

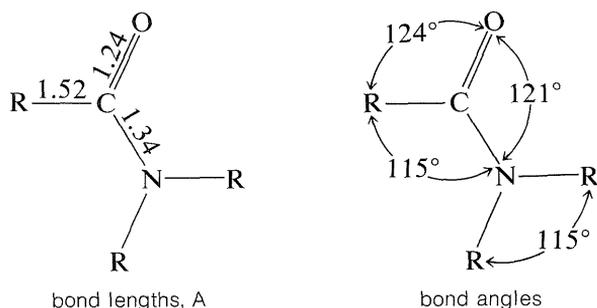
ORGANONITROGEN COMPOUNDS II. AMIDES, NITRILES, NITRO COMPOUNDS, AND SOME SUBSTANCES WITH N–N BONDS

The properties of the simple amides are relevant to the chemistry of peptides and proteins, substances that are fundamental to all life as we know it. Indeed, the characteristics of peptides and proteins are primarily due to their polyamide structures. For this reason, it is important to know and understand the chemistry of simple amides.

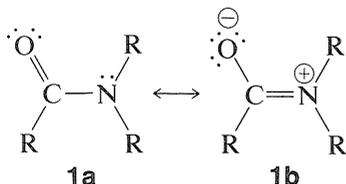
24-1 STRUCTURAL, PHYSICAL, AND SPECTRAL CHARACTERISTICS OF AMIDES

24-1A Molecular Structure

The structural parameters of the amide group have been determined carefully and the following diagram gives a reasonable idea of the molecular dimensions:

