26

MORE ON AROMATIC COMPOUNDS. ARYL OXYGEN COMPOUNDS; SIDE-CHAIN DERIVATIVES

Generally, the reactivity of a substituent on an aromatic ring is greatly modified from that of its aliphatic counterpart. Likewise, the substituent can influence the reactivity of the ring. We have seen this interplay between ring and substituent in the chemistry of aryl halides (Section 14-6), of arenamines (Sections 23-7C and 23-9F), and in electrophilic substitution reactions of aromatic compounds (Section 22-5). It is particularly manifest in the chemistry of substances that have oxygen attached directly to arene rings. We shall discuss aryl oxygen compounds and some of their oxidation products called **quinones** in this chapter. We also shall discuss aromatic substances that have carbon substituents in the form of alkyl, haloalkyl (such as $—CH_2Cl$, $—CHCl_2$, $—CCl_3$), aldehyde (—CHO), and carboxylic acid ($—CO_2H$) groups. We classify such substances as aromatic side-chain derivatives (for want of a better term).

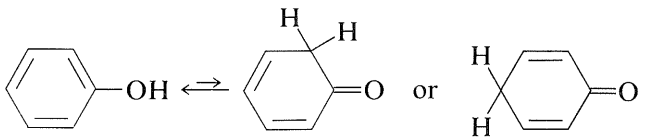
26-1 ARYL OXYGEN COMPOUNDS

26-1A Phenols (Arenols)—Physical Properties

Phenols are enols, and enols normally are unstable with respect to the corresponding carbonyl compounds (Section 17-1D). Thus

$$CH_2{=}CHOH \longrightarrow CH_3CH{=}O \qquad \Delta H^0_{\text{calc. (gas)}} \cong -15 \text{ kcal mole}^{-1}$$

The situation is different for phenols because of the inclusion of the carbon–carbon double bond into the aromatic ring and the associated aromatic stabilization. Phenol (benzenol) exists exclusively in the enol form:

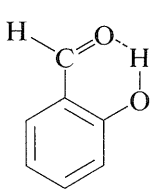


$\Delta H^0_{\text{calc. (gas)}} \cong +20$ kcal mole^{-1}

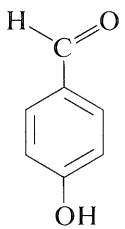
The *physical properties* of some representative phenols are summarized in Table 26-1. In general, phenols are somewhat more polar than the corresponding saturated alcohols. The magnitudes of the differences are well illustrated by comparison of the physical properties of benzenol and cyclohexanol, shown in Table 26-2. The determining factor appears to be the greater acidity of the phenolic hydroxyl group, which means that, in the undissociated form, the O–H bond is more strongly polarized as $\overset{\delta\ominus}{O}—\overset{\delta\oplus}{H}$ than for alcohols. Phenols therefore form stronger hydrogen bonds than alcohols, thereby resulting in higher boiling points, higher water solubility, and increased ability to act as solvents for reasonably polar organic molecules.

The wavelengths of the ultraviolet absorption maxima of the arenols shown in Table 26-1 indicate a considerable effect of substituents on these absorptions, which correspond to the 200-nm and 255-nm absorptions of benzene (Section 22-3B).

Substances such as 2-hydroxybenzaldehyde, 2-hydroxybenzoic acid, and 2-nitrobenzenol form *intra-* rather than intermolecular hydrogen bonds. This effectively reduces intermolecular attraction, thereby reducing boiling points and increasing solubility in nonpolar solvents as compared to the meta and para isomers, which only form *inter*molecular hydrogen bonds:



*intra*molecular
hydrogen bond
bp 196.5°; mp −7°



only *inter*molecular
hydrogen bonds
bp 250°; mp 115°

Table 26-1
Physical Properties of Some Representative Phenols

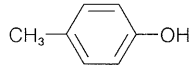
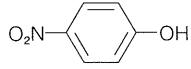
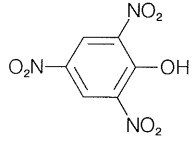
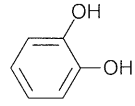
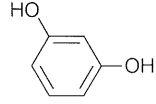
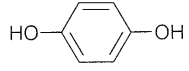
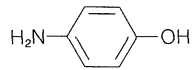
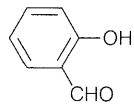
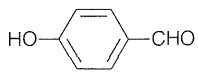
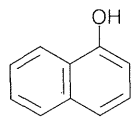
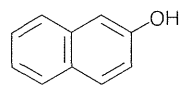
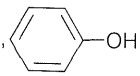
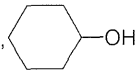
Name	Formula	Mp, °C	Bp, °C	K_a H_2O, 25°C	λ_{max},[a] nm	ϵ	λ_{max},[b] nm	ϵ
benzenol (phenol)	C_6H_5OH	43	182	1.3×10^{-10}	211	6,200	270	1,450
4-methylbenzenol (*para*-cresol)		34	203	1.5×10^{-10}	225	7,400	280	1,995
4-nitrobenzenol (*para*-nitrophenol)		114		6.5×10^{-8}	318	10,000		
2,4,6-trinitrobenzenol (picric acid)		123			380	13,450		
1,2-benzenediol (catechol)		105	246	3.3×10^{-10}[c]	214	6,300	276	2,300
1,3-benzenediol (resorcinol)		110	280	3.6×10^{-10}[c]	216	6,800	274	1,900
1,4-benzenediol (hydroquinone)		170	285	1×10^{-10}			290	2,800

Table 26-1 (continued)
Physical Properties of Some Representative Phenols

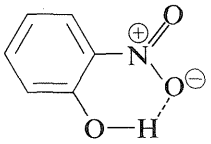
Name	Formula	Mp, °C	Bp, °C	K_a H_2O, 25°C	λ_{max},[a] nm	ϵ	λ_{max},[b] nm	ϵ
4-aminobenzenol (*para*-aminophenol)		186		6.6×10^{-9}[c]	233	8,000	280	3,200
2-hydroxybenzenecarbaldehyde (salicylaldehyde)		−7	197		256	12,600	324	3,400
4-hydroxybenzenecarbaldehyde (*para*-hydroxybenzaldehyde)		115	250	2.2×10^{-8}	284	16,000		
1-naphthalenol (1-naphthol)		94	288	1×10^{-8}				
2-naphthalenol (2-naphthol)		123	285					

[a]To be compared with the 200-nm band of benzene (Table 22-3).
[b]To be compared with the 250-nm band of benzene (Table 22-4).
[c]At 18°C.

Table 26-2
Comparative Physical Properties of Benzenol and Cyclohexanol

	Benzenol, 	Cyclohexanol, 
mp, °C	43	25.5
bp, °C	182	161
water solubility, g/100 g, 20°	9.3	3.6
K_a	1.3×10^{-10}	$\sim 10^{-18}$

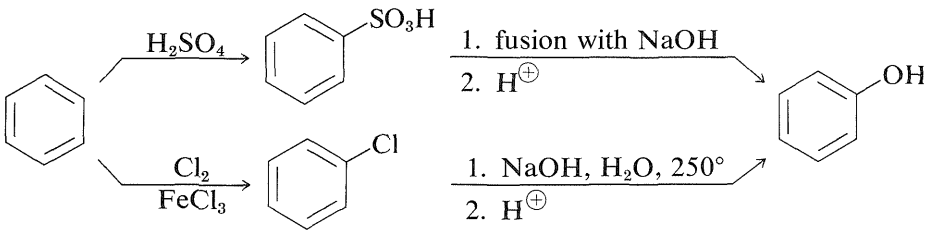
Formation of *intra*molecular hydrogen bonds shows up clearly in the proton nmr spectra, as we have seen previously for the enol form of 2,4-pentanedione (Section 17-1D, Figure 17-1). Figure 26-1 shows the proton resonances of the nitrobenzenol isomers, and you will see that the ortho isomer has the OH proton resonance at much lower field than either the meta or para isomer. Only for the ortho isomer are the nitro and hydroxyl groups sufficiently close together to form an intramolecular hydrogen bond:



26-1B Synthesis of Phenols

Benzenol and the 2-, 3-, and 4-methylbenzenols (cresols) can be isolated from coal tar (Section 22-11). Benzenol itself is used commercially in such large quantities that alternate methods of preparation are necessary and most of these start with benzene or alkylbenzenes. Direct oxidation of benzene is not satisfactory because benzenol is oxidized more readily than is benzene.

At one time, benzenol was made industrially by sulfonating or chlorinating benzene and then introducing the hydroxyl group by nucleophilic substitution with strong alkali:



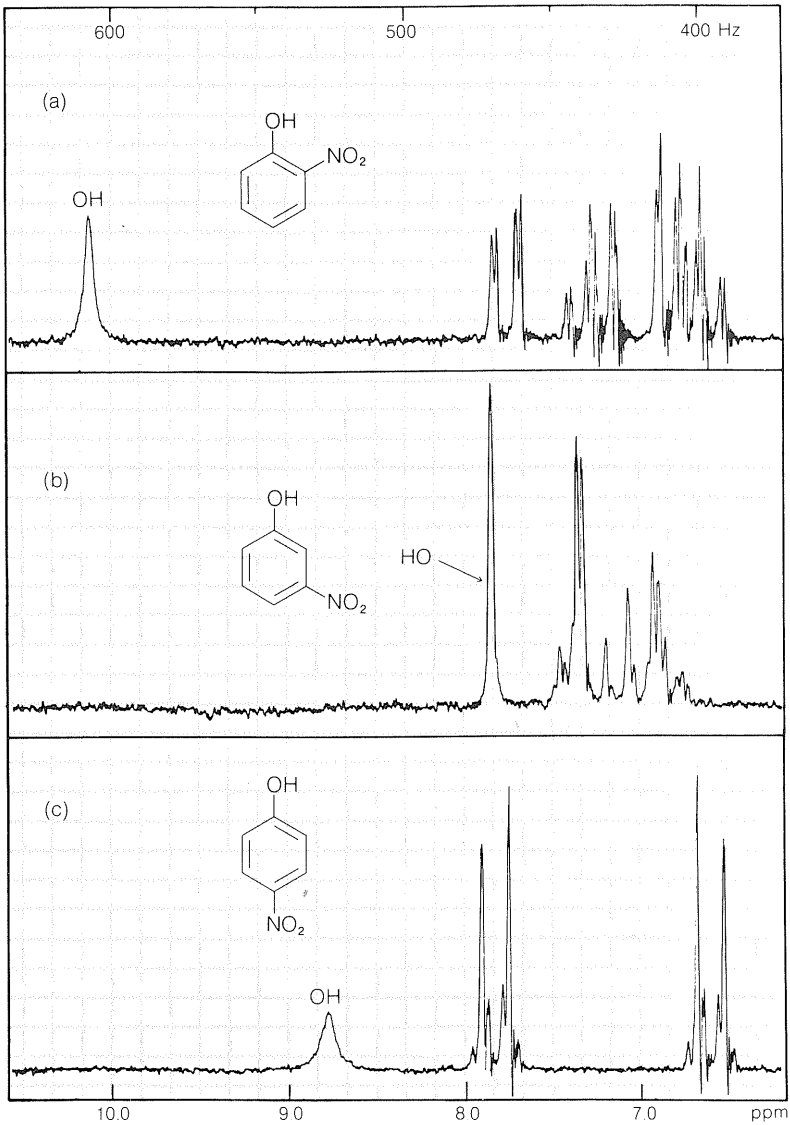
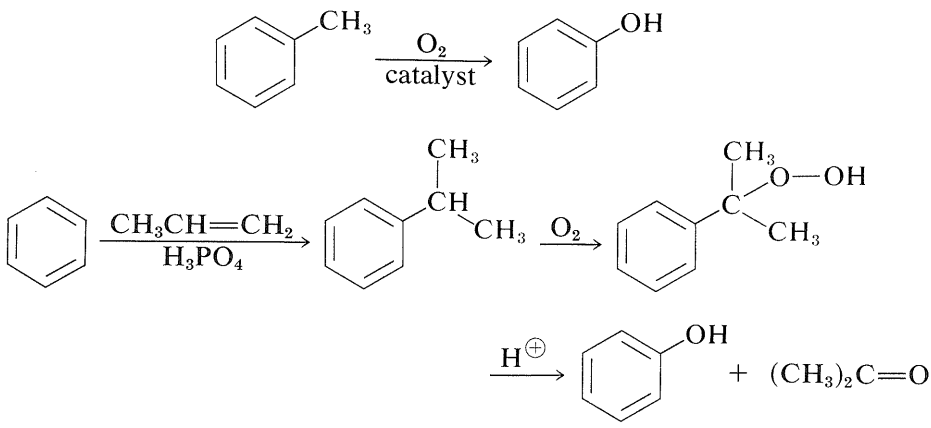


Figure 26-1 Nuclear magnetic resonance spectra at 60 MHz of (a) 2-nitrobenzenol, (b) 3-nitrobenzenol, and (c) 4-nitrobenzenol in ethoxyethane solution (the solvent bands are not shown).

Current commercial syntheses of benzenol involve oxidation of methylbenzene or isopropylbenzene (Section 16-9E). Oxidation of isopropylbenzene is economically feasible for the production of benzenol because 2-propanone

(acetone) also is a valuable product:

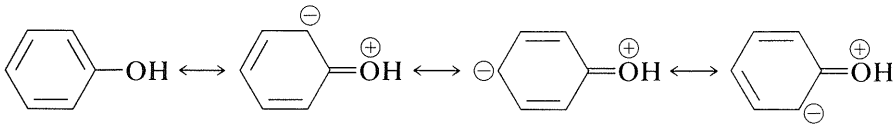


A common laboratory procedure converts an aromatic amine to a phenol by way of the arenediazonium salt, $ArNH_2 \longrightarrow ArN_2^{\oplus} \longrightarrow ArOH$ (Section 23-10B).

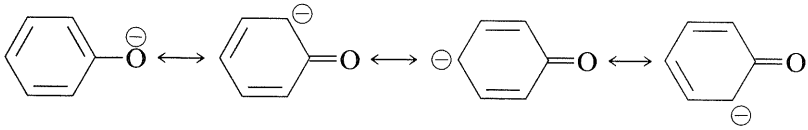
26-1C Reactions of Phenols Involving the O–H Bonds

The reactions of the hydroxyl groups of phenols, wherein the O–H bonds are broken, are similar to those of alcohols. Thus phenols are weak acids ($K_a = 10^{-10}$ to 10^{-8}; Table 26-1), intermediate in strength between carboxylic acids and alcohols.

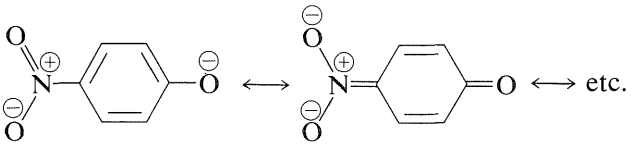
Enols are stronger acids than alcohols because of the increase in electron delocalization in enolate anions as compared to the neutral enols (see Section 15-8A). The stabilization energy of benzenol (Table 21-1) is 48 kcal $mole^{-1}$, 5 kcal greater than that of benzene. We can ascribe this increase to delocalization of an unshared electron pair from oxygen:



When the OH proton is removed by a base the resulting anion has even greater stabilization, because the corresponding valence-bond structures do not involve charge separation:



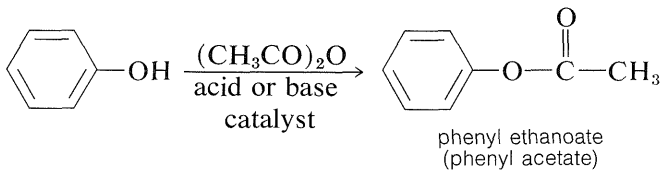
We can be confident that substituent groups that stabilize the anion will increase the acidity. Thus 4-nitrobenzenol is about 500 times stronger as an acid than benzenol, because of the increased delocalization of charge to the nitro group:



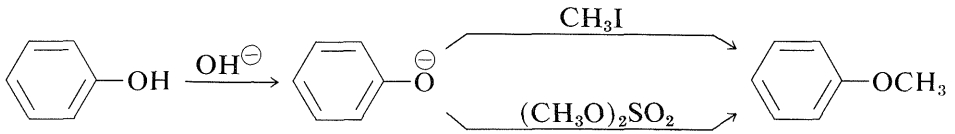
Exercise 26-1 Predict which one of the following pairs of compounds will be the stronger acid. Give your reasoning.

a. 3-nitrobenzenol or 4-nitrobenzenol
b. 3,5-dimethyl-4-nitrobenzenol or 2,6-dimethyl-4-nitrobenzenol
c. 4-methoxybenzenol or 3-methoxybenzenol
d. azabenzen-4-ol or azabenzen-3-ol

It is possible to prepare esters of phenols with carboxylic acid anhydrides or acid halides, and phenyl ethers by reaction of benzenolate anion with halides, sulfate esters, sulfonates, or other alkyl derivatives that react well by the S_N2 mechanism:

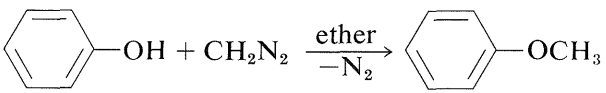


phenyl ethanoate
(phenyl acetate)



methoxybenzene
(anisole)

Phenols (like carboxylic acids; Section 24-7C and Table 18-6) are converted to methoxy derivatives with diazomethane:

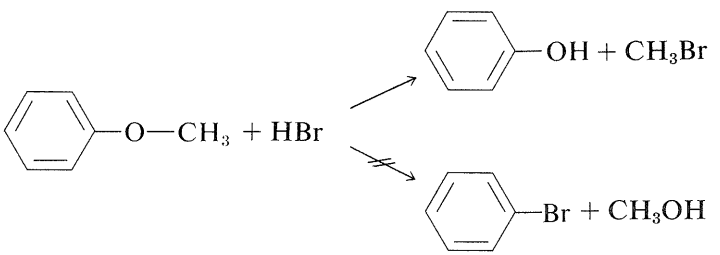


Almost all phenols and enols (such as those of 1,3-diketones) give colors with ferric chloride in dilute water or alcohol solutions. Benzenol

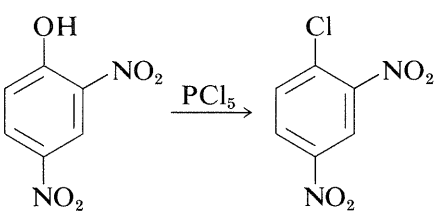
itself produces a violet color with ferric chloride, and the methylbenzenols give a blue color. The products apparently are ferric arenolate salts, which absorb visible light to give an excited state having electrons delocalized over both the iron atom and the unsaturated system.

26-1D Reactions of Phenols Involving the C–O Bonds

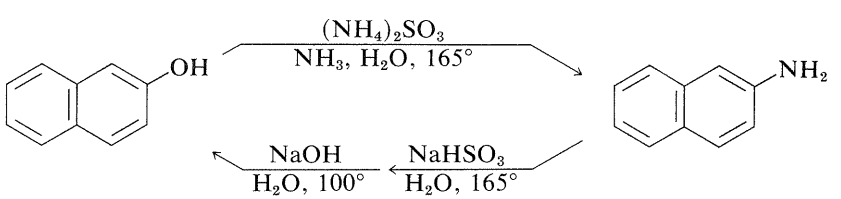
In general, it is very difficult to break the aromatic C–O bond of arenols. Thus concentrated halogen acids do *not* convert simple arenols to aryl halides, and alkoxyarenes are cleaved with hydrogen bromide or hydrogen iodide in the manner ArO—R rather than Ar—OR:



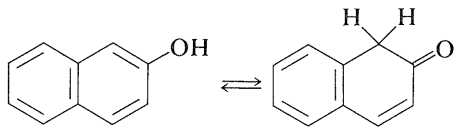
(Diaryl ethers, such as diphenyl ether, do not react with hydrogen iodide even at 200°.) There is no easy way to convert arenols to aryl halides, except where activation is provided by 2- or 4-nitro groups. Thus 2,4-dinitrobenzenol is converted to 1-chloro-2,4-dinitrobenzene with phosphorus pentachloride:



An exception to the generalization that C—O bonds to aromatic systems are difficult both to make and to break is provided by reversible conversion of benzenediols and 1- or 2-naphthalenols to the corresponding amines, usually at elevated temperatures with sodium hydrogen sulfite or an acidic catalyst. The sodium hydrogen sulfite-induced reaction is called the **Bucherer reaction:**

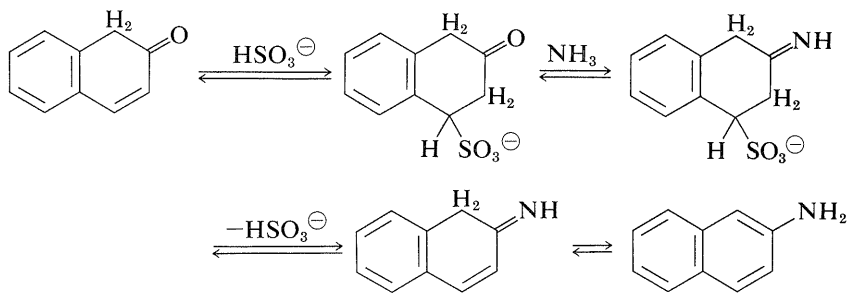


These reactions do not work well with simple benzenols because the key step is formation of the keto isomer of the arenol—a process that is unfavorable for simple benzenols:



(26-1)

The role of the hydrogen sulfite is participation in a reversible 1,4-addition to the unsaturated ketone to hold it in the ketone form that then is converted to the imine by NH_3 (Section 16-4C) and hence to the arenamine:



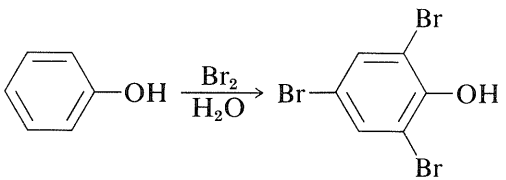
Exercise 26-2* Use bond and stabilization energies to calculate $\Delta H^0(g)$ for the reaction of Equation 26-1 on the assumption that the extra stabilization energy of 2-naphthalenol relative to naphthalene is 5 kcal mole^{-1} (see Tables 4-3 and 21-1). Compare your answer to ΔH^0 calculated for the corresponding reactions of benzenol (Section 26-1A).

Exercise 26-3* Treatment of 1,3-benzenediol (resorcinol) with an ammonia-ammonium chloride solution under pressure at 200° (no sulfite) gives 3-aminobenzenol. Write a reasonable mechanism for this transformation. Would you expect benzenol itself to react similarly? Why?

26-1E Substitution Reactions at the Ring Carbons of Arenols

The electron-rich π-orbital systems of arenols and especially of arenolate ions make these compounds very susceptible to electrophilic substitution. Arenols typically react rapidly with bromine in aqueous solution to substitute

the positions ortho or para to the hydroxyl group. Benzenol itself gives 2,4,6-tribromobenzenol in high yield:

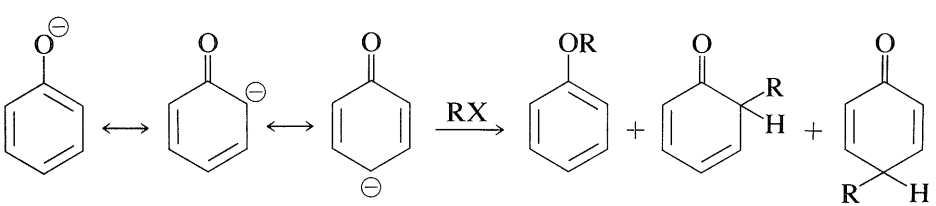


Exercise 26-4* Explain why benzenol with bromine gives tribromobenzenol readily in water solution but 2- and 4-monobromobenzenol in nonpolar solvents. Notice that 2,4,6-tribromobenzenol is at least a 300-fold stronger acid than phenol in water solution.

Exercise 26-5 When 2-naphthalenol is treated with bromine in ethanoic acid it first gives 1-bromo-2-naphthalenol then 1,6-dibromo-2-naphthalenol. Explain the order of substitution, giving attention to why disubstitution does not lead to 1,3-dibromo-2-naphthalenol.

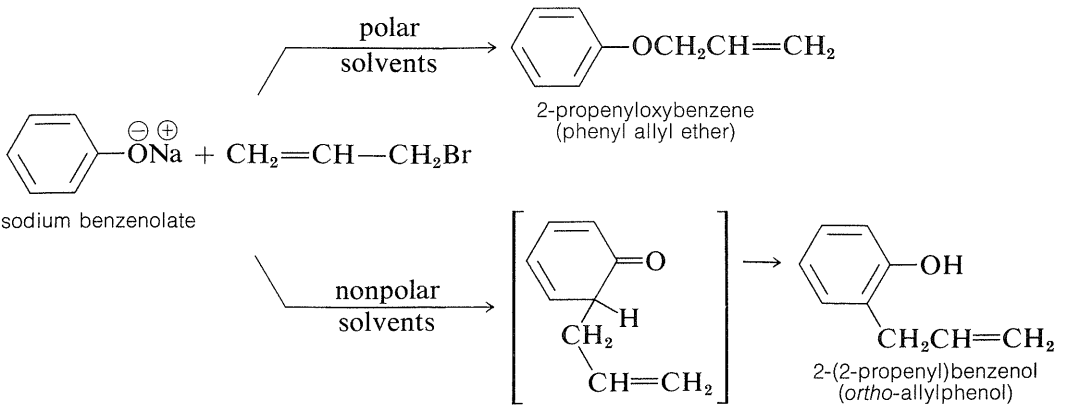
Exercise 26-6 The herbicide "2,4-D" is (2,4-dichlorophenoxy)ethanoic acid. Show how this substance could be synthesized starting from benzenol and ethanoic acid.

Several important reactions of arenols involve aromatic substitution of arenolate ions with *carbon* electrophiles. In a sense, these reactions are alkylation and acylation reactions as discussed for arenes (Sections 22-4E and 22-4F). In another sense, they are alkylation and acylation reactions of *enolate anions* and therefore could give rise to products by C- and O-alkylation, or C- and O-acylation (Section 17-4). Thus:

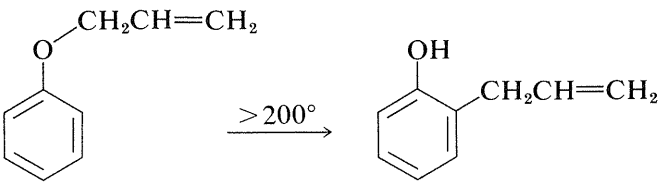


In most cases, O-alkylation predominates. However, with 2-propenyl halides either reaction can be made essentially the exclusive reaction by proper choice of solvent. With sodium benzenolate the more polar solvents, such as

2-propanone, lead to 2-propenyloxybenzene, whereas in nonpolar solvents, such as benzene, 2-(2-propenyl)benzenol is the favored product:

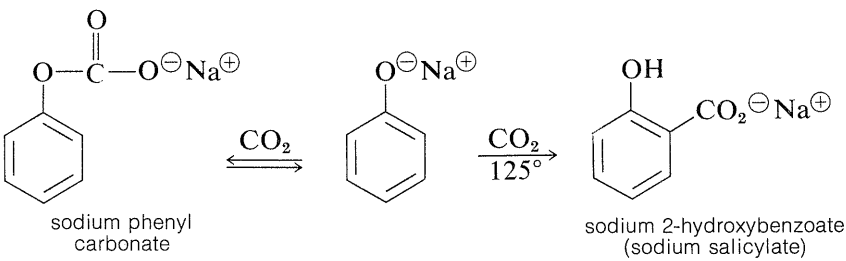


It should be noted that formation of 2-(2-propenyl)benzenol in nonpolar solvents is *not* the result of O-propenylation *followed* by rearrangement, even though the C-propenylation product is thermodynamically more stable. Rearrangement in fact does occur, but at much higher temperatures (above 200°) than required to propenylate sodium benzenolate:

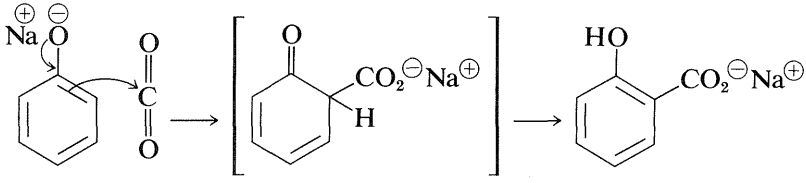


Such rearrangements are quite general for aryl allyl ethers and are called **Claisen rearrangements.** They are examples of the pericyclic reactions discussed in Section 21-10D. (See Exercise 26-45.)

The **Kolbe-Schmitt reaction** produces O- and C-carboxylation through the reaction of carbon dioxide with sodium benzenolate at 125°:



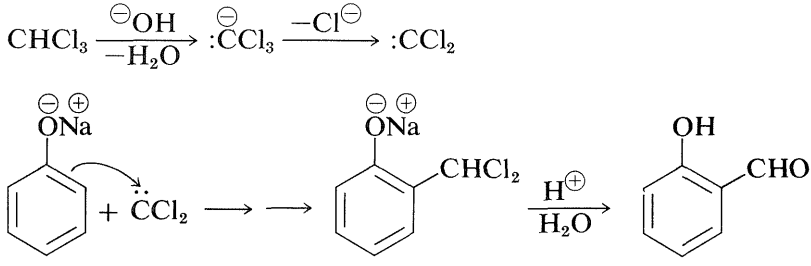
Sodium benzenolate absorbs carbon dioxide at room temperature to form sodium phenyl carbonate (O-carboxylation) and, when this is heated to 125° under a pressure of several atmospheres of carbon dioxide, it rearranges to sodium 2-hydroxybenzoate (sodium salicylate). However, there is no evidence that this reaction is other than a dissociation–recombination process, in which the important step involves electrophilic attack by carbon dioxide on the aromatic ring of the benzenolate ion (C-carboxylation):



With the sodium benzenolate at temperatures of 125° to 150°, ortho substitution occurs; at higher temperatures (250° to 300°), particularly with the potassium salt, the para isomer is favored.

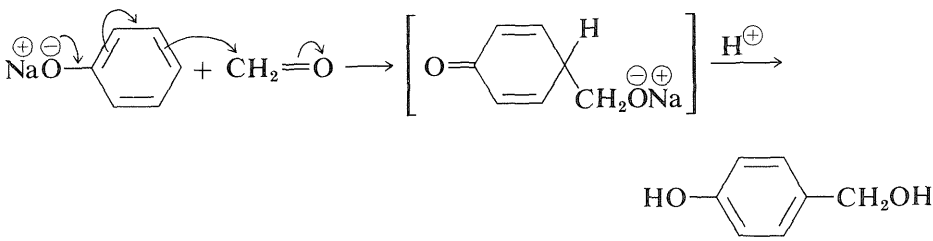
> The Kolbe-Schmitt reaction is related to enzymatic carboxylations as of D-ribulose 1,5-diphosphate with carbon dioxide, a key step in photosynthesis (Section 20-9). The overall result is C—C bond formation by addition of CO_2 to an enolate salt or its enamine equivalent.

In the somewhat related **Reimer-Tiemann reaction,** sodium benzenolate with trichloromethane in alkaline solution forms the sodium salt of 2-hydroxybenzenecarbaldehyde (salicylaldehyde). The electrophile in this case probably is dichlorocarbene (Section 14-7B):



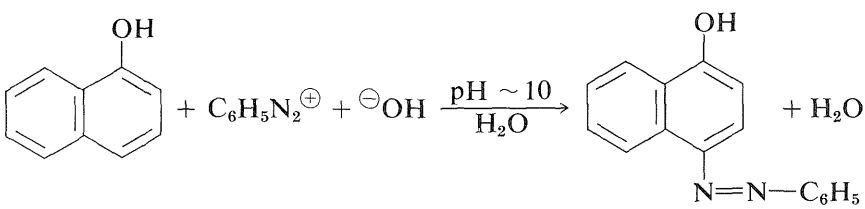
Exercise 26-7 1,3-Benzenediol (resorcinol) can be converted to a carboxylic acid with carbon dioxide and alkali. Would you expect 1,3-benzenediol to react more, or less, readily than benzenol? Why? Which is the most likely point of monosubstitution? Explain.

Many phenols undergo aldol-like addition reactions with carbonyl compounds in the presence of acids or bases. Thus benzenol reacts with methanal under mild alkaline conditions to form (4-hydroxyphenyl)methanol:



The use of this type of reaction in the formation of polymers will be discussed in Chapter 29.

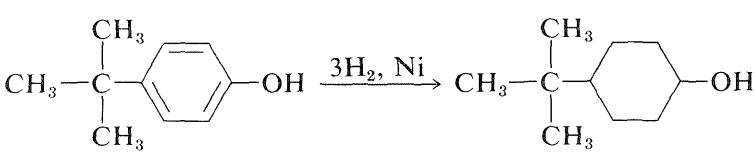
Arenols usually will undergo diazo coupling reactions with aryldiazonium salts at pH values high enough to convert some of the arenol to the more powerfully nucleophilic arenolate anions:



However, if the pH is too high, coupling is inhibited because the diazonium salt is transformed into $ArN{=}N{-}O^{\ominus}$, which is the nonelectrophilic conjugate base of a diazotic acid (Table 23-4).

