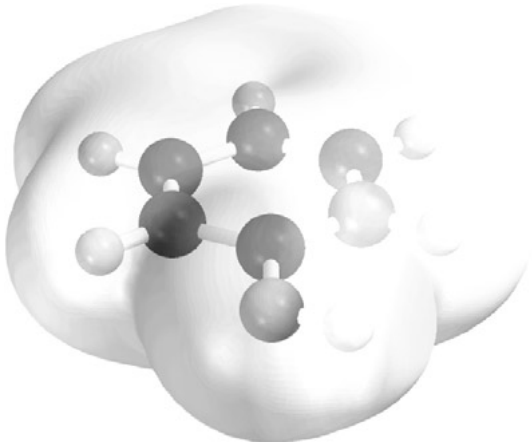
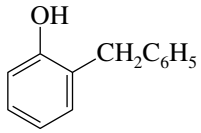


CHAPTER 24

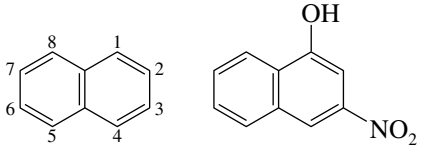
PHENOLS

SOLUTIONS TO TEXT PROBLEMS

24.1 (*b*) A benzyl group ($C_6H_5CH_2$—) is ortho to the phenolic hydroxyl group in *o*-benzylphenol.

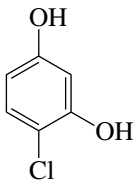


(*c*) Naphthalene is numbered as shown. 3-Nitro-1-naphthol has a hydroxyl group at C-1 and a nitro group at C-3.

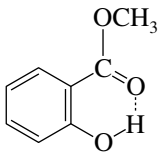


Naphthalene 3-Nitro-1-naphthol

(*d*) Resorcinol is 1,3-benzenediol. 4-Chlororesorcinol is therefore



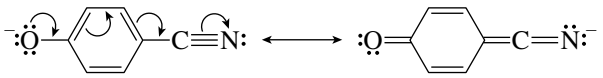
24.2 Intramolecular hydrogen bonding between the hydroxyl group and the ester carbonyl can occur when these groups are ortho to each other.



Methyl salicylate

Intramolecular hydrogen bonds form at the expense of intermolecular ones, and intramolecularly hydrogen-bonded phenols have lower boiling points than isomers in which only intermolecular hydrogen-bonding is possible.

24.3 (*b*) A cyano group withdraws electrons from the ring by resonance. A *p*-cyano substituent is conjugated directly with the negatively charged oxygen and stabilizes the anion more than does an *m*-cyano substituent.

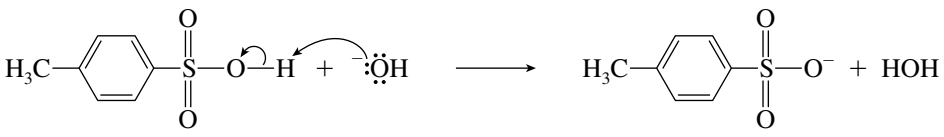


p-Cyanophenol is slightly more acidic than *m*-cyanophenol, the K_a values being 1.0×10^{-8} and 2.8×10^{-9}, respectively.

(*c*) The electron-withdrawing inductive effect of the fluorine substituent will be more pronounced at the ortho position than at the para. *o*-Fluorophenol ($K_a = 1.9 \times 10^{-9}$) is a stronger acid than *p*-fluorophenol ($K_a = 1.3 \times 10^{-10}$).

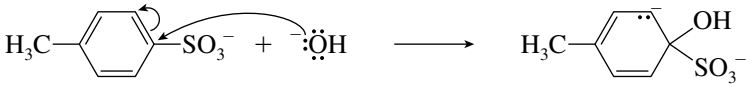
24.4 The text points out that the reaction proceeds by the addition–elimination mechanism of nucleophilic aromatic substitution.

Under the strongly basic conditions of the reaction, *p*-toluenesulfonic acid is first converted to its anion.



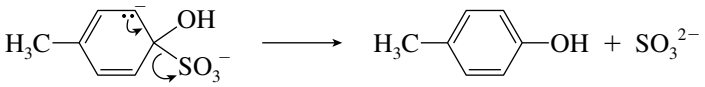
p-Toluenesulfonic acid | Hydroxide ion | *p*-Toluenesulfonate ion | Water

Nucleophilic addition of hydroxide ion gives a cyclohexadienyl anion intermediate.



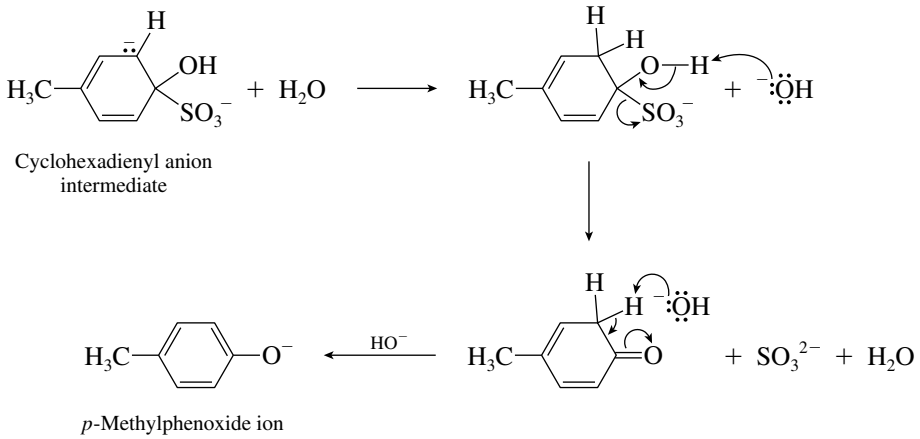
p-Toluenesulfonate ion | Hydroxide | Cyclohexadienyl anion

Loss of sulfite ion (SO_3^{2-}) gives *p*-cresol.

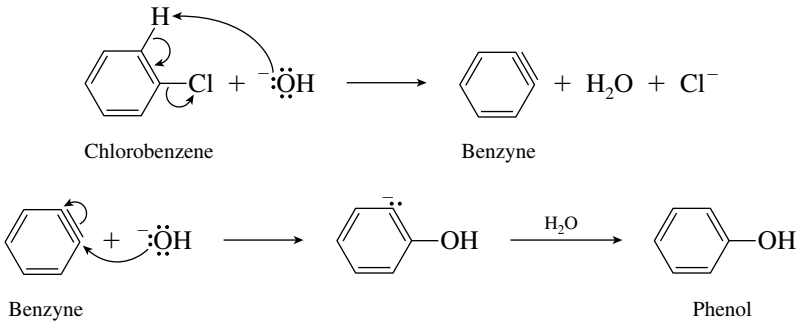


Cyclohexadienyl anion | *p*-Cresol

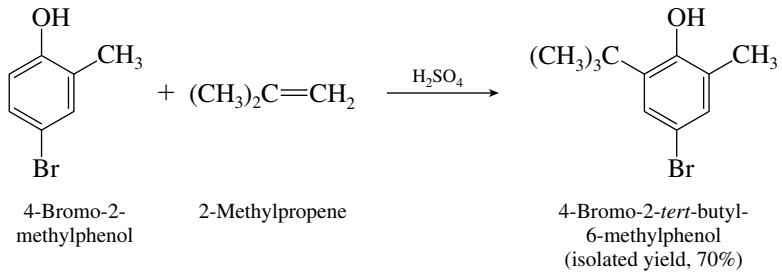
It is also possible that the elimination stage of the reaction proceeds as follows:



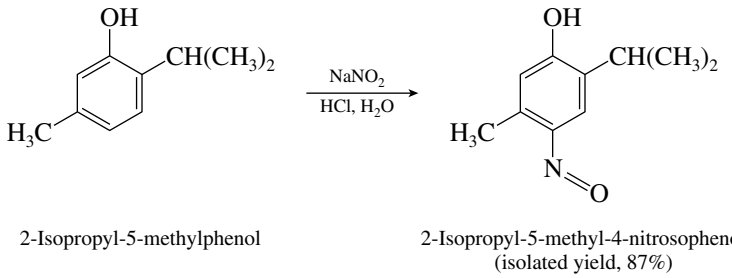
24.5 The text states that the hydrolysis of chlorobenzene in base follows an elimination–addition mechanism.



24.6 (*b*) The reaction is Friedel–Crafts alkylation. Proton transfer from sulfuric acid to 2-methylpropene gives *tert*-butyl cation. Because the position para to the hydroxyl substituent already bears a bromine, the *tert*-butyl cation attacks the ring at the position ortho to the hydroxyl.



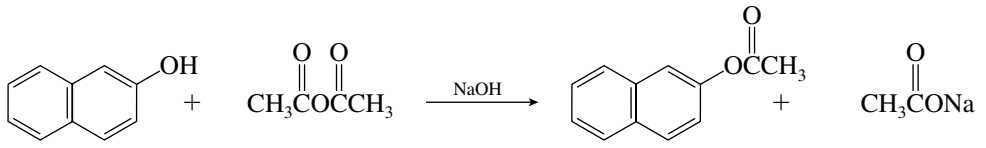
(*c*) Acidification of sodium nitrite produces nitrous acid, which nitrosates the strongly activated aromatic ring of phenols.



