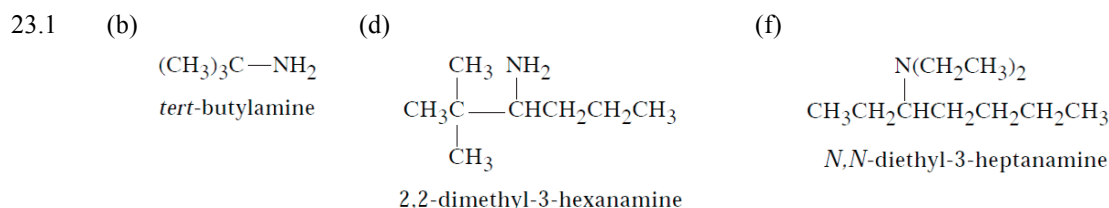


# Chapter 23

## The Chemistry of Amines

### Solutions to In-Text Problems

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- 23.2 (b) *N,N*-Dimethyl-*p*-nitroaniline (common), or 1-dimethylamino-4-nitrobenzene  
(c) Dicyclohexylamine (common), or *N*-cyclohexylcyclohexanamine

- 23.3 (b) Apply the principle used in part (a). The order of increasing carbon–nitrogen bond length is

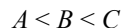


Compound *B* has a true carbon–nitrogen single bond, and hence has the longest carbon–nitrogen bond. Compound *A* has a true carbon–nitrogen double bond, and hence has the shortest carbon–nitrogen bond. The carbon–nitrogen bond of *C* has some double-bond character because of resonance interaction of the nitrogen unshared pair with the double bond. (Draw the appropriate resonance structure.) Another way to compare the C–N bond lengths of compounds *B* and *C* is to note that the C–N bond in *B* is an  $sp^3-sp^3$  single bond, whereas the C–N bond in *C* is an  $sp^2-sp^3$  single bond, and to remember that  $\sigma$  bonds with greater *s* character are shorter. (See discussion on text pp. 127 and 678.)

- 23.5 The NMR spectrum indicates the presence of only two phenyl hydrogens, and the singlet absorptions at  $\delta$  2.07 and  $\delta$  2.16 indicate the presence of chemically nonequivalent methyl groups in the ratio 2:1. Only compound (2), 2,4,6-trimethylaniline, fits the data. The two resonances at  $\delta$  2.07 and  $\delta$  2.16 correspond to the ortho and para methyl groups, respectively, and the  $\delta$  3.19 resonance to the  $-\text{NH}_2$  protons of the amine.

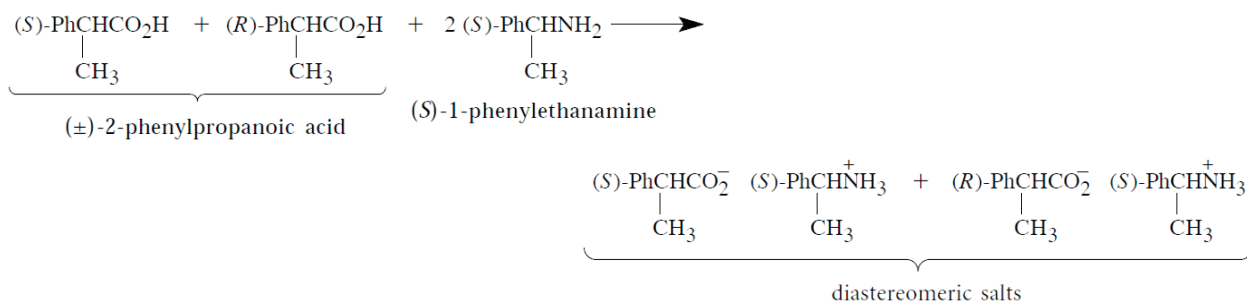
- 23.6 (a) 2,2-Dimethyl-1-propanamine (neopentylamine,  $(\text{CH}_3)_3\text{CCH}_2\text{NH}_2$ ) has a maximum of three resonances in its CMR spectrum. 2-Methyl-2-butanamine,  $\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)_2\text{NH}_2$ , should have four resonances in its CMR spectrum.

- 23.8 From Table 23.1, text p. 1123, we see that the basicity order is as follows:

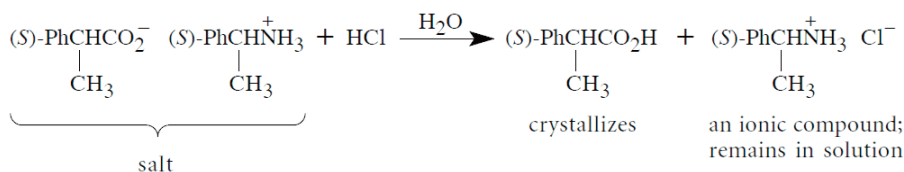


The basicities of all these amines are reduced by resonance interaction of the nitrogen unshared electron pair with the ring. The electron-withdrawing polar effect of the nitro group lowers basicity further, and resonance interaction of the nitrogen unshared pair with the *p*-nitro group stabilizes *p*-nitroaniline and lowers its basicity even more. (Resonance structures depicting this interaction are shown in the solution to Problem 23.3(a) on p. 610 of the Study Guide and Solutions Manual.)

- 23.10 Mix the racemic acid with one equivalent of the enantiomerically pure amine. (The *S* enantiomer of the amine is utilized in the equation below, but either *pure* enantiomer of the amine could be used.) The carboxylic acids will react with the amine to give a mixture of *diastereomeric* salts.

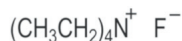


Because these salts have different properties, they can be separated by differential solubility, for example, by fractional crystallization from some solvent, probably an alcohol. After separating the salts, aqueous acid is added to each. The amine resolving agent dissolves in the aqueous acid solution (from which it can be recovered), leaving the enantiomerically pure free carboxylic acid as a solid that can be isolated by filtration and recrystallized.



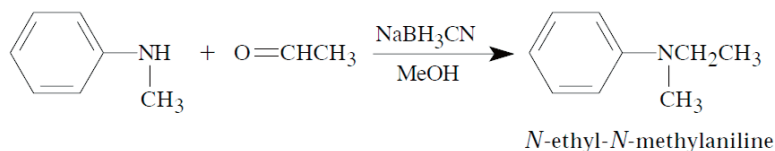
Notice that not only is amine basicity important in forming the initial salt, but also it is important in separating the amine resolving agent from the resolved carboxylic acid.

23.11 (a)

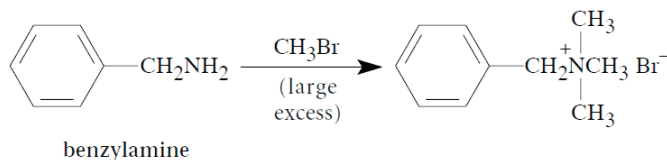


tetraethylammonium fluoride

23.14 The ethyl group could originate from acetaldehyde:

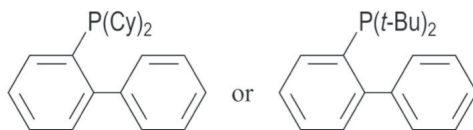


23.15 (b) Exhaustively methylate benzylamine with a large excess of methyl bromide.