26-1F Addition Reactions

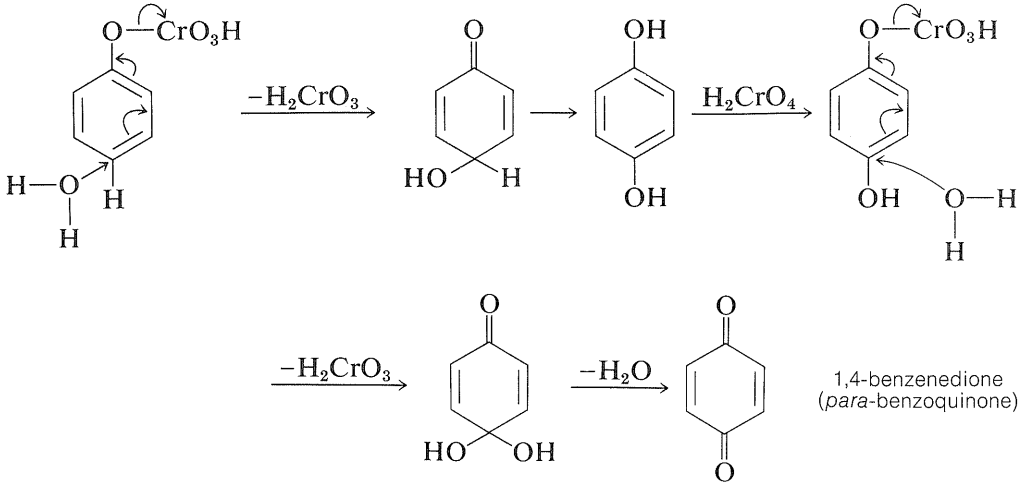
Arenols can be reduced successfully with hydrogen over nickel catalysts to the corresponding cyclohexanols. A variety of alkyl-substituted cyclohexanols can be prepared in this way:



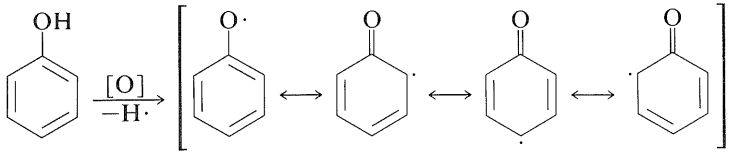
26-1G Oxidation of Arenols

Benzenol can be oxidized to 1,4-benzenedione (*para*-benzoquinone) by chromic acid. The reaction may proceed by way of phenyl hydrogen-chromate

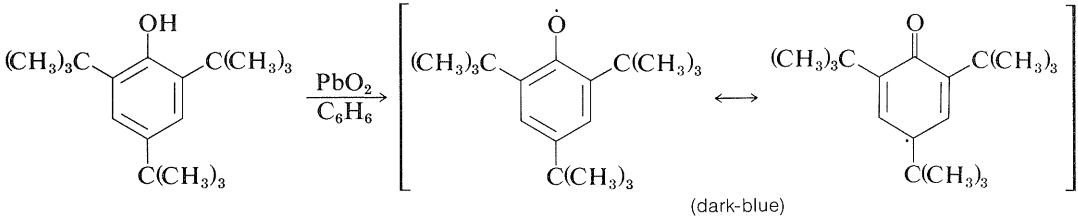
(Section 15-6B) as follows:



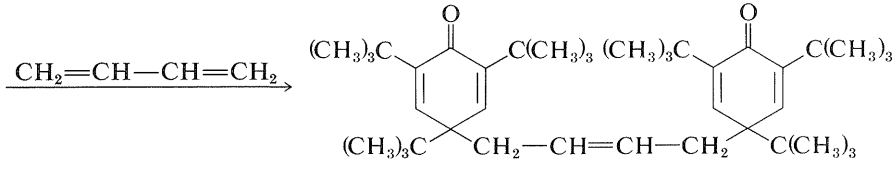
Oxidation reactions of arenols with other oxidants are complex. Oxidative attack seems to involve, as the first step, removal of the hydroxyl hydrogen to yield a phenoxy radical:



The subsequent course depends upon the substituents on the aromatic ring. With 2,4,6-tri-*tert*-butylbenzenol, the radical is reasonably stable in benzene solution and its presence is indicated by both its dark-blue color and the fact that it adds to 1,3-butadiene:

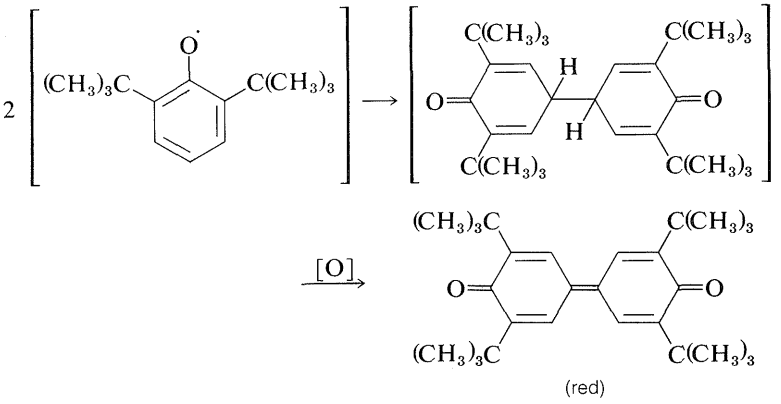


(dark-blue)

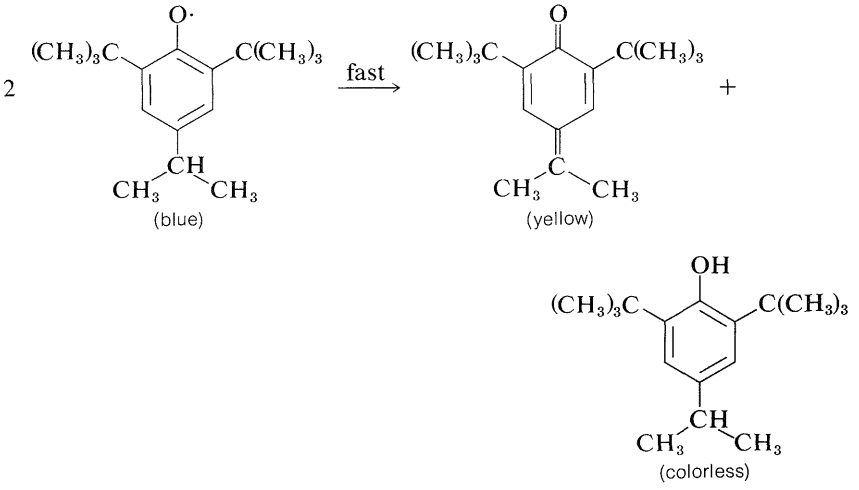


Apparently, dimerization of the above phenoxy radical through either oxygen or the ring is inhibited by the bulky *tert*-butyl groups. With fewer or smaller substituents, the phenoxy radicals may form dimerization or disproportionation products. Examples of these reactions follow.

Dimerization:



Disproportionation:

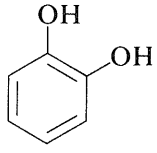


Exercise 26-8 Explain how you would use proton nmr spectra to show that the product of oxidation of 2,4,6-tri-*tert*-butylbenzenol in the presence of butadiene links the aromatic rings at the 4-position, not at the 2-position.

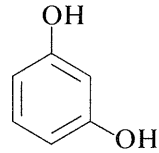
Exercise 26-9* Benzenol samples that have been allowed to stand in air always are pink or red because of oxidation. Write a mechanism for the oxidation of benzenol by oxygen that could lead to one or more products that may be expected to be colored.

26-1H Arene Polyols

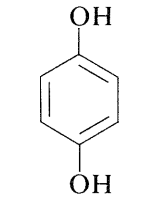
Several important aromatic compounds have more than one arene hydroxyl group. These most often are derivatives of the following dihydric and trihydric arenols, all of which have commonly used (but poorly descriptive) names:



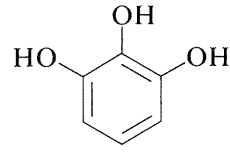
1,2-benzenediol (catechol)



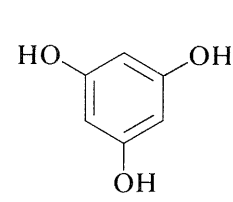
1,3-benzenediol (resorcinol)



1,4-benzenediol (hydroquinone)

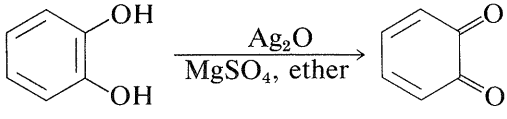


1,2,3-benzenetriol (pyrogallol)

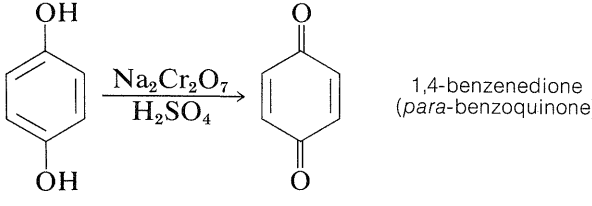


1,3,5-benzenetriol (phloroglucinol)

All are exceptionally reactive towards electrophilic reagents, particularly in alkaline solution, and all are readily oxidized. The 1,2- and 1,4-benzenediols, but not 1,3-benzenediol, are oxidized to quinones:

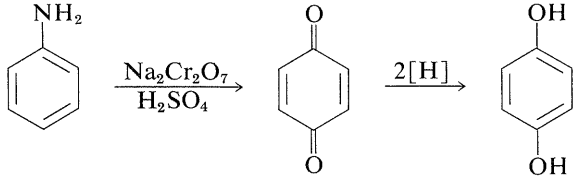


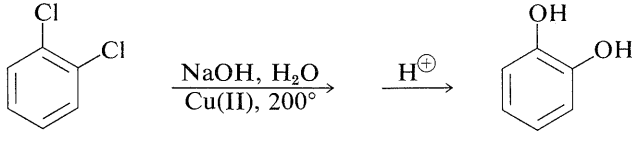
1,2-benzenedione (*ortho*-benzoquinone)

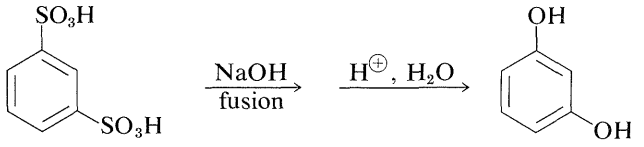


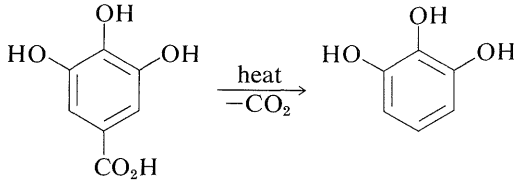
1,4-benzenedione (*para*-benzoquinone)

The preparation of these substances can be achieved by standard methods for synthesizing arenols, but most of them actually are made on a commercial scale by rather special procedures, some of which are summarized as follows:

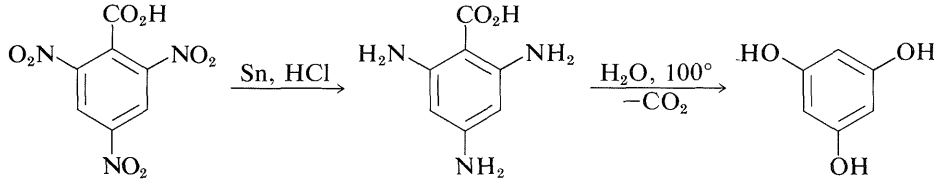








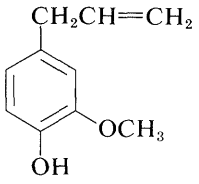
gallic acid



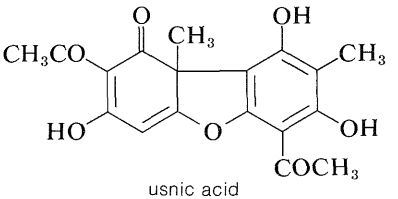
Exercise 26-10* Explain why gallic acid decarboxylates on heating more readily than benzoic acid. Would you expect 2,5-dihydroxybenzoic acid to decarboxylate as readily as its 2,4 isomer? Explain.

Exercise 26-11* Work out the course of hydrolysis and decarboxylation of 2,4,6-triaminobenzoic acid to 1,3,5-benzenetriol.

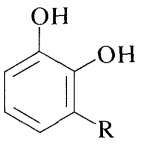
The gallic acid used in the preparation of 1,2,3-benzenetriol can be obtained by microbial degradation of **tannins,** which are complex combinations of glucose and gallic acid obtained from oak bark and gallnuts. A few other representatives of the many types of naturally occurring derivatives of polyhydric arenols are



eugenol
(oil of cloves)

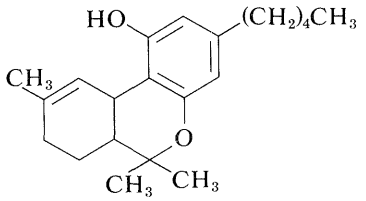


usnic acid
(lichen pigment with
antibiotic properties)

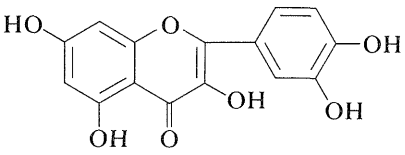


$R = -(CH_2)_{14}CH_3$
$R = -(CH_2)_7CH{=}CH(CH_2)_5CH_3$
$R = -(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_2CH_3$
$R = -(CH_2)_7CH{=}CHCH_2CH{=}CHCH_2CH{=}CH_2$

urushiol (poison ivy, mixture of different R groups)



tetrahydrocannabinol
(active constituent of marijuana or hashish)



quercetin
(in the form of glucosides, as a coloring matter in plants)

Exercise 26-12* Devise a reasonable sequence of synthetic steps for conversion of eugenol to the flavoring material vanillin, which is 3-methoxy-4-hydroxybenzenecarbaldehyde (Section 26-5).

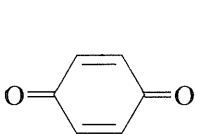
Exercise 26-13* Reduction of the carbonyl group of quercetin gives a substance that loses water readily to give a brilliant-violet compound. This compound, when treated with hydrochloric acid, is converted reversibly to a red salt. Consider possible ways that the reduction product could dehydrate to give a violet substance and show how addition of a proton to it could occur in such a way as to give a substantial color change.

Exercise 26-14* Natural usnic acid is optically active but racemizes on heating *without need for acid or base catalysts.* Write a mechanism involving a reversible electrocyclic reaction for this racemization that also accounts for the fact that when usnic acid is heated in ethanol, an optically inactive ethyl ester of a *carboxylic acid* is formed. (Review Sections 21-10D and 17-6B.)

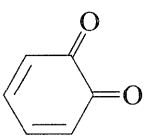
26-2 QUINONES

Quinones are not aromatic compounds but are conjugated cyclic diketones. Yet it is convenient to discuss their chemistry at this point because quinones and the related aromatic arenols are readily interconverted, and their chemistry is largely interdependent.

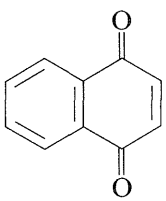
A variety of quinonelike structures have been prepared, the most common of which are the 1,2- and 1,4-quinones as exemplified by 1,2- and 1,4-benzenediones. Usually the 1,2-quinones are more difficult to make and are more reactive than the 1,4-quinones. A few 1,6- and 1,8-quinones also are known.



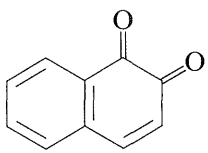
1,4-benzenedione
(*para*-benzoquinone)



1,2-benzenedione
(*ortho*-benzoquinone)

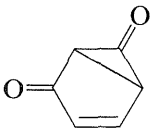


1,4-naphthalenedione
(1,4-naphthoquinone)

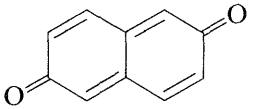


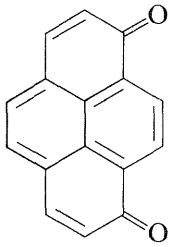
1,2-naphthalenedione
(1,2-naphthoquinone)

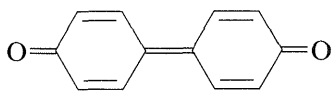
No 1,3-quinones are known, possibly because they would have nonplanar, highly strained structures and therefore would be unstable:


(unknown)

A number of quinones are known in which the quinone arrangement extends over more than one ring. Examples are:

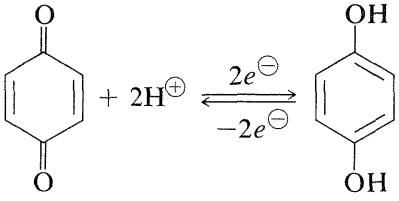

2,6-naphthalenedione
(2,6-naphthoquinone)


1,8-pyrenedione
(1,8-pyrenequinone)


4,4′-biphenyldione
(4,4′-diphenoquinone)

26-2A Reduction of Quinones

A characteristic and important reaction of quinones is reduction to the corresponding arenediols. The reduction products of 1,4-quinones are called **hydroquinones:**


(26-2)

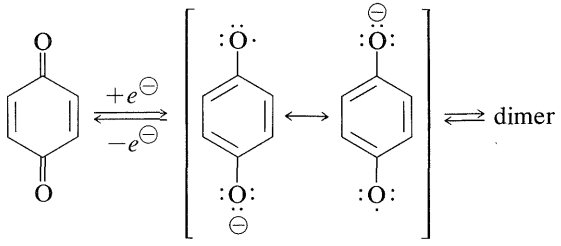
Reduction can be achieved electrochemically and with a variety of reducing agents (metals in aqueous acid, catalytic hydrogenation). Such reductions are unusual among organic reactions in being sufficiently rapid and reversible to give easily reproducible electrode potentials in an electrolytic cell. The position of the 1,4-benzenediol-1,4-benzenedione equilibrium (Equation 26-2) is proportional to the square of the hydrogen-ion concentration. Therefore the electrode potential is sensitive to pH; a change of one unit of pH in water solution changes the potential of the electrode by 0.059 V. Before the invention of the glass-electrode pH meter, the half-cell potential developed by this equilibrium was used widely to determine pH values of aqueous solutions. The method is not very useful above pH 9 because the quinone reacts irreversibly with alkali.

Numerous studies have been made of the relationship between half-cell reduction potentials and the structures of quinones. As might be expected, the potentials are greatest when the resonance stabilization associated with formation of the aromatic ring is greatest.

Exercise 26-15 Arrange the following quinones in the order of expected increasing half-cell potential for reduction (the larger the potential the greater the tendency for reduction): 1,4-benzenedione, 4,4′-biphenyldione, *cis*-2,2′-dimethyl-4,4′-biphenyldione, 9,10-anthracenedione, and 1,4-naphthalenedione. Your reasoning should be based on differences expected in the stabilization of the arenediones and arenediols, including steric factors, if any.

When alcoholic solutions of hydroquinone and quinone are mixed, a brown-red color develops and a green-black 1:1 complex crystallizes that is known as **quinhydrone.** This substance is a charge-transfer complex (Section 24-6C), with the diol acting as the electron donor and the dione as the electron acceptor. Quinhydrone is not very soluble and dissociates considerably to its components in solution.

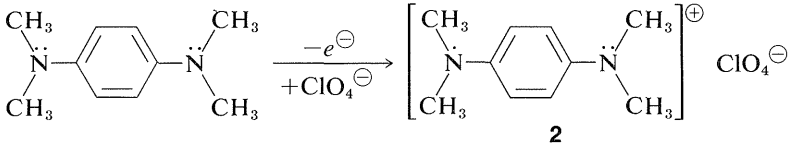
The reduction of a quinone requires two electrons, and it is possible that these electrons could be transferred either together or one at a time. The product of a single-electron transfer leads to what appropriately is called a **semiquinone, 1**, with both a negative charge and an odd electron (a radical anion):



a semiquinone radical anion, **1**

The formation of relatively stable semiquinone radicals by electrolytic reduction of quinones has been established by a variety of methods. Some semiquinone radicals undergo reversible dimerization reactions to form peroxides.