(*d*) Friedel–Crafts acylation occurs ortho to the hydroxyl group.

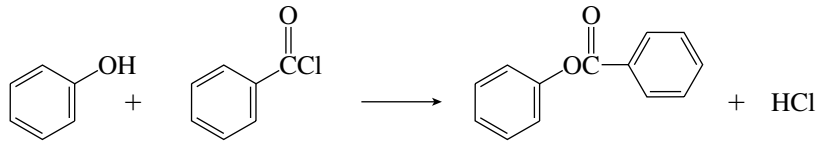
p-Cresol | Propanoyl chloride | 1-(2-Hydroxy-5-methylphenyl)-1-propanone (isolated yield, 87%)

24.7 (*b*) The hydroxyl group of 2-naphthol is converted to the corresponding acetate ester.



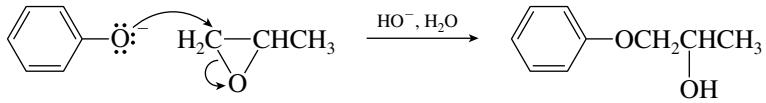
2-Naphthol | Acetic anhydride | 2-Naphthyl acetate | Sodium acetate

(*c*) Benzoyl chloride acylates the hydroxyl group of phenol.



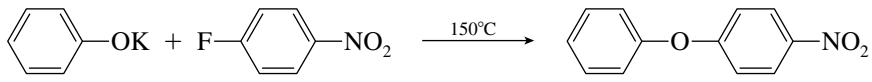
Phenol | Benzoyl chloride | Phenyl benzoate | Hydrogen chloride

24.8 Epoxides are sensitive to nucleophilic ring-opening reactions. Phenoxide ion attacks the less hindered carbon to yield 1-phenoxy-2-propanol.



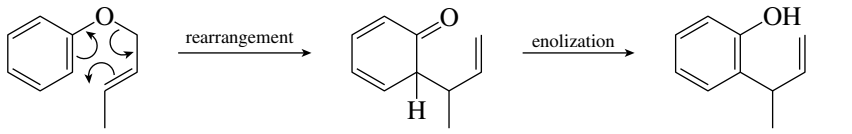
Phenoxide ion | 1,2-Epoxypropane | 1-Phenoxy-2-propanol

24.9 The aryl halide must be one that is reactive toward nucleophilic aromatic substitution by the addition–elimination mechanism. *p*-Fluoronitrobenzene is far more reactive than fluorobenzene. The reaction shown yields *p*-nitrophenyl phenyl ether in 92% yield.



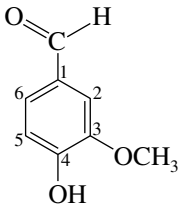
Potassium phenoxide | *p*-Fluoronitrobenzene | *p*-Nitrophenyl phenyl ether

24.10 Substituted allyl aryl ethers undergo a Claisen rearrangement similar to the reaction described in text Section 24.13 for allyl phenyl ether. 2-Butenyl phenyl ether rearranges on heating to give *o*-(1-methyl-2-propenyl)phenol.



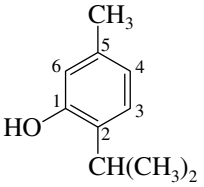
2-Butenyl phenyl ether | *o*-(1-Methyl-2-propenyl)-phenol

24.11 (*a*) The parent compound is benzaldehyde. Vanillin bears a methoxy group (CH_3O) at C-3 and a hydroxyl group (HO) at C-4.

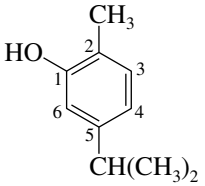


Vanillin
(4-hydroxy-3-methoxybenzaldehyde)

(*b*, *c*) Thymol and carvacrol differ with respect to the position of the hydroxyl group.

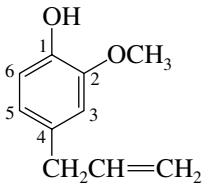


Thymol
(2-isopropyl-5-methylphenol)



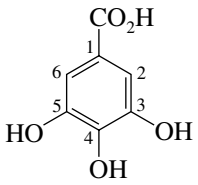
Carvacrol
(5-isopropyl-2-methylphenol)

(*d*) An allyl substituent is $—CH_2CH═CH_2$.



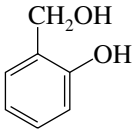
Eugenol
(4-allyl-2-methoxyphenol)

(*e*) Benzoic acid is $C_6H_5CO_2H$. Gallic acid bears three hydroxyl groups, located at C-3, C-4, and C-5.



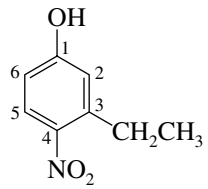
Gallic acid
(3,4,5-trihydroxybenzoic acid)

(*f*) Benzyl alcohol is $C_6H_5CH_2OH$. Salicyl alcohol bears a hydroxyl group at the ortho position.



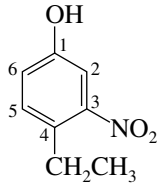
Salicyl alcohol
(*o*-hydroxybenzyl alcohol)

24.12 (*a*) The compound is named as a derivative of phenol. The substituents (ethyl and nitro) are cited in alphabetical order with numbers assigned in the direction that gives the lowest number at the first point of difference.



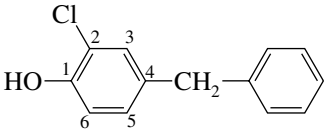
3-Ethyl-4-nitrophenol

(*b*) An isomer of the compound in part (*a*) is 4-ethyl-3-nitrophenol.



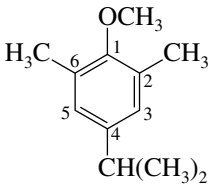
4-Ethyl-3-nitrophenol

(*c*) The parent compound is phenol. It bears, in alphabetical order, a benzyl group at C-4 and a chlorine at C-2.



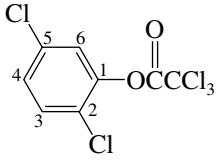
4-Benzyl-2-chlorophenol

(*d*) This compound is named as a derivative of anisole, $C_6H_5OCH_3$. Because multiplicative prefixes (di, tri-, etc.) are not considered when alphabetizing substituents, isopropyl precedes dimethyl.



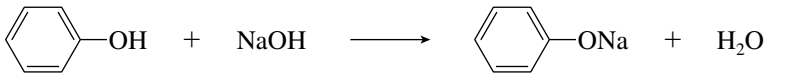
4-Isopropyl-2,6-dimethylanisole

(*e*) The compound is an aryl ester of trichloroacetic acid. The aryl group is 2,5-dichlorophenyl.



2,5-Dichlorophenyl trichloroacetate

24.13 (*a*) The reaction is an acid–base reaction. Phenol is the acid; sodium hydroxide is the base.

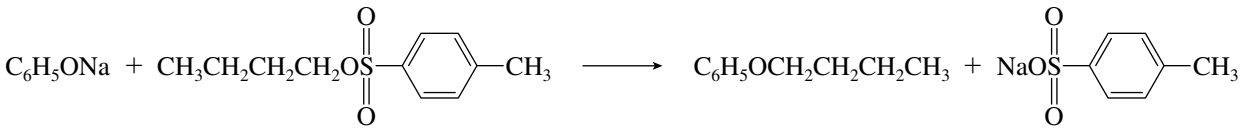


Phenol (stronger acid) | Sodium hydroxide (stronger base) | Sodium phenoxide (weaker base) | Water (weaker acid)

(*b*) Sodium phenoxide reacts with ethyl bromide to yield ethyl phenyl ether in a Williamson reaction. Phenoxide ion acts as a nucleophile.

Sodium phenoxide | Ethyl bromide | Ethyl phenyl ether | Sodium bromide

(*c*) *p*-Toluenesulfonate esters behave much like alkyl halides in nucleophilic substitution reactions. Phenoxide ion displaces *p*-toluenesulfonate from the primary carbon.

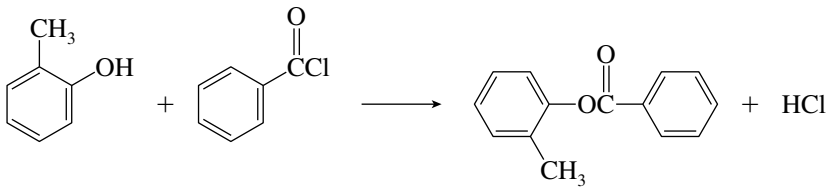


Sodium phenoxide | Butyl *p*-toluenesulfonate | Butyl phenyl ether | Sodium *p*-toluenesulfonate

(*d*) Carboxylic acid anhydrides react with phenoxide anions to yield aryl esters.

