Chapter 24 Phenols

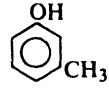
24.1 Structure and nomenclature

Phenols are compounds of the general formula ArOH, where Ar is **phenyl**, substituted phenyl, or one of the other aryl groups we shall study later (e.g., naphthyl, Chap. 30). *Phenols differ from alcohols in having the* —OH *group attached directly to an aromatic ring.*

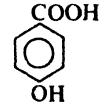
Phenols are generally named as derivatives of the simplest member of the family, **phenol**. The methylphenols are given the special name of *cresols*. Occasionally phenols are named as *hydroxy*– compounds.

Phenol

o-Chlorophenol



m-Cresol



p-Hydroxybenzoic acid

Catechol

Resorcinol

Hydroquinone

Salicylic acid

Both phenols and alcohols contain the —OH group, and as a result the two families resemble each other to a limited extent. We have already seen, for example, that both alcohols and phenols can be converted into ethers and esters. In most of their properties, however, and in their preparations, the two kinds of compound differ so greatly that they well deserve to be classified as different families.

24.2 Physical properties

The simplest phenols are liquids or low-melting solids; because of hydrogen bonding, they have quite high boiling points. Phenol itself is somewhat soluble

in water (9 g per 100 g of water), presumably because of hydrogen bonding with the water; most other phenols are essentially insoluble in water. Unless some group capable of producing color is present, phenols themselves are colorless. However, like aromatic amines, they are easily oxidized; unless carefully purified, many phenols are colored by oxidation products.

Table 24.1 PHENOLS

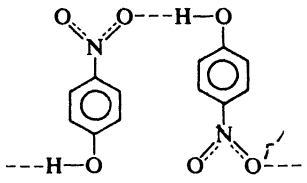
Name	M.p., °C	B.p., °C	Solub., g/100 g H_2O at 25°	K_a
Phenol	41	182	9.3	1.1×10^{-10}
o-Cresol	31	191	2.5	0.63
m-Cresol	11	201	2.6	0.98
p-Cresol	35	202	2.3	0.67
o-Fluorophenol	16	152		15
m-Fluorophenol	14	178		5.2
p-Fluorophenol	48	185		1.1
o-Chlorophenol	9	173	2.8	77
m-Chlorophenol	33	214	2.6	16
p-Chlorophenol	43	220	2.7	6.3
o-Bromophenol	5	194		41
m-Bromophenol	33	236		14
p-Bromophenol	64	236	1.4	5.6
o-Iodophenol	43			34
m-Iodophenol	40			13
p-Iodophenol	94			6.3
o-Aminophenol	174		1.7[0]	2.0
m-Aminophenol	123		2.6	69
p-Aminophenol	186		1.1[0]	
o-Nitrophenol	45	217	0.2	600
m-Nitrophenol	96		1.4	50
p-Nitrophenol	114		1.7	690
2,4-Dinitrophenol	113		0.6	1000000
2,4,6-Trinitrophenol (picric acid)	122		1.4	very large
Catechol	104	246	45	1
Resorcinol	110	281	123	3
Hydroquinone	173	286	8	2

An important point emerges from a comparison of the physical properties of the isomeric nitrophenols (Table 24.2). We notice that *o*-nitrophenol has a much lower boiling point and much lower solubility in water than its isomers; it is the only one of the three that is readily steam-distillable. How can these differences be accounted for?

Table 24.2 PROPERTIES OF THE NITROPHENOLS

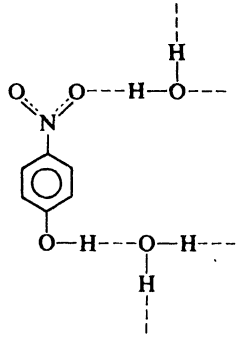
	B.p., °C at 70 mm	Solub., g/100 g H_2O	
o-Nitrophenol	100	0.2	Volatile in steam
m-Nitrophenol	194	1.35	Non-volatile in steam
p-Nitrophenol	*dec.*	1.69	Non-volatile in steam

Let us consider first the *m*- and *p*-isomers. They have very high boiling points because of intermolecular hydrogen bonding:



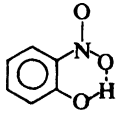
Intermolecular hydrogen bonding

Their solubility in water is due to hydrogen bonding with water molecules:



Steam distillation depends upon a substance having an appreciable vapor pressure at the boiling point of water; by lowering the vapor pressure, intermolecular hydrogen bonding inhibits steam distillation of the *m*- and *p*-isomers.

What is the situation for the *o*-isomer? Examination of models shows that the $-NO_2$ and $-OH$ groups are located exactly right for the formation of a



o-Nitrophenol

Intramolecular hydrogen bonding: chelation

hydrogen bond *within a single molecule*. This **intramolecular hydrogen bonding** takes the place of *inter*molecular hydrogen bonding with other phenol molecules and with water molecules; therefore *o*-nitrophenol does not have the low volatility of an associated liquid, nor does it have the solubility characteristic of a compound that forms hydrogen bonds with water.

The holding of a hydrogen or metal atom between two atoms of a single molecule is called **chelation** (Greek: *chele*, claw). See, for example, *chlorophyll* (p. 1004) and *hemin* (p. 1152).

Intramolecular hydrogen bonding seems to occur whenever the structure of a compound permits; we shall encounter other examples of its effect on physical properties.

Problem 24.1 Interpret the following observations. The O—H bands (Sec. 15.4) for the isomeric nitrophenols in solid form (KBr pellets) and in $CHCl_3$ solution are:

	KBr	$CHCl_3$
o-	3200 cm^{-1}	3200 cm^{-1}
m-	3330	3520
p-	3325	3530

Problem 24.2 In which of the following compounds would you expect intramolecular hydrogen bonding to occur: *o*-nitroaniline, *o*-cresol, *o*-hydroxybenzoic acid (salicylic acid), *o*-hydroxybenzaldehyde (salicylaldehyde), *o*-fluorophenol, *o*-hydroxybenzonitrile.

24.3 Salts of phenols

Phenols are fairly acidic compounds, and in this respect differ markedly from alcohols, which are even more weakly acidic than water. Aqueous hydroxides convert phenols into their salts; aqueous mineral acids convert the salts back into the free phenols. As we might expect, phenols and their salts have opposite solubility properties, the salts being soluble in water and insoluble in organic solvents.

$$\underset{\text{A phenol (acid)}}{\text{ArOH}} \underset{H^+}{\overset{OH^-}{\rightleftharpoons}} \underset{\text{A phenoxide ion (salt)}}{\text{ArO}^-}$$

Insoluble in water — *Soluble in water*

Most phenols have K_a's in the neighborhood of 10^{-10}, and are thus considerably weaker acids than the carboxylic acids (K_a's about 10^{-5}). Most phenols are weaker than carbonic acid, and hence, unlike carboxylic acids, do not dissolve in aqueous bicarbonate solutions. Indeed, phenols are conveniently liberated from their salts by the action of carbonic acid.

$$\underset{}{CO_2 + H_2O} \rightleftharpoons \underset{\text{Stronger acid}}{H_2CO_3} + \underset{\textit{Soluble in water}}{ArO^-Na^+} \longrightarrow \underset{\text{Weaker acid}}{ArOH} + \underset{}{Na^+HCO_3^-}$$

Insoluble in water

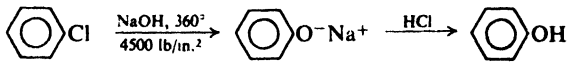
The acid strength of phenols and the solubility of their salts in water are useful both in analysis and in separations. A water-insoluble substance that dissolves in aqueous hydroxide but not in aqueous bicarbonate must be more acidic than water, but less acidic than a carboxylic acid; most compounds in this range of acidity are phenols. A phenol can be separated from non-acidic compounds by means of its solubility in base; it can be separated from carboxylic acids by means of its insolubility in bicarbonate.

Problem 24.3 Outline the separation by chemical methods of a mixture of *p*-cresol, *p*-toluic acid, *p*-toluidine, and *p*-nitrotoluene. Describe exactly what you would *do* and *see*.

