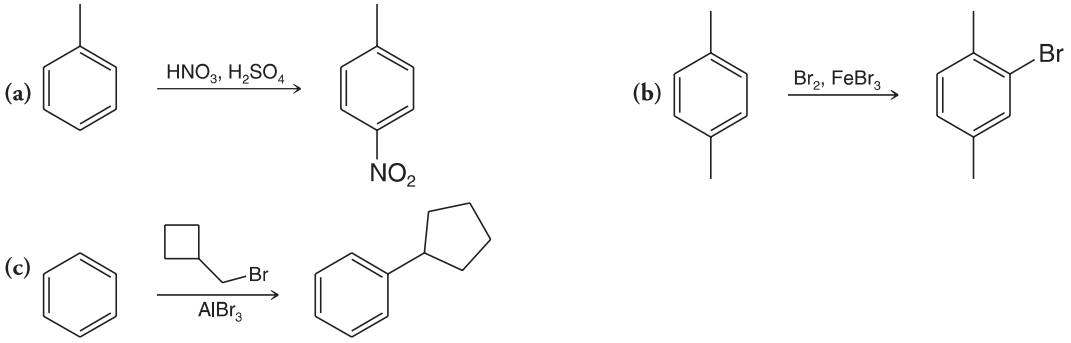
PROBLEMS

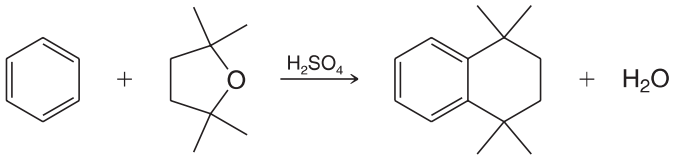
Note to Instructors: Many of the homework problems are available for assignment via *WileyPLUS*, an online teaching and learning solution.

MECHANISMS

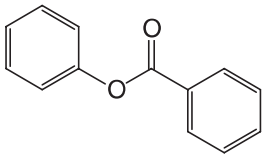
15.22 Provide a detailed mechanism for each of the following reactions. Include contributing resonance structures and the resonance hybrid for the arenium ion intermediates.



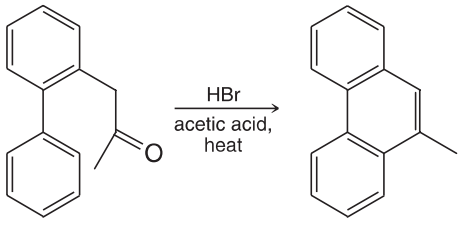
15.23 Provide a detailed mechanism for the following reaction.



15.24 One ring of phenyl benzoate undergoes electrophilic aromatic substitution much more readily than the other. **(a)** Which one is it? **(b)** Explain your answer.



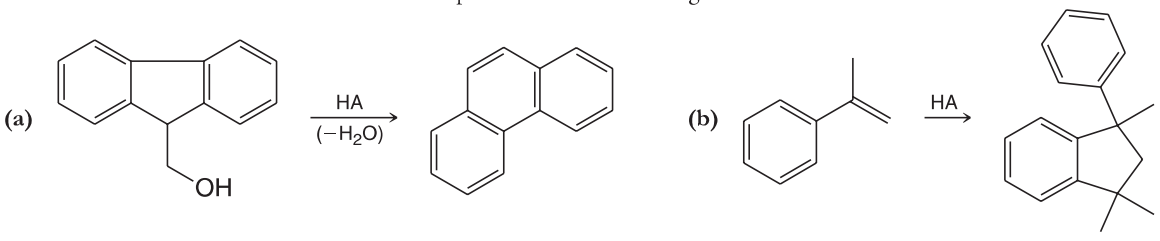
15.25 Many polycyclic aromatic compounds have been synthesized by a cyclization reaction known as the **Bradsher reaction** or **aromatic cyclodehydration**. This method can be illustrated by the following synthesis of 9-methylphenanthrene:



9-Methylphenanthrene

An arenium ion is an intermediate in this reaction, and the last step involves the dehydration of an alcohol. Propose a plausible mechanism for this example of the Bradsher reaction.