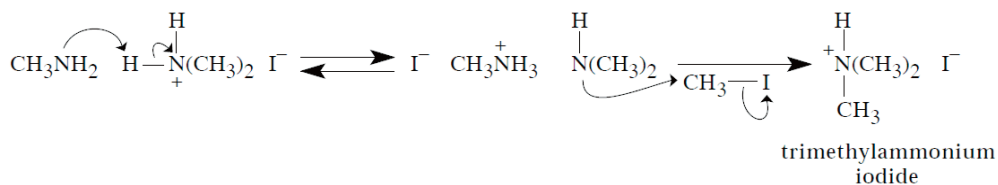


23.16 (a) Caleb has forgotten, if he ever knew, that aryl halides such as bromobenzene do not undergo  $\text{S}_{\text{N}}2$  reactions (Sec. 18.1).

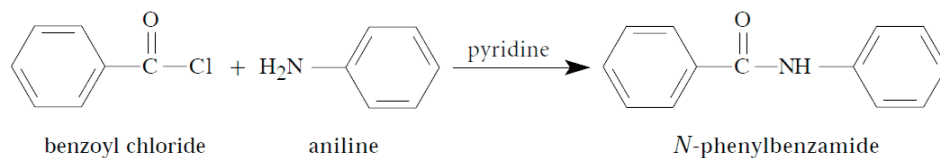
(b) A Pd(0) catalyst of the type  $\text{PdL}_2$ . This reaction is discussed in Sec. 23.11C, where L is:



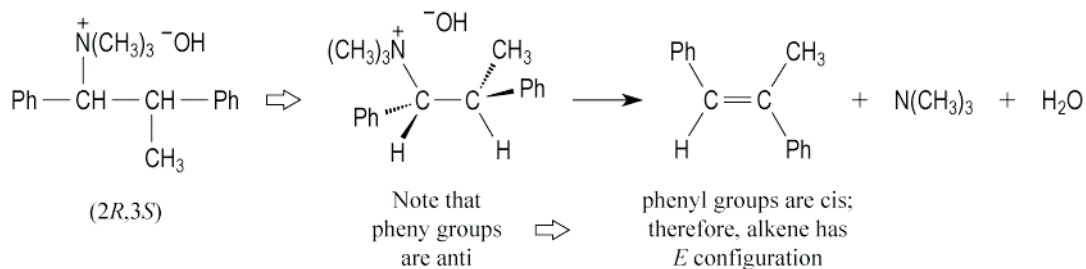
23.17 The dimethylammonium ion can lose a proton to give dimethylamine, which can then be alkylated by methyl iodide.



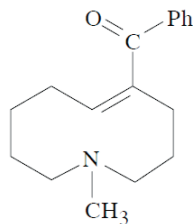
23.18 (a)



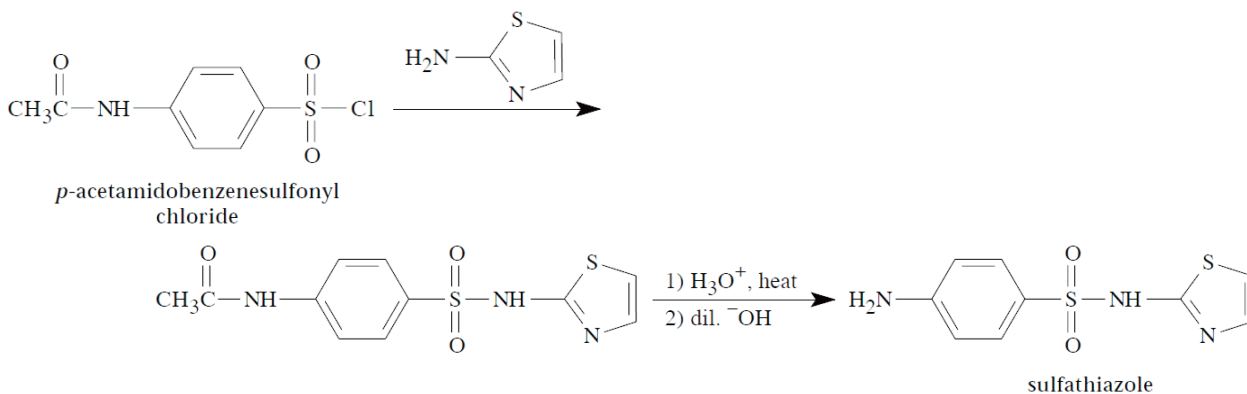
23.19 (b) Draw the molecule in a conformation in which the trimethylammonium group is anti to the  $\beta$ -hydrogen, and examine the relative positions of the phenyl groups. In this part, the alkene product must have the *E* configuration.



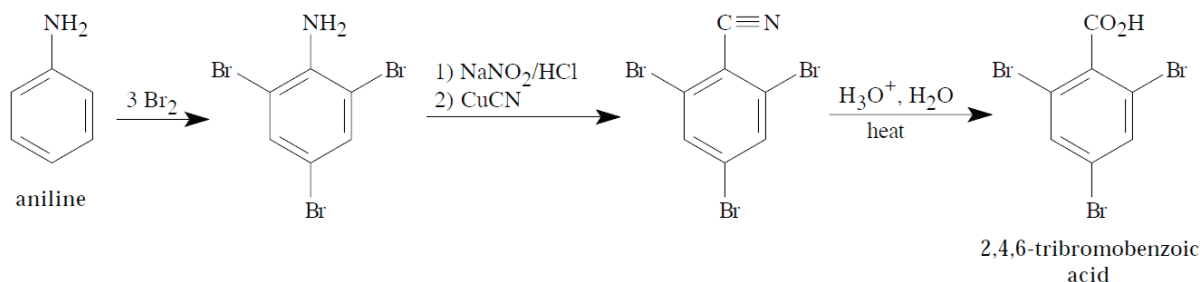
23.20 (b) The hydrogen  $\alpha$  to the carbonyl group is removed because it is considerably more acidic than the other  $\beta$ -hydrogens.



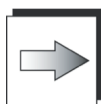
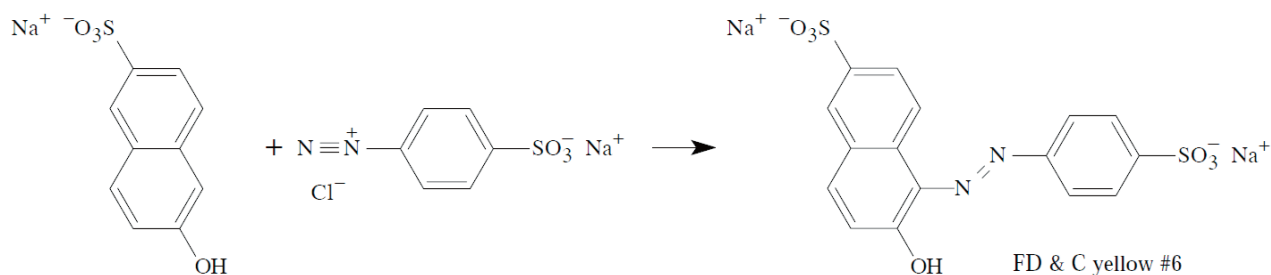
23.23 (b) Begin with *p*-acetamidobenzenesulfonyl chloride, prepared as shown in the solution to Problem 23.22, p. 614 of the Study Guide and Solutions Manual.



