sex attractant of the Egyptian cotton leafworm has been prepared in the following way. On the basis of this synthesis what structure or structures can you assign to this pheromone (and to all intermediates)? (b) At one point in the synthesis, it is necessary to separate a pair of isomers. At which point is this, and what are the isomers?

9-bromo-1-nonanol + DHP, H^+ $\longrightarrow$ A ($C_{14}H_{27}O_2Br$)

A + Ph_3P; then base $\longrightarrow$ B ($C_{32}H_{41}O_2P$)

B + (*E*)-2-penten-1-al $\longrightarrow$ C ($C_{19}H_{34}O_2$)

C + H_2O, HCl $\longrightarrow$ D ($C_{14}H_{26}O$)

D + Ac_2O, pyridine $\longrightarrow$ E, the pheromone ($C_{16}H_{28}O_2$)

22. *Bombykol*, the sex pheromone of the silkworm moth, has been prepared in the following way. What is the structure of bombykol? What uncertainties, if any, are there in your answer?

1-pentyne + *n*-C_4H_9MgBr $\longrightarrow$ F (C_5H_7MgBr)

F + HCHO; then H^+ $\longrightarrow$ G ($C_6H_{10}O$)

G + PBr_3 $\longrightarrow$ H (C_6H_9Br)

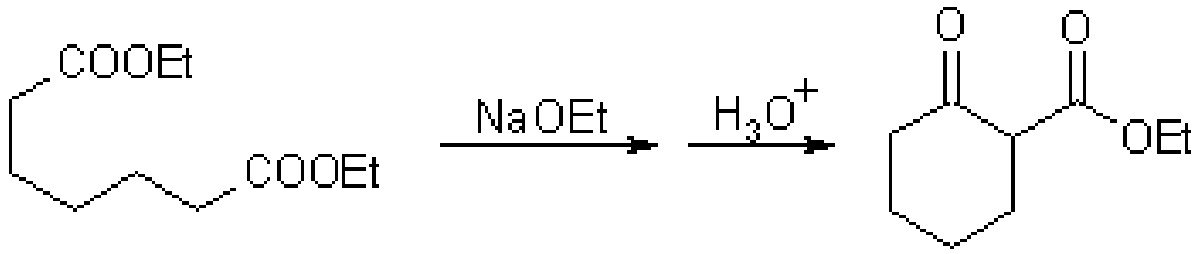
H + Ph_3P, base $\longrightarrow$ I ($C_{24}H_{23}P$)

I + ethyl 10-oxodecanoate $\longrightarrow$ J ($C_{18}H_{30}O_2$)

J + H_2, Lindlar catalyst $\longrightarrow$ K ($C_{18}H_{32}O_2$)

K + $LiAlH_4$ $\longrightarrow$ *bombykol* ($C_{16}H_{30}O$)

Dieckmann Condensation



The base-catalyzed intramolecular condensation of a diester. The Dieckmann Condensation works well to produce 5- or 6-membered cyclic ß-keto esters, and is usually effected with sodium alkoxide in alcoholic solvent.