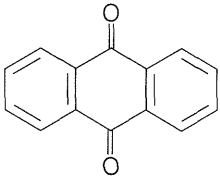
A particularly stable cation-radical of the semiquinone type is formed by mild oxidation of *N,N,N′,N′*-tetramethyl-1,4-benzenediamine. The cation, which is isolable as a brilliant-blue perchlorate salt, **2**, is called "Wurster's Blue":



2

Wurster's Blue

Exercise 26-16 Reduction of 9,10-anthracenedione with tin and hydrochloric acid in ethanoic acid produces a solid, pale-yellow ketone (mp 156°), which has the formula $C_{14}H_{10}O$. This ketone is not soluble in cold alkali but does dissolve when heated with alkali. Acidification of cooled alkaline solutions of the ketone precipitates a brown-yellow *isomer* of the ketone (mp 120°), which gives a color with ferric chloride, couples with diazonium salts (Section 23-10C), reacts with bromine, and slowly reverts to the isomeric ketone.



9,10-anthracenedione
(9,10-anthraquinone)

What are the likely structures of the ketone and its isomer? Write equations for the reactions described and calculate ΔH^0 for interconversion of the isomers in the vapor phase. (Review Sections 26-1 and 21-7.)

Exercise 26-17* Write resonance structures that account for the stability of the cation of Wurster's salts, such as Wurster's Blue, **2**. Explain why *N,N,N′,N′*-2,3,5,6-octamethyl-1,4-benzenediamine does not form a similarly stable cation radical.

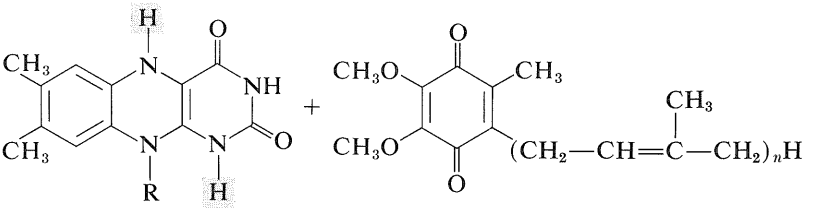
Exercise 26-18* Acidification of a solution containing semiquinone radicals such as **1** tends to cause the radicals to disproportionate to the arenediol and arenedione. Why should acid cause changes in the relative stabilities of the semiquinones and the corresponding diol–dione pairs?

26-2B Quinones of Biological Importance

Oxidation and reduction in biochemical systems involve many reactions that are similar to the arenediol–arenedione couple. We have mentioned several previously: $NADP^{\oplus} \rightleftharpoons NADPH$ (Section 20-9), and $FADH_2 \rightleftharpoons FAD$ (Section 15-6C).

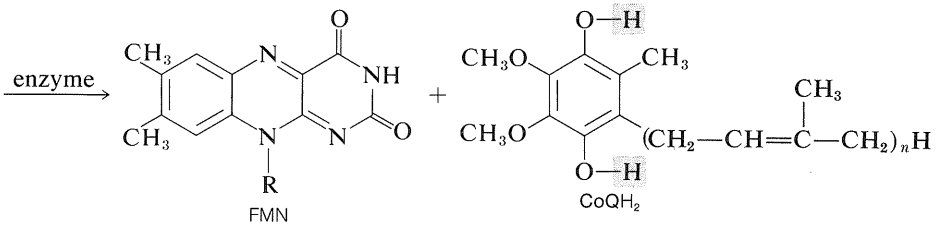
An important question in metabolic oxidation is just how reduction of oxygen ($\frac{1}{2}O_2 + 2H^{\oplus} + 2e \longrightarrow H_2O$) is linked to the oxidation of NADH ($NADH \longrightarrow NAD^{\oplus} + H^{\oplus} + 2e$). The route for transfer of electrons from NADH to oxygen (oxidation plus phosphorylation; Section 20-10) is indirect, complicated, and involves, in an early stage, oxidation of NADH by flavin mononucleotide (FMN) by the reaction $FMN + NADH + H^{\oplus} \longrightarrow FMNH_2 + NAD^{\oplus}$. But the reduced form of FMN, $FMNH_2$, does not react directly

with oxygen. Instead, it reduces a quinone called **coenzyme Q (CoQ)** to the corresponding arenediol:



$FMNH_2$ CoQ $n = 6\text{–}10$

$[R = -CH_2(CHOH)_3CH_2OPO_3^{2\ominus}]$

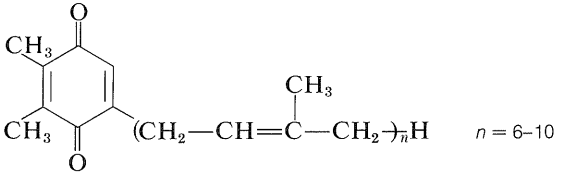


FMN $CoQH_2$

The effect of this step is to form a slightly polar reductant ($\mathbf{CoQH_2}$) from a strongly polar reductant ($FMNH_2$), and this permits the reduced material to penetrate into a less polar region of the oxidative apparatus. The reduced **CoQ** does not react directly with oxygen but is a participant in a chain of oxidation-reduction reactions involving electron transfer between a number of iron-containing proteins known as *cytochromes*. At the end of this chain of reactions, the reduced form of a copper-containing cytochrome actually reacts with oxygen. The sequence of electron-carriers may be summarized as

$$NADH \longrightarrow FMNH_2 \longrightarrow \mathbf{CoQH_2} \longrightarrow \text{cytochromes} \longrightarrow O_2$$

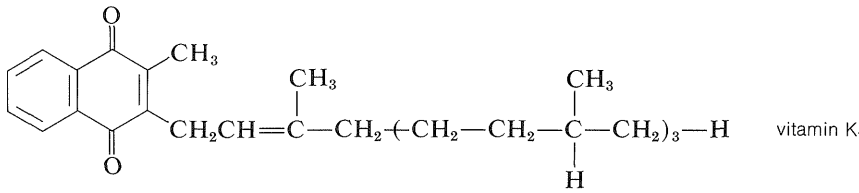
A related process occurs in photosynthesis (Section 20-9). You will recall that a critical part of photosynthesis involves the transfer of electrons from the photosystem that oxidizes water ($H_2O \longrightarrow {}^1/_2O_2 + 2H^{\oplus} + 2e$) to the photosystem that reduces $NADP^{\oplus}$ ($NADP^{\oplus} + 2H^{\oplus} + 2e \longrightarrow NADPH + H^{\oplus}$). As in oxidative phosphorylation, the electron-transfer route is complex. However, one of the electron carriers is a quinone called **plastoquinone** that closely resembles coenzyme Q found in animals. Plastoquinone, like coenzyme Q, is reduced to the hydroquinone form, which is part of an electron-transport chain involving iron- and copper-containing proteins:



$n = 6\text{–}10$

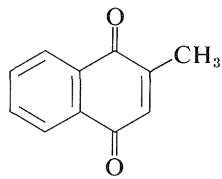
plastoquinone

Among other naturally occurring substances having quinone-type structures, one of the most important is the blood antihemorrhagic factor, vitamin K_1, which occurs in green plants and is a substituted 1,4-naphthalenedione:



vitamin K_1

The structure of vitamin K_1 has been established by degradation and by synthesis. Surprisingly, the long alkyl side chain of vitamin K_1 is not necessary for its action in aiding blood clotting because 2-methyl-1,4-naphthoquinone is almost equally active on a molar basis.



2-methyl-1,4-naphthalenedione (menadione)

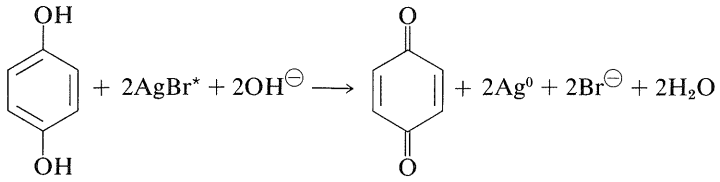
Besides playing a vital role in the oxidation–reduction processes of living organisms, quinones occur widely as natural pigments found mainly in plants, fungi, lichens, marine organisms, and insects (see alizarin, Section 28-4A, as representative of a natural anthraquinone-type dye).

Exercise 26-19* The biologically important quinone called plastoquinone is similar to CoQ, except that the CH_3O— groups of CoQ are replaced by CH_3— groups. What differences in properties would you expect between plastoquinone and CoQ and their respective reduction products? Consider half-cell potentials (see Exercise 26-15), solubility in polar and nonpolar solvents, and relative acidity.

26-2C Photographic Developers

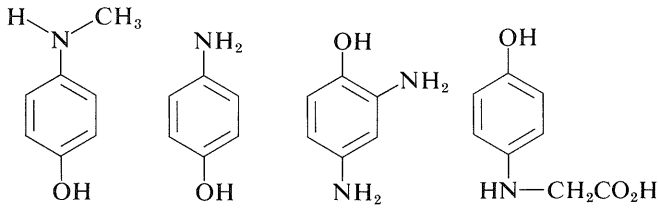
Photography makes important practical use of the arenediol–arenedione oxidation–reduction system. Exposure of the minute grains of silver bromide in a photographic emulsion to blue light (or any visible light in the presence of suitably sensitizing dyes) produces a stable activated form of silver bromide, the activation involving generation of some sort of crystal defect. Subsequently, when the emulsion is brought into contact with a developer, which may be an alkaline aqueous solution of 1,4-benzenediol (hydroquinone) and sodium sulfite, the particles of activated silver bromide are reduced to silver metal much more rapidly than the ordinary silver bromide. Removal of the unreduced silver

bromide with sodium thiosulfate ("fixing") leaves a suspension of finely divided silver in the emulsion in the form of the familiar photographic negative.

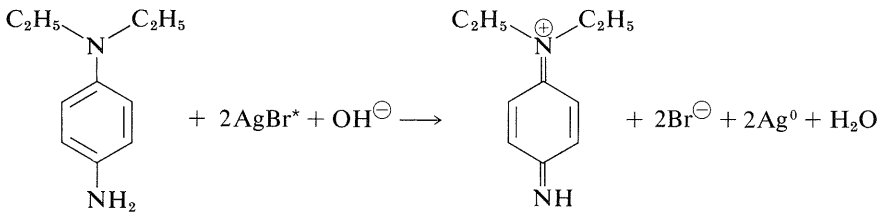


AgBr* = light-activated silver bromide

A variety of compounds are used as photographic developing agents. They are not all arenediols. In fact, most are aromatic aminoalcohols or diamines, but irrespective of their structural differences, they all possess the ability to undergo redox reactions of the type described for 1,4-benzenediol. Structural formulas and commercial names for several important developers are



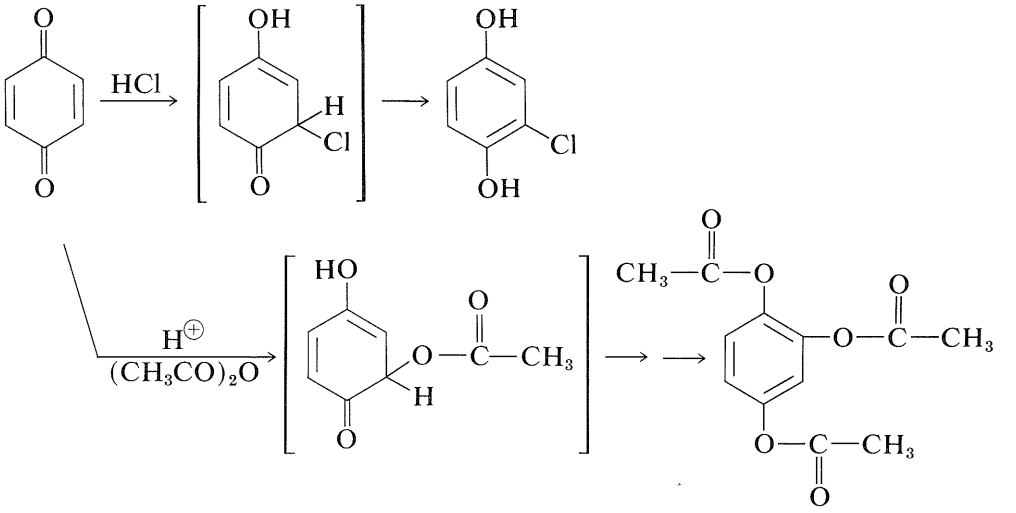
1,4-Benzenediamine also is an effective developing agent, but it may cause dermatitis in sensitive individuals. *N,N*-Diethyl-1,4-benzenediamine is used as a developer in color photography. These substances react with silver bromide to produce benzenediimine derivatives:



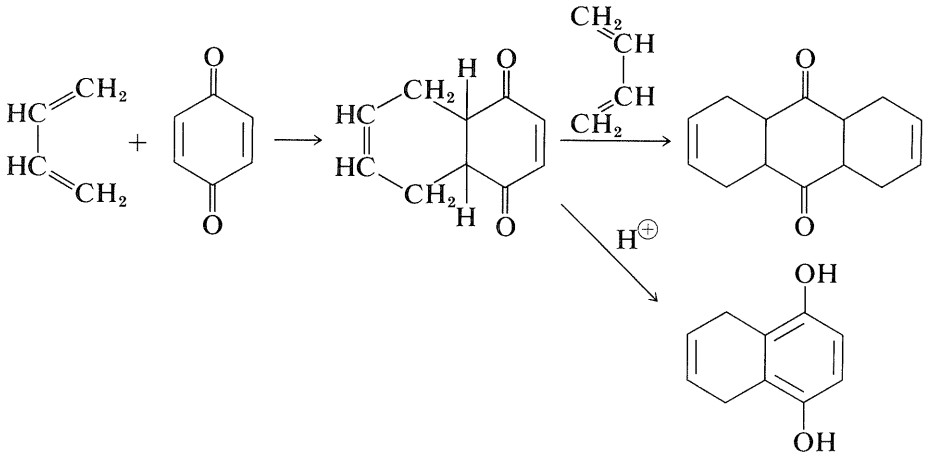
26-2D Addition Reactions of Quinones

Being α,β-unsaturated ketones, quinones have the potential of forming 1,4-addition products in the same way as their open-chain analogs (Section 17-5B). 1,4-Benzenedione undergoes such additions rather readily. The products are unstable and undergo enolization to give substituted 1,4-benzenediols. Two examples are the addition of hydrogen chloride and the acid-catalyzed addition of ethanoic anhydride. In the latter reaction, the hydroxyl groups of the

adduct are acylated by the anhydride. Hydrolysis of the product yields 1,2,4-benzenetriol:



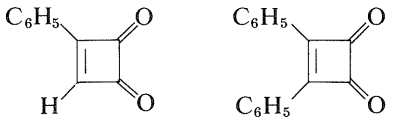
Quinones usually undergo Diels–Alder additions readily, provided that they have at least one double bond that is not part of an aromatic ring. With 1,4-benzenedione and 1,3-butadiene, either the mono- or diadduct can be obtained. The monoadduct enolizes under the influence of acid or base to a 1,4-benzenediol derivative:



Exercise 26-20* You will see that the natural quinones, vitamin K_1, plastoquinone, and CoQ, all have three or four groups on the quinone ring. What kind of possible destructive side reactions would ring substituents tend to prevent? Give your reasoning.

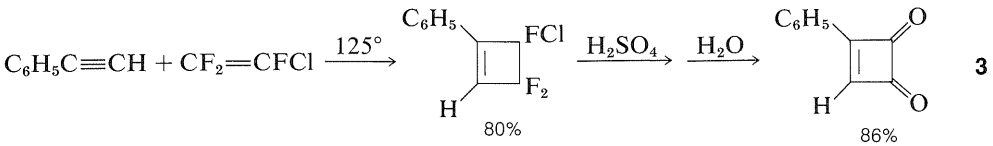
26-2E Quinones of Cyclobutadiene

Benzoquinones owe their unusual properties as α,β-unsaturated ketones to the ease by which they are transformed to stable aromatic systems. How would these properties change if the quinone were derived from nonaromatic structures, such as cyclobutadiene, cyclooctatetraene, or pentalene? There is no final answer to this question because few such substances have been prepared, the best known so far being the mono- and diphenylcyclobutenediones:



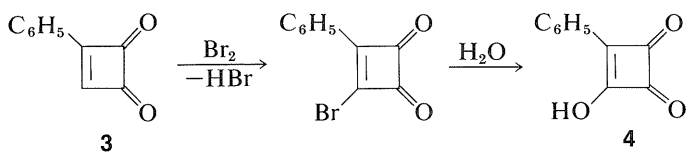
3

For example, **3** can be prepared from sulfuric acid hydrolysis of the cycloaddition product of ethynylbenzene and trifluorochloroethene (Section 13-3D):



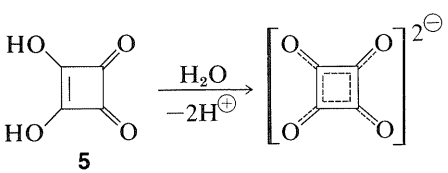
3

The dione, **3**, is a yellow crystalline solid that, despite its strained four-membered ring, is much less reactive than 1,2-benzenedione (*ortho*-benzoquinone). It cannot be reduced to a cyclobutadienediol, does not undergo Diels–Alder reactions, and with bromine gives a substitution product rather than addition. The bromo compound so formed hydrolyzes rapidly to a hydroxy compound, **4**, which is an extraordinarily strong acid having an ionization constant about 10^9 times that of benzenol:



3 **4**

A related compound, 3,4-dihydroxy-1,2-cyclobutenedione, **5**, also has been prepared and is a very strong dibasic acid. It is sometimes called "squaric acid":



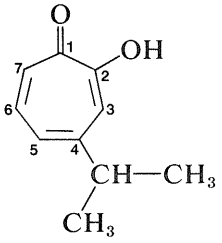
5

From the data so far available, it appears that the quinones corresponding to cyclobutadiene have more aromatic character than do the cyclobutadienes themselves.