24.4 · Industrial source

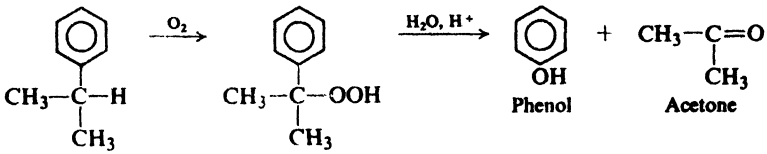
Most phenols are made industrially by the same methods that are used in the laboratory; these are described in Sec. 24.5. There are, however, special ways of obtaining certain of these compounds on a commercial scale, including the most important one, phenol. In quantity produced, phenol ranks near the top of the list of synthetic aromatic compounds. Its principal use is in the manufacture of the phenol–formaldehyde polymers (Sec. 32.7).

A certain amount of phenol, as well as the cresols, is obtained from coal tar (Sec. 12.4). Most of it (probably over 90%) is synthesized. One of the synthetic processes used is the fusion of sodium benzenesulfonate with alkali (Sec. 30.12); another is the Dow process, in which chlorobenzene is allowed to react with aqueous sodium hydroxide at a temperature of about 360°. Like the synthesis of aniline from chlorobenzene (Sec. 22.7), this second reaction involves nucleophilic substitution under conditions that are not generally employed in the laboratory (Sec. 25.4).



Chlorobenzene Sodium phenoxide Phenol

An increasingly important process for the synthesis of phenol starts with *cumene*, isopropylbenzene. Cumene is converted by air oxidation into cumene hydroperoxide, which is converted by aqueous acid into phenol and acetone.

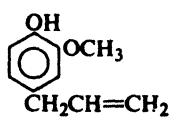


Cumene Cumene hydroperoxide Phenol Acetone

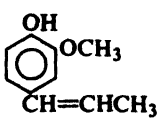
(The mechanism of this reaction is discussed in Sec. 28.6.)

Problem 24.4 Outline a synthesis of cumene from cheap, readily available hydrocarbons.

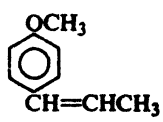
Certain phenols and their ethers are isolated from the *essential oils* of various plants (so called because they contain the *essence*—odor or flavor—of the plants). A few of these are:



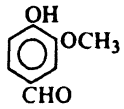
Eugenol
Oil of cloves



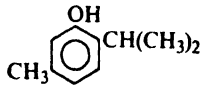
Isoeugenol
Oil of nutmeg



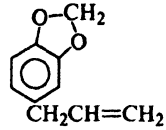
Anethole
Oil of aniseed



Vanillin
Oil of vanilla bean



Thymol
Oil of thyme and mint



Safrole
Oil of sassafras

24.5 Preparation

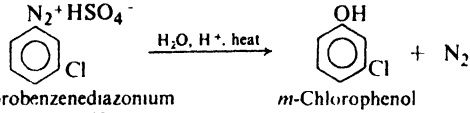
In the laboratory, phenols are generally prepared by one of the two methods outlined below.

PREPARATION OF PHENOLS

1. Hydrolysis of diazonium salts. Discussed in Sec. 23.14.

$$ArN_2^+ + H_2O \longrightarrow ArOH + H^+ + N_2$$

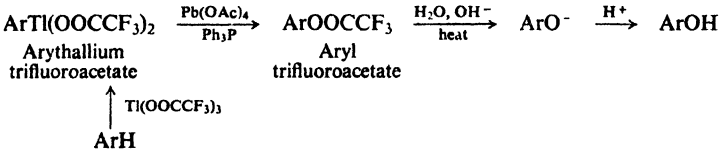
Example:



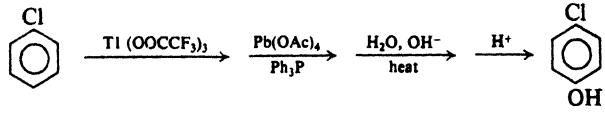
m-Chlorobenzenediazonium hydrogen sulfate

m-Chlorophenol

2. Oxidation of arylthallium compounds. Discussed in Sec. 24.5.



Example:



Chlorobenzene

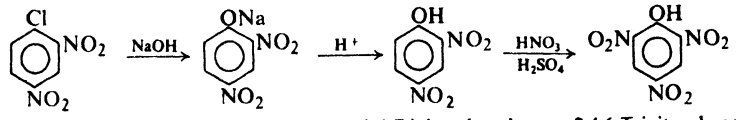
p-Chlorophenol
Only isomer

3. Alkali fusion of sulfonates. Discussed in Sec. 30.12.

Hydrolysis of diazonium salts is a highly versatile method of making phenols. It is the last step in a synthetic route that generally begins with nitration (Secs. 23.11 and 23.14).

Much simpler and more direct is a recently developed route via thallation. An arylthallium compound is oxidized by lead tetraacetate (in the presence of triphenylphosphine, Ph_3P) to the phenolic ester of trifluoroacetic acid, which on hydrolysis yields the phenol. The entire sequence, including thallation, can be carried out without isolation of intermediates. Although the full scope of the method has not yet been reported, it has two advantages over the diazonium route: (a) the speed and high yield made possible by the fewer steps; and (b) orientation control in the thallation step. (Review Secs. 11.7 and 11.13.)

Of limited use is the hydrolysis of aryl halides containing strongly electron-withdrawing groups *ortho* and *para* to the halogen (Sec. 25.9); 2,4-dinitrophenol and 2,4,6-trinitrophenol (*picric acid*) are produced in this way on a large scale:



2,4-Dinitrochlorobenzene — Sodium 2,4-dinitrophenoxide — 2,4-Dinitrophenol — 2,4,6-Trinitrophenol — Picric acid

Problem 24.5 Outline all steps in the synthesis *from toluene* of: (a) *p*-cresol via diazotization; (b) *p*-cresol via thallation; (c) and (d) *m*-cresol via each route. (*Hint:* See Secs. 23.16 and 11.13.)

24.6 Reactions

Aside from acidity, the most striking chemical property of a phenol is the extremely high reactivity of its ring toward electrophilic substitution. Even in ring substitution, acidity plays an important part; ionization of a phenol yields the $-O^-$ group, which, because of its full-fledged negative charge, is even more strongly electron-releasing than the —OH group.

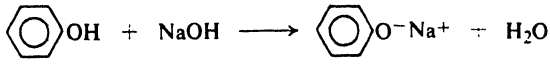
Phenols undergo not only those electrophilic substitution reactions that are typical of most aromatic compounds, but also many others that are possible only because of the unusual reactivity of the ring. We shall have time to take up only a few of these reactions.

REACTIONS OF PHENOLS

1. Acidity. Salt formation. Discussed in Secs. 24.3 and 24.7.

$$ArOH + H_2O \rightleftharpoons ArO^- + H_3O^+$$

Example:

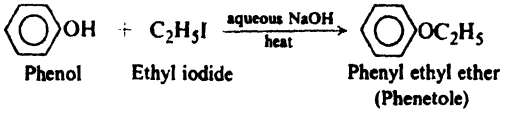


Phenol — Sodium phenoxide

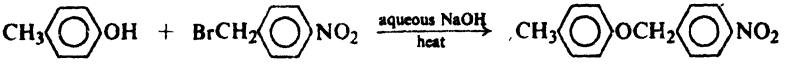
2. Ether formation. Williamson synthesis. Discussed in Secs. 17.5 and 24.8.

$$ArO^- + RX \longrightarrow ArOR + X^-$$

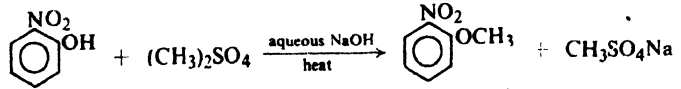
Examples:



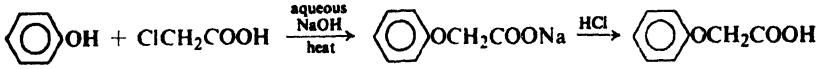
Phenol Ethyl iodide Phenyl ethyl ether (Phenetole)



p-Cresol *p*-Nitrobenzyl bromide *p*-Tolyl *p*-nitrobenzyl ether

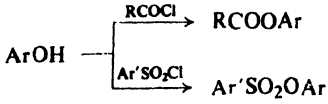


o-Nitrophenol Methyl sulfate *o*-Nitroanisole (*o*-Nitrophenyl methyl ether)

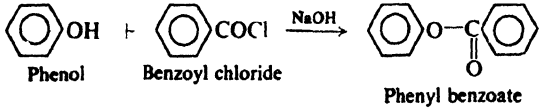


Phenol Chloroacetic acid Phenoxyacetic acid

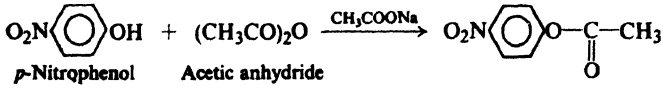
3. **Ester formation.** Discussed in Secs. 20.8, 20.15, and 24.9.