23.24 (b)

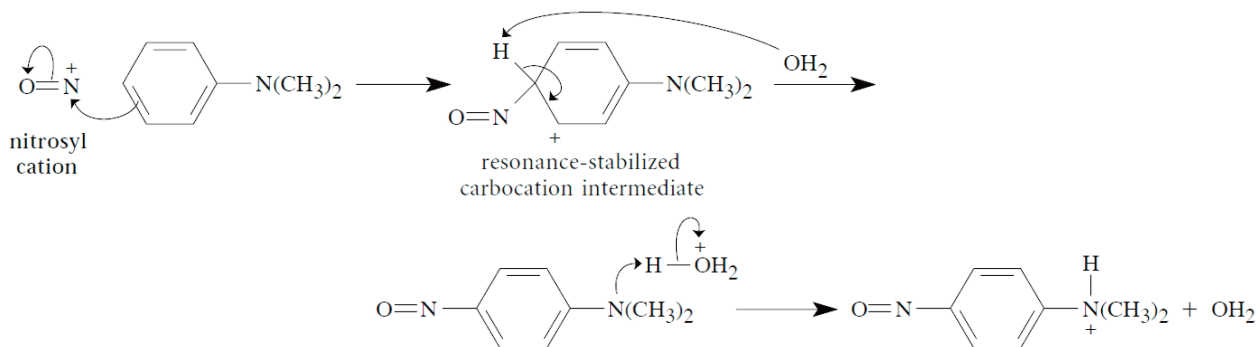


23.27 The following compounds would react to give FD &amp; C Yellow No. 6:

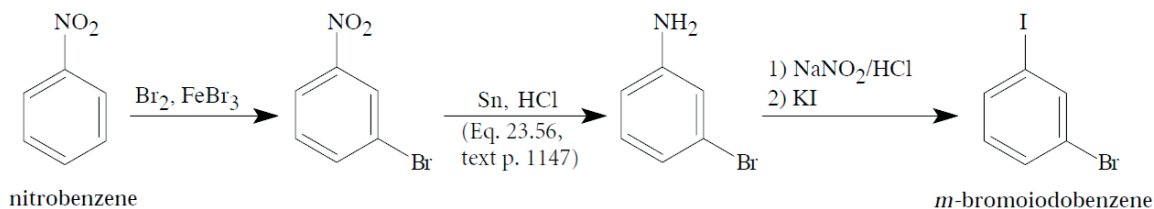


The position next to the ring junction (called the  $\alpha$ -position) in a naphthalene ring is more reactive in electrophilic substitution than the ring position one carbon removed. Hence, of the two positions "ortho" to the phenolic  $\text{—OH}$  group, the  $\alpha$ -position is the more reactive and gives the observed product.

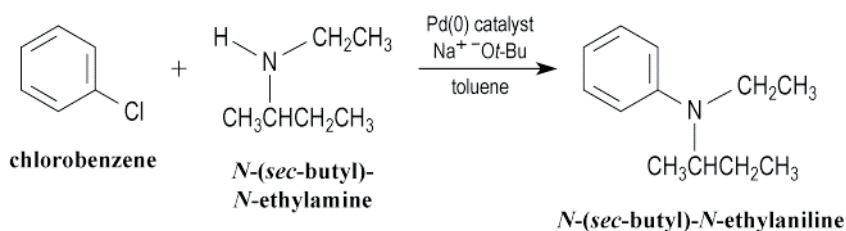
23.28 (b) The loss of  $\text{H}_2\text{O}$  from protonated nitrous acid provides the nitrosyl cation, as shown in the solution to part (a) of this problem. This cation then serves as the electrophile in an electrophilic aromatic substitution reaction:



23.30 (b)

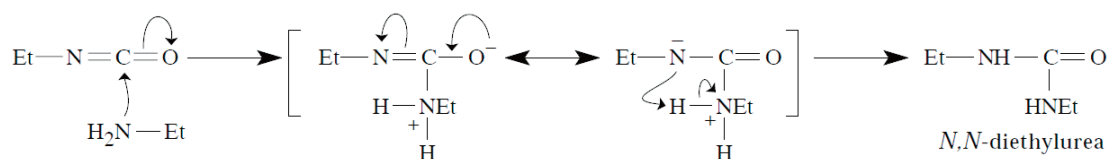


23.31 (a)

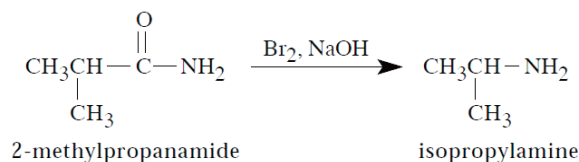


23.32 (a) *Tert*-butylamine cannot be prepared by the Gabriel synthesis because it would require that the nitrogen of phthalimide be alkylated with *tert*-butyl bromide in an  $\text{S}_{\text{N}}2$  reaction. Tertiary alkyl halides generally do not undergo  $\text{S}_{\text{N}}2$  reactions but, under basic conditions, undergo E2 reactions instead.

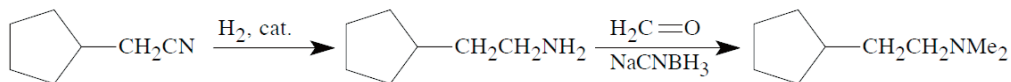
23.33 (b) The curved-arrow mechanism for the reaction of ethylamine with ethyl isocyanate to give *N,N'*-diethylurea:



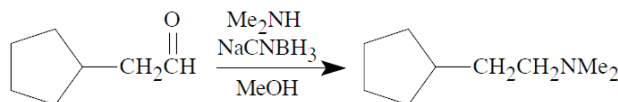
23.34 (b) In aqueous NaOH, hydroxide is the nucleophile that reacts with the isocyanate, and the resulting carbamic acid (or its salt) decarboxylates to give the corresponding amine.



23.36 (b)

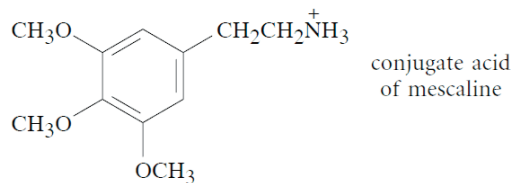


(d) One synthesis involves a reductive amination of the aldehyde:



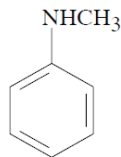
A second synthesis involves oxidation of the aldehyde to the carboxylic acid starting material of part (a) with aqueous  $\text{H}_2\text{CrO}_4$ ,  $\text{KMnO}_4$ , or other common oxidant, and then proceeding as in part (a).