Exercise 26-21* Devise a synthesis of dimethoxy- and dihydroxy-1,2-cyclobutenedione based on the expected dimerization product of trifluorochloroethene (Section 13-3D).

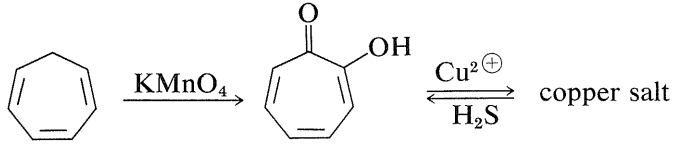
26-3 TROPOLONES AND RELATED COMPOUNDS

The tropolones make up a very interesting class of nonbenzenoid aromatic compound that was discovered first in several quite different kinds of natural products. As one example, the substance called β-thujaplicin or hinokitiol has been isolated from the oil of the Formosan cedar and is 4-isopropyltropolone:



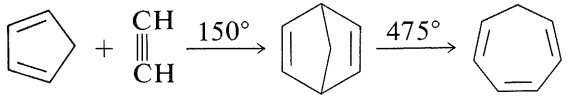
4-isopropyltropolone
(β-thujaplicin)

Tropolone itself can be prepared in a number of ways, the most convenient of which involves oxidation of 1,3,5-cycloheptatriene with alkaline potassium permanganate. The yield is low but the product is isolated readily as the cupric salt:



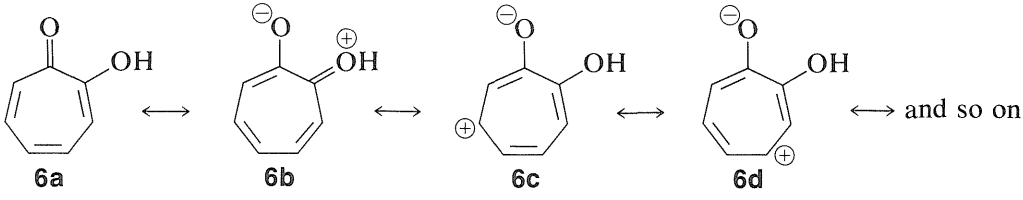
tropolone

The cycloheptatriene for this synthesis can be obtained best by thermal rearrangement of the Diels–Alder addition product of cyclopentadiene and ethyne:



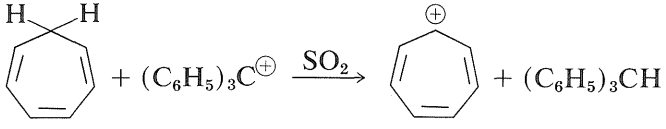
Tropolone is an acid with an ionization constant of 10^{-7}, which is intermediate between the K_a of ethanoic acid and the K_a of benzenol. Like most

arenols, tropolones form colored complexes with ferric chloride solution. Tropolone has many properties that attest to its aromatic character—it resists hydrogenation, undergoes diazo coupling, and can be nitrated, sulfonated, and substituted with halogens. The aromaticity of tropolone can be attributed to resonance involving the two nonequivalent VB structures **6a** and **6b**, and to several dipolar structures, such as **6c** and **6d**, in which the ring has the stable tropylium cation structure with six π electrons (Section 21-9B):



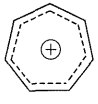
6a **6b** **6c** **6d**

The tropylium cation is prepared easily by transfer of a hydride ion from cycloheptatriene to triphenylmethyl cation in sulfur dioxide solution. This reaction is related to the hydride ion transfer, $(CH_3)_3C^{\oplus} + RH \longrightarrow (CH_3)_3CH + R^{\oplus}$, discussed in Section 10-9:



tropylium cation

Seven equivalent VB structures can be written for the tropylium cation so only one seventh of the positive charge is expected to be on each carbon. Because the cation has six π electrons, it is expected from Hückel's $(4n+2)\pi$-electron rule to be unusually stable for a carbocation.



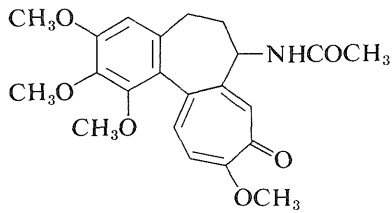
hybrid structure for tropylium ion

The infrared and Raman spectra of tropylium bromide in hydrobromic acid solution have no common bands, which means that the cation exists in a highly symmetrical form in this solution (see Section 9-8). At higher pH, reversible formation of the hydroxy compound occurs:

$$C_7H_7^{\oplus} + OH^{\ominus} \rightleftharpoons C_7H_7OH$$

The equilibrium constant for this reaction is such that the cation is half converted to the hydroxy compound at about pH 5.

Colchicine is an important naturally occurring tropolone derivative. It is isolated from the autumn crocus and is used in medicine for the treatment of gout. It also has an effect on cell division and is used in plant genetic studies to cause doubling of chromosomes. The structure has been confirmed by total synthesis.

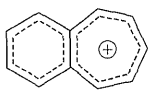


colchicine

Exercise 26-22 Tropone (2,4,6-cycloheptatrienone) is an exceptionally strong base for a ketone. Explain.

Exercise 26-23 At which position would you expect tropolone to substitute most readily with nitric acid? Explain.

Exercise 26-24 Would you expect benzotropylium ion to form the corresponding OH derivative more readily or less readily than tropylium ion itself in water solution? At which position would you expect the C–O bond to be formed? Explain.



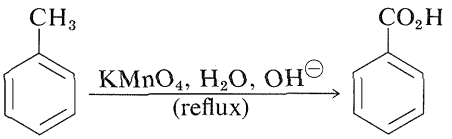
benzotropylium ion

26-4 SOME AROMATIC SIDE-CHAIN COMPOUNDS

We have discussed in this chapter and in previous chapters how the reactivity of halogen, amino, and hydroxy substituents are modified when linked to aromatic carbons rather than to saturated carbons. Other substituents, particularly those linked to an aromatic ring through a carbon–carbon bond, also are influenced by the ring, although usually to a lesser degree. Examples include $-CH_2OH$, $-CH_2OCH_3$, $-CH_2Cl$, $-CHO$, $-COCH_3$, $-CO_2H$, and $-CN$, and we shall refer to aromatic compounds containing substituents of this type as **aromatic side-chain compounds.** Our interest in such compounds will be directed mainly to reactions at the side chain, with particular reference to the effect of the aromatic ring on reactivity. In this connection, we shall discuss the relatively stable triarylmethyl cations, anions, and radicals, as well as a quantitative correlation of rates of organic reactions by what is known as the Hammett equation.

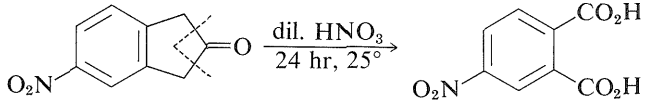
26-4A Preparation of Aromatic Side-Chain Compounds

Carboxylic acids can be obtained from most alkylbenzenes by oxidation of the side chain with reagents such as potassium permanganate, potassium dichromate, or nitric acid:



benzoic acid

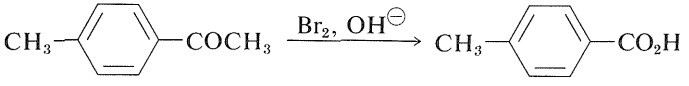
Under the conditions of oxidation, higher alkyl or alkenyl groups are degraded and ring substituents, other than halogen and nitro groups, often fail to survive. As an example, oxidation of 5-nitro-2-indanone with dilute nitric acid leads to 4-nitro-1,2-benzenedicarboxylic acid:



5-nitro-2-indanone

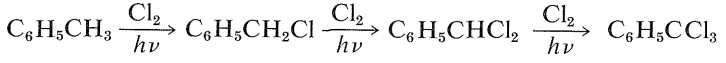
4-nitro-1,2-benzene-dicarboxylic acid

To retain a side-chain substituent, selective methods of oxidation are required. For example, 4-methylbenzoic acid can be prepared from 1-(4-methylphenyl)-ethanone by the haloform reaction (Section 17-2B):



Many side-chain halogen compounds can be synthesized by reactions that also are applicable to alkyl halides (see Table 14-5), but there are other methods especially useful for the preparation of arylmethyl halides. The most important of these are the chloromethylation of aromatic compounds (to be discussed later in this section) and radical halogenation of alkylbenzenes.

Light-induced, radical chlorination or bromination of alkylbenzenes with molecular chlorine or bromine was discussed previously (Section 14-3C). Under these conditions, methylbenzene reacts with chlorine to give successively phenylchloromethane, phenyldichloromethane, and phenyltrichloromethane:



methylbenzene (toluene)

phenylchloro-methane (benzyl chloride)

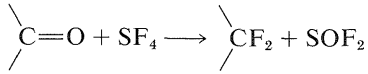
phenyldichloro-methane (benzal chloride)

phenyltrichloro-methane (benzo-trichloride)

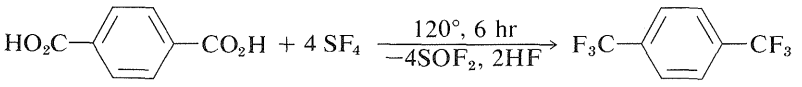
Related reactions occur with other reagents, notably sulfuryl chloride, SO_2Cl_2; *tert*-butyl hypochlorite, $(CH_3)_3COCl$; and *N*-bromobutanimide,

$(CH_2CO)_2NBr$. The α substitution of alkylbenzenes is the result of radical-chain reactions (Section 14-3C).

Side-chain fluorine compounds with the groupings $—CHF_2$, $—CF_2—$, and $—CF_3$ are available by the reaction of sulfur tetrafluoride or molybdenum hexafluoride with carbonyl compounds (see Section 16-4D):

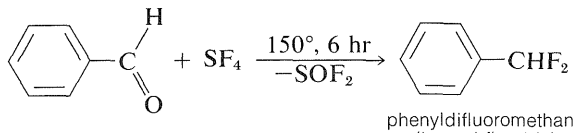


Some specific examples follow:



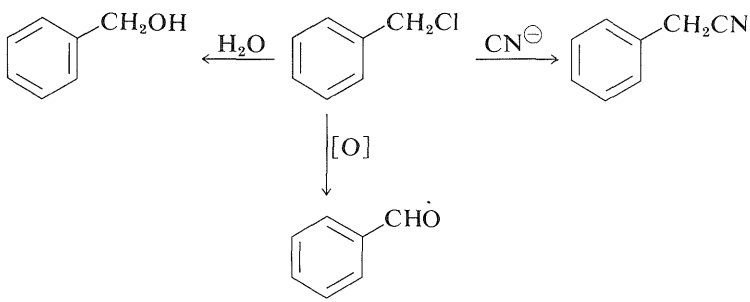
1,4-benzenedicarboxylic acid (terephthalic acid)

1,4-di-(trifluoromethyl)benzene 76%

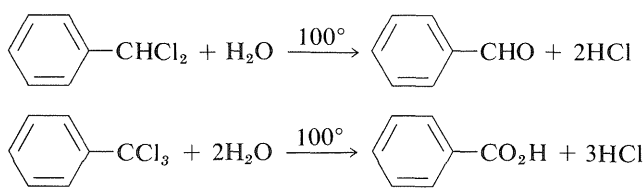


phenyldifluoromethane (benzal fluoride) 81%

Arylmethyl chlorides or bromides are quite reactive compounds that are readily available or easily prepared, and as a result they are useful intermediates for the synthesis of other side-chain derivatives. Thus phenylmethyl chloride can be hydrolyzed to phenylmethanol, converted to phenylethanenitrile with alkali-metal cyanides, and oxidized to benzenecarbaldehyde (benzaldehyde):



Phenyldichloromethane hydrolyzes readily to benzaldehyde, and phenyltrichloromethane to benzoic acid:



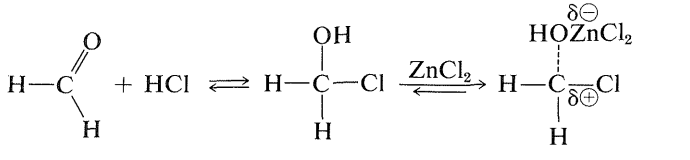
Carbon side chains also may be introduced by direct substitution and several such reactions have been discussed in detail previously. These include Friedel–

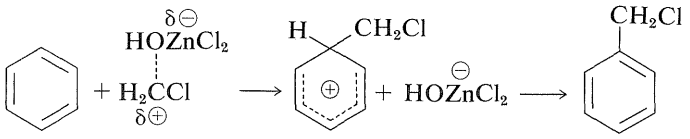
Crafts alkylation and acylation (Section 22-4E and 22-4F), the Gattermann–Koch reaction for preparation of aldehydes from arenes and carbon monoxide (Section 22-4F), and the Kolbe–Schmitt, Reimer–Tiemann, and Gattermann reactions for synthesis of acids and aldehydes from arenols (Section 26-1E).

Chloromethylation is a useful method for substitution of $-CH_2Cl$ for an aromatic hydrogen, provided one starts with a reasonably reactive arene. The reagents are methanol and hydrogen chloride in the presence of zinc chloride:

$$C_6H_6 + CH_2O + HCl \xrightarrow{ZnCl_2} C_6H_5CH_2Cl + H_2O$$

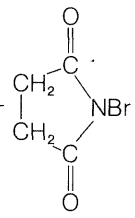
The mechanism of the chloromethylation reaction is related to that of Friedel–Crafts alkylation and acylation and probably involves an incipient chloromethyl cation, $^{\oplus}CH_2Cl$:





$$+ ZnCl_2 + H_2O$$

Exercise 26-25 What principal product would you expect from each of the following reactions? Show the steps involved.

a. $(CH_3)_3C-C_6H_4-CH_3 +$  $\xrightarrow{CCl_4,\ h\nu}$

b. $CH_3CH_2-C_6H_5 + Cl_2 \xrightarrow[h\nu]{150^\circ\text{ (vapor phase)}}$

c. $CH_3-C_6H_5 \xrightarrow{CH_2O,\ HCl,\ ZnCl_2}$

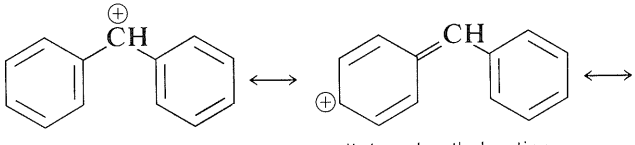
d. $C_6H_6 \xrightarrow[AlCl_3]{(CH_3)_3CCl} \xrightarrow[AlCl_3]{CH_3COCl} \xrightarrow{Cl_2,\ NaOH}$

Exercise 26-26 Devise syntheses of the following compounds from the specified starting materials, giving reagents and approximate reaction conditions. (If necessary, review the reactions of Chapter 22 as well as reactions discussed in previous sections of this chapter.)

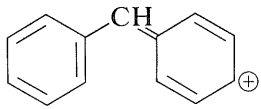
a. 4-aminobenzenecarbaldehyde from methylbenzene
b. 2,2′-biphenyldicarboxylic acid [$C_6H_4(2\text{-}CO_2H)C_6H_4(2'\text{-}CO_2H)$] from phenanthrene
c. 4-nitrotrifluoromethylbenzene from methylbenzene
d. 9,9,10,10-tetrafluoro-9,10-dihydroanthracene from 1,2-dimethylbenzene and benzene
e. 4-methylphenylethanenitrile from methylbenzene
f. 4-chlorobenzenecarbaldehyde from methylbenzene
g. 2-hydroxy-3-methylbenzenecarbaldehyde from methylbenzene
h. 4-ethylphenylmethanol from benzene, methylbenzene, or ethylbenzene
i. 2-chloro-4-ethoxybenzenecarbaldehyde from benzene or methylbenzene

26-4B Triarylmethyl Cations

Phenylmethyl halides are similar in S_N1 reactivity to 2-propenyl halides. The S_N1 reactivity of phenylmethyl derivatives can be ascribed mainly to stabilization of the cation by electron delocalization. Diphenylmethyl halides, $(C_6H_5)_2CHX$, are still more reactive and this is reasonable because the diphenylmethyl cation has two phenyl groups over which the positive charge can be delocalized and therefore should be more stable relative to the starting halide than is the phenylmethyl cation:



diphenylmethyl cation



$\longleftrightarrow$ etc.

Accordingly, we might expect triphenylmethyl (or trityl) halides, $(C_6H_5)_3C—X$, to be even more reactive. In fact, the C–X bonds of such compounds are extremely labile. In liquid sulfur dioxide, triarylmethyl halides ionize reversibly, although the equilibria are complicated by ion-pair association:

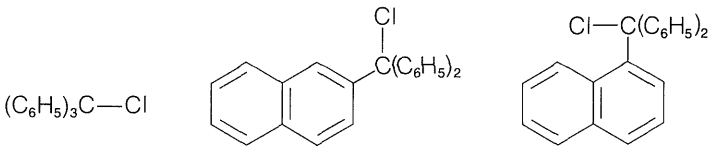
$$(C_6H_5)_3C—Cl \xrightleftharpoons{SO_2,\ 0^\circ} \underset{\text{ion pair}}{(C_6H_5)_3C^{\oplus}Cl^{\ominus}} \rightleftharpoons \underset{\text{dissociated ions}}{(C_6H_5)_3C^{\oplus} + Cl^{\ominus}}$$

Triarylmethyl cations are among the most stable carbocations known. They are intensely colored and are formed readily when the corresponding triarylmethanols are dissolved in strong acids:

$$(C_6H_5)_3C{-}OH \xrightleftharpoons{H_2SO_4} (C_6H_5)_3C{-}\overset{\oplus}{O}H_2 \xrightleftharpoons{-H_2O} (C_6H_5)_3C^{\oplus}$$

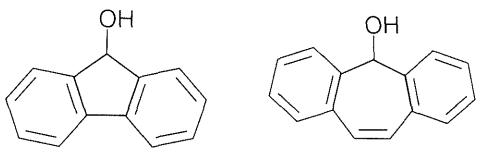
triphenylmethanol (colorless) — triphenylmethyl cation (orange-yellow)

Exercise 26-27 a. Explain why the energy of ionic dissociation of triarylmethyl chlorides in liquid sulfur dioxide decreases in the order **7** > **8** > **9**. (Review Section 22-8A and also consider possible effects of steric hindrance in the starting material and the cations formed.)