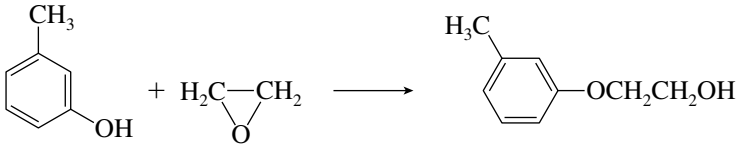
Sodium phenoxide | Acetic anhydride | Phenyl acetate | Sodium acetate

(*e*) Acyl chlorides convert phenols to aryl esters.



o-Cresol | Benzoyl chloride | 2-Methylphenyl benzoate | Hydrogen chloride

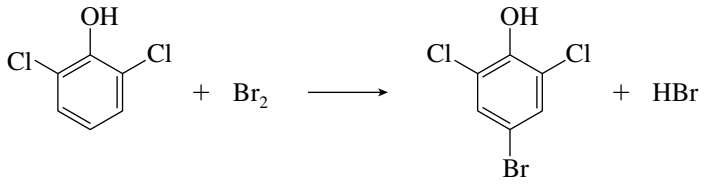
(*f*) Phenols react as nucleophiles toward epoxides.



m-Cresol | Ethylene oxide | 2-(3-Methylphenoxy)ethanol

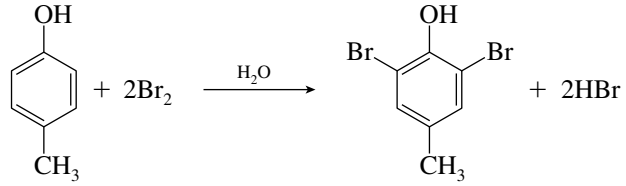
The reaction as written conforms to the requirements of the problem that a balanced equation be written. Of course, the reaction will be much faster if catalyzed by acid or base, but the catalysts do not enter into the equation representing the overall process.

(*g*) Bromination of the aromatic ring of 2,6-dichlorophenol occurs para to the hydroxy group. The more activating group (—OH) determines the orientation of the product.



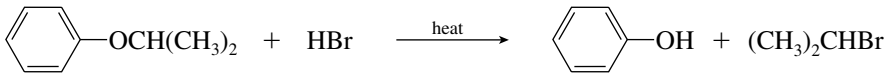
2,6-Dichlorophenol — Bromine — 4-Bromo-2,6-dichlorophenol — Hydrogen bromide

(*h*) In aqueous solution bromination occurs at all the open positions that are ortho and para to the hydroxyl group.



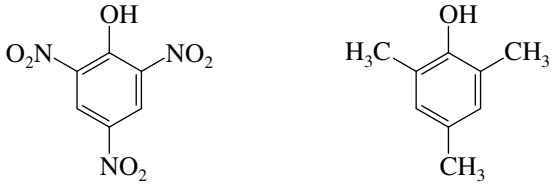
p-Cresol — Bromine — 2,6-Dibromo-4-methylphenol — Hydrogen bromide

(*i*) Hydrogen bromide cleaves ethers to give an alkyl halide and a phenol.



Isopropyl phenyl ether — Hydrogen bromide — Phenol — Isopropyl bromide

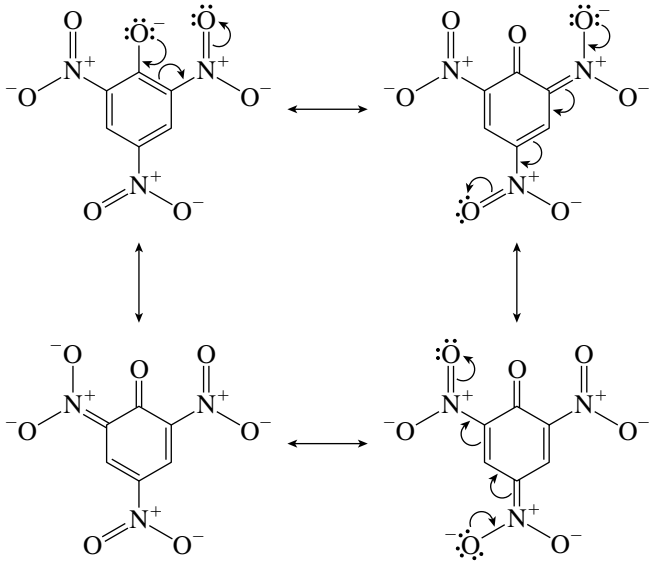
24.14 (*a*) Strongly electron-withdrawing groups, particularly those such as —NO_2, increase the acidity of phenols by resonance stabilization of the resulting phenoxide anion. Electron-releasing substituents such as —CH_3 exert a very small acid-weakening effect.



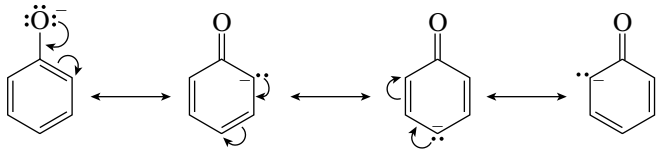
2,4,6-Trinitrophenol, more acidic ($K_a = 3.8 \times 10^{-1}$, $pK_a = 0.4$)

2,4,6-Trimethylphenol, less acidic ($K_a = 1.3 \times 10^{-11}$, $pK_a = 10.9$)

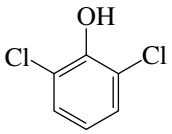
Picric acid (2,4,6-trinitrophenol) is a stronger acid by far than 2,4,6-trimethylphenol. All three nitro groups participate in resonance stabilization of the picrate anion.



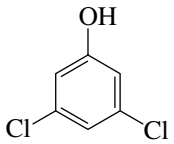
(*b*) Stabilization of a phenoxide anion is most effective when electron-withdrawing groups are present at the ortho and para positions, because it is these carbons that bear most of the negative charge in phenoxide anion.



2,6-Dichlorophenol is therefore expected to be (and is) a stronger acid than 3,5-dichlorophenol.

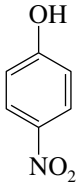


2,6-Dichlorophenol, more acidic
($K_a = 1.6 \times 10^{-7}$, $pK_a = 6.8$)

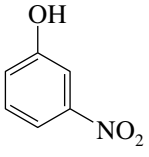


3,5-Dichlorophenol, less acidic
($K_a = 6.5 \times 10^{-9}$, $pK_a = 8.2$)

(*c*) The same principle is at work here as in part (*b*). A nitro group para to the phenol oxygen is directly conjugated to it and stabilizes the anion better than one at the meta position.



4-Nitrophenol, stronger acid
($K_a = 1.0 \times 10^{-8}$, $pK_a = 7.2$)



3-Nitrophenol, weaker acid
($K_a = 4.1 \times 10^{-9}$, $pK_a = 8.4$)

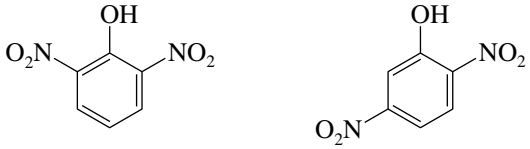
(*d*) A cyano group is strongly electron-withdrawing, and so 4-cyanophenol is a stronger acid than phenol.

4-Cyanophenol, more acidic ($K_a = 1.1 \times 10^{-8}$, $pK_a = 8.0$)

Phenol, less acidic ($K_a = 1 \times 10^{-10}$, $pK_a = 10$)

There is resonance stabilization of the 4-cyanophenoxide anion.

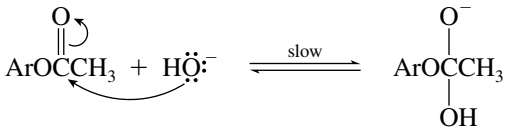
(*e*) The 5-nitro group in 2,5-dinitrophenol is meta to the hydroxyl group and so does not stabilize the resulting anion as much as does an ortho or a para nitro group.



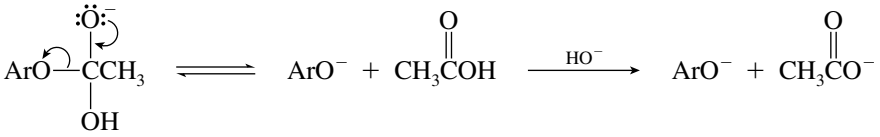
2,6-Dinitrophenol, more acidic ($K_a = 2.0 \times 10^{-4}$, $pK_a = 3.7$)

2,5-Dinitrophenol, less acidic ($K_a = 6.0 \times 10^{-6}$, $pK_a = 5.2$)

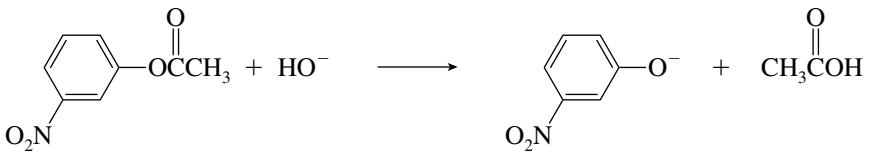
24.15 (*a*) The rate-determining step of ester hydrolysis in basic solution is formation of the tetrahedral intermediate.



Because this intermediate is negatively charged, there will be a small effect favoring its formation when the aryl group bears an electron-withdrawing substituent. Furthermore, this intermediate can either return to starting materials or proceed to products.



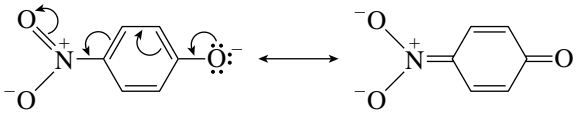
The proportion of the tetrahedral intermediate that goes on to products increases as the leaving group ArO^- becomes less basic. This is strongly affected by substituents; electron-withdrawing groups stabilize ArO^-. The prediction is that *m*-nitrophenyl acetate undergoes hydrolysis in basic solution faster than phenol. Indeed, this is observed to be the case; *m*-nitrophenyl acetate reacts some ten times faster than does phenyl acetate at 25°C.



m-Nitrophenyl acetate (more reactive)

m-Nitrophenoxide anion (a better leaving group than phenoxide because it is less basic)

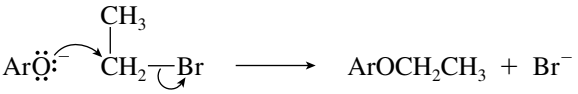
(*b*) The same principle applies here as in part (*a*). *p*-Nitrophenyl acetate reacts faster than *m*-nitrophenyl acetate (by about 45%) largely because *p*-nitrophenoxide is less basic and thus a better leaving group than *m*-nitrophenoxide.