15.26 Write mechanisms that account for the products of the following reactions:



15.27 The addition of a hydrogen halide (hydrogen bromide or hydrogen chloride) to 1-phenyl-1,3-butadiene produces (only) 1-phenyl-3-halo-1-butene. **(a)** Write a mechanism that accounts for the formation of this product. **(b)** Is this 1,4 addition or 1,2 addition to the butadiene system? **(c)** Is the product of the reaction consistent with the formation of the most stable intermediate carbocation? **(d)** Does the reaction appear to be under kinetic control or equilibrium control? Explain.

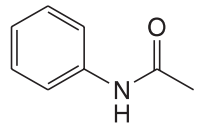
REACTIONS AND SYNTHESIS

15.28 Predict the major product (or products) formed when each of the following reacts with Cl_2 and $FeCl_3$:

(a) Ethylbenzene
(b) Anisole (methoxybenzene)
(c) Fluorobenzene
(d) Benzoic acid
(e) Nitrobenzene
(f) Chlorobenzene
(g) Biphenyl ($C_6H_5—C_6H_5$)
(h) Ethyl phenyl ether

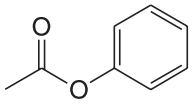
15.29 Predict the major product (or products) formed when each of the following reacts with a mixture of concentrated HNO_3 and H_2SO_4.

(a)



Acetanilide

(b)

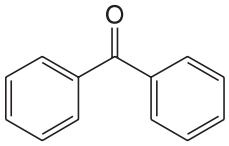


Phenyl acetate

(c) 4-Chlorobenzoic acid

(d) 3-Chlorobenzoic acid

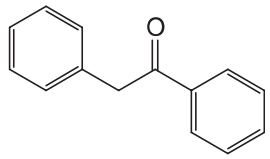
(e)



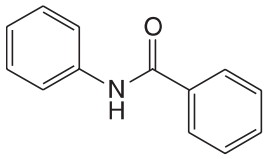
Benzophenone

15.30 What monobromination product (or products) would you expect to obtain when the following compounds undergo ring bromination with Br_2 and $FeBr_3$?

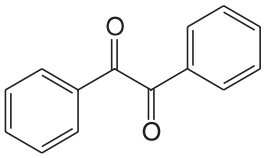
(a)



(b)

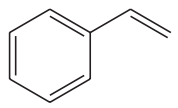


(c)



15.31 Predict the major products of the following reactions:

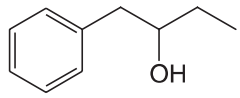
(a)



Styrene

(b) 2-Bromo-1-phenylpropane $\xrightarrow{EtONa}$

(c)



$\xrightarrow{HA,\ heat}$

(d) Product of (c) + HBr $\xrightarrow{peroxides}$

(e) Product of (c) + H_2O $\xrightarrow[heat]{HA}$

(f) Product of (c) + H_2 (1 molar equivalent) $\xrightarrow[25\ °C]{Pt}$

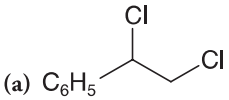
(g) Product of (f) $\xrightarrow[(2)\ H_3O^+]{(1)\ KMnO_4,\ HO^-,\ heat}$

15.32 Starting with benzene, outline a synthesis of each of the following:

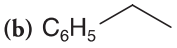
(a) Isopropylbenzene
(b) *tert*-Butylbenzene
(c) Propylbenzene
(d) Butylbenzene
(e) 1-*tert*-Butyl-4-chlorobenzene
(f) 1-Phenylcyclopentene
(g) *trans*-2-Phenylcyclopentanol
(h) *m*-Dinitrobenzene
(i) *m*-Bromonitrobenzene
(j) *p*-Bromonitrobenzene
(k) *p*-Chlorobenzenesulfonic acid
(l) *o*-Chloronitrobenzene
(m) *m*-Nitrobenzenesulfonic acid