23.37 (b) The most basic atom in mescaline is the amine nitrogen. Thus, the conjugate acid of mescaline has the following structure:



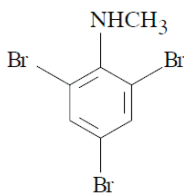
## Solutions to Additional Problems

23.39 The structure of *N*-methylaniline is

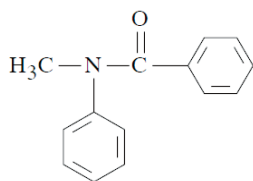


*N*-methylaniline

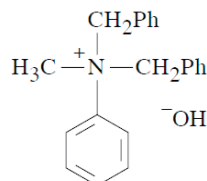
(a)



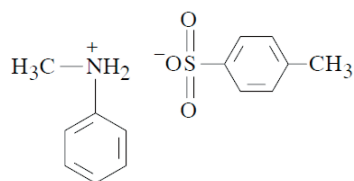
(b)



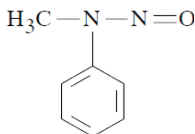
(c)



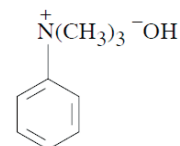
(d)



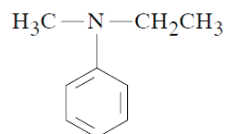
(e)



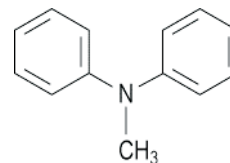
(f)



(g)

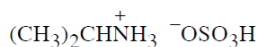


(h)



23.40 The structure of isopropylamine is  $(\text{CH}_3)_2\text{CH}-\text{NH}_2$

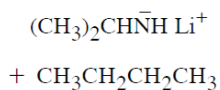
(a)



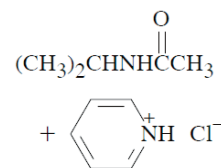
(b)

no reaction

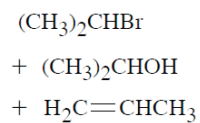
(c)



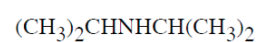
(d)



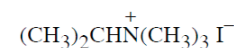
(e)



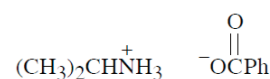
(f)



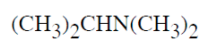
(g)



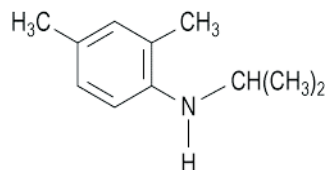
(h)



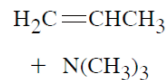
(i)



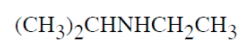
(j)

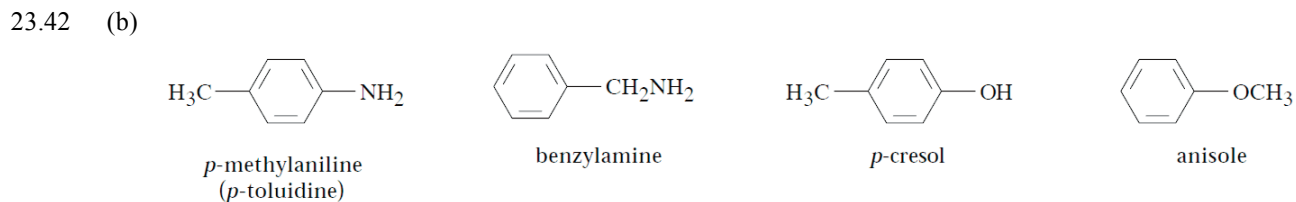
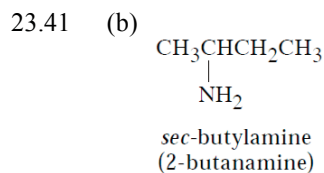


(k)



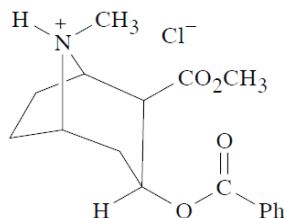
(l)



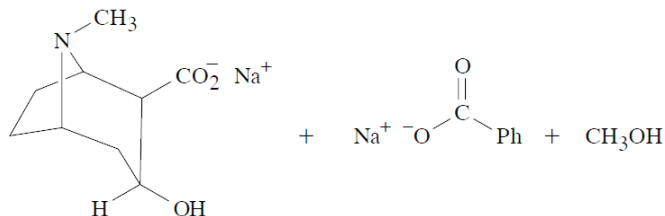


Only the two amines, *p*-methylaniline and benzylamine, are soluble (as their conjugate-acid ammonium ions) in dilute HCl. Only the phenol *p*-cresol is soluble (as its conjugate-base phenolate) in dilute NaOH solution. Anisole is soluble in neither dilute acid nor dilute base. Only benzylamine gives off a gas ( $\text{N}_2$ ) when diazotized at  $0^\circ$  with  $\text{HNO}_2$ . *p*-Methylaniline gives off  $\text{N}_2$  when the corresponding diazonium salt is heated.

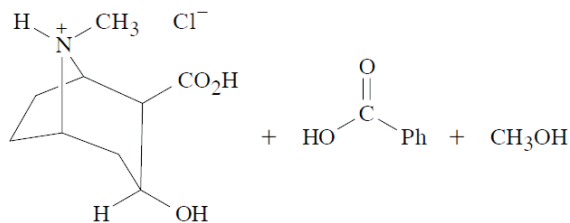
23.44 (a) In 1 *M* HCl solution, cocaine is protonated on its amino nitrogen.



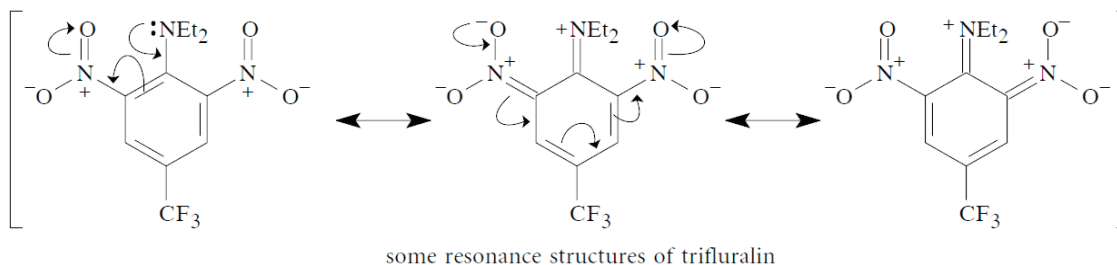
(b) Hot aqueous NaOH would bring about saponification of the ester groups:



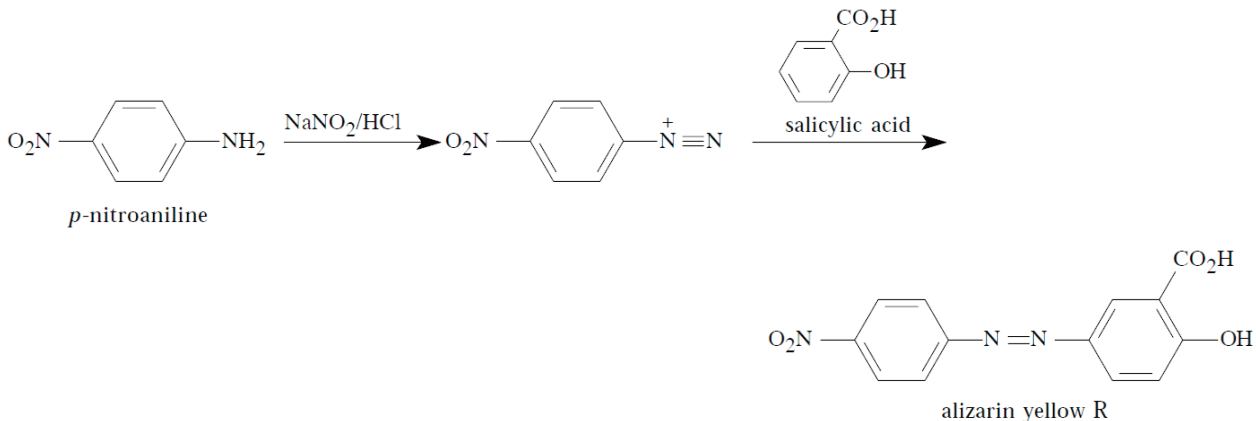
(c) Concentrated, hot aqueous HCl would protonate the amine nitrogen (as in part (a)) and would bring about hydrolysis of the two ester groups.