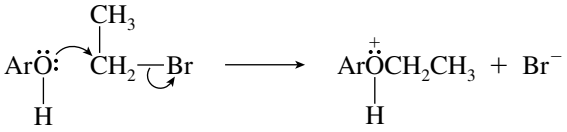
Resonance in *p*-nitrophenoxide is particularly effective because the *p*-nitro group is directly conjugated to the oxyanion; direct conjugation of these groups is absent in *m*-nitrophenoxide.

(*c*) The reaction of ethyl bromide with a phenol is an S_N2 reaction in which the oxygen of the phenol is the nucleophile. The reaction is much faster with sodium phenoxide than with phenol, because an anion is more nucleophilic than a corresponding neutral molecule.

Faster reaction:

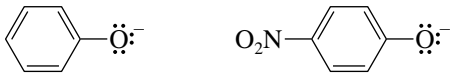


Slower reaction:



(*d*) The answer here also depends on the nucleophilicity of the attacking species, which is a phenoxide anion in both reactions.

The more nucleophilic anion is phenoxide ion, because it is more basic than *p*-nitrophenoxide.

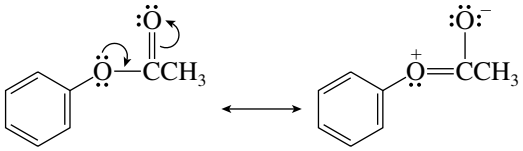


More basic; better nucleophile

Better delocalization of negative charge makes this less basic and less nucleophilic.

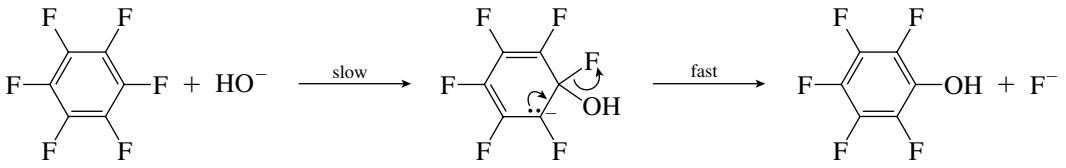
Rate measurements reveal that sodium phenoxide reacts 17 times faster with ethylene oxide (in ethanol at 70°C) than does its *p*-nitro derivative.

(*e*) This reaction is electrophilic aromatic substitution. Because a hydroxy substituent is more activating than an acetate group, phenol undergoes bromination faster than does phenyl acetate.



Resonance involving ester group reduces tendency of oxygen to donate electrons to ring.

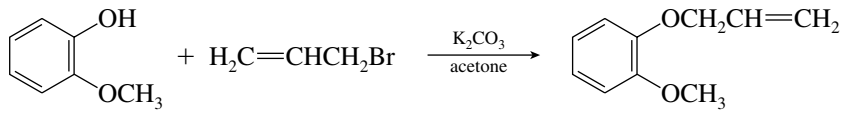
24.16 Nucleophilic aromatic substitution by the elimination–addition mechanism is impossible, owing to the absence of any protons that might be abstracted from the substrate. The addition–elimination pathway is available, however.



Hexafluorobenzene Pentafluorophenol

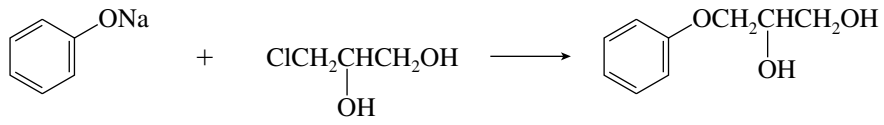
This pathway is favorable because the cyclohexadienyl anion intermediate formed in the rate-determining step is stabilized by the electron-withdrawing inductive effect of its fluorine substituents.

24.17 (*a*) Allyl bromide is a reactive alkylating agent and converts the free hydroxyl group of the aryl compound (a natural product known as *guaiacol*) to its corresponding allyl ether.



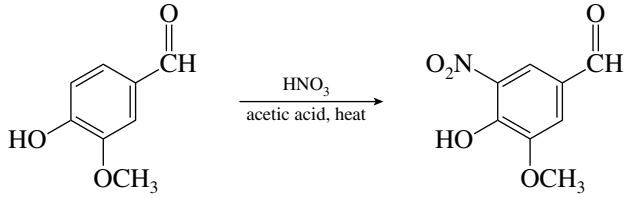
Guaiacol Allyl bromide 2-Allyloxyanisole (80–90%)

(*b*) Sodium phenoxide acts as a nucleophile in this reaction and is converted to an ether.



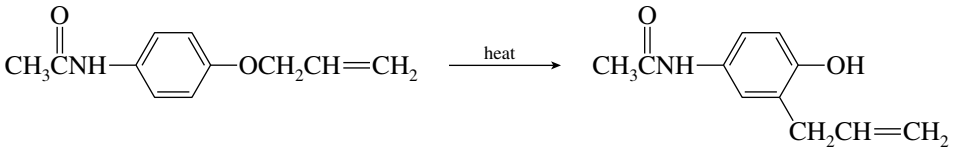
Sodium phenoxide 3-Chloro-1,2-propanediol 3-Phenoxy-1,2-propanediol (61–63%)

(*c*) Orientation in nitration is governed by the most activating substituent, in this case the hydroxyl group.



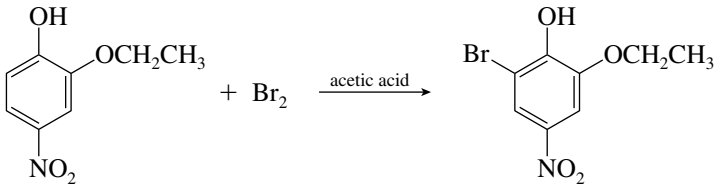
Vanillin 4-Hydroxy-3-methoxy-5-nitrobenzaldehyde (83%)

(*d*) Allyl aryl ethers undergo a Claisen rearrangement on heating. Heating *p*-acetamidophenyl allyl ether gave an 83% yield of 4-acetamido-2-allylphenol.



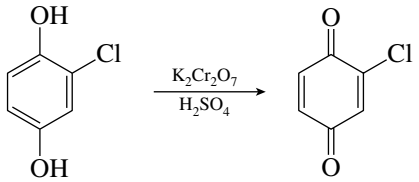
p-Acetamidophenyl allyl ether 4-Acetamido-2-allylphenol

(*e*) The hydroxyl group, as the most activating substituent, controls the orientation of electrophilic aromatic substitution. Bromination takes place ortho to the hydroxyl group.



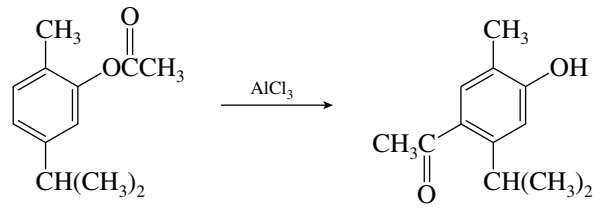
2-Ethoxy-4-nitrophenol — 2-Bromo-6-ethoxy-4-nitrophenol (65%)

(*f*) Oxidation of hydroquinone derivatives (*p*-dihydroxybenzenes) with Cr(VI) reagents is a method for preparing quinones.



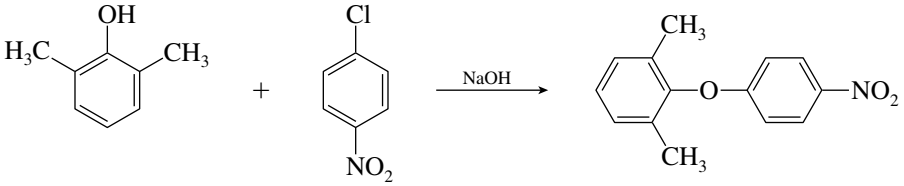
2-Chloro-1,4-benzenediol — 2-Chloro-1,4-benzoquinone (88%)

(*g*) Aryl esters undergo a reaction known as the **Fries rearrangement** on being treated with aluminum chloride, which converts them to acyl phenols. Acylation takes place para to the hydroxyl in this case.



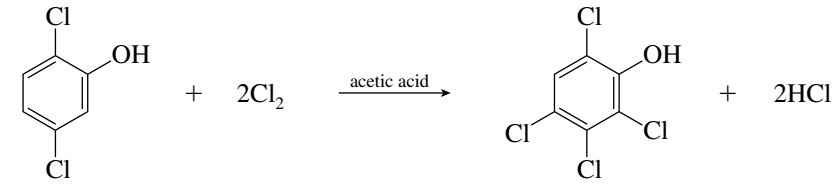
5-Isopropyl-2-methylphenyl acetate — 4-Hydroxy-2-isopropyl-5-methylacetophenone (90%)

(*h*) Nucleophilic aromatic substitution takes place to yield a diaryl ether. The nucleophile is the phenoxide ion derived from 2,6-dimethylphenol.