15.33 Starting with styrene, outline a synthesis of each of the following:

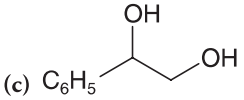
(a)



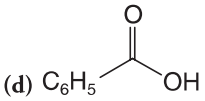
(b)



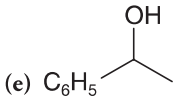
(c)



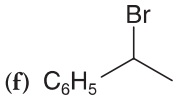
(d)



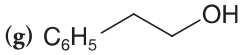
(e)



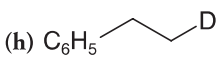
(f)



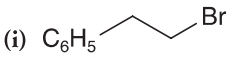
(g)



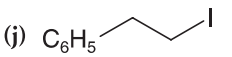
(h)



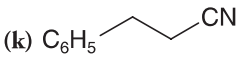
(i)



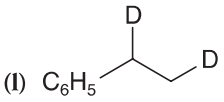
(j)



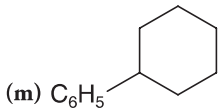
(k)



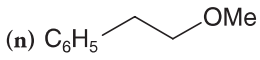
(l)



(m)



(n)



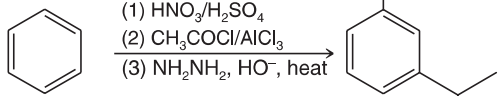
15.34 Starting with toluene, outline a synthesis of each of the following:

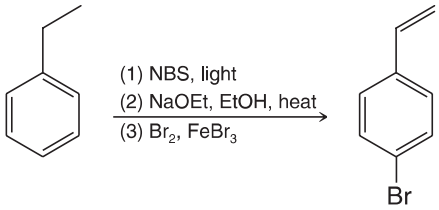
(a) *m*-Chlorobenzoic acid
(b) *p*-Methylacetophenone
(c) 2-Bromo-4-nitrotoluene
(d) *p*-Bromobenzoic acid
(e) 1-Chloro-3-trichloromethylbenzene
(f) *p*-Isopropyltoluene (*p*-cymene)
(g) 1-Cyclohexyl-4-methylbenzene
(h) 2,4,6-Trinitrotoluene (TNT)
(i) 4-Chloro-2-nitrobenzoic acid
(j) 1-Butyl-4-methylbenzene

15.35 Starting with aniline, outline a synthesis of each of the following:

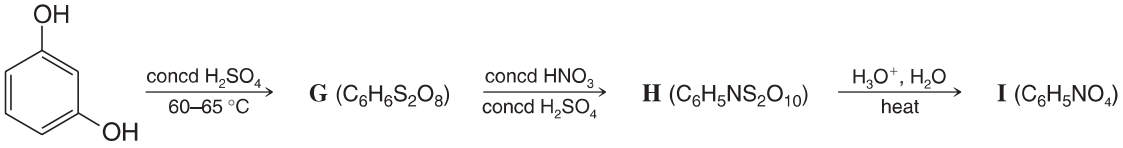
(a) *p*-Bromoaniline
(b) *o*-Bromoaniline
(c) 2-Bromo-4-nitroaniline
(d) 4-Bromo-2-nitroaniline
(e) 2,4,6-Tribromoaniline

15.36 Both of the following syntheses will fail. Explain what is wrong with each one.

(a) 