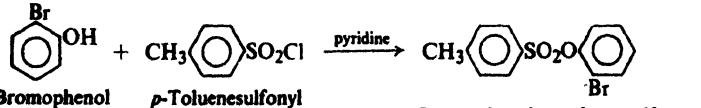
Examples:



Phenol Benzoyl chloride Phenyl benzoate



p-Nitrophenol Acetic anhydride *p*-Nitrophenyl acetate



o-Bromophenol *p*-Toluenesulfonyl chloride *o*-Bromophenyl *p*-toluenesulfonate

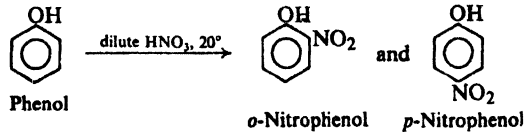
4. **Ring substitution.** Discussed in Sec. 24.10.

—OH, —O⁻ } Activate powerfully, and direct *ortho,para* in electrophilic aromatic substitution.

—OR: Less powerful activator than —OH.

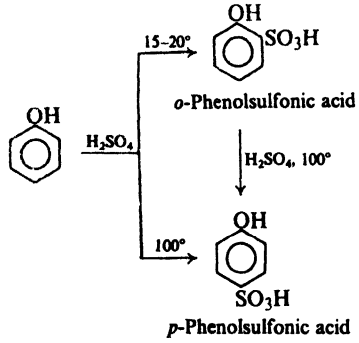
(a) **Nitration.** Discussed in Sec. 24.10.

Example:



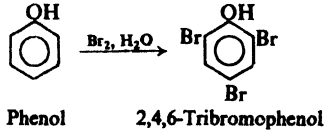
(b) **Sulfonation.** Discussed in Sec. 24.10.

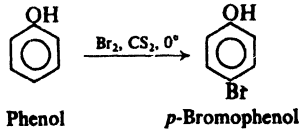
Example:



(c) **Halogenation.** Discussed in Sec. 24.10.

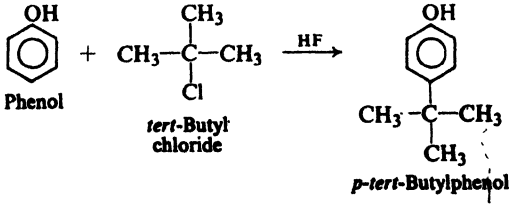
Examples:





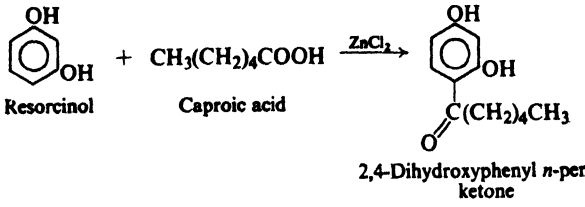
(d) **Friedel-Crafts alkylation.** Discussed in Sec. 24.10.

Example:

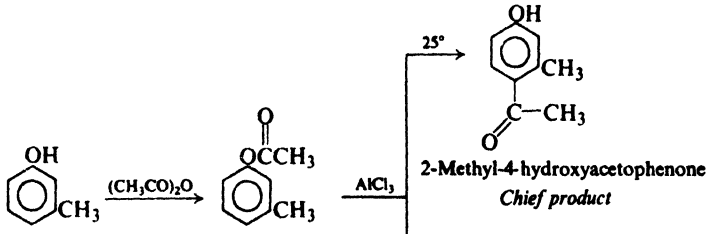


(e) Friedel-Crafts acylation. Fries rearrangement. Discussed in Secs. 24.9 and 24.10.

Examples:



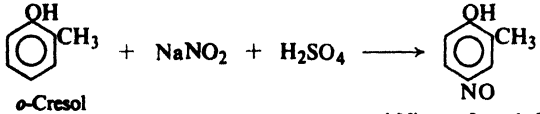
Resorcinol Caproic acid 2,4-Dihydroxyphenyl *n*-pentyl ketone



m-Cresol *m*-Cresyl acetate

(f) Nitrosation. Discussed in Sec. 24.10.

Example:

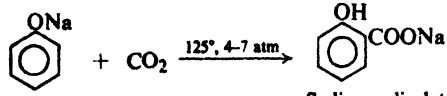


o-Cresol 4-Nitroso-2-methylphenol

(g) Coupling with diazonium salts. Discussed in Secs. 23.17 and 24.10.

(h) Carbonation. Kolbe reaction. Discussed in Sec. 24.11.

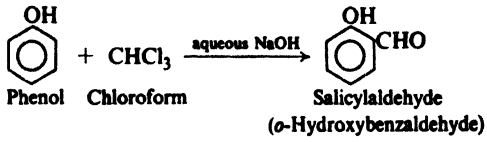
Example:



Sodium phenoxide Sodium salicylate (Sodium *o*-hydroxybenzoate)

(i) Aldehyde formation. Reimer-Tiemann reaction. Discussed in Sec. 24.12.

Example:



(j) Reaction with formaldehyde. Discussed in Sec. 32.7.

24.7 Acidity of phenols

Phenols are converted into their salts by aqueous hydroxides, but not by aqueous bicarbonates. The salts are converted into the free phenols by aqueous mineral acids, carboxylic acids, or carbonic acid.

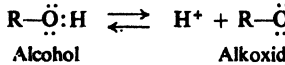
$$\underset{\text{Stronger acid}}{ArOH} + OH^- \longrightarrow \underset{\text{Weaker acid}}{ArO^-} + H_2O$$

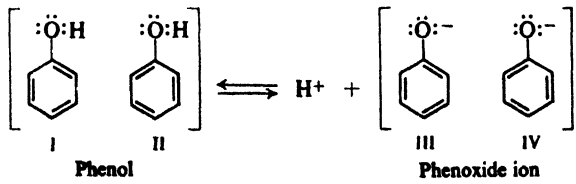
$$\underset{\text{Stronger acid}}{ArO^-} + H_2CO_3 \longrightarrow \underset{\text{Weaker acid}}{ArOH} + HCO_3^-$$

Phenols must therefore be considerably stronger acids than water, but considerably weaker acids than the carboxylic acids. Table 24.1 (p. 788) shows that this is indeed so: most phenols have K_a's of about 10^{-10}, whereas carboxylic acids have K_a's of about 10^{-5}.

Although weaker than carboxylic acids, phenols are tremendously more acidic than alcohols, which have K_a's in the neighborhood of 10^{-16} to 10^{-18} How does it happen that an —OH attached to an aromatic ring is so much more acidic than an —OH attached to an alkyl group? The answer is to be found in an examination of the structures involved. As usual we shall assume that differences in acidity are due to differences in stabilities of reactants and products (Sec. 18.12).

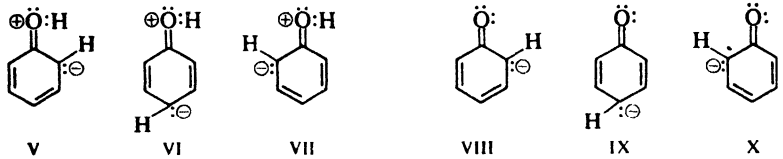
Let us examine the structures of reactants and products in the ionization of an alcohol and of phenol. We see that the alcohol and the alkoxide ion are each represented satisfactorily by a single structure. Phenol and the phenoxide ion





contain a benzene ring and therefore must be hybrids of the Kekulé structures I and II, and III and IV. This resonance presumably stabilizes both molecule and ion to the same extent. It lowers the energy content of each by the same number of kcal/mole, and hence does not affect the *difference* in their energy contents. If there were no other factors involved, then, we might expect the acidity of a phenol to be about the same as the acidity of an alcohol.

However, there are additional structures to be considered. Being basic, oxygen can share more than a pair of electrons with the ring; this is indicated by contribution from structures V–VII for phenol, and VIII–X for the phenoxide ion.



V VI VII VIII IX X

Phenol Phenoxide ion

Now, are these two sets of structures equally important? Structures V-VII for phenol carry both positive and negative charges; structures VIII–X for phenoxide ion carry only a negative charge. Since energy must be supplied to separate opposite charges, the structures for the phenol should contain more energy and hence be less stable than the structures for phenoxide ion. (We have already encountered the effect of *separation of charge* on stability in Sec. 18.12.) The net effect of resonance is therefore to stabilize the phenoxide ion to a greater extent than the phenol, and thus to shift the equilibrium toward ionization and make K_a larger than for an alcohol (Fig. 24.1).

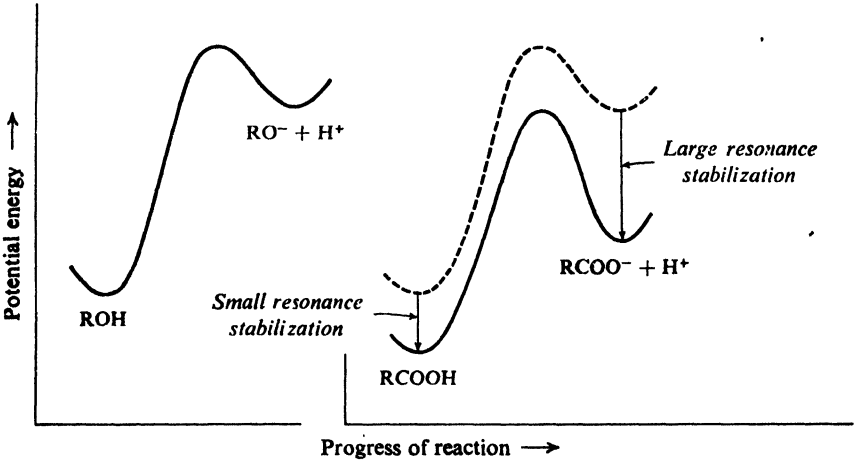


Figure 24.1. Molecular structure and position of equilibrium. Phenol yields resonance-stabilized anion; is stronger acid than alcohol. (Plots aligned with each other for easy comparison.)

We have seen (Sec. 23.3) that aromatic amines are weaker bases than aliphatic amines, since resonance stabilizes the free amine to a greater extent than it does the ion. Here we have exactly the opposite situation, phenols being stronger acids than their aliphatic counterparts, the alcohols, because resonance stabilizes the ion to a greater extent than it does the free phenol. (Actually, of course, resonance with the ring exerts the *same* effect in both cases; it stabilizes—and thus weakens—the base: amine or phenoxide ion.)

In Table 24.1 (p. 788) we see that electron-attracting substituents like —X or $-NO_2$ increase the acidity of phenols, and electron-releasing substituents like $-CH_3$ decrease acidity. Thus substituents affect acidity of phenols in the same way that they affect acidity of carboxylic acids (Sec. 18.14); it is, of course, opposite to the way these groups affect basicity of amines (Sec. 23.4). Electron-attracting substituents tend to disperse the negative charge of the phenoxide ion, whereas electron-releasing substituents tend to intensify the charge.

Problem 24.6 How do you account for the fact that, unlike most phenols, 2,4-dinitrophenol and 2,4,6-trinitrophenol are soluble in aqueous sodium bicarbonate?

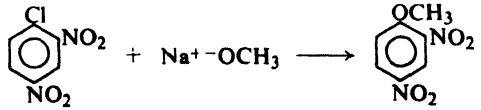
We can see that a group attached to an aromatic ring affects *position of equilibrium* in reversible reactions in the same way that it affects *rate* in irreversible reactions. An electron-releasing group favors reactions in which the ring becomes more positive, as in electrophilic substitution or in the conversion of an amine into its salt. An electron-withdrawing group favors reactions in which the ring becomes more negative, as in nucleophilic substitution (Chap. 25) or in the conversion of a phenol or an acid into its salt.

24.8 Formation of ethers. Williamson synthesis

As already discussed (Sec. 17.5), phenols are converted into ethers by reaction in alkaline solution with alkyl halides; methyl ethers can also be prepared by reaction with methyl sulfate. In alkaline solutions a phenol exists as the phenoxide ion which, acting as a nucleophilic reagent, attacks the halide (or the sulfate) and displaces halide ion (or sulfate ion).

$$ArOH \xrightarrow{OH^-} ArO^- \begin{cases} \xrightarrow{RX} Ar{-}O{-}R \cdot X^- \\ \xrightarrow{(CH_3)_2SO_4} Ar{-}O{-}CH_3 \cdot CH_3OSO_3^- \end{cases}$$

Certain ethers can be prepared by the reaction of unusually active aryl halides with sodium alkoxides. For example:

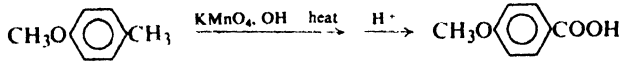


2,4-Dinitrochlorobenzene

2,4-Dinitroanisole
(2,4-Dinitrophenyl methyl ether)

While alkoxy groups are activating and *ortho,para*-directing in electrophilic aromatic substitution, they are considerably less so than the —OH group. As a result ethers do not generally undergo those reactions (Secs. 24.10–24.12) which require the especially high reactivity of phenols: coupling, Kolbe reaction, Reimer-Tiemann reaction, etc. This difference in reactivity is probably due to the fact that, unlike a phenol, an ether cannot ionize to form the extremely reactive phenoxide ion.

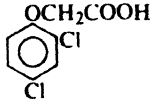
As a consequence of the lower reactivity of the ring, an aromatic ether is less sensitive to oxidation than a phenol. For example:



p-Methylanisole Anisic acid

We have already discussed the cleavage of ethers by acids (Sec. 17.7). Cleavage of methyl aryl ethers by concentrated hydriodic acid is the basis of an important analytical procedure (the *Zeisel procedure*, Sec. 17.16).

Problem 24.7 2,4-Dichlorophenoxyacetic acid is the important weed-killer known as 2,4-D. Outline the synthesis of this compound starting from benzene or toluene and acetic acid.



2,4-Dichlorophenoxyacetic acid
(2,4-D)

Problem 24.8 The *n*-propyl ether of 2-amino-4-nitrophenol is one of the sweetest compounds ever prepared, being about 5000 times as sweet as the common sugar sucrose. It can be made from the dinitro compound by reduction with ammonium bisulfide. Outline the synthesis of this material starting from benzene or toluene and any aliphatic reagents.

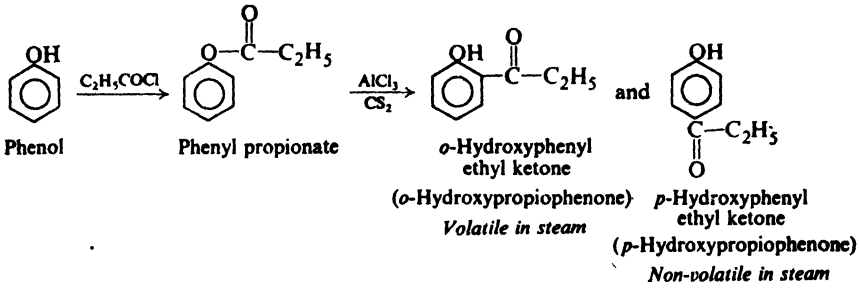
24.9 Ester formation. Fries rearrangement

Phenols are usually converted into their esters by the action of acids, acid chlorides, or anhydrides as discussed in Secs. 18.16, 20.8, and 20.15.

Problem 24.9 Predict the products of the reaction between phenyl benzoate and one mole of bromine in the presence of iron.

When esters of phenols are heated with aluminum chloride, the acyl group migrates from the phenolic oxygen to an *ortho* or *para* position of the ring, thus yielding a ketone. This reaction, called the *Fries rearrangement*, is often used

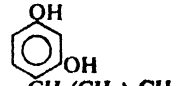
instead of direct acylation for the synthesis of phenolic ketones. For example:



In at least some cases, rearrangement appears to involve generation of an acylium ion, RCO^+, which then attacks the ring as in ordinary Friedel-Crafts acylation.

Problem 24.10 A mixture of *o*- and *p*-isomers obtained by the Fries rearrangement can often be separated by steam distillation, only the *o*-isomer distilling. How do you account for this?