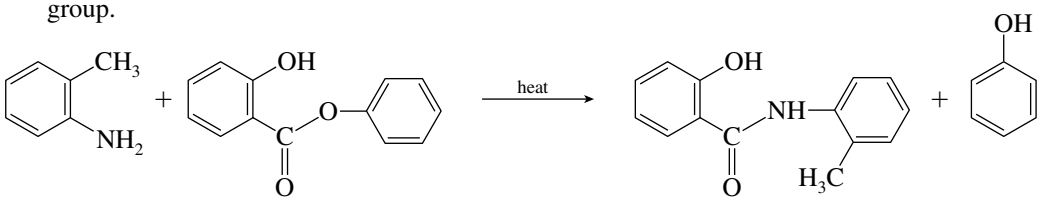
2,6-Dimethylphenol — *p*-Chloronitrobenzene — 2,6-Dimethylphenyl *p*-nitrophenyl ether (82%)

(*i*) Chlorination with excess chlorine occurs at all available positions that are ortho and para to the hydroxyl group.



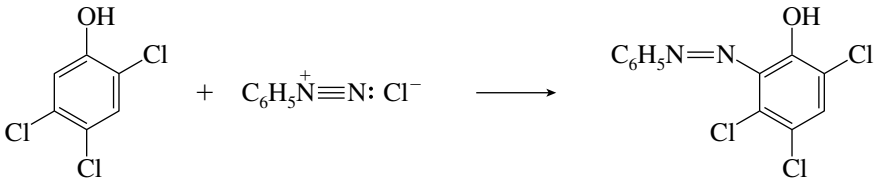
2,5-Dichlorophenol — Chlorine — 2,3,4,6-Tetrachlorophenol (isolated yield, 100%) — Hydrogen chloride

(*j*) Amines react with esters to give amides. In the case of a phenyl ester, phenol is the leaving group.



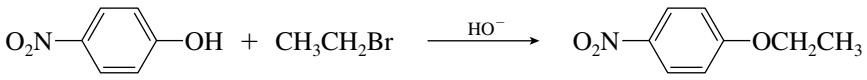
o-Methylaniline — Phenyl salicylate — *N*-(*o*-Methylphenyl)salicylamide (isolated yield, 73–77%) — Phenol

(*k*) Aryl diazonium salts attack electron-rich aromatic rings, such as those of phenols, to give the products of electrophilic aromatic substitution.



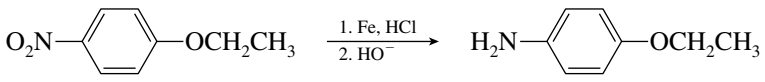
2,4,5-Trichlorophenol — Benzenediazonium chloride — 2-Benzeneazo-3,4,6-trichlorophenol (80%)

24.18 In the first step *p*-nitrophenol is alkylated on its phenolic oxygen with ethyl bromide.



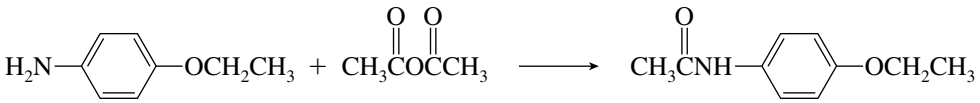
p-Nitrophenol — Ethyl bromide — Ethyl *p*-nitrophenyl ether

Reduction of the nitro group gives the corresponding arylamine.



Ethyl *p*-nitrophenyl ether — *p*-Ethoxyaniline

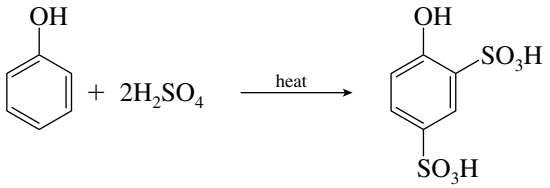
Treatment of *p*-ethoxyaniline with acetic anhydride gives phenacetin.



p-Ethoxyaniline — Acetic anhydride — *p*-Ethoxyacetanilide (phenacetin)

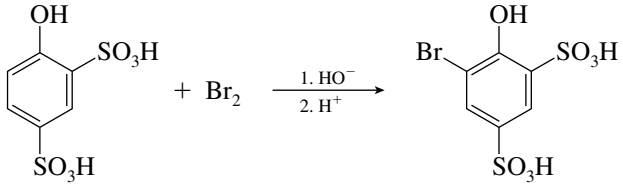
24.19 The three parts of this problem make up the series of steps by which *o*-bromophenol is prepared.

(*a*) Because direct bromination of phenol yields both *o*-bromophenol and *p*-bromophenol, it is essential that the para position be blocked prior to the bromination step. In practice, what is done is to disulfonate phenol, which blocks the para and one of the ortho positions.



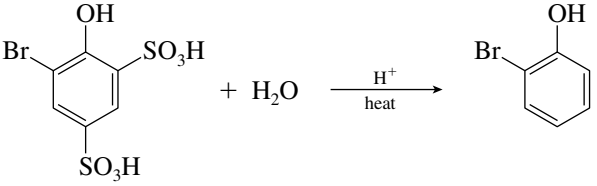
Phenol — 4-Hydroxy-1,3-benzenedisulfonic acid (compound A)

(*b*) Bromination then can be accomplished cleanly at the open position ortho to the hydroxyl group.



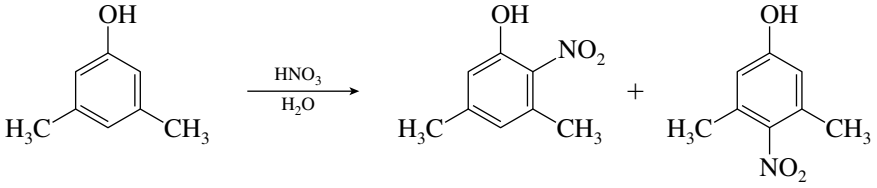
Compound A — 5-Bromo-4-hydroxy-1,3-benzenedisulfonic acid (compound B)

(*c*) After bromination the sulfonic acid groups are removed by acid-catalyzed hydrolysis.



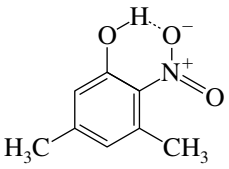
Compound B — *o*-Bromophenol (compound C)

24.20 Nitration of 3,5-dimethylphenol gives a mixture of the 2-nitro and 4-nitro derivatives.



3,5-Dimethylphenol — 3,5-Dimethyl-2-nitrophenol — 3,5-Dimethyl-4-nitrophenol

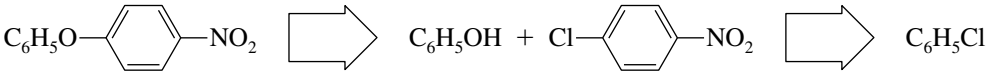
The more volatile compound (compound A), isolated by steam distillation, is the 2-nitro derivative. Intramolecular hydrogen bonding is possible between the nitro group and the hydroxyl group.



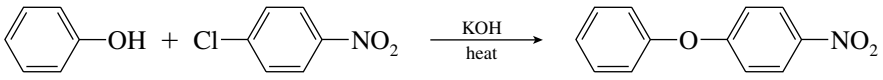
Intramolecular hydrogen bonding
in 3,5-dimethyl-2-nitrophenol

The 4-nitro derivative participates in intermolecular hydrogen bonds and has a much higher boiling point; it is compound B.

24.21 The relationship between the target molecule and the starting materials tells us that two processes are required, formation of a diaryl ether linkage and nitration of an aromatic ring. The proper order of carrying out these two separate processes is what needs to be considered.

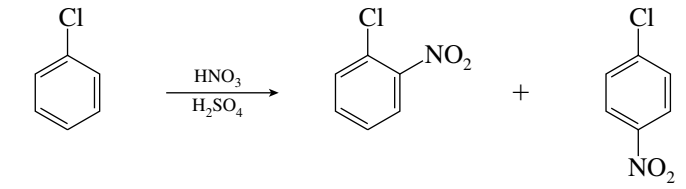


The critical step is ether formation, a step that is feasible for the reactants shown:



Phenol *p*-Chloronitrobenzene 4-Nitrophenyl phenyl ether

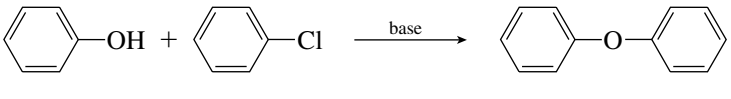
The reason this reaction is suitable is that it involves nucleophilic aromatic substitution by the addition–elimination mechanism on a *p*-nitro-substituted aryl halide. Indeed, this reaction has been carried out and gives an 80–82% yield. A reasonable synthesis would therefore begin with the preparation of *p*-chloronitrobenzene.



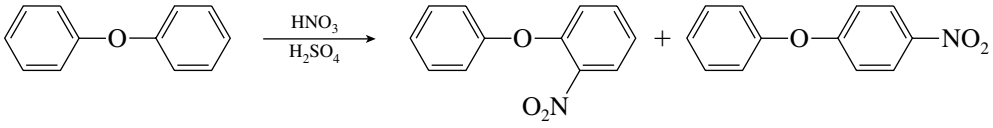
Chlorobenzene *o*-Chloronitrobenzene *p*-Chloronitrobenzene

Separation of the *p*-nitro-substituted aryl halide and reaction with phenoxide ion complete the synthesis.