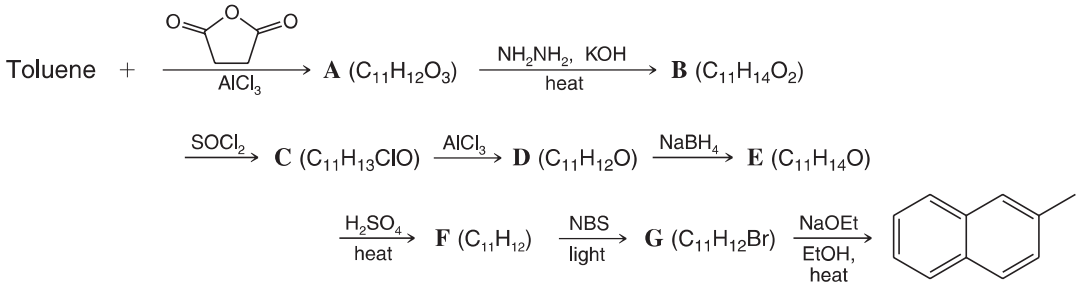
(b) 

15.37 Propose structures for compounds **G–I:**

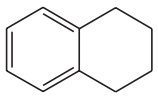
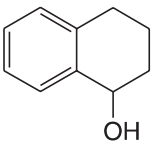


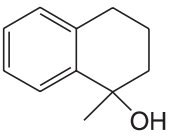
15.38 2,6-Dichlorophenol has been isolated from the females of two species of ticks (*Amblyomma americanum* and *A. maculatum*), where it apparently serves as a sex attractant. Each female tick yields about 5 ng of 2,6-dichlorophenol. Assume that you need larger quantities than this and outline a synthesis of 2,6-dichlorophenol from phenol. (*Hint*: When phenol is sulfonated at 100 °C, the product is chiefly *p*-hydroxybenzenesulfonic acid.)

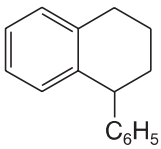
15.39 2-Methylnaphthalene can be synthesized from toluene through the following sequence of reactions. Write the structure of each intermediate.



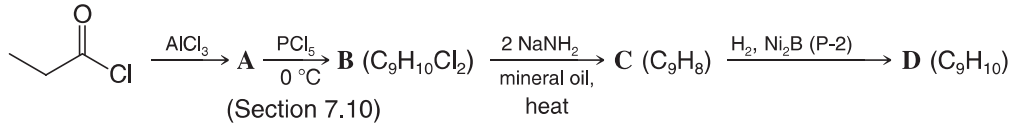
15.40 Show how you might synthesize each of the following starting with α-tetralone (Section 15.9):

(a) 
(b) 

(c) 

(d) 

15.41 Give structures (including stereochemistry where appropriate) for compounds **A–G:**

(a) 

(*Hint*: The ^{1}H NMR spectrum of compound **C** consists of a multiplet at δ 7.20 (5H) and a singlet at δ 2.0 (3H).)

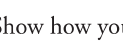
(b) **C** $\xrightarrow[\text{(2) } NH_4Cl \text{ (Section 7.15B)}]{\text{(1) Li, } EtNH_2}$ **E** (C_9H_{10})

(c) **D** $\xrightarrow[\text{2-5 °C}]{Br_2}$ **F** + enantiomer (major products)

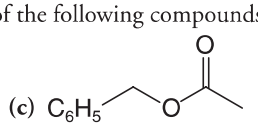
(d) **E** $\xrightarrow[\text{2-5 °C}]{Br_2}$ **G** + enantiomer (major products)

GENERAL PROBLEMS

15.42 Show how you might synthesize each of the following compounds starting with either benzyl bromide or allyl bromide:

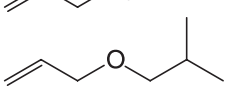
(a) 

(b)

(c) 

(d)

(e) 

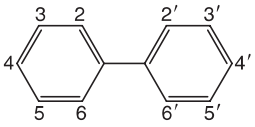
(f) 

15.43 Provide structures for compounds **A** and **B**:

$$\text{Benzene} \xrightarrow[\text{liq. } NH_3,\ EtOH]{Na} \mathbf{A}\ (C_6H_8) \xrightarrow{NBS} \mathbf{B}\ (C_6H_7Br)$$

15.44 Ring nitration of a dimethylbenzene (a xylene) results in the formation of only one dimethylnitrobenzene. Which dimethylbenzene isomer was the reactant?

15.45 The compound phenylbenzene ($C_6H_5—C_6H_5$) is called *biphenyl*, and the ring carbons are numbered in the following manner:



Use models to answer the following questions about substituted biphenyls. **(a)** When certain large groups occupy three or four of the *ortho* positions (e.g., 2, 6, 2′, and 6′), the substituted biphenyl may exist in enantiomeric forms. An example of a biphenyl that exists in enantiomeric forms is the compound in which the following substituents are present: 2-NO_2, 6-CO_2H, 2′-NO_2, 6′-CO_2H. What factors account for this? **(b)** Would you expect a biphenyl with 2-Br, 6-CO_2H, 2′-CO_2H, 6′-H to exist in enantiomeric forms? **(c)** The biphenyl with 2-NO_2, 6-NO_2, 2′-CO_2H, 6′-Br cannot be resolved into enantiomeric forms. Explain.

15.46 Treating cyclohexene with acetyl chloride and $AlCl_3$ leads to the formation of a product with the molecular formula $C_8H_{13}ClO$. Treating this product with a base leads to the formation of 1-acetylcyclohexene. Propose mechanisms for both steps of this sequence of reactions.

15.47 The *tert*-butyl group can be used as a blocking group in certain syntheses of aromatic compounds. **(a)** How would you introduce a *tert*-butyl group? **(b)** How would you remove it? **(c)** What advantage might a *tert*-butyl group have over a $—SO_3H$ group as a blocking group?

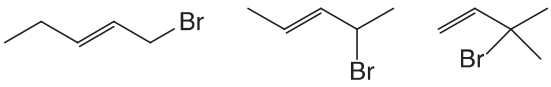
15.48 When toluene is sulfonated (concentrated H_2SO_4) at room temperature, predominantly (about 95% of the total) ortho and para substitution occurs. If elevated temperatures (150–200 °C) and longer reaction times are employed, meta (chiefly) and para substitution account for some 95% of the products. Account for these differences in terms of kinetic and thermodynamic pathways. (*Hint: m*-Toluenesulfonic acid is the most stable isomer.)

15.49 A C—D bond is harder to break than a C—H bond, and, consequently, reactions in which C—D bonds are broken proceed more slowly than reactions in which C—H bonds are broken. What mechanistic information comes from the observation that perdeuterated benzene, C_6D_6, is nitrated at the same rate as normal benzene, C_6H_6?

15.50 Heating 1,1,1-triphenylmethanol with ethanol containing a trace of a strong acid causes the formation of 1-ethoxy-1,1,1-triphenylmethane. Write a plausible mechanism that accounts for the formation of this product.

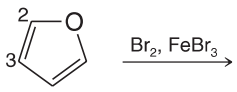
15.51

(a) Which of the following halides would you expect to be most reactive in an S_N2 reaction? **(b)** In an S_N1 reaction? Explain your answers.



CHALLENGE PROBLEMS

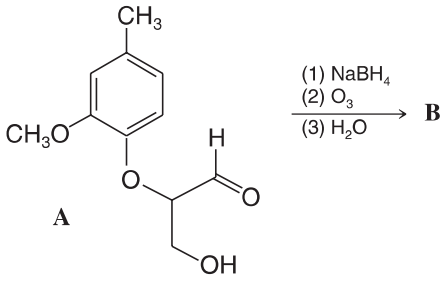
15.52 Furan undergoes electrophilic aromatic substitution. Use resonance structures for possible arenium ion intermediates to predict whether furan is likely to undergo bromination more rapidly at C2 or at C3.



Furan

15.53 Acetanilide was subjected to the following sequence of reactions: (1) concd H_2SO_4; (2) HNO_3, heat; (3) H_2O, H_2SO_4, heat, then HO^-. The ^{13}C NMR spectrum of the final product gives six signals. Write the structure of the final product.