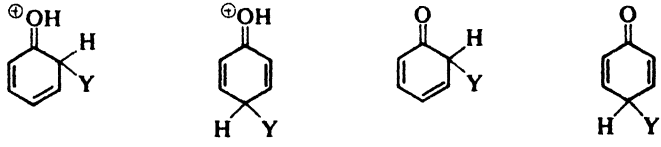
Problem 24.11 4-*n*-Hexylresorcinol is used in certain antiseptics. Outline its preparation starting with resorcinol and any aliphatic reagents.



4-*n*-Hexylresorcinol

24.10 Ring substitution

Like the amino group, the phenolic group powerfully activates aromatic rings toward electrophilic substitution, and in essentially the same way. The intermediates are hardly carbonium ions at all, but rather oxonium ions (like I and II), in which every atom (except hydrogen) has a complete octet of electrons;

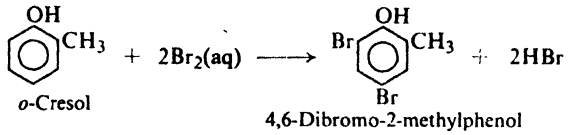


I II III IV

they are formed tremendously faster than the carbonium ions derived from benzene itself. Attack on a phenoxide ion yields an even more stable—and even more rapidly formed—intermediate, an unsaturated ketone (like III and IV).

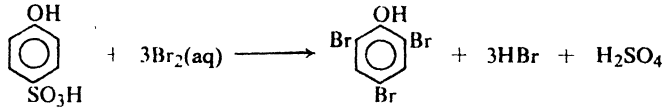
With phenols, as with amines, special precautions must often be taken to prevent polysubstitution and oxidation.

Treatment of phenols with aqueous solutions of bromine results in replacement of every hydrogen *ortho* or *para* to the —OH group, and may even cause displacement of certain other groups. For example:



o-Cresol

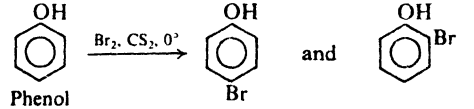
4,6-Dibromo-2-methylphenol



p-Phenolsulfonic acid

2,4,6-Tribromophenol

If halogenation is carried out in a solvent of low polarity, such as chloroform, carbon tetrachloride, or carbon disulfide, reaction can be limited to monohalogenation. For example:

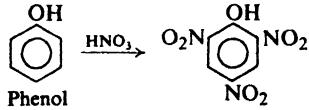


Phenol

p-Bromophenol
Chief product

o-Bromophenol

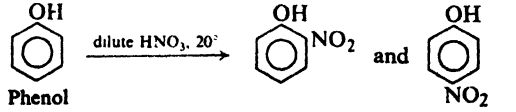
Phenol is converted by concentrated nitric acid into 2,4,6-trinitrophenol (*picric acid*), but the nitration is accompanied by considerable oxidation. To



Phenol

2,4,6-Trinitrophenol
(Picric acid)

obtain mononitrophenols, it is necessary to use dilute nitric acid at a low temperature; even then the yield is poor. (The isomeric products are readily separated by



Phenol

o-Nitrophenol
40% yield

p-Nitrophenol
13% yield

steam distillation. *Why?*)

Problem 24.12 Picric acid can be prepared by treatment of 2,4-phenoldisulfonic acid with nitric acid. (a) Show in detail the mechanism by which this happens. (b) What advantage does this method of synthesis have over the direct nitration of phenol?

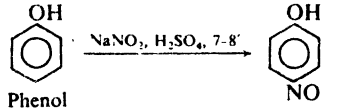
Alkylphenols can be prepared by Friedel-Crafts alkylation of phenols, but the yields are often poor.

Although phenolic ketones can be made by direct acylation of phenols, they are more often prepared in two steps by means of the Fries rearrangement (Sec. 24.9).

Problem 24.13 The product of sulfonation of phenol depends upon the temperature of reaction: chiefly *ortho* at 15-20°, chiefly *para* at 100°. Once formed, *o*-phenolsulfonic acid is converted into the *p*-isomer by sulfuric acid at 100°. How do you account for these facts? (*Hint:* See Sec. 8.22.)

In addition, phenols undergo a number of other reactions that also involve electrophilic substitution, and that are possible only because of the especially high reactivity of the ring.

Nitrous acid converts phenols into nitrosophenols:



Phenol

p-Nitrosophenol
80% yield

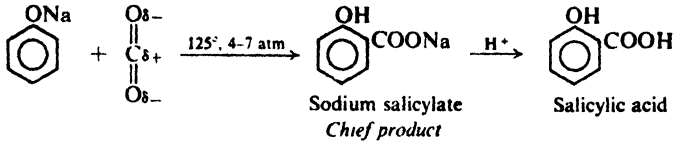
Phenols are one of the few classes of compounds reactive enough to undergo attack by the weakly electrophilic nitrosonium ion, ^+NO.

Problem 24.14 The —NO group is readily oxidized to the $—NO_2$ group by nitric acid. Suggest a better way to synthesize *p*-nitrophenol than the one given earlier in this section

As we have seen, the ring of a phenol is reactive enough to undergo attack by diazonium salts, with the formation of azo compounds. This reaction is discussed in detail in Sec. 23.17.

24.11 Kolbe reaction. Synthesis of phenolic acids

Treatment of the salt of a phenol with carbon dioxide brings about substitution of the carboxyl group, —COOH, for hydrogen of the ring. This reaction is known as the **Kolbe reaction**; its most important application is in the conversion of phenol itself into *o*-hydroxybenzoic acid, known as *salicylic acid.* Although some *p*-hydroxybenzoic acid is formed as well, the separation of the two isomers can be



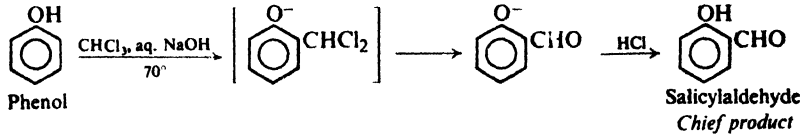
carried out readily by steam distillation, the *o*-isomer being the more volatile. (Why?)

It seems likely that CO_2 attaches itself initially to phenoxide oxygen rather than to the ring. In any case, the final product almost certainly results from electrophilic attack by electron-deficient carbon on the highly reactive ring.

Problem 24.15 *Aspirin* is acetylsalicylic acid (*o*-acetoxybenzoic acid, *o*-CH_3COO-C_6H_4COOH); *oil of wintergreen* is the ester, methyl salicylate. Outline the synthesis of these two compounds from phenol.

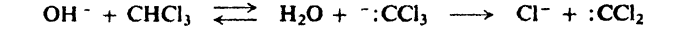
24.12 Reimer-Tiemann reaction. Synthesis of phenolic aldehydes. Dichlorocarbene

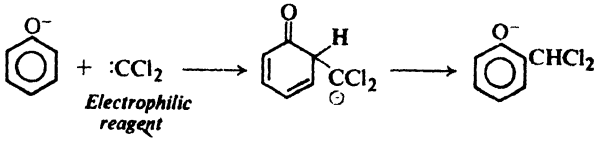
Treatment of a phenol with chloroform and aqueous hydroxide introduces an aldehyde group, —CHO, into the aromatic ring, generally *ortho* to the —OH. This reaction is known as the **Reimer-Tiemann reaction**. For example:



A substituted benzal chloride is initially formed, but is hydrolyzed by the alkaline reaction medium.

The Reimer-Tiemann reaction involves electrophilic substitution on the highly reactive phenoxide ring. The electrophilic reagent is dichlorocarbene, $:CCl_2$, generated from chloroform by the action of base. Although electrically neutral, dichlorocarbene contains a carbon atom with only a sextet of electrons and hence is strongly electrophilic.





We encountered dichlorocarbene earlier (Sec. 9.16) as a species adding to carbon–carbon double bonds. There, as here, it is considered to be formed from chloroform by the action of a strong base.

The formation of dichlorocarbene by the sequence

(1) $CHCl_3 + OH^- \rightleftharpoons CCl_3^- + H_2O$

(2) $CCl_3^- \rightleftharpoons Cl^- + :CCl_2$

$\xrightarrow{\text{fast}}$ products (addition to alkenes, Reimer-Tiemann reaction, hydrolysis, etc.)

is indicated by many lines of evidence, due mostly to elegant work by Jack Hine of the Ohio State University.

Problem 24.16 What bearing does each of the following facts have on the mechanism above? Be specific.