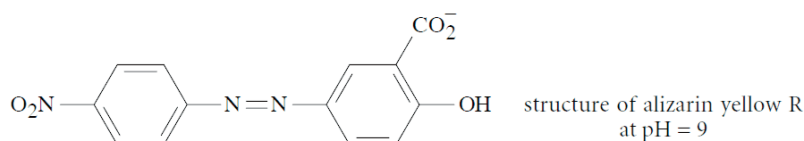
23.46 The basicity of trifluralin is much less than that of *N,N*-diethylaniline. The electron-withdrawing polar effects of both the nitro substituents and the trifluoromethyl substituent destabilize the conjugate acid of trifluralin, and resonance interaction of the nitrogen unshared electron pair with the two nitro groups stabilizes trifluralin itself; this interaction is absent in the ammonium ion. (In fact, trifluralin is not basic enough to dissolve in dilute HCl.)



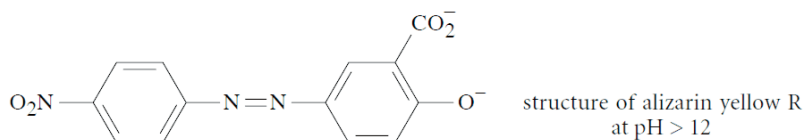
- 23.48 (a) First prepare *p*-nitroaniline from aniline as shown in Study Problem 23.4 on text p. 1138. Then diazotize this amine to give the diazonium salt. Couple the diazonium salt to salicylic acid to obtain alizarin yellow R.



- (b) From the solution to the Problem (23.47 on p. 620 of the Study Guide and Solutions Manual), or from the information in the problem, the  $pK_a$  of a protonated diazo group should be around 5. Consequently, at a pH value well above 5, the diazo nitrogens are unprotonated. The  $pK_a$  of the carboxy group should be around 4. Therefore, at pH = 9, the carboxy group should be ionized. The group that ionizes between 10 and 12 should affect the conjugated  $\pi$ -electron system because it affects the color. Since this group is not the diazo group, it must be the phenol. If the phenol has a  $pK_a$  of about 11, then at pH = 9 it is un-ionized.



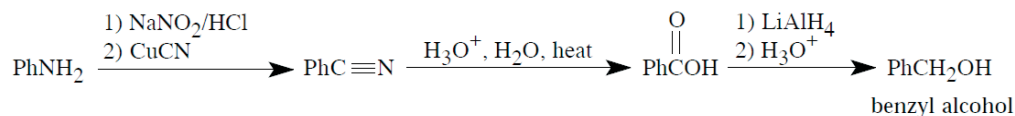
- (c) At pH > 12, both the carboxy group and the phenol are ionized. (Show the resonance structures for the delocalization of the phenolate ion throughout the  $\pi$ -electron system of the rings, the diazo group, and the *p*-nitro group. This interaction is the basis for the color change.)



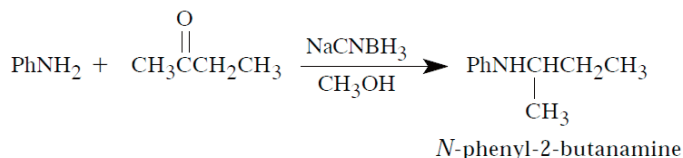
- 23.49 (b) Excess methyl iodide will form the quaternary salt  $(CH_3)_3CN^+(CH_3)_3 I^-$ ; the reaction will not stop at the secondary amine shown in the problem.
- (d) Although the aldehyde will indeed be reduced, so will the nitro group. (See Eq. 23.57 on text p. 1147.)
- (f) Amanda is attempting to carry out an  $S_N2$  reaction on a tertiary alkyl halide. Unfortunately, tertiary alkyl halides do not undergo  $S_N2$  reactions. If a reaction occurs at all, it will be the competing  $E2$  process.



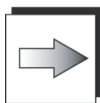
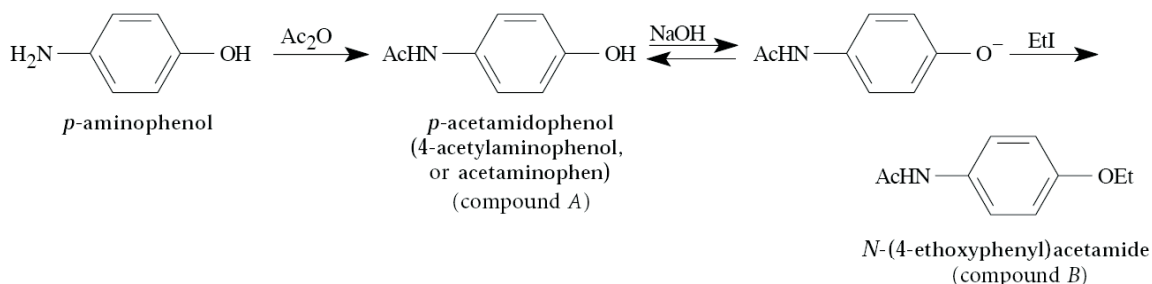
23.50 (b)



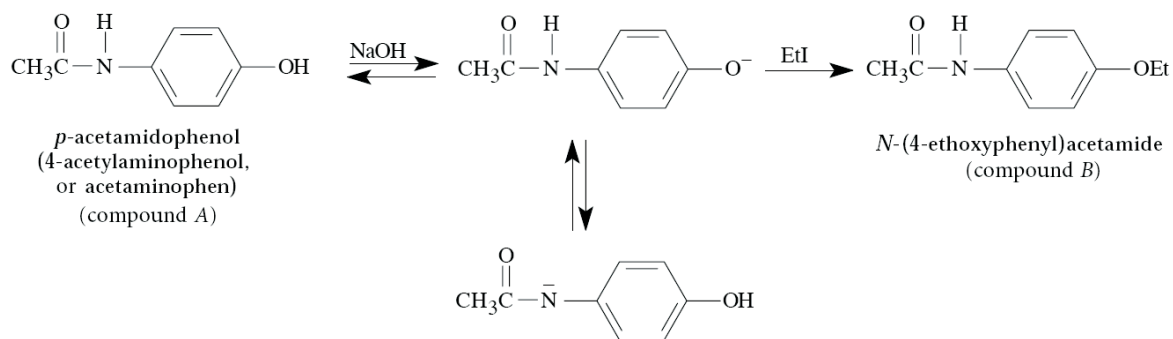
(d)



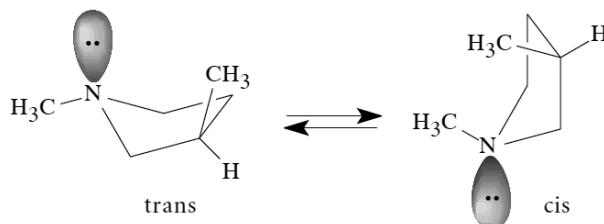
- 23.51 The acetic anhydride treatment acetylates either the amino group or the hydroxy group. Because the initially formed product *A* can form an ethyl ether, its —OH group is not affected in the first reaction. Consequently, compound *A* is *p*-acetamidophenol and compound *B* is its ethyl ether. This is reasonable because, so long as the hydroxy group is not ionized, the amino group is the most basic group in the molecule, and is thus the more nucleophilic group. Compound *A* dissolves in base because the hydroxy proton can ionize.