7 **8** **9**

b. Which alcohol would you expect to form a carbocation more readily in sulfuric acid, **10** or **11**? Explain.



10 **11**

c. When triphenylmethanol is dissolved in 100% sulfuric acid, it gives a freezing-point depression that corresponds to formation of *four moles* of particles *per mole* of alcohol dissolved. Explain.

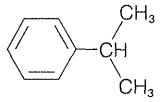
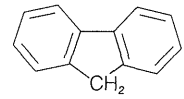
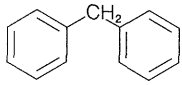
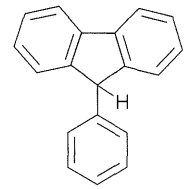
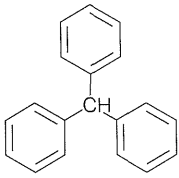
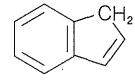
26-4C Triarylmethyl Anions

In addition to stable cations, triarylmethyl compounds form stable carbanions. Because of this the corresponding hydrocarbons are relatively acidic compared to simple alkanes. They react readily with strong bases such as sodium amide, and the resulting carbanions, like the cations, are intensely colored:

$$(C_6H_5)_3CH + Na^{\oplus}NH_2^{\ominus} \xrightleftharpoons{\text{ether}} (C_6H_5)_3C{:}^{\ominus}Na^{\oplus} + NH_3$$

triphenylmethane (colorless) — triphenylmethylsodium (blood red)

Table 26-3
Strengths of Some Hydrocarbon Acids

Compound	K_a	Compound	K_a
 isopropylbenzene (cumene)	10^{-37}	 dibenzocyclopentadiene[a] (fluorene)	10^{-25}
 diphenylmethane	10^{-35}	 5-phenyldibenzocyclopentadiene[a] (9-phenylfluorene)	10^{-21}
 triphenylmethane	10^{-33}	 benzocyclopentadiene[a] (indene)	10^{-21}

[a]According to the IUPAC rules for naming polycyclic compounds, when a benzene ring is "ortho-fused" to another ring the prefix "benzo" is attached to the name of the parent ring. This is contracted to "benz" when preceding a vowel, as in benzanthracene.

The acid strengths of arylmethanes are listed in Table 26-3. All are quite weak acids relative to water but vary over many powers of ten relative to one another. The stronger acids form the more stable carbanions, and the carbanion stability generally is determined by the effectiveness with which the negative charge can be delocalized over the substituent aryl groups.

Exercise 26-28 Explain why 9-phenylfluorene is a stronger acid than triphenylmethane.

26-4D Triarylmethyl Radicals

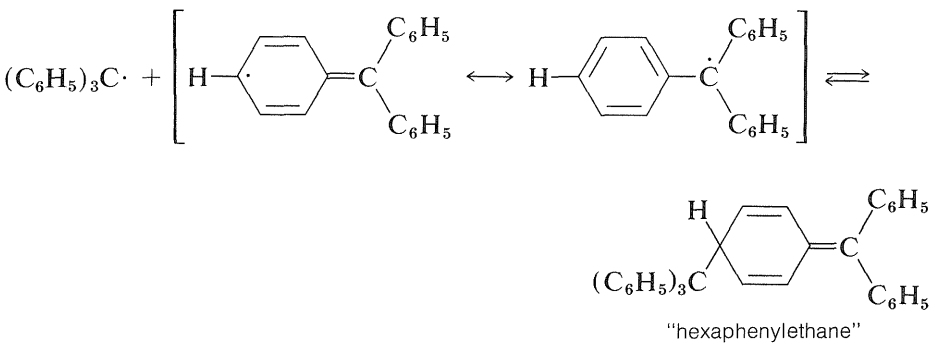
Triarylmethyl compounds also form rather stable triarylmethyl radicals, and indeed the first stable carbon free radical to be reported was the triphenyl-

methyl radical, $(C_6H_5)_3C\cdot$, prepared inadvertently by M. Gomberg in 1900. Gomberg's objective was to prepare hexaphenylethane by a Wurtz coupling reaction of triphenylmethyl chloride with metallic silver:

$$2(C_6H_5)_3C{-}Cl + 2Ag \xrightarrow{\text{benzene}} \underset{\text{hexaphenylethane}}{(C_6H_5)_3C{-}C(C_6H_5)_3} + 2AgCl$$

However, he found that unless air was carefully excluded from the system, the product was triphenylmethyl peroxide, $(C_6H_5)_3COOC(C_6H_5)_3$, rather than the expected hexaphenylethane.

Gomberg believed that the yellow solution obtained from the reaction of triphenylmethyl chloride with silver in benzene in the absence of air contained the triphenylmethyl radical. However, subsequent investigations showed that the molecular weight of the dissolved substance was closer to that for $C_{38}H_{30}$, hexaphenylethane. A bitter battle raged over the nature of the product and its reactions. The controversy finally was thought to have been settled by the demonstration that the hydrocarbon $C_{38}H_{30}$ dissociates rapidly, but only slightly, to triphenylmethyl radicals at room temperature in inert solvents ($K = 2.2 \times 10^{-4}$ at 24° in benzene). For many years thereafter, the hydrocarbon $C_{38}H_{30}$ was believed to be the hexaphenylethane. Now it is known that this conclusion was incorrect. The product is a dimer of triphenylmethyl, but it is formed by the addition of one radical to the 4-position of a phenyl ring of the other:



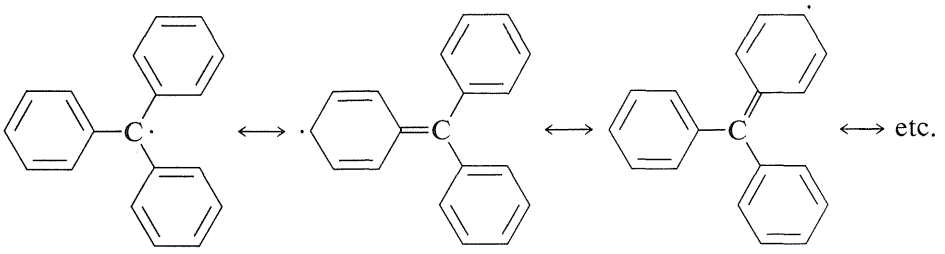
"hexaphenylethane"

Formation of the peroxide in the presence of oxygen is explained as follows:

$$(C_6H_5)_3C\cdot + O_2 \longrightarrow (C_6H_5)_3COO\cdot \xrightarrow{(C_6H_5)_3C\cdot} \underset{\text{triphenylmethyl peroxide}}{(C_6H_5)_3COOC(C_6H_5)_3}$$

Although the foregoing reactions involving the triphenylmethyl radical seemed very unreasonable at the time they were discovered, the stability of the radical now has been established beyond question by a variety of methods such as

esr spectroscopy (Section 27-9). This stability can be attributed to delocalization of the odd electron over the attached phenyl groups:

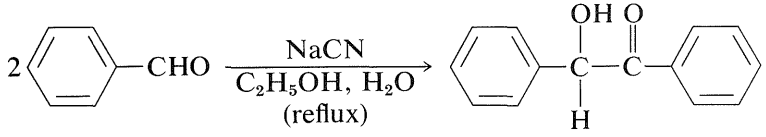


Exercise 26-29 **a.** Why should 3-phenyl-1-propene be appreciably more reactive than methylbenzene in hydrogen-abstraction reactions?
b. Would you expect 1-phenyl-1-propene ($C_6H_5CH{=}CHCH_3$) to be more, or less, reactive than 3-phenyl-1-propene ($C_6H_5CH_2CH{=}CH_2$) if account is taken of the stabilization of the ground state as well as the stabilization of the radicals?

Exercise 26-30 Which of the following pairs of compounds would you expect to be the more reactive under the specified conditions? Give your reasons and write equations for the reactions involved.
a. 4-$NO_2C_6H_4CH_2Br$ or 4-$CH_3OC_6H_4CH_2Br$ on hydrolysis in 2-propanone-water solution
b. $(C_6H_5)_3CH$ or $C_6H_5CH_3$ in the presence of phenyllithium
c. $(C_6H_5)_3C{-}C(C_6H_5)_3$ or $(C_6H_5)_2CH{-}CH(C_6H_5)_2$ on heating
d. $(C_6H_5)_2N{-}N(C_6H_5)_2$ or $(C_6H_5)_2CH{-}CH(C_6H_5)_2$ on heating
e. $(C_6H_5CH_2CO_2)_2$ or $(C_6H_5CO_2)_2$ on heating
f. $C_6H_5COC_6H_5$ or $C_6H_5CH_2COCH_2C_6H_5$ on reduction with sodium borohydride.

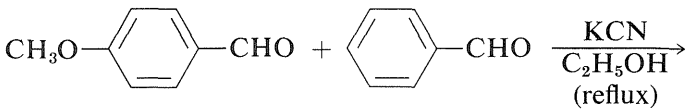
26-4E Aromatic Aldehydes. The Benzoin Condensation

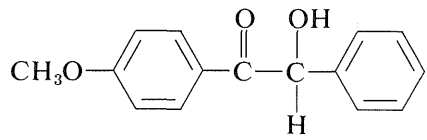
Most of the reactions of aromatic aldehydes, ArCHO, are those expected of aldehydes with no α hydrogens and most of these will not be reviewed here. One reaction that usually is regarded as being characteristic of aromatic aldehydes (although, in fact, it does occur with other aldehydes having no α hydrogens), is known as the **benzoin condensation.** This reaction essentially is a dimerization of two aldehyde molecules through the catalytic action of sodium or potassium cyanide:



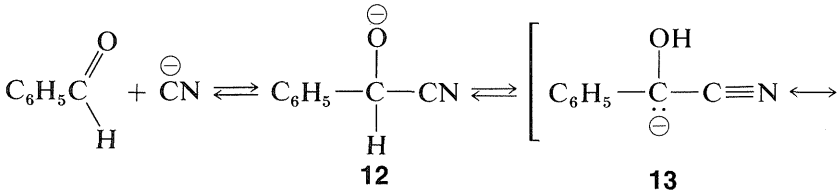
2-hydroxy-1,2-diphenylethanone
(benzoin) 90%

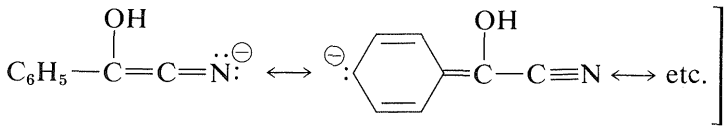
Unsymmetrical or mixed benzoins may be obtained in good yield from two different aldehydes:

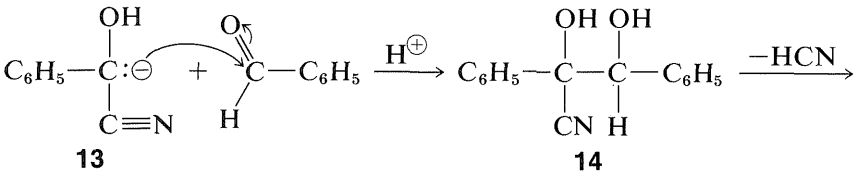


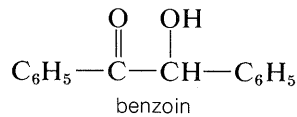


As to the mechanism of benzoin formation, cyanide ion adds to the aldehyde to form **12**. This anion is in equilibrium with **13**, wherein the negative charge can be delocalized over the phenyl and nitrile groups. A subsequent aldol-type addition of **13** to the carbonyl carbon of a second aldehyde molecule gives the addition product **14**, and loss of HCN from **14** leads to the benzoin:



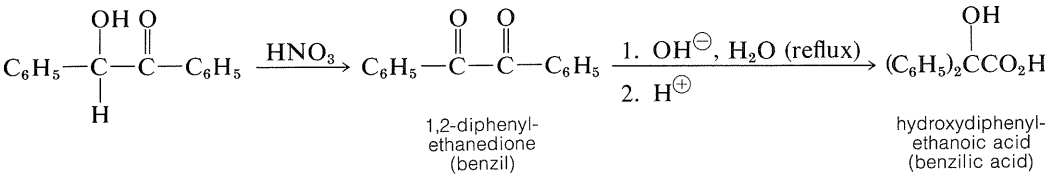






Benzoins are useful intermediates for the synthesis of other compounds because they can be oxidized to 1,2-diones and reduced in stages to various products, depending upon the reaction conditions. The 1,2-diketone known as benzil, which is obtained by nitric acid oxidation of benzoin, undergoes a base-

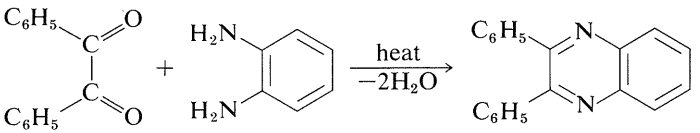
catalyzed hydration rearrangement reaction to form an α-hydroxy acid, commonly called the **benzilic acid rearrangement** (see Section 17-7):



1,2-diphenylethanedione (benzil)

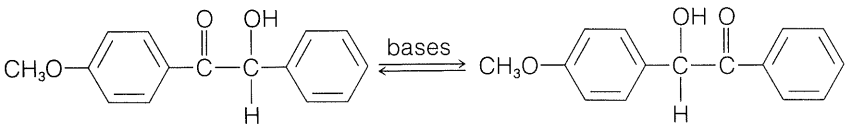
hydroxydiphenylethanoic acid (benzilic acid)

Benzils, like other 1,2-diones, react with 1,2-benzenediamines to form diazaarenes known as quinoxalines. This kind of reaction is an important general procedure for the synthesis of aromatic ring systems containing nitrogen:



2,3-diphenylquinoxaline

Exercise 26-31 The following equilibrium is established readily in the presence of bases:



The mechanism of the reaction could be either a base-induced enolization reaction (Section 17-1) or ionization of the OH proton followed by a Cannizzaro-type reaction (Section 16-4E). Write each mechanism in detail and devise experiments that could be used to distinguish between them.

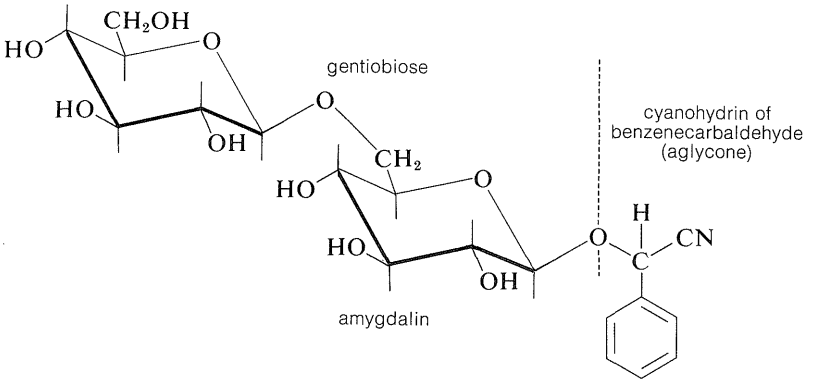
Exercise 26-32 Devise methods of synthesis of the following compounds based on the given starting materials:

a. 1,2-di-(4-methoxyphenyl)ethane from 4-methoxybenzenecarbaldehyde
b. 4-(2-nitrophenyl)-3-buten-2-one from benzene or methylbenzene
c. 2-methyl-1-azanaphthalene (quinaldine) from 4-(2-nitrophenyl)-3-buten-2-one
d. diphenylmethanone (benzophenone) from benzenecarbaldehyde

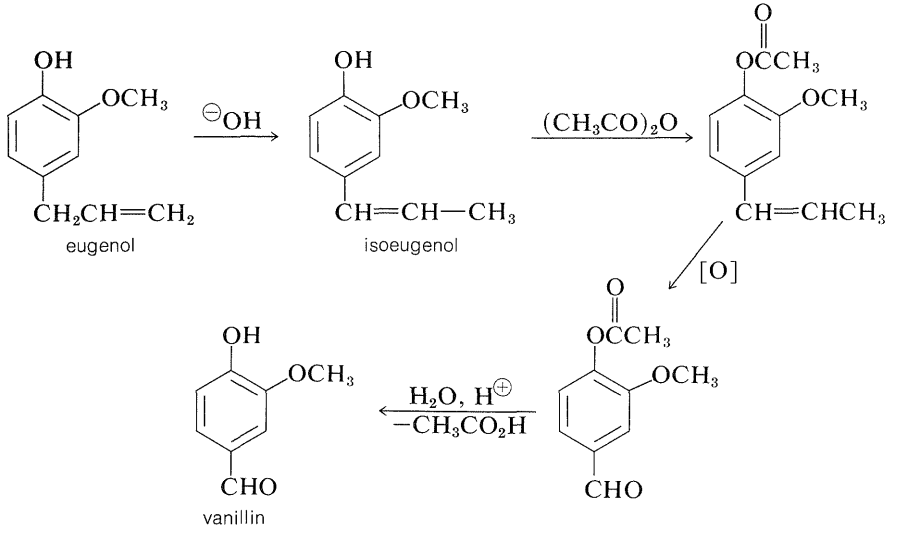
Exercise 26-33 Write a mechanism based on analogy for the formation of quinoxalines from benzils and 1,2-benzenediamines. (Review Section 16-4C.)