(a) $CHCl_3$ undergoes alkaline hydrolysis much more rapidly than CCl_4 or CH_2Cl_2.

(b) Hydrolysis of ordinary chloroform is carried out in D_2O in the presence of OD^-. When the reaction is interrupted, and unconsumed chloroform is recovered, it is found to contain deuterium. (*Hint:* See Sec. 20.17.)

(c) The presence of added Cl^- *slows down* alkaline hydrolysis of $CHCl_3$.

(d) When alkaline hydrolysis of $CHCl_3$ in the presence of I^- is interrupted, there is recovered not only $CHCl_3$ but also $CHCl_2I$. (In the absence of base, $CHCl_3$ does not react with I^-.)

(e) In the presence of base, $CHCl_3$ reacts with acetone to give 1,1,1-trichloro-2-methyl-2-propanol.

24.13 Analysis of phenols

The most characteristic property of phenols is their particular degree of acidity. Most of them (Secs. 24.3 and 24.7) are stronger acids than water but weaker acids than carbonic acid. Thus, a water-insoluble compound that dissolves in aqueous sodium hydroxide but *not* in aqueous sodium bicarbonate is most likely a phenol.

Many (but not all) phenols form colored complexes (ranging from green through blue and violet to red) with ferric chloride. (This test is also given by *enols*.)

Phenols are often identified through bromination products and certain esters and ethers.

Problem 24.17 Phenols are often identified as their aryloxyacetic acids, $ArOCH_2COOH$. Suggest a reagent and a procedure for the preparation of these derivatives. (*Hint:* See Sec. 24.8.) Aside from melting point, what other property of the aryloxyacetic acids would be useful in identifying phenols? (*Hint:* See Sec. 18.21.)

24.14 Spectroscopic analysis of phenols

Infrared. As can be seen in Fig. 24.2 (p. 806), phenols show a strong, broad band due to O—H stretching in the same region, 3200–3600 cm^{-1}, as alcohols.

O—H stretching, *strong, broad*

Phenols (or alcohols), 3200–3600 cm^{-1}

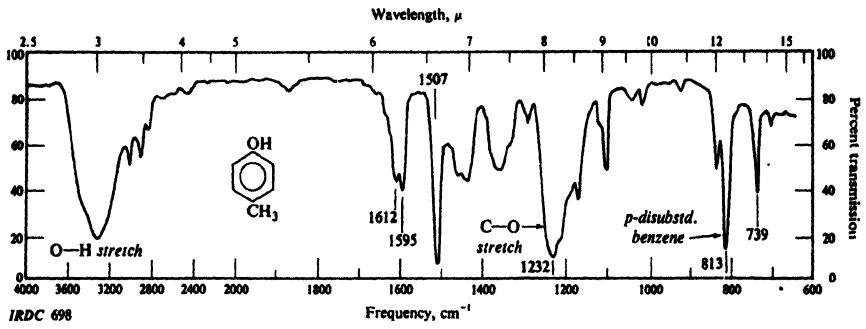


Figure 24.2. Infrared spectrum of *p*-cresol.

Phenols differ from alcohols, however, in the position of the C—O stretching band (compare Sec. 16.13).

C—O stretching, *strong, broad*

Phenols, about 1230 cm^{-1} Alcohols, 1050–1200 cm^{-1}

Phenolic ethers do not, of course, show the O—H band, but do show C—O stretching.

C—O stretching, *strong, broad*

Aryl and vinyl ethers, 1200–1275 cm^{-1}, and weaker, 1020–1075 cm^{-1}

Alkyl ethers, 1060–1150 cm^{-1}

(For a comparison of certain oxygen compounds, see Table 20.3, p. 689.)

Nmr. Absorption by the O—H proton of a phenol, like that of an alcohol (Sec. 16.13), is affected by the degree of hydrogen bonding, and hence by the temperature, concentration, and nature of the solvent. The signal may appear anywhere in the range δ 4–7, or, if there is intramolecular hydrogen bonding, still lower: δ 6–12.

PROBLEMS

1. Write structural formulas for.

(a) 2,4-dinitrophenol
(b) *m*-cresol
(c) hydroquinone
(d) resorcinol
(e) 4-*n*-hexylresorcinol
(f) catechol
(g) picric acid
(h) phenyl acetate
(i) anisole
(j) salicylic acid
(k) ethyl salicylate

2. Give the reagents and any critical conditions necessary to prepare phenol from:

(a) aniline
(b) benzene
(c) chlorobenzene
(d) cumene (isopropylbenzene)

3. Outline the steps in a possible industrial synthesis of:

(a) catechol from *guaiacol*, *o*-$CH_3OC_6H_4OH$, found in beech-wood tar
(b) catechol from phenol
(c) resorcinol from benzene
(d) picric acid from chlorobenzene
(e) *veratrole*, *o*-$C_6H_4(OCH_3)_2$, from catechol

4. Outline a possible laboratory synthesis of each of the following compounds from benzene and/or toluene, using any needed aliphatic and inorganic reagents.

(a)–(c) the three cresols
(d) *p*-iodophenol
(e) *m*-bromophenol
(f) *o*-bromophenol
(g) 3-bromo-4-methylphenol
(h) 2-bromo-4-methylphenol
(i) 2-bromo-5-methylphenol
(j) 5-bromo-2-methylphenol
(k) 2,4-dinitrophenol
(l) *p*-isopropylphenol
(m) 2,6-dibromo-4-isopropylphenol
(n) 2-hydroxy-5-methylbenzaldehyde
(o) *o*-methoxybenzyl alcohol

5. Give structures and names of the principal organic products of the reaction (if any) of *o*-cresol with:

(a) aqueous NaOH
(b) aqueous $NaHCO_3$
(c) hot conc. HBr
(d) methyl sulfate, aqueous NaOH
(e) benzyl bromide, aqueous NaOH
(f) bromobenzene, aqueous NaOH
(g) 2,4-dinitrochlorobenzene, aqueous NaOH
(h) acetic acid, H_2SO_4
(i) acetic anhydride
(j) phthalic anhydride
(k) *p*-nitrobenzoyl chloride, pyridine
(l) benzenesulfonyl chloride, aqueous NaOH
(m) product (i) + $AlCl_3$
(n) thionyl chloride
(o) ferric chloride solution
(p) H_2, Ni, 200°, 20 atm.
(q) cold dilute HNO_3
(r) H_2SO_4, 15°
(s) H_2SO_4, 100°
(t) bromine water
(u) Br_2, CS_2
(v) $NaNO_2$, dilute H_2SO_4
(w) product (v) + HNO_3
(x) *p*-nitrobenzenediazonium chloride
(y) CO_2, NaOH, 125°, 5 atm.
(z) $CHCl_3$, aqueous NaOH, 70°

6. Answer Problem 5 for anisole.

7. Answer Problem 5, parts (a) through (o), for benzyl alcohol.

8. Without referring to tables, arrange the compounds of each set in order of acidity:

(a) benzenesulfonic acid, benzoic acid, benzyl alcohol, phenol
(b) carbonic acid, phenol, sulfuric acid, water
(c) *m*-bromophenol, *m*-cresol, *m*-nitrophenol, phenol
(d) *p*-chlorophenol, 2,4-dichlorophenol, 2,4,6-trichlorophenol

9. Describe simple chemical tests that would serve to distinguish between:

(a) phenol and *o*-xylene
(b) *p*-ethylphenol, *p*-methylanisole, and *p*-methylbenzyl alcohol
(c) 2,5-dimethylphenol, phenyl benzoate, *m*-toluic acid
(d) anisole and *o*-toluidine
(e) acetylsalicylic acid, ethyl acetylsalicylate, ethyl salicylate, and salicylic acid
(f) *m*-dinitrobenzene, *m*-nitroaniline, *m*-nitrobenzoic acid, and *m*-nitrophenol

Tell exactly what you would *do* and *see*.

10. Describe simple chemical methods for the separation of the compounds of Problem 9, parts (a), (c), (d), and (f), recovering each component in essentially pure form.