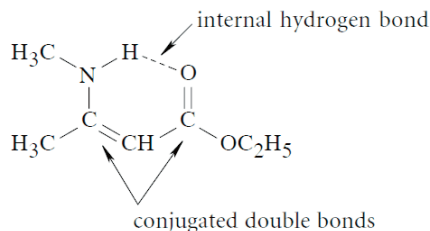
In compound *A* the acidity of the amide N—H is likely to be comparable to that of the phenol (why?). Hence, the conjugate-base anion of the phenoxide is in equilibrium with the phenoxide ion. If both ions are indeed present, evidently the conjugate base phenolate is alkylated more rapidly. Alkylation of the oxygen then pulls the equilibrium between the anions towards the phenoxide:



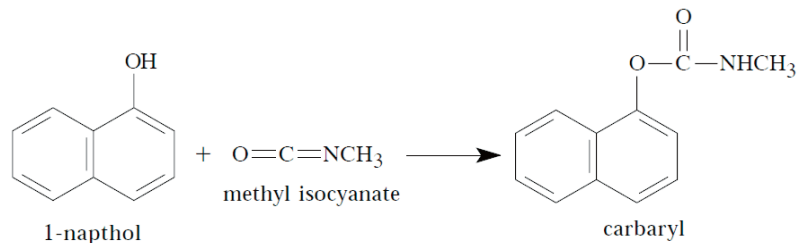
- 23.53 (b) *Cis*- and *trans*-1,3-dimethylpyrrolidine rapidly interconvert because all that is required for this process is amine inversion, which is very rapid.



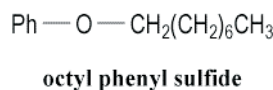
- (d) This compound exists as an enamine for the same reason that  $\beta$ -diketones exist as enols: internal hydrogen bonding and conjugation stabilize the enamine form.



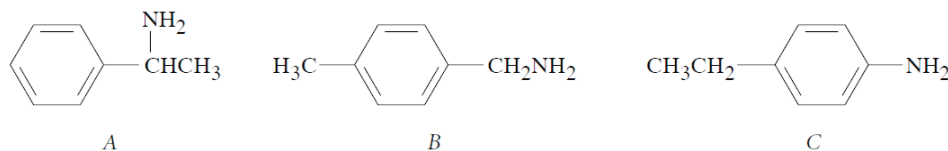
- 23.55 Carbaryl can be prepared by the reaction of 1-naphthol with methyl isocyanate.



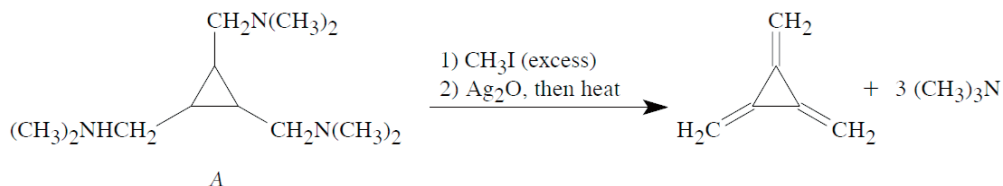
- 23.56 (a) Sodium benzenethiolate,  $\text{Na}^+ \text{PhS}^-$ , is a salt and thus soluble in water but not an organic solvent; 1-bromooctane is relatively nonpolar and thus insoluble in water. No reaction occurs initially because the two reactants cannot interact; however, with the addition of the phase-transfer catalyst tetrabutylammonium bromide,  $(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2)_4\text{N}^+ \text{Br}^-$ , the two reactants can interact to form octyl phenyl sulfide. (See text p. 1130.)



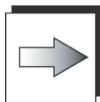
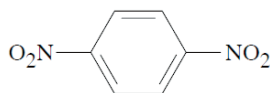
- 23.58 The oxidation data reveal that compound *A* contains a monosubstituted benzene ring, compounds *B* and *C* contain *para*-disubstituted benzene rings, and compound *C* additionally has an amino group directly attached to the ring. The  $\text{p}K_a$  of compound *C* additionally confirms that it is an aniline derivative, and the fact that compound *C*, following diazotization, requires warming to evolve a gas ( $\text{N}_2$ ) also indicates that it is an aniline derivative. Compound *A* is chiral, and furthermore, it must be the racemate, because it evidently forms diastereomeric salts with (+)-tartaric acid. Because six carbons are involved in a benzene ring, the problem is to determine how the remaining two carbons are arranged so that the resulting structures are consistent with the data. The following structures are the only reasonable possibilities:



- 23.59 (c) The triamide resulting from treatment of the acid chloride is reduced with  $\text{LiAlH}_4$  to give triamine *A*, which is exhaustively methylated and then subjected to Hofmann elimination to give the product, which is an isomer of benzene.

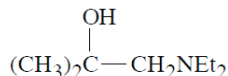


- (e) In this variation of the Sandmeyer reaction, copper(I) nitrite introduces a nitro group into the ring.

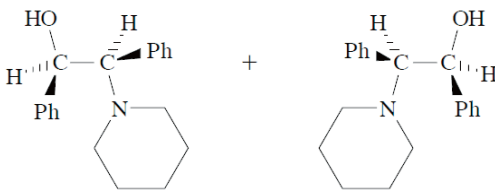


*p*-Dinitrobenzene would be very difficult to prepare by electrophilic aromatic substitution; can you see why?

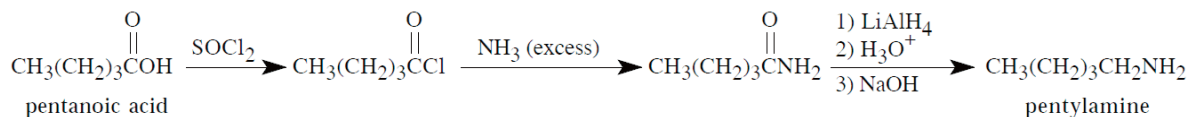
- (g) The amine reacts with the epoxide at the carbon with fewer alkyl substituents.



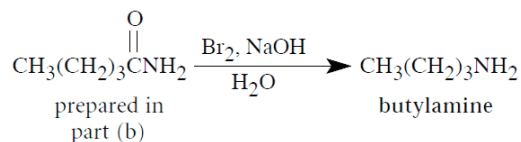
- (i) The amine reacts with the epoxide with inversion of configuration. Because both starting materials are achiral (the epoxide is the meso stereoisomer), the product is the racemate; one enantiomer results from reaction at one carbon of the epoxide, and the other enantiomer results from reaction at the other carbon.