26-5 NATURAL OCCURRENCE AND USES OF SOME AROMATIC SIDE-CHAIN COMPOUNDS

Derivatives of aromatic aldehydes occur naturally in the seeds of plants. For example, amygdalin is a substance occurring in the seeds of the bitter almond. It is a derivative of gentiobiose, which is a disaccharide made up of two glucose units; one of the glucose units is bonded by a β-glucoside linkage to the OH group of the cyanohydrin of benzenecarbaldehyde:



The flavoring vanillin occurs naturally as glucovanillin (a glucoside) in the vanilla bean (Section 20-5). It is made commercially in several ways. One is from eugenol, itself a constituent of several essential oils:



Methyl 2-hydroxybenzoate (methyl salicylate, oil of wintergreen) occurs in many plants, but it also is readily prepared synthetically by esterification of

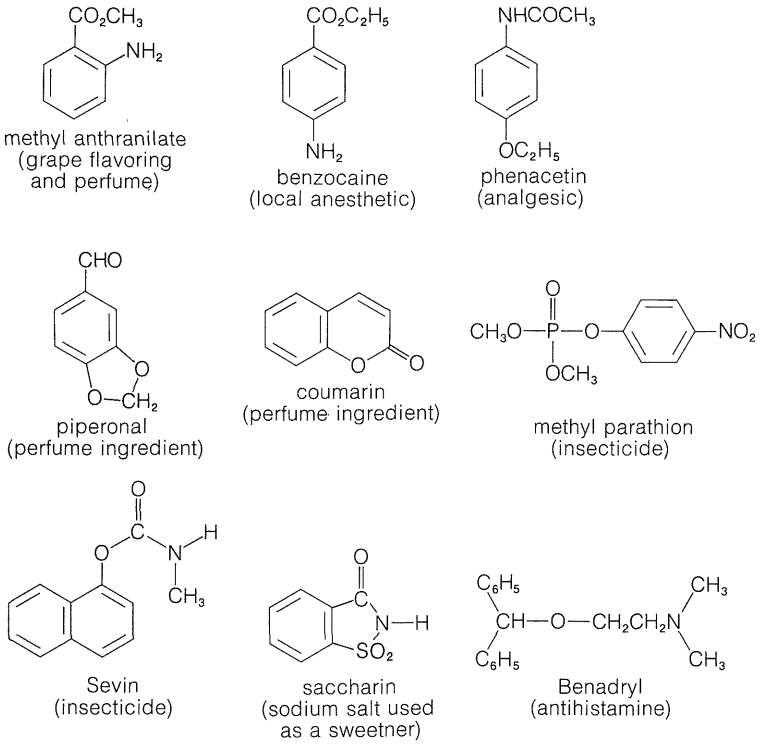
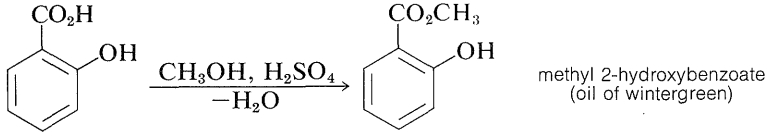
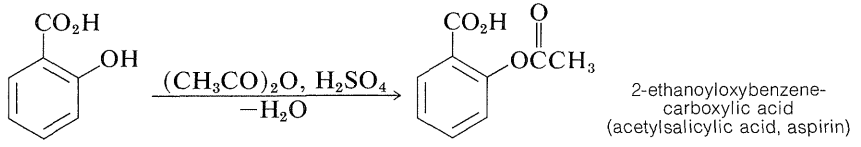


Figure 26-2 Some synthetic and natural aromatic compounds and their uses

2-hydroxybenzoic acid, which in turn is made from benzenol (see Section 26-1E):



The ethanoyl derivative of 2-hydroxybenzoic acid is better known as *aspirin* and is prepared from the acid with ethanoic anhydride, using sulfuric acid as catalyst:



The structures and common names of several other aromatic compounds that have direct use as flavorings, perfumes, therapeutic drugs, or insecticides are shown in Figure 26-2. Many other such compounds that contain nitrogen are shown in Figures 23-1 through 23-3.

26-6 CORRELATIONS OF STRUCTURE WITH REACTIVITY OF AROMATIC COMPOUNDS

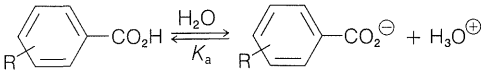
This section is concerned with the quantitative correlation of reaction rates and equilibria of organic reactions with the structure of the reactants. We will restrict the discussion to benzene derivatives. The focus is on a remarkably simple treatment developed by L. P. Hammett in 1935, which has been tremendously influential. Hammett's correlation covers chemical reactivity, spectroscopy and other physical properties, and even the biological activity of drugs. Virtually all quantitative treatments of reactivity of organic compounds in solution start with the kinds of correlations that are discussed in this section.

26-6A The Hammett Equation

If we compare the acid strengths (K_a) of a series of substituted benzoic acids with the strength of benzoic acid itself (Table 26-4), we see that there are considerable variations with the nature of the substituent and its ring position, ortho, meta, or para. Thus all three nitrobenzoic acids are appreciably stronger than benzoic acid in the order ortho $\gg$ para $>$ meta. A methoxy substituent in the ortho or meta position has a smaller acid-strengthening effect, and in the para position decreases the acid strength relative to benzoic acid. Rate effects also are produced by different substituents, as is evident from the data in Table 26-5 for basic hydrolysis of some substituted ethyl benzoates. A nitro substituent increases the rate, whereas methyl and methoxy substituents decrease the rate relative to that of the unsubstituted ester.

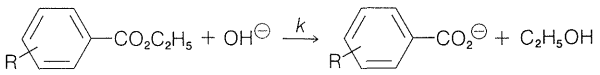
If we now plot the logarithms of the dissociation constants K_a of Table 26-4 against the logarithms of the rate constants k of Table 26-5, we find that

Table 26-4
Dissociation Constants ($10^{-5} \times K_a$) of Some Substituted Benzoic Acids in Water at 25°



R	H	CH_3	OCH_3	F	Cl	NO_2
ortho	6.27	12.3	8.06	54.1	114	671
meta	6.27	5.35	8.17	13.6	14.8	32.1
para	6.27	4.24	3.38	7.22	10.5	37.0

Table 26-5
Specific Rate Constants[a] for Alkaline Hydrolysis of Some Substituted Ethyl Benzoates in 85% Ethanol–Water Solution at 30°



R	H	CH_3	OCH_3	F	Cl	NO_2
ortho	81.7	15.8		462	267	912
meta	81.7	57.7			605	5180
para	81.7	38.2	17.5	251	353	8480

[a] 10^5k, liter $mole^{-1}$ sec^{-1}.

the data for the meta- and para-substituted compounds fall on a straight line, whereas data for the ortho derivatives are badly scattered (see Figure 26-3). The linear correlation for meta and para substituents is observed for the rates or equilibrium constants for many other reactions. For example, straight lines are obtained on plotting log K for the dissociation of phenylethanoic acids (*meta-* and *para-*$RC_6H_4CH_2CO_2H$) against log K' for the dissociation of phenylammonium ions (*meta-* and *para-*$RC_6H_4\overset{\oplus}{N}H_3$), or against log k for the rate of hydrolysis of phenylmethyl halides (*meta-* and *para-*$RC_6H_4CH_2X$).

The straight line in Figure 26-3 can be expressed conveniently by Equation 26-3, in which the two variables are log k and log K, the slope of the line is ρ, and the intercept is C:

$$\log k = \rho \log K + C \tag{26-3}$$

For the particular case for which the ring substituent is hydrogen (R = H), Equation 26-3 becomes

$$\log k_0 = \rho \log K_0 + C \tag{26-4}$$

in which K_0 is the dissociation constant of benzoic acid and k_0 is the rate of hydrolysis of ethyl benzoate. Subtracting Equation 26-4 from Equation 26-3 we obtain

$$\log \frac{k}{k_0} = \rho \log \frac{K}{K_0} \tag{26-5}$$

This equation could be tested on the ratios of any rates or equilibrium constants, but it is convenient to reserve log (K/K_0) for the dissociation of benzoic

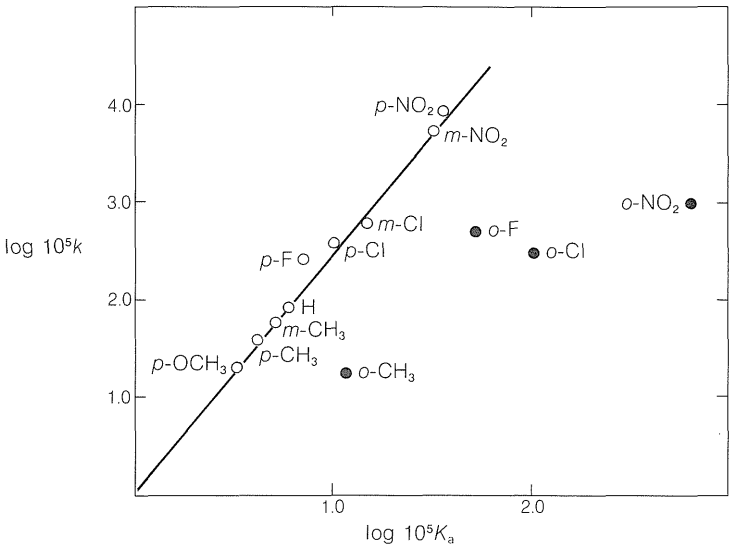


Figure 26-3 Plot of log 10^5 K_a for the dissociation of substituted benzoic acids in water at 25° against log 10^5 k for the rates of alkaline hydrolysis of substituted ethyl benzoates in 85% ethanol–water at 30°

acids in water at 25° (Table 26-4) and correlate the rate or equilibrium constants for all other processes with log (K/K_0). The common procedure is to rewrite Equation 26-5 as Equation 26-6:

$$\log \frac{k}{k_0} = \rho\sigma \tag{26-6}$$

in which σ is defined as:

$$\sigma = \log \frac{K}{K_0} \tag{26-7}$$

Equation 26-6 is known as the **Hammett equation,** but before we discuss its general applications, it will be helpful to say more about the σ term in Equation 26-7.

The *relative strength* of a substituted benzoic acid and hence the value of σ depends on the *nature* and *position* of the substituent in the ring. For this reason, σ is called the **substituent constant.** Table 26-6 lists several substituent constants and these will be seen to correspond to the polar character of the respective substituents. Thus the more electron-attracting a substituent is, by either resonance or induction, the more acid-strengthening it is, and the more *positive* is its σ value (relative to H as 0.000). Conversely, the more strongly a substituent donates electrons by resonance or induction, the more

Table 26-6
Hammett Substituent Constants

	σ			σ	
Substituent	Meta	Para	Substituent	Meta	Para
$O^{\ominus}$	−0.71	−1.00	F	+0.34	+0.06
OH	+0.12	−0.37	Cl	+0.37	+0.23
OCH_3	+0.12	−0.27	CO_2H	+0.36	+0.41
NH_2	−0.16	−0.66	$COCH_3$	+0.38	+0.50
CH_3	−0.07	−0.17	CF_3	+0.43	+0.54
$(CH_3)_3Si$	−0.04	−0.07	NO_2	+0.71	+0.78
C_6H_5	+0.06	−0.01	$(CH_3)_3N^{\oplus}$	+0.88	+0.82
H	0.00	0.00	$N_2^{\oplus}$	+1.76	+1.91
SH	+0.25	+0.15	$(CH_3)_2S^{\oplus}$	+1.00	+0.90
SCH_3	+0.15	0.00			

negative is its σ value. We expect that among the more electron-attracting and electron-donating substituents will be those with electric charges, positive and negative respectively. Indeed, a diazonium group ($-N_2^{\oplus}$) in the para position has a very large σ value of +1.91, whereas a para $-O^{\ominus}$ group has a σ value of −1.00. In general, meta σ constants correspond to the inductive effect of the substituent while the para σ constants represent the *net* influence of inductive and resonance effects. If there is a substantial resonance effect, and it and the inductive effect operate in the same direction, σ_{para} will have a considerably greater magnitude than σ_{meta}. The converse will be true if the resonance and inductive effects operate in opposite directions.

Exercise 26-34 The ionization constants of 3- and 4-cyanobenzoic acids at 30° are 2.51×10^{-4} and 2.82×10^{-4}, respectively. Benzoic acid has K_a of 6.76×10^{-5} at 30°. Calculate σ_{meta} and σ_{para} for the cyano substituent.

Exercise 26-35 The magnitudes and signs of the σ constants associated with meta and para substituents can be rationalized in terms of inductive and electron-delocalization influences. Show how it is possible, within this framework, to account for the following facts:

a. Fluorine has a sizable positive σ constant when meta but almost zero when para.

b. The σ constant of the methoxy group ($-OCH_3$) is positive in the meta position and negative in the para position.

c. The $-\overset{\oplus}{N}(CH_3)_3$ group has a slightly larger positive σ constant in the meta position than in the para position, but the reverse is true for the $-N_2^{\oplus}$ group.

d.* The σ constant of the $-CF_3$ group is more positive when para than when meta.

Exercise 26-36 Predict whether the meta and para σ constants for the following groups would be positive or negative, and large or small. Give your reasoning.

a. $-C{\equiv}N$ **b.** $-CH_2\overset{\oplus}{N}(CH_3)_3$ **c.** $-OCF_2H$ **d.** $-CO_2^{\ominus}$

The Hammett equation (26-6) states that the relative reactivity (expressed in logarithmic form) of a substituted benzene derivative is proportional to the substituent constant σ. For a given reaction, a plot of log (k/k_0) or of log (K/K_0) versus σ should be linear with slope ρ. Some idea of the validity of the Hammett equation can be gained from Figure 26-4, which shows plots of log (k/k_0) or of log (K/K_0) against σ for several different reactions. For the examples given, the fit to the Hammett equation is fair. A number of ρ values (slopes) are listed separately in Table 26-7. It can be seen that ρ values vary

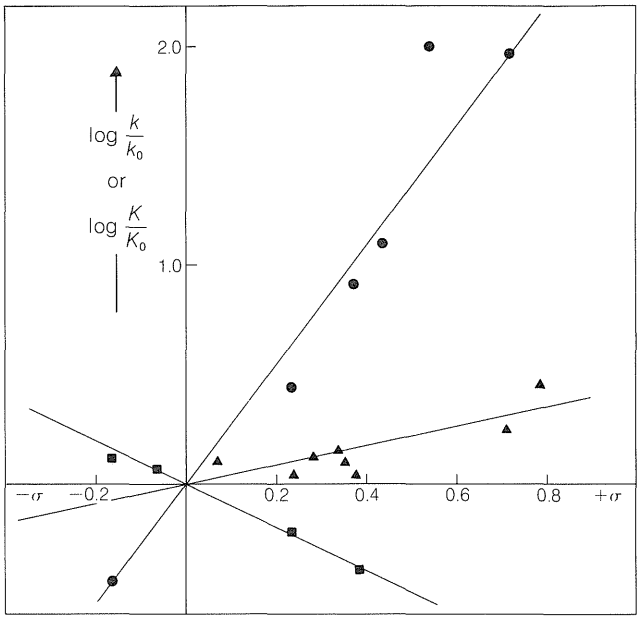


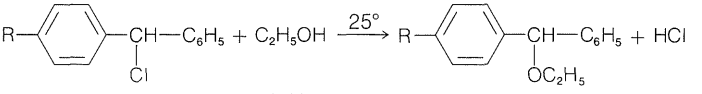
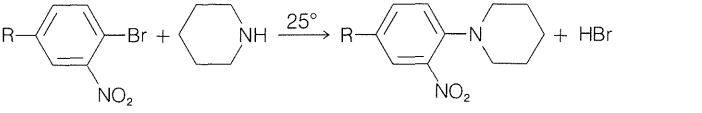
Figure 26-4 Plot of log (k/k_0) or log (K/K_0) against σ for the following reactions, in which RC_6H_4- is a meta- or para-substituted benzene ring.