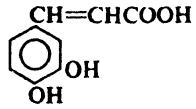
11. Outline all steps in a possible laboratory synthesis of each of the following compounds starting from the aromatic source given, and using any needed aliphatic and inorganic reagents:

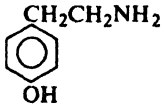
(a) 2,4-diaminophenol (Amidol, used as a photographic developer) from chlorobenzene
(b) 4-amino-1,2-dimethoxybenzene from catechol
(c) 2-nitro-1,3-dihydroxybenzene from resorcinol (*Hint:* See Problem 11.7, p. 350.)
(d) 2,4,6-trimethylphenol from mesitylene
(e) *p-tert*-butylphenol from phenol
(f) 4-(*p*-hydroxyphenyl)-2,2,4-trimethylpentane from phenol
(g) 2-phenoxy-1-bromoethane from phenol (*Hint:* Together with $C_6H_5OCH_2CH_2OC_6H_5$.)
(h) phenyl vinyl ether from phenol

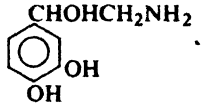
(i) What will phenyl vinyl ether give when heated with acid?
(j) 2,6-dinitro-4-*tert*-butyl-3-methylanisole (synthetic musk) from *m*-cresol
(k) 5-methyl-1,3-dihydroxybenzene (*orcinol*, the parent compound of the litmus dyes) from toluene

12. Outline a possible synthesis of each of the following from benzene, toluene, or any of the natural products shown in Sec. 24.4, using any other needed reagents.

(a) *caffeic acid*, from coffee beans
(b) *tyramine*, found in ergot (*Hint:* See Problem 21.22a, p. 714.)
(c) *noradrenaline*, an adrenal hormone


Caffeic acid


Tyramine

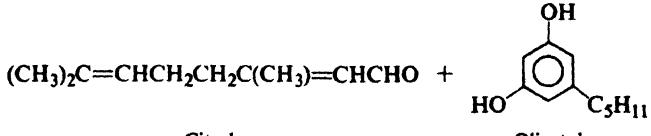

Noradrenaline

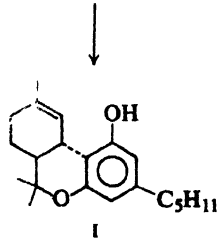
13. The reaction between benzyl chloride and sodium phenoxide follows second-order kinetics in a variety of solvents; the nature of the products, however, varies considerably. (a) In dimethylformamide, dioxane, or tetrahydrofuran, reaction yields only benzyl phenyl ether. Show in detail the mechanism of this reaction. To what general class does it belong? (b) In aqueous solution, the yield of ether is cut in half, and there is obtained, in addition, *o*- and *p*-benzylphenol. Show in detail the mechanism by which the latter products are formed. To what general class (or classes) does the reaction belong? (c) What is a possible explanation for the difference between (a) and (b)? (*Hint:* See Sec. 1.21.) (d) In methanol or ethanol, reaction occurs as in (a); in liquid phenol or 2,2,2-trifluoroethanol, reaction is as in (b). How can you account for these differences?

14. When *phloroglucinol*, 1,3,5-trihydroxybenzene, is dissolved in concentrated $HClO_4$, its nmr spectrum shows two peaks of equal area at δ 6.12 and δ 4.15. Similar solutions of 1,3,5-trimethoxybenzene and 1,3,5-triethoxybenzene show similar nmr peaks. On dilution, the original compounds are recovered unchanged. Solutions of these compounds in D_2SO_4 also show these peaks, but on standing the peaks gradually disappear.

How do you account for these observations? What is formed in the acidic solutions? What would you expect to recover from the solution of 1,3,5-trimethoxybenzene in D_2SO_4?

15. When the terpene *citral* is allowed to react in the presence of dilute acid with *olivetol*, there is obtained a mixture of products containing I, the racemic form of one of the physiologically active components of hashish (marijuana). (C_5H_{11} is *n*-pentyl.) Show all steps in a likely mechanism for the formation of I.


Citral Olivetol


I

Δ^1-3,4-*trans*-Tetrahydrocannabinol

16. Give structures of all compounds below:

(a) *p*-nitrophenol + C_2H_5Br + NaOH (aq) $\longrightarrow$ A ($C_8H_9O_3N$)
A + Sn + HCl $\longrightarrow$ B ($C_8H_{11}ON$)
B + $NaNO_2$ + HCl, then phenol $\longrightarrow$ C ($C_{14}H_{14}O_2N_2$)
C + ethyl sulfate + NaOH (aq) $\longrightarrow$ D ($C_{16}H_{18}O_2N_2$)
D + $SnCl_2$ $\longrightarrow$ E ($C_8H_{11}ON$)
E + acetyl chloride $\longrightarrow$ *phenacetin* ($C_{10}H_{13}O_2N$), an analgesic ("pain-killer") and antipyretic ("fever-killer")

(b) β-(*o*-hydroxyphenyl)ethyl alcohol + HBr $\longrightarrow$ F (C_8H_9OBr)
F + KOH $\longrightarrow$ *coumarane* (C_8H_8O), insoluble in NaOH

(c) phenol + $ClCH_2COOH$ + NaOH (aq), then HCl $\longrightarrow$ G ($C_8H_8O_3$)
G + $SOCl_2$ $\longrightarrow$ H ($C_8H_7O_2Cl$)
H + $AlCl_3$ $\longrightarrow$ *3-cumaranone* ($C_8H_6O_2$)

(d) *p*-cymene (*p*-isopropyltoluene) + conc. H_2SO_4 $\longrightarrow$ I + J (both $C_{10}H_{14}O_3S$)
I + KOH + heat, then H^+ $\longrightarrow$ *carvacrol* ($C_{10}H_{14}O$), found in some essential oils
J + KOH + heat, then H^+ $\longrightarrow$ *thymol* ($C_{10}H_{14}O$), from oil of thyme
I + HNO_3 $\longrightarrow$ K ($C_8H_8O_5S$)
p-toluic acid + fuming sulfuric acid $\longrightarrow$ K

(e) anethole (p. 791) + HBr $\longrightarrow$ L ($C_{10}H_{13}OBr$)
L + Mg $\longrightarrow$ M ($C_{20}H_{26}O_2$)
M + HBr, heat $\longrightarrow$ *hexestrol* ($C_{18}H_{22}O_2$), a synthetic estrogen (female sex hormone)

17. The adrenal hormone (−)-*adrenaline* was the first hormone isolated and the first synthesized. Its structure was proved by the following synthesis:

catechol + $ClCH_2COCl$ $\xrightarrow{POCl_3}$ N ($C_8H_7O_3Cl$)
N + CH_3NH_2 $\longrightarrow$ O ($C_9H_{11}O_3N$)
O + H_2, Pd $\longrightarrow$ (±)-adrenaline ($C_9H_{13}O_3N$)
N + NaOI, then H^+ $\longrightarrow$ 3,4-dihydroxybenzoic acid

What is the structure of adrenaline?

18. (−)-*Phellandral*, $C_{10}H_{16}O$, is a terpene found in eucalyptus oils. It is oxidized by Tollens' reagent to (−)-phellandric acid, $C_{10}H_{16}O_2$, which readily absorbs only one mole of hydrogen, yielding dihydrophellandric acid. $C_{10}H_{18}O_2$. (±)-Phellandral has been synthesized as follows:

isopropylbenzene + H_2SO_4 + SO_3 $\longrightarrow$ P ($C_9H_{12}O_3S$)
P + KOH, fuse $\longrightarrow$ Q ($C_9H_{12}O$)
Q + H_2, Ni $\longrightarrow$ R ($C_9H_{18}O$)
R + $K_2Cr_2O_7$, H_2SO_4 $\longrightarrow$ S ($C_9H_{16}O$)
S + KCN + H^+ $\longrightarrow$ T ($C_{10}H_{17}ON$)
T + acetic anhydride $\longrightarrow$ U ($C_{12}H_{19}O_2N$)
U + heat (600°) $\longrightarrow$ V ($C_{10}H_{15}N$) + CH_3COOH
V + H_2SO_4 + H_2O $\longrightarrow$ W ($C_{10}H_{16}O_2$)
W + $SOCl_2$ $\longrightarrow$ X ($C_{10}H_{15}OCl$)
X $\xrightarrow{\text{reduction}}$ (±)-phellandral

(a) What is the most likely structure of phellandral? (b) Why is synthetic phellandral optically inactive? At what stage in the synthesis does inactivity of this sort first appear? (c) Dihydrophellandric acid is actually a mixture of two optically inactive isomers. Give the structures of these isomers and account for their optical inactivity.