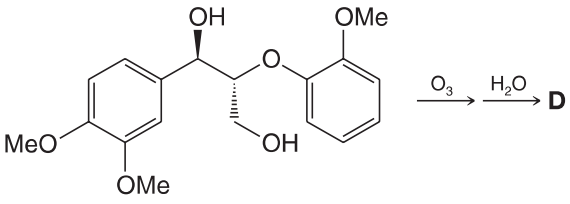
15.54 The lignins are macromolecules that are major components of the many types of wood, where they bind cellulose fibers together in these natural composites. The lignins are built up out of a variety of small molecules (most having phenylpropane skeletons). These precursor molecules are covalently connected in varying ways, and this gives the lignins great complexity. To explain the formation of compound **B** below as one of many products obtained when lignins are ozonized, lignin model compound **A** was treated as shown. Use the following information to determine the structure of **B**.



A

To make **B** volatile enough for GC/MS (gas chromatography–mass spectrometry, Section 9.19), it was first converted to its tris(*O*-trimethylsilyl) derivative, which had M^+ 308 *m/z*. ["Tris" means that three of the indicated complex groups named (e.g., trimethylsilyl groups here) are present. The capital, italicized *O* means these are attached to oxygen atoms of the parent compound, taking the place of hydrogen atoms. Similarly, the prefix "bis" indicates the presence of two complex groups subsequently named, and "tetrakis" (used in the problem below), means four.] The IR spectrum of **B** had a broad absorption at 3400 cm^{-1}, and its ^1H NMR spectrum showed a single multiplet at δ 3.6. What is the structure of **B**?

15.55 When compound **C**, which is often used to model a more frequently occurring unit in lignins, was ozonized, product **D** was obtained. In a variety of ways it has been established that the stereochemistry of the three-carbon side chain of such lignin units remains largely if not completely unchanged during oxidations like this.

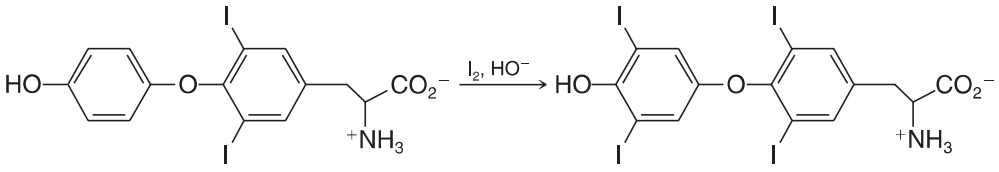


C

For GC/MS, **D** was converted to its tetrakis(*O*-trimethylsilyl) derivative, which had M^+ 424 *m/z*. The IR spectrum of **D** had bands at 3000 cm^{-1} (broad, strong) and 1710 cm^{-1} (strong). Its ^1H NMR spectrum had peaks at δ 3.7 (multiplet, 3H) and δ 4.2 (doublet, 1H) after treatment with D_2O. Its DEPT ^{13}C NMR spectra had peaks at δ 64 (CH_2), δ 75 (CH), δ 82 (CH), and δ 177 (C). What is the structure of **D**, including its stereochemistry?

LEARNING GROUP PROBLEMS

1. The structure of thyroxine, a thyroid hormone that helps to regulate metabolic rate, was determined in part by comparison with a synthetic compound believed to have the same structure as natural thyroxine. The final step in the laboratory synthesis of thyroxine by Harington and Barger, shown below, involves an electrophilic aromatic substitution. Draw a detailed mechanism for this step and explain why the iodine substitutions occur ortho to the phenolic hydroxyl and not ortho to the oxygen of the aryl ether. [One reason iodine is required in our diet (e.g., in iodized salt) is for the biosynthesis of thyroxine.]



Thyroxine

2. Synthesize 2-chloro-4-nitrobenzoic acid from toluene and any other reagents necessary. Begin by writing a retrosynthetic analysis.

3. Deduce the structures of compounds **E–L** in the roadmap below.