The following alternative route is less satisfactory:



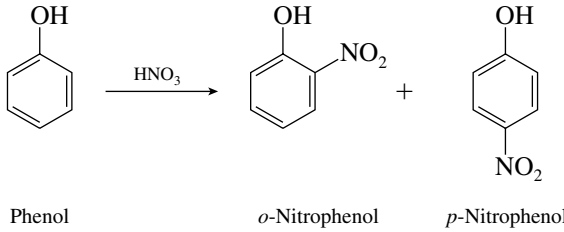
Phenol Chlorobenzene Diphenyl ether



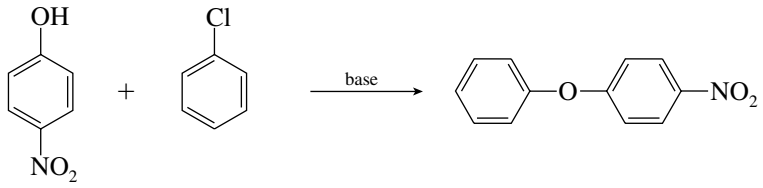
Diphenyl ether 2-Nitrophenyl phenyl ether 4-Nitrophenyl phenyl ether

The difficulty with this route concerns the preparation of diphenyl ether. Direct reaction of phenoxide ion with chlorobenzene is very slow and requires high temperatures because chlorobenzene is a poor substrate for nucleophilic substitution.

A third route is also unsatisfactory because it, too, requires nucleophilic substitution on chlorobenzene.

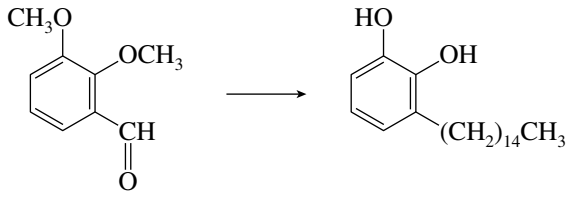


Phenol *o*-Nitrophenol *p*-Nitrophenol



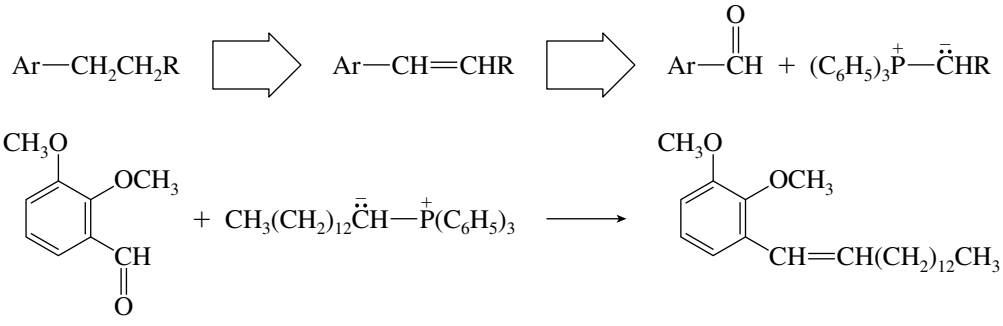
p-Nitrophenol Chlorobenzene 4-Nitrophenyl phenyl ether

24.22 The overall transformation that needs to be effected is



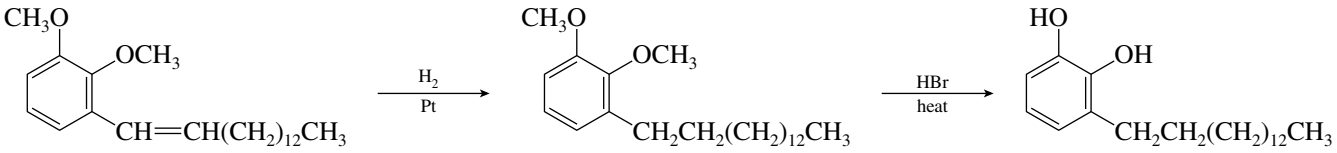
2,3-Dimethoxybenzaldehyde 3-Pentadecylcatechol

A reasonable place to begin is with the attachment of the side chain. The aldehyde function allows for chain extension by a Wittig reaction.



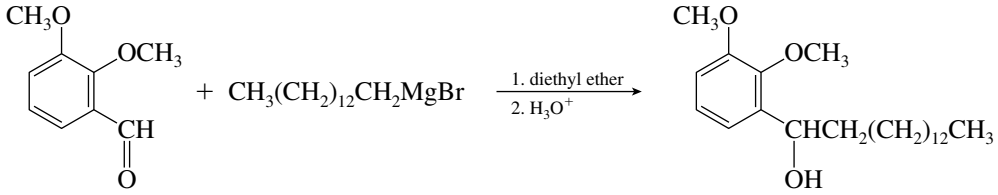
2,3-Dimethoxybenzaldehyde

Hydrogenation of the double bond and hydrogen halide cleavage of the ether functions complete the synthesis.



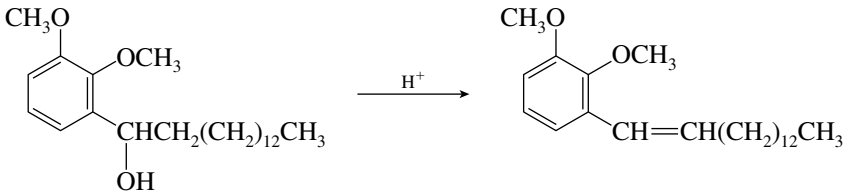
3-Pentadecylcatechol

Other synthetic routes are of course possible. One of the earliest approaches used a Grignard reaction to attach the side chain.



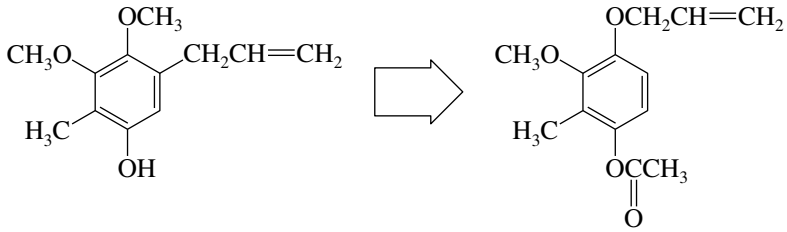
2,3-Dimethoxybenzaldehyde

The resulting secondary alcohol can then be dehydrated to the same alkene intermediate prepared in the preceding synthetic scheme.

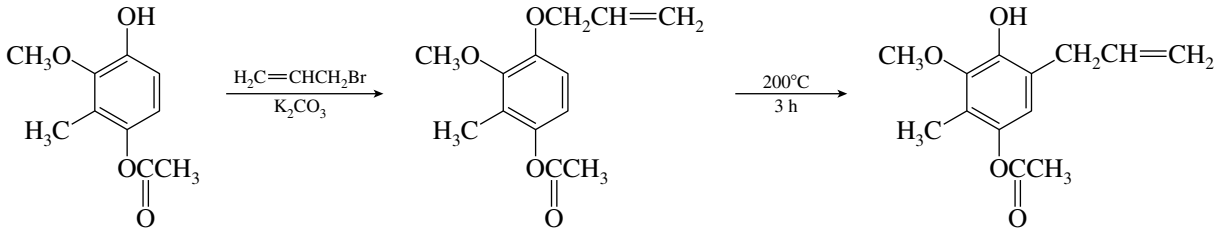


Again, hydrogenation of the double bond and ether cleavage leads to the desired 3-pentadecylcatechol.

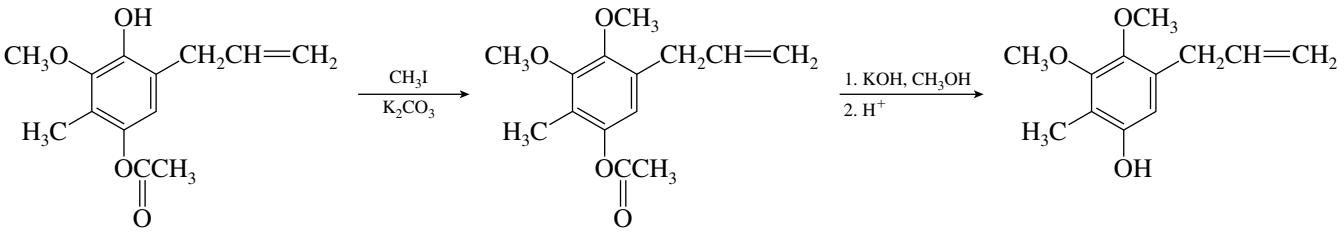
24.23 Recall that the Claisen rearrangement converts an aryl allyl ether to an ortho-substituted allyl phenol. The presence of an allyl substituent in the product ortho to an aryl ether thus suggests the following retrosynthesis:



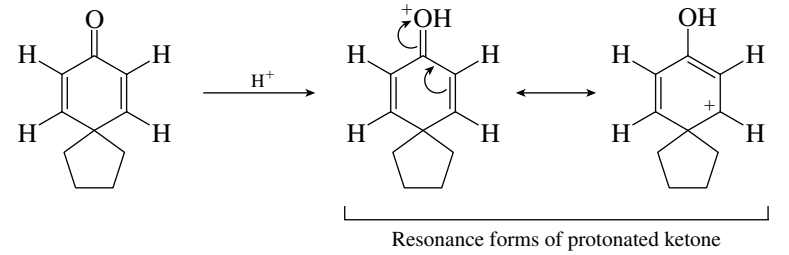
As reported in the literature synthesis, the starting phenol may be converted to the corresponding allyl ether by reaction with allyl bromide in the presence of base. This step was accomplished in 80% yield. Heating the allyl ether yields the *o*-allyl phenol.