19. Compound Y, C_7H_8O, is insoluble in water, dilute HCl, and aqueous $NaHCO_3$; it dissolves in dilute NaOH. When Y is treated with bromine water it is converted rapidly into a compound of formula $C_7H_5OBr_3$. What is the structure of Y?

20. Two isomeric compounds, Z and AA, are isolated from oil of bay leaf; both are found to have the formula $C_{10}H_{12}O$. Both are insoluble in water, dilute acid, and

dilute base. Both give positive tests with dilute $KMnO_4$ and Br_2/CCl_4. Upon vigorous oxidation, both yield anisic acid, *p*-$CH_3OC_6H_4COOH$.

(a) At this point what structures are possible for Z and AA?
(b) Catalytic hydrogenation converts Z and AA into the same compound, $C_{10}H_{14}O$. Now what structures are possible for Z and AA?
(c) Describe chemical procedures (other than synthesis) by which you could assign structures to Z and AA.
(d) Compound Z can be synthesized as follows:

p-bromoanisole + Mg + ether, then allyl bromide $\longrightarrow$ Z

What is the structure of Z?
(e) Z is converted into AA when heated strongly with concentrated base. What is the most likely structure for AA?
(f) Suggest a synthetic sequence starting with *p*-bromoanisole that would independently confirm the structure assigned to AA.

21. Compound BB ($C_{10}H_{12}O_3$) was insoluble in water, dilute HCl, and dilute aqueous $NaHCO_3$; it was soluble in dilute NaOH. A solution of BB in dilute NaOH was boiled, and the distillate was collected in a solution of NaOI, where a yellow precipitate formed.

The alkaline residue in the distillation flask was acidified with dilute H_2SO_4; a solid, CC, precipitated. When this mixture was boiled, CC steam-distilled and was collected. CC was found to have the formula $C_7H_6O_3$; it dissolved in aqueous $NaHCO_3$ with evolution of a gas.

(a) Give structures and names for BB and CC. (b) Write complete equations for all the above reactions.

22. *Chavibetol*, $C_{10}H_{12}O_2$, is found in betel-nut leaves. It is soluble in aqueous NaOH but not in aqueous $NaHCO_3$.

Treatment of chavibetol (a) with methyl sulfate and aqueous NaOH gives compound DD, $C_{11}H_{14}O_2$; (b) with hot hydriodic acid gives methyl iodide; (c) with hot concentrated base gives compound EE, $C_{10}H_{12}O_2$.

Compound DD is insoluble in aqueous NaOH, and readily decolorizes dilute $KMnO_4$ and Br_2/CCl_4. Treatment of DD with hot concentrated base gives FF, $C_{11}H_{14}O_2$.

Ozonolysis of EE gives a compound that is isomeric with vanillin (p. 792).

Ozonolysis of FF gives a compound that is identical with the one obtained from the treatment of vanillin with methyl sulfate.

What is the structure of chavibetol?

23. *Piperine*, $C_{17}H_{19}O_3N$, is an alkaloid found in black pepper. It is insoluble in water, dilute acid, and dilute base. When heated with aqueous alkali, it yields *piperic acid*, $C_{12}H_{10}O_4$, and the cyclic secondary amine *piperidine* (see Sec. 31.12), $C_5H_{11}N$.

Piperic acid is insoluble in water, but soluble in aqueous NaOH and aqueous $NaHCO_3$. Titration gives an equivalent weight of 215 ± 6. It reacts readily with Br_2/CCl_4, without evolution of HBr, to yield a compound of formula $C_{12}H_{10}O_4Br_4$. Careful oxidation of piperic acid yields *piperonylic acid*, $C_8H_6O_4$, and *tartaric acid*, HOOCCHOHCHOHCOOH.

When piperonylic acid is heated with aqueous HCl at 200° it yields formaldehyde and *protocatechuic acid*, 3,4-dihydroxybenzoic acid.

(a) What kind of compound is piperine? (b) What is the structure of piperonylic acid? Of piperic acid? Of piperine?

(c) Does the following synthesis confirm your structure?

catechol + $CHCl_3$ + NaOH $\longrightarrow$ GG ($C_7H_6O_3$)
GG + CH_2I_2 + NaOH $\longrightarrow$ HH ($C_8H_6O_3$)
HH + CH_3CHO + NaOH $\longrightarrow$ II ($C_{10}H_8O_3$)
II + acetic anhydride + sodium acetate $\longrightarrow$ piperic acid ($C_{12}H_{10}O_4$)
piperic acid + PCl_5 $\longrightarrow$ JJ ($C_{12}H_9O_3Cl$)
JJ + piperidine $\longrightarrow$ piperine

24. *Hordinene*, $C_{10}H_{15}ON$, is an alkaloid found in germinating barley. It is soluble in dilute HCl and in dilute NaOH; it reprecipitates from the alkaline solution when CO_2 is bubbled in. It reacts with benzenesulfonyl chloride to yield a product KK that is soluble in dilute acids.

When hordinene is treated with methyl sulfate and base, a product, LL, is formed. When LL is oxidized by alkaline $KMnO_4$, there is obtained anisic acid, *p*-$CH_3OC_6H_4$-COOH. When LL is heated strongly there is obtained *p*-methoxystyrene.

(a) What structure or structures are consistent with this evidence? (b) Outline a synthesis or syntheses that would prove the structure of hordinene.

25. The structure of the terpene *α-terpineol* (found in oils of cardamom and marjoram) was proved in part by the following synthesis:

p-toluic acid + fuming sulfuric acid $\longrightarrow$ MM ($C_8H_8O_5S$)
MM + KOH $\xrightarrow{\text{fusion}}$ NN ($C_8H_8O_3$)
NN + Na, alcohol $\longrightarrow$ OO ($C_8H_{14}O_3$)
OO + HBr $\longrightarrow$ PP ($C_8H_{13}O_2Br$)
PP + base, heat $\longrightarrow$ QQ ($C_8H_{12}O_2$)
QQ + C_2H_5OH, HCl $\longrightarrow$ RR ($C_{10}H_{16}O_2$)
RR + CH_3MgI, then H_2O $\longrightarrow$ α-terpineol ($C_{10}H_{18}O$)

What is the most likely structure for α-terpineol?

26. *Coniferyl alcohol*, $C_{10}H_{12}O_3$, is obtained from the sap of conifers. It is soluble in aqueous NaOH but not in aqueous $NaHCO_3$.

Treatment of coniferyl alcohol (a) with benzoyl chloride and pyridine gives compound SS, $C_{24}H_{20}O_5$; (b) with cold HBr gives $C_{10}H_{11}O_2Br$; (c) with hot hydriodic acid gives a volatile compound identified as methyl iodide; (d) with methyl iodide and aqueous base gives compound TT, $C_{11}H_{14}O_3$.

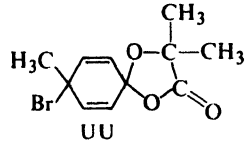
Both SS and TT are insoluble in dilute NaOH, and rapidly decolorize dilute $KMnO_4$ and Br_2/CCl_4.

Ozonolysis of coniferyl alcohol gives vanillin.

What is the structure of coniferyl alcohol?

Write equations for all the above reactions.

27. When α-(*p*-tolyloxy)isobutyric acid (prepared from *p*-cresol) is treated with Br_2, there is obtained UU.



UU

(a) To what class of compounds does UU belong? Suggest a mechanism for its formation.

(b) Give structural formulas for compounds VV, WW, and XX.

UU + $AgNO_3$, CH_3OH $\longrightarrow$ VV ($C_{12}H_{16}O_4$)
VV + H_2, Rh $\longrightarrow$ WW ($C_{12}H_{20}O_4$)
WW + H_2O, OH^- $\longrightarrow$ XX ($C_8H_{14}O$)

(c) The reactions outlined in (b) can be varied. Of what general synthetic utility do you think this general process might be?

28. Compounds AAA–FFF are phenols or related compounds whose structures are given in Problem 19, p. 650, or Sec. 24.4. Assign a structure to each one on the basis of infrared and/or nmr spectra shown as follows.

AAA, BBB, and CCC: infrared spectra in Fig. 24.3 (p. 812)
nmr spectra in Fig. 24.4 (p. 813)
DDD: nmr spectrum in Fig. 24.5 (p. 814)
EEE and FFF: infrared spectra in Fig. 24.6 (p. 814)

(*Hint:* After you have worked out some of the structures, compare infrared spectra.)