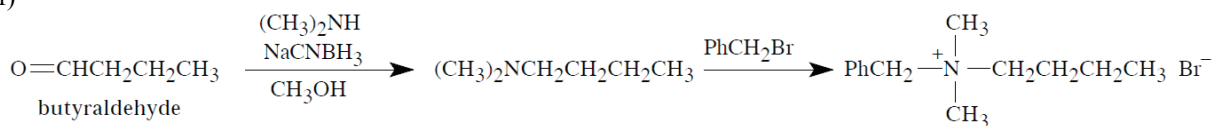
23.60 (b)



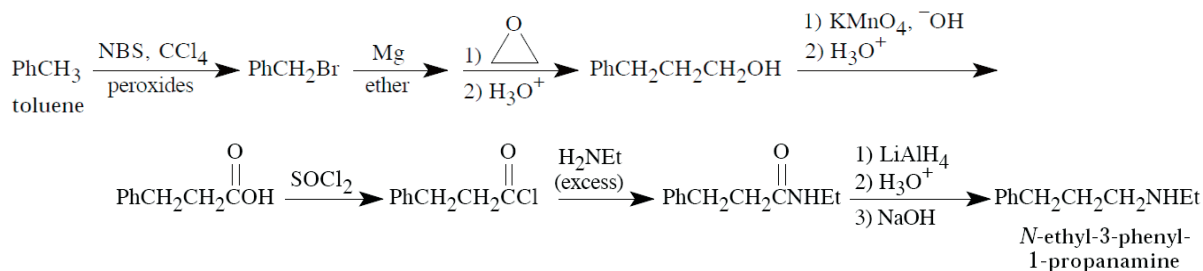
(d)



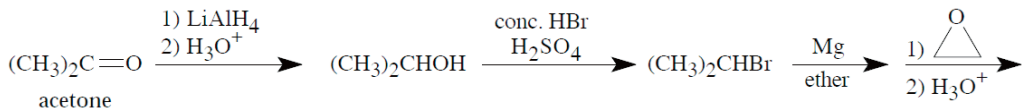
(f)

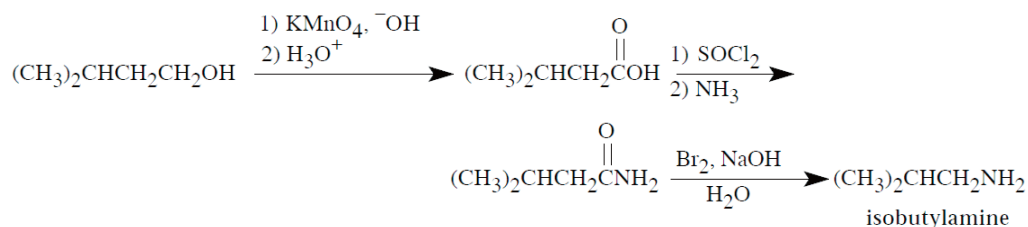


(g)

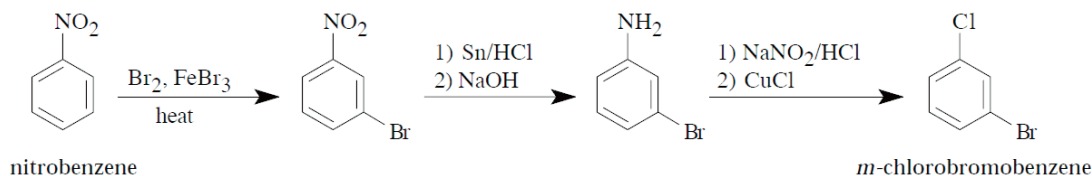


(i)

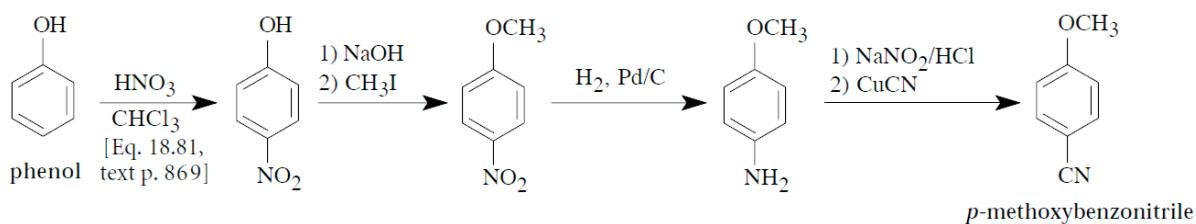




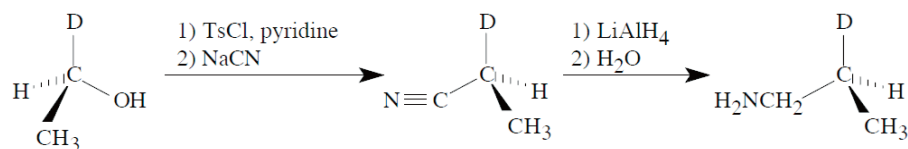
(k)



(m)

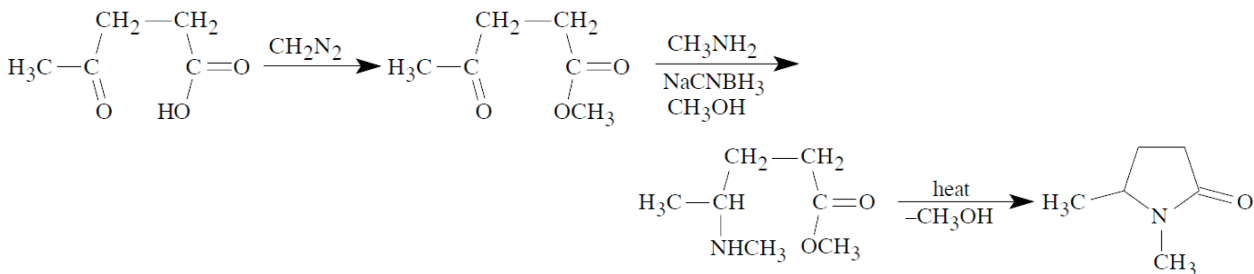


(n)

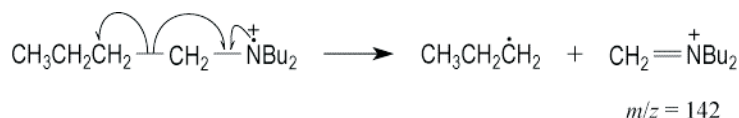


Note that the  $\text{S}_{\text{N}}2$  reaction of cyanide ion proceeds with inversion of configuration.

(o)



23.61 (b) The  $\alpha$ -cleavage of tributylamine produces a major peak at  $m/z = 142$ :



23.64 Assume that the  $\text{—NH}_2$  or  $\text{—NH}$  protons of the amine rapidly exchange, so that they are not coupled to adjacent protons on carbon.

Compound *C* should have the resonance at greatest chemical shift, because the proton  $\alpha$  to the nitrogen is also benzylic and is a methine proton. This proton should be a triplet.

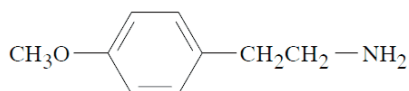
Compound *B* should have the resonance at the next greatest chemical shift, because the protons  $\alpha$  to the nitrogen are also benzylic, but are methylenes, which have smaller chemical shifts than methine protons by about

0.5–0.7 ppm. These  $\alpha$ -protons should be a singlet. The relative integrations of the  $\alpha$ -protons of *B* and *C* are different, as well.

Between compounds *A* and *D*, compound *A* has the resonance at smallest chemical shift—the methyl group, which should be a doublet. These methyl protons are neither benzylic nor  $\alpha$  to a nitrogen; thus, they should have a resonance not far from  $\delta$  1.

All of the resonances of compound *D* are in the  $\delta$  2–3.5 range. This spectrum should consist of two triplets and a singlet (plus the NH proton). Other features of these spectra might be cited as well.