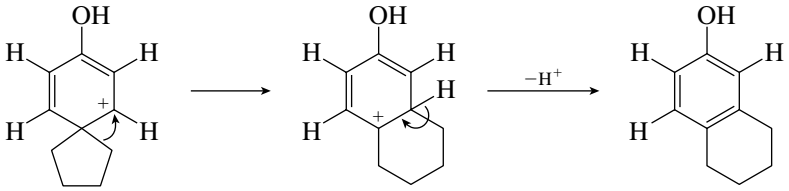


The synthesis is completed by methylation of the phenolic oxygen and saponification of the acetate ester. The final three steps of the synthesis proceeded in an 82% overall yield.



24.24 The driving force for this reaction is the stabilization that results from formation of the aromatic ring. A reasonable series of steps begins with protonation of the carbonyl oxygen.

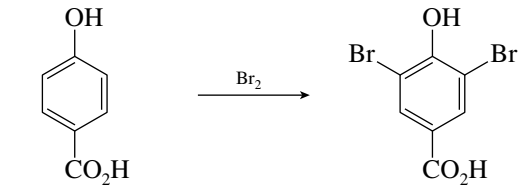




Protonated ketone can rearrange by alkyl migration.

Aromatization of this intermediate occurs by loss of a proton.

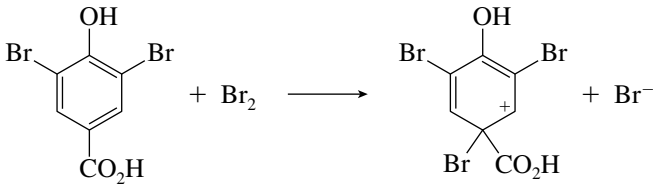
24.25 Bromination of *p*-hydroxybenzoic acid takes place in the normal fashion at both positions ortho to the hydroxy group.



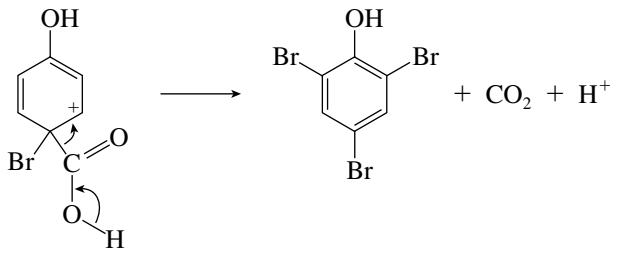
p-Hydroxybenzoic acid

3,5-Dibromo-4-hydroxybenzoic acid

A third bromination step, this time at the para position, leads to the intermediate shown.

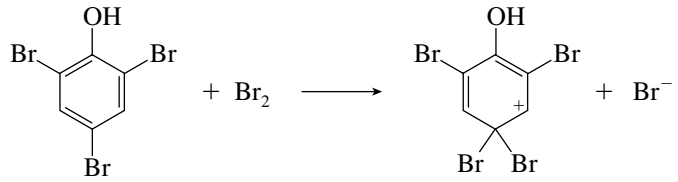


Aromatization of this intermediate occurs by decarboxylation.



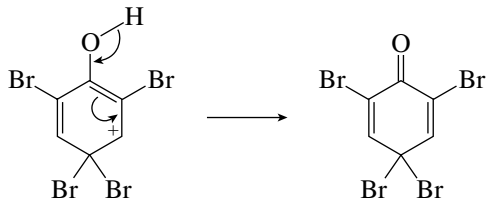
2,4,6-Tribromophenol

24.26 Electrophilic attack of bromine on 2,4,6-tribromophenol leads to a cationic intermediate.



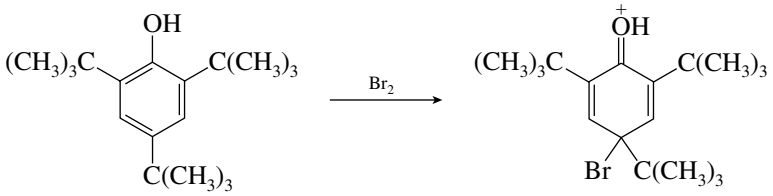
2,4,6-Tribromophenol

Loss of the hydroxyl proton from this intermediate generates the observed product.



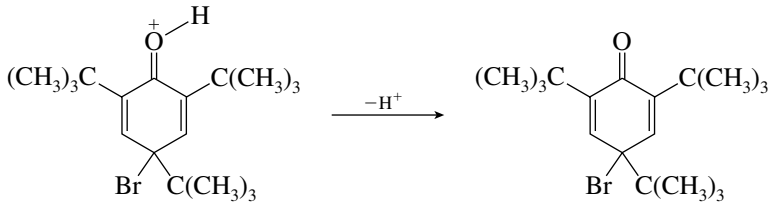
2,4,4,6-Tetrabromo-cyclohexadienone

24.27 A good way to approach this problem is to assume that bromine attacks the aromatic ring of the phenol in the usual way, that is, para to the hydroxyl group.



2,4,6-Tri-*tert*-butylphenol

This cation cannot yield the product of electrophilic aromatic substitution by loss of a proton from the ring but can lose a proton from oxygen to give a cyclohexadienone derivative.



4-Bromo-2,4,6-tri-*tert*-butyl-2,5-cyclohexadienone

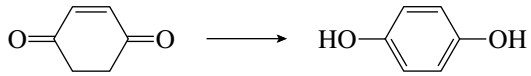
This cyclohexadienone is the compound $C_{18}H_{29}BrO$, and the peaks at 1655 and 1630 cm^{-1} in the infrared are consistent with C═O and C═C stretching vibrations. The compound's symmetry is consistent with the observed ^1H NMR spectrum; two equivalent *tert*-butyl groups at C-2 and C-6 appear as an 18-proton singlet at δ 1.3 ppm, the other *tert*-butyl group is a 9-proton singlet at δ 1.2 ppm, and the 2 equivalent vinyl protons of the ring appear as a singlet at δ 6.9 ppm.

24.28 Because the starting material is an acetal and the reaction conditions lead to hydrolysis with the production of 1,2-ethanediol, a reasonable reaction course is

Compound A 1,2-Ethanediol Compound B

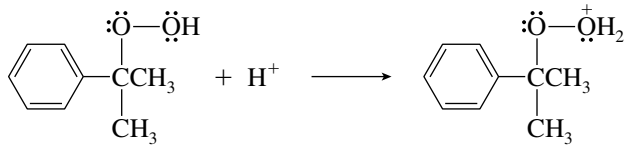
Indeed, dione B satisfies the spectroscopic criteria. Carbonyl bands are seen in the infrared spectrum, and compound B has two sets of protons to be seen in its ^{1}H NMR spectrum. The two vinyl protons are equivalent and appear at low field, δ 6.7 ppm; the 4 methylene protons are equivalent to each other and are seen at δ 2.9 ppm.

Compound B is the doubly ketonic tautomeric form of hydroquinone, compound C, to which it isomerizes on standing in water.



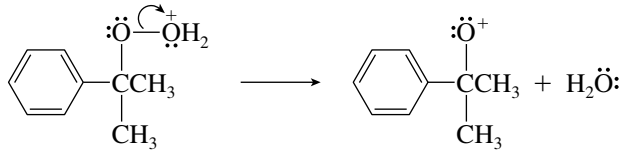
Compound B — Compound C (hydroquinone)

24.29 A reasonable first step is protonation of the hydroxyl oxygen.

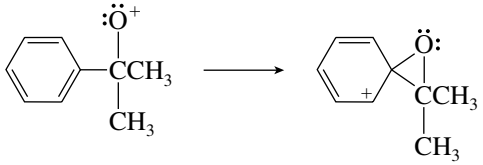


Cumene hydroperoxide

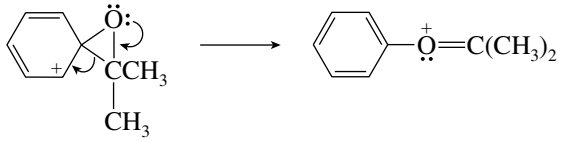
The weak oxygen–oxygen bond can now be cleaved, with loss of water as the leaving group.



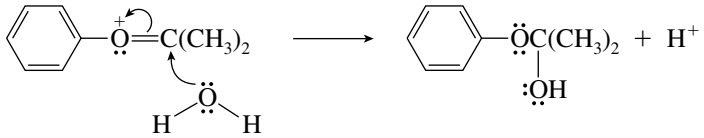
This intermediate bears a positively charged oxygen with only six electrons in its valence shell. Like a carbocation, such a species is highly electrophilic. The electrophilic oxygen attacks the π system of the neighboring aromatic ring to give an unstable intermediate.



Ring opening of this intermediate is assisted by one of the lone pairs of oxygen and restores the aromaticity of the ring.