● $RC_6H_4{-}NH_3^{\oplus} + H_2O \overset{25°}{\rightleftharpoons} RC_6H_4{-}NH_2 + H_3O^{\oplus}$

▲ $RC_6H_4{-}COCH_3 + Br_2 \xrightarrow[CH_3CO_2^{\ominus}]{CH_3CO_2H,\ 35°} RC_6H_4{-}COCH_2Br + HBr$

■ $RC_6H_4{-}O^{\ominus} + C_2H_5I \xrightarrow[42.5°]{C_2H_5OH} RC_6H_4{-}OC_2H_5 + I^{\ominus}$

Table 26-7
Reaction Constants for meta- and para-Substituted Benzene Derivatives (RC_6H_4—)

No.	Equilibria	ρ
1	$RC_6H_4—CO_2H \underset{25°}{\overset{H_2O}{\rightleftharpoons}} RC_6H_4—CO_2^{\ominus} + H^{\oplus}$	1.00
2	$RC_6H_4—CH_2CO_2H \underset{25°}{\overset{H_2O}{\rightleftharpoons}} RC_6H_4—CH_2CO_2^{\ominus} + H^{\oplus}$	0.49
3	$RC_6H_4—\overset{\oplus}{N}H_3 \underset{25°}{\overset{H_2O}{\rightleftharpoons}} RC_6H_4—NH_2 + H^{\oplus}$	2.77
4	$RC_6H_4—CHO + HCN \overset{95\%\ C_2H_5OH}{\rightleftharpoons} RC_6H_4—CH(OH)CN$	−1.49
5	$RC_6H_4—OH \underset{25°}{\overset{H_2O}{\rightleftharpoons}} RC_6H_4—O^{\ominus} + H^{\oplus}$	2.11
No.	**Reaction rates**	ρ
6	$RC_6H_4—CO_2C_2H_5 + OH^{\ominus} \xrightarrow[30°]{85\%\ C_2H_5OH} RC_6H_4—CO_2^{\ominus} + C_2H_5OH$	2.43
7	$RC_6H_4—CO_2H + CH_3OH \xrightarrow[25°]{H^{\oplus}} RC_6H_4—CO_2CH_3 + H_2O$	−0.23
8	$RC_6H_4—OH + C_6H_5COCl \xrightarrow{20°} RC_6H_4—OCOC_6H_5 + HCl$	0.56
9	$RC_6H_4—O^{\ominus} + C_2H_5I \xrightarrow[42.5°]{C_2H_5OH} RC_6H_4—OC_2H_5 + I^{\ominus}$	−0.99
10	$RC_6H_4—CH_2Cl + OH^{\ominus} \xrightarrow[30°]{H_2O} RC_6H_4—CH_2OH + Cl^{\ominus}$	−0.33
11	$RC_6H_4—CH_2Cl + H_2O \xrightarrow[30°]{48\%\ C_2H_5OH} RC_6H_4—CH_2OH + HCl$	−2.18
12		−5.09
13	$RC_6H_4—NH_2 + C_6H_5COCl \xrightarrow[26°]{C_6H_6} RC_6H_4—NHCOC_6H_5 + HCl$	−2.78
14	$RC_6H_4—COCH_3 + Br_2 \xrightarrow[CH_3CO_2^{\ominus}]{CH_3CO_2H,\ 35°} RC_6H_4—COCH_2Br + HBr$	0.42
15	$RC_6H_4—H + NO_2^{\oplus} \xrightarrow[18°]{(CH_3CO)_2O} RC_6H_4—NO_2 + H^{\oplus}$	−5.93
16		4.92

with the type of reaction and are appropriately called **reaction constants.** However, the real significance of ρ is that it measures the sensitivity of the reaction to the electrical effects of substituents in meta and para positions. A large ρ constant, positive or negative, means a high sensitivity to substituent influences. Reactions that are assisted by high electron density at the reaction site characteristically have *negative* ρ values (e.g., Reaction 15, Table 26-7), whereas reactions that are favored by withdrawal of electrons from the reaction site have *positive* ρ values (e.g., Reaction 16, Table 26-7).

Usually, ρ for a given reaction is influenced by conditions such as the temperature and composition of the solvent. However, the changes normally are not large unless an actual change in mechanism occurs with a change in the reaction conditions.

26-6B Scope of the Hammett Equation

The Hammett treatment provides a correlation of much experimental data. Tables 26-6 and 26-7 contain 38 substituent constants and 16 reaction constants. This means that we can calculate relative k or K values for 608 individual reactions. To illustrate, let us suppose that we need to estimate the relative rates of Reaction 16 of Table 26-7 for the para-substituents $R = OCH_3$ and $R = CF_3$. According to the ρ value of 4.92 for this reaction and the σ values of p-OCH_3 and p-CF_3 in Table 26-6, we may write

$$\log \frac{k_{p\text{-}OCH_3}}{k_0} = 4.92 \times (-0.27), \text{ and } \log \frac{k_{p\text{-}CF_3}}{k_0} = 4.92 \times (0.54)$$

Subtracting these two equations gives the result:

$$\log \frac{k_{p\text{-}OCH_3}}{k_{p\text{-}CF_3}} = 4.92 \times (-0.27 - 0.54) = -4.0 \qquad \text{or} \qquad \frac{k_{p\text{-}OCH_3}}{k_{p\text{-}CF_3}} = 10^{-4}$$

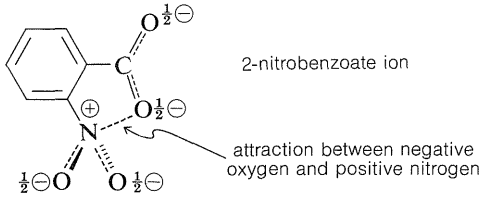
This then is a rate ratio of 1/10,000. If we have a further table of the sixteen k_0 or K_0 values for the reactions listed in Table 26-7, we can calculate actual k or K values for 608 different reactions. It should be recognized that neither Table 26-6 nor Table 26-7 is a complete list; at least 80 substituent constants[1] and several hundred ρ constants are now available.

The Hammett relationship formalizes and puts into quantitative terms much of the qualitative reasoning we have used for reactions involving aliphatic, alicyclic, and aromatic compounds. Considerable effort has been made to extend the Hammett idea to cover reactions other than of meta- and para-substituted benzene derivatives, but these will not be discussed here.[1]

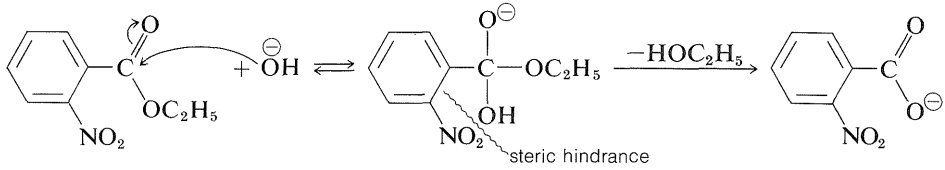
[1]J. Hine, *Structural Effects on Equilibria in Organic Chemistry,* Wiley-Interscience, New York, 1975, p. 65. This book offers a very broad coverage of quantitative correlations of substituent effects on processes as diverse as radical formation and rates of rotation around single C–C bonds.

26-6C Limitations of the Hammett Equation

The effects of substituents in ortho positions on the reactivity of benzene derivatives do not correlate well with the Hammett equation, as can be seen in Figure 26-3. The problem is that ortho substituents are close enough to the reaction site to exert significant "proximity" effects, which may be polar as well as steric in origin. Thus the enhanced acid strength of 2-nitrobenzoic acid over the 3- and 4-isomers (see Table 26-4) may be due to a polar stabilization of the acid anion by the neighboring positive nitrogen, which of course is not possible with the 3- and 4-isomers:



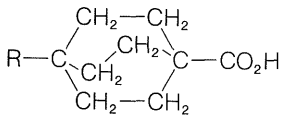
In contrast, the slower rate of alkaline hydrolysis of ethyl 2-nitrobenzoate than of its 3- and 4-isomers is more likely due to a steric hindrance effect of the 2-nitro group (see Table 26-5):



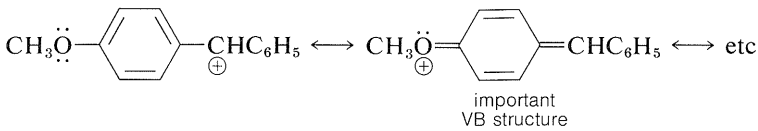
Because the effect of steric hindrance on different types of reactions is not expected to be the same, a given substituent is unlikely to exert the same relative steric effect in one reaction as in another. Consequently we cannot hope to find a very simple relationship such as the Hammett equation that will correlate structure and reactivity of ortho-substituted compounds.

The Hammett equation also fails for open-chain aliphatic derivatives. For example, there is no simple linear relationship between log K for a series of substituted ethanoic acids (RCH_2CO_2H) and log k for the hydrolysis rates of similarly substituted ethyl ethanoates ($RCH_2CO_2C_2H_5$). The freedom of motion available to a flexible open-chain compound permits a much wider range of variations in steric effects than for meta- and para-substituted aromatic compounds.

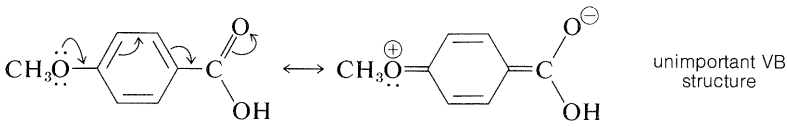
Exercise 26-37 Would you expect a Hammett type of relationship to correlate data for the dissociation of acids of the following type with rate data for hydrolysis of the corresponding esters? Explain.



The Hammett equation sometimes fails for meta- and para-substituted aromatic compounds. This failure may be expected whenever the opportunity arises for strong electron delocalization between the substituent and the reaction site. Generally, reactions that are strongly assisted by donation of electrons to the reaction site, as in S_N1 reactions and electrophilic aromatic substitution, will be facilitated by electron-delocalization effects of substituents with unshared electron pairs adjacent to the aromatic group (e.g., $—OCH_3$, —OH, $—O^{\ominus}$, $—NH_2$, and —Cl). Such reactions generally give a poor Hammett correlation. Thus a diphenylmethyl chloride with one 4-methoxy group solvolyzes in ethanol at 25° at a rate much faster than predicted by the Hammett equation, because of the resonance stabilization provided by the substituent to the intermediate carbocation:



The same type of stabilization by a 4-methoxy group does not appear to be important in influencing the ionization of 4-methoxybenzoic acid.



Similarly, those reactions that are strongly assisted by *withdrawal of electrons* from the reaction site, such as nucleophilic aromatic substitution, give a poor fit to a Hammett plot for the substituents that are capable of withdrawing electrons by delocalization ($—NO_2$, $—N_2^{\oplus}$, $—C{\equiv}N$, and so on). An example is Reaction 16 in Table 26-7. To correlate reactivity data with structures where strong resonance effects operate, different sets of substituent constants are required.[1]

Exercise 26-38 Account for the large difference in the ρ values of Reactions 10 and 11 of Table 26-7.

Exercise 26-39 The ρ constant for the ionization of benzoic acid is 1.000 for water solutions at 25°. Would you expect ρ for acid ionization to increase, or decrease, in going to a less polar solvent such as methanol? Explain.

Exercise 26-40 Explain why ρ for ionization of benzoic acids is larger than ρ for phenylethanoic acids. Estimate a value of ρ for the ionization of substituted 4-phenylbutanoic acids. Why should we expect the value of ρ for alkaline hydrolysis of ethyl benzoates to be larger than for acid ionization and to have the same sign?

Exercise 26-41 From the data of Tables 26-6 and 26-7 and given that K_a for benzenol at 25° is 1.3×10^{-10}, calculate K_a for 3-nitrobenzenol and 4-nitrobenzenol. The experimental values are 1.0×10^{-8} for 3-nitrobenzenol and 6.5×10^{-8} for 4-nitrobenzenol.

Do the calculated and experimental values agree satisfactorily (within a factor of 2 to 3) and, if not, why?

Exercise 26-42 From appropriate ρ values (Table 26-7) and σ values (Table 26-6), calculate the rates of hydrolysis of 4-CH_3-, 4-CH_3O-, 4-NO_2-phenylmethyl chlorides relative to phenylmethyl chloride (a) in water at 30° in the presence of base, and (b) in 48% ethanol at 30°. Explain why there is a greater spread in the relative rates in (b) than in (a).

Additional Reading

J. Hine, *Structural Effects on Equilibria in Organic Chemistry,* Wiley-Interscience, New York, 1975, Chapter 2.

C. A. Buehler and D. E. Pearson, *Survey of Organic Syntheses,* Wiley-Interscience, 1970, Chapter 5 (phenols), Chapter 12 (quinones and related substances), Chapter 20 (nitro compounds).

L. F. and M. Fieser, *Advanced Organic Chemistry,* Van Nostrand Reinhold Co., New York, 1961, Chapters 16–26. The quintessence of experts in the area of aromatic chemistry; magnificent descriptive chemistry of aromatic compounds.

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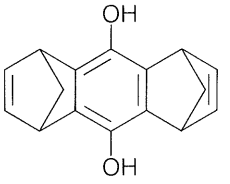
Supplementary Exercises

26-43 For each of the following pairs of compounds give a chemical test, preferably a test-tube reaction, that will distinguish between the two compounds. Write a structural formula for each compound and equations for the reactions involved.

a. benzenol and cyclohexanol
b. methyl 4-hydroxybenzoate and 4-methoxybenzoic acid
c. 1,4- and 1,3-benzenediol
d. 1,4-benzenediol and tropolone
e. 9,10-anthracenedione and 1,4-anthracenedione

26-44 Show by means of equations how each of the following substances may be synthesized, starting with the indicated materials. Specify reagents and approximate reaction conditions.

a. methyl 2-methoxybenzoate from benzenol
b. 1,3-dibromo-5-*tert*-butyl-2-methoxybenzene from benzenol
c. (4-cyanophenoxy)ethanoic acid from benzenol
d. 2-hydroxy-5-nitrobenzoic acid from benzenol
e. 2-naphthalenamine from naphthalene
f. tetramethyl-1,4-benzenedione from 1,2,4,5-tetramethylbenzene
g. 2-cyano-1,4-benzenedione from 1,4-benzenediol

h.  from 1,4-benzenedione

26-45 Rearrangement of 2-propenyloxybenzene labeled with radioactive carbon (^{14}C) at C3 of the 2-propenyl group forms 2-propenylbenzenol labeled at C1 of the 2-propenyl group. Can the rearrangement mechanism involve dissociation into $C_6H_5O\cdot$ and $^{14}CH_2{=}CH{-}CH_2\cdot$ followed by recombination? Can the rearrangement be a concerted pericyclic reaction (Section 21-10)? Where would you expect the ^{14}C label to be found in the rearrangement of 2,6-dimethyl(2-propenyloxy)benzene to 2,6-dimethyl-4-(2-propenyl)benzenol?

26-46 Write structural formulas for substances (one for each part) that fit the following descriptions:

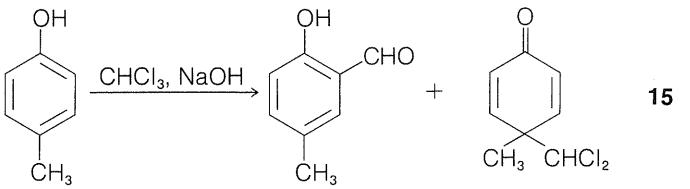
a. an arenol that would be a stronger acid than benzenol itself
b. the dichlorobenzenol isomer that is the strongest acid
c. the Claisen rearrangement product from 1,3-dimethyl-2-(1-methyl-2-propenyloxy)-benzene
d. a quinone that would not undergo Diels–Alder addition
e. a quinone that would be a better charge-transfer agent than 1,4-benzenedione
f. the expected product from addition of hydrogen cyanide to 2-cyano-1,4-benzenedione

26-47 Predict the positions to which coupling would occur (or whether coupling would occur at all) with benzenediazonium chloride in slightly alkaline solution for the following compounds. Give your reasoning.

a. 2,4,6-trimethylbenzenol
b. 2-naphthalenol
c. 1-methyl-2-naphthalenol
d. 9-phenanthrenol

26-48 When 2-hydroxybenzoic acid (salicylic acid) is treated with excess bromine in aqueous solution, it forms 2,4,6-tribromobenzenol. Write a reasonable mechanism for this reaction. Would you expect the same type of reaction to occur with 3-hydroxybenzoic acid?

26-49 Account for the formation of the by-product, **15,** in the reaction of 4-methylbenzenol with trichloromethane in alkali:

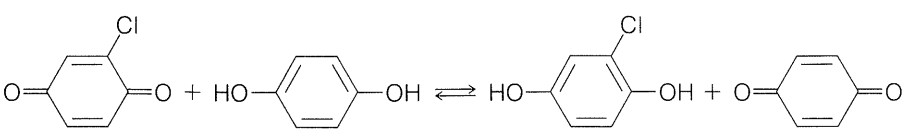


15

26-50 The important polymer intermediate "bis-phenol A" [2,2-bis-(4-hydroxyphenyl)propane] used, among other things, in epoxy resins, is made by an acid-induced condensation of 2-propanone and benzenol. Write a stepwise mechanism for this reaction that is consistent with the nature of the reactants and the products. (Review Section 15-4E on electrophilic reactions of  compounds, Section 22-4E, and Section 26-1E.)

26-51* Devise syntheses from benzene of each of the photographic developers whose structure is shown in Section 26-2C. Some reactions you will need are discussed in Chapters 22 and 23.

26-52 Addition of hydrogen chloride to 1,4-benzenedione yields, among other products, 2,3,5,6-tetrachloro-1,4-benzenedione. Explain how this substance might be formed, with the knowledge that equilibria such as the following are established rapidly:



26-53 Nitrous acid can substitute the more reactive aromatic derivatives by attack of $NO^{\oplus}$ on the ring and form Ar—N=O compounds. A product obtained from benzenol by this kind of reaction has the formula $C_6H_5O_2N$. Exactly the same substance is formed from treatment of one mole of 1,4-benzenedione with one mole of azanol (hydroxylamine; Section 16-4C). On the basis of the reactions by which it is formed, write two likely structures for this substance and explain how you would decide which one was correct on the basis of chemical and spectroscopic tests.

26-54 Consider possible benzil–benzilic acid-type rearrangements occurring with 9,10-phenanthrenedione and 9,10-anthracenedione. Give your reasoning as to how easily these rearrangements might occur, relative to rearrangement of benzil itself (Section 26-4E).

26-55 The [2 + 2] cycloadduct of tetrafluoroethene and 1,3-cyclopentadiene, when pyrolyzed at 700° to 750° and 5-mm pressure, produces (as the result of a sigmatropic rearrangement; Section 21-10) a mixture of two new substances, each having two double bonds. The pyrolysis mixture, when heated in aqueous ethanoic acid containing potassium ethanoate, forms tropolone in 70% yield. Write equations for the reactions involved, with particular attention to possible structures for the pyrolysis products.

26-56 How would you expect the properties of 3- and 4-hydroxy-2,4,6-cycloheptatrienone to compare with those of tropolone? Explain.

26-57 Make an atomic-orbital model of benzenol, showing in detail the orbitals and electrons at the oxygen atom. From your model, would you expect one, or both, pairs of unshared electrons on oxygen to be delocalized over the ring? What would be the most favorable orientation of the hydrogen of the hydroxyl group for maximum delocalization of an unshared electron pair?

26-58 It has been reported that compound **16** with alkali rearranges to phenyl-1,2-cyclobutenedione, **3** (Section 26-2E). This reaction appears to be the first reported reverse benzil-benzilic acid rearrangement (Section 26-4E). Explain how and why this process occurs.