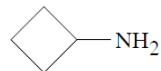
- 23.65 (a) With an unsaturation number of 4 and clear evidence for a para-substituted benzene ring (the four-proton pair of doublets centered at about  $\delta$  7), no other unsaturations are possible. The NMR indicates partial structures —OCH<sub>3</sub> and —CH<sub>2</sub>CH<sub>2</sub>—. With no other unsaturation, the nitrogen has to be an amine, and the broad, two-proton resonance near  $\delta$  1 suggests an —NH<sub>2</sub> group. The only structure that fits all the data is



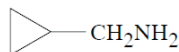
2-(4-methoxyphenyl)ethylamine  
(compound *A*)

- 23.67 (a) The chemical data indicate the presence of a primary amine. The compound has one degree of unsaturation, and the chemical shifts in the CMR are too small for any carbon to be involved in a double bond. Hence, compound *A* contains a ring, and only CH and CH<sub>2</sub> groups are present. The presence of only three resonances means that two carbons are equivalent. Compound *A* is cyclobutylamine.

Cyclopropylmethanamine is ruled out by the fact that the carbon bound to one hydrogen has the largest chemical shift and therefore must be bound to the nitrogen.

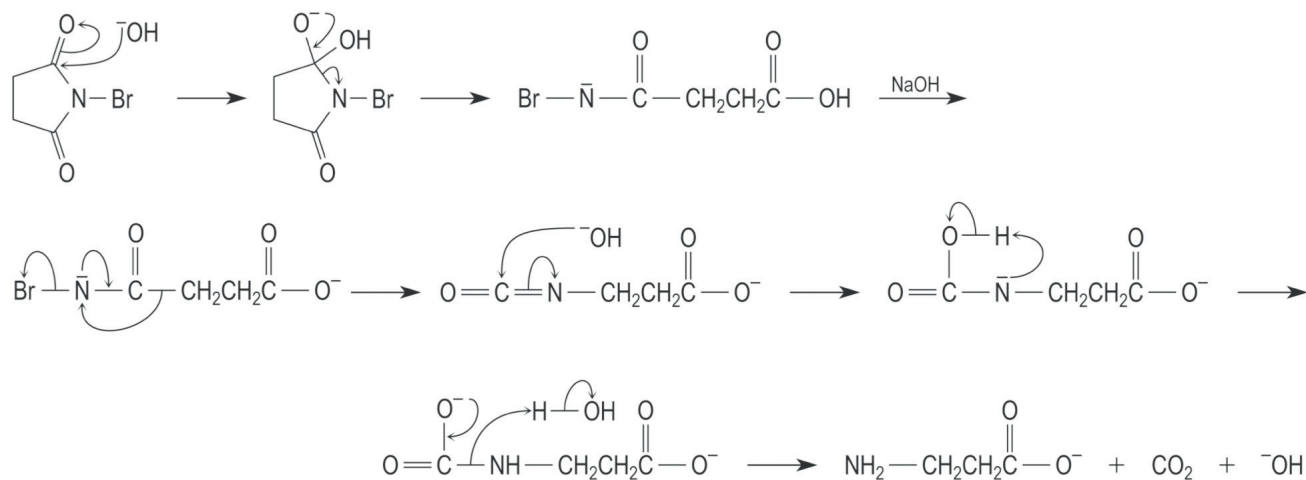


cyclobutylamine  
(compound *A*)



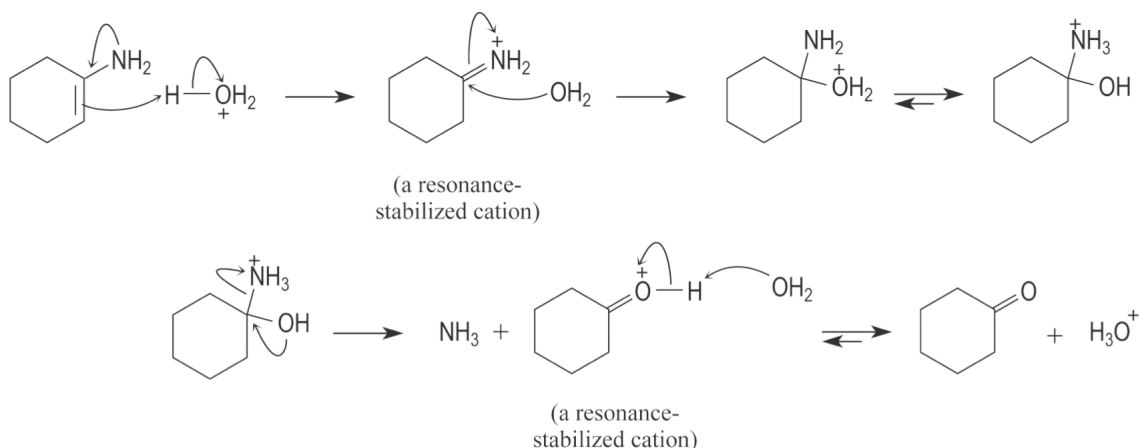
cyclopropylmethanamine  
(ruled out)

- 23.68 (b) This reaction is related to the Hofmann rearrangement. Reaction with hydroxide on the carbonyl carbon of *N*-bromosuccinimide gives an *N*-bromo anion, which undergoes a Hofmann rearrangement to the corresponding isocyanate, which in turn, hydrolyzes and decarboxylates to the amine product.

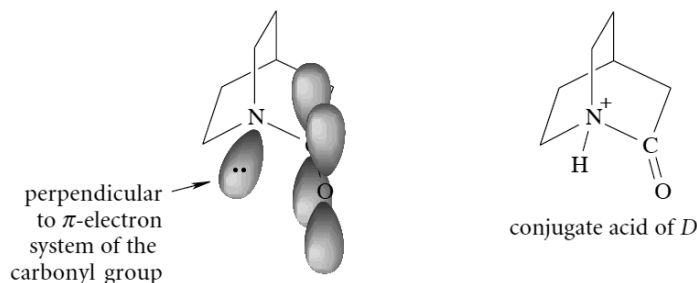


- 23.70 An intermediate in the formation of 1-pentanamine is the imine *A*. The other products arise from the fact that 1-pentanamine, *B*, can react with either the starting aldehyde, pentanal, or with imine *A* to give a new imine *C*. (Give the mechanism for this reaction.) Imine *C* can also undergo hydrogenation to the second product,





- 23.74 The data show that the conjugate-acid  $pK_a$  values of a bicyclic tertiary amine *C* (which is the same as amine *C* in the previous problem) and a monocyclic tertiary amine *B* are not very different. Hence, the additional ring has no unusual effect on  $pK_a$ . The conjugate-acid  $pK_a$  of amide *A* is also fairly normal for an amide that is protonated on the carbonyl oxygen. (See Eq. 21.4b on text p. 1001.) The  $pK_a$  of amide *D*, then, is unusual. Normally, amides protonate on the carbonyl oxygen because the resulting carbocation is resonance-stabilized. In this case, however, the bicyclic structure of the ring prevents the overlap of the nitrogen unshared electron pair with the  $\pi$ -electron system of the carbonyl group. Hence, the electronic character of this nitrogen is more like that of an amine with a neighboring electron-withdrawing substituent (the carbonyl group) than it is like that of an amide. Thus, this amide behaves like an amine: it protonates on nitrogen. What about the hydrolysis rate? Recall that ordinary amides hydrolyze slowly because they are resonance-stabilized. (See Sec. 21.7E, text p. 1011.) When resonance stabilization is not present, as in the case of compound *D*, an amide hydrolyzes rapidly. In acidic solution, when the nitrogen is protonated, its hydrolysis rate is more like that of an acid chloride!



(See also the sidebar on text pp. 1002–1003 for a discussion of this case.)