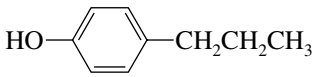


The cation formed by ring opening is captured by a water molecule to yield the hemiacetal product.



24.30 (*a*) The molecular formula of the compound ($C_9H_{12}O$) tells us that it has a total of four double bonds and rings (index of hydrogen deficiency = 4). The prominent peak in the infrared spectrum is the hydroxyl absorption of an alcohol or a phenol at 3300 cm^{-1}.

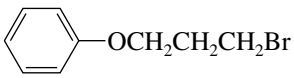
Peaks in the δ 110–160 ppm region of the ^{13}C NMR spectrum suggest an aromatic ring, which accounts for six of the nine carbon atoms and all its double bonds and rings. The presence of four peaks in this region, two of which are C and two CH, indicates a para-disubstituted aromatic derivative. That the remaining three carbons are sp^3-hybridized is indicated by the upfield absorptions at δ 15, 26, and 38 ppm. None of these carbons has a chemical shift below δ 40 ppm, and so none of them can be bonded to the hydroxyl group. Thus the hydroxyl group must be bonded to the aromatic ring. The compound is 4-propylphenol.



4-Propylphenol

(*b*) Once again the molecular formula ($C_9H_{11}BrO$) indicates a total of four double bonds and rings. The four peaks in the δ 110–160 ppm region of the spectrum, three of which represent CH, suggest a monosubstituted aromatic ring.

The remaining atoms to be accounted for are O and Br. Because all the unsaturations are accounted for by the benzene ring and the infrared spectrum lacks any hydroxyl absorption, the oxygen atom must be part of an ether function. The three CH_2 groups indicated by the absorptions at δ 32, 35, and 66 ppm in the ^{13}C NMR spectrum allow the compound to be identified as 3-bromopropyl phenyl ether.



3-Bromopropyl phenyl ether

SELF-TEST

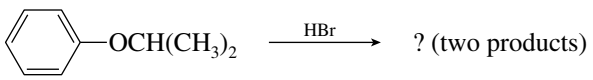
PART A

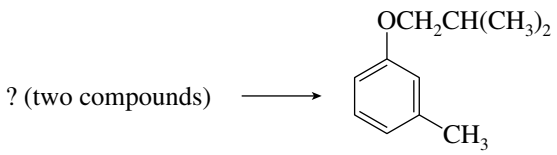
A-1. Which is the stronger acid, *m*-hydroxybenzaldehyde or *p*-hydroxybenzaldehyde? Explain your answer, using resonance structures.

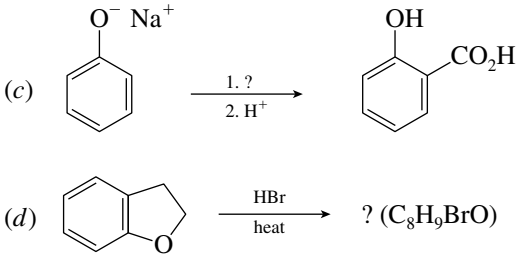
A-2. The cresols are methyl-substituted phenols. Predict the major products to be obtained from the reactions of *o*-, *m*-, and *p*-cresol with dilute nitric acid.

A-3. Give the structure of the product from the reaction of *p*-cresol with propanoyl chloride, $CH_3CH_2\overset{\overset{O}{\|}}{C}Cl$, in the presence of $AlCl_3$. What product is obtained in the absence of $AlCl_3$?

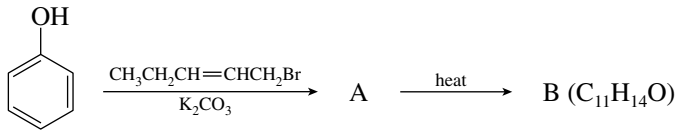
A-4. Provide the structure of the reactant, reagent, or product omitted from each of the following:

(*a*) 

(*b*) 



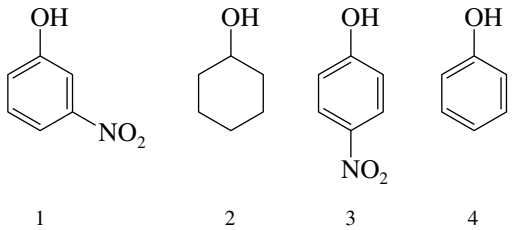
A-5. Provide the structures of compounds A and B in the following sequence of reactions:



A-6. Prepare *p-tert*-butylphenol from *tert*-butylbenzene using any necessary organic or inorganic reagents.

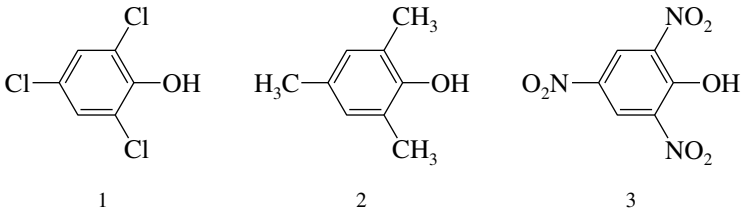
PART B

B-1. Rank the following in order of decreasing acid strength (most acidic → least acidic):



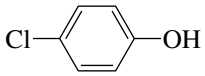
(*a*) 2 > 4 > 1 > 3
(*b*) 3 > 1 > 2 > 4
(*c*) 1 > 3 > 4 > 2
(*d*) 3 > 1 > 4 > 2

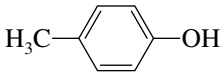
B-2. Rank the following compounds in order of increasing acidity (weakest acid first).

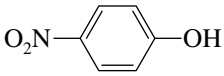


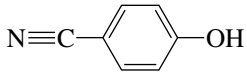
(*a*) 2 < 3 < 1
(*b*) 3 < 2 < 1
(*c*) 3 < 1 < 2
(*d*) 2 < 1 < 3
(*e*) 1 < 2 < 3

B-3. Which of the following phenols has the largest pK_a value (i.e., is least acidic)?

(*a*) 

(*b*) 

(*c*) 

(*d*) 

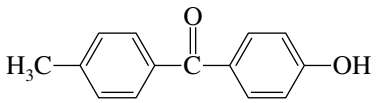
B-4. Which of the following reactions is a more effective method for preparing phenyl propyl ether?

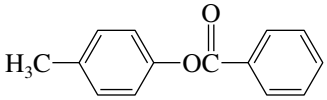
I: $C_6H_5ONa + CH_3CH_2CH_2Br \longrightarrow$

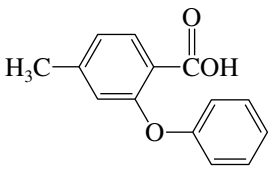
II: $CH_3CH_2CH_2ONa + C_6H_5Br \longrightarrow$

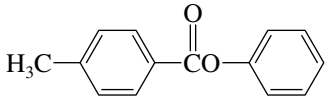
(*a*) Reaction I is more effective.
(*b*) Reaction II is more effective.
(*c*) Both reactions I and II are effective.
(*d*) Neither reaction I nor reaction II is effective.

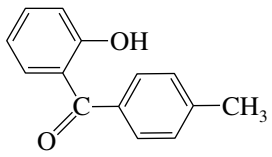
B-5. What reactant gives the product shown on heating with aluminum chloride?



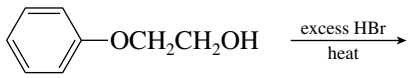
(*a*) 

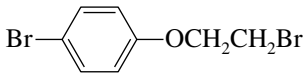
(*b*) 

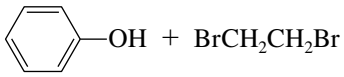
(*c*) 

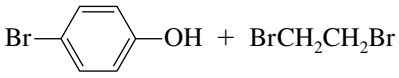
(*d*) 

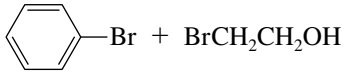
B-6. What are the products of the following reaction?

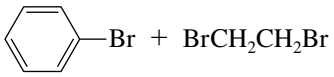


(*a*) 

(*b*) 

(*c*) 

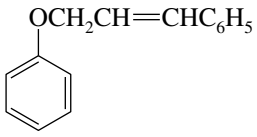
(*d*) 

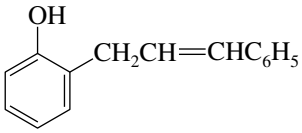
(*e*) 

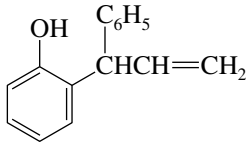
B-7. Which of the following sets of reagents, used in the order shown, would enable preparation of *p*-chlorophenol from *p*-chloronitrobenzene?

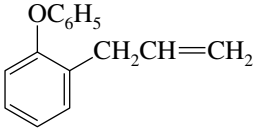
(*a*) 1. Fe, HCl; 2. NaOH; 3. $NaNO_2$, H_2SO_4; 4. H_3PO_2
(*b*) 1. Fe, HCl; 2. NaOH; 3. $NaNO_2$, H_2SO_4; 4. H_2O, heat
(*c*) 1. Fe, HCl; 2. NaOH; 3. $NaNO_2$, H_2SO_4; 4. ethanol
(*d*) 1. NaOH, heat; 2. HCl

B-8. What is the product obtained by heating the following allylic ether of phenol?



(*a*) 

(*c*) 

(*b*) 

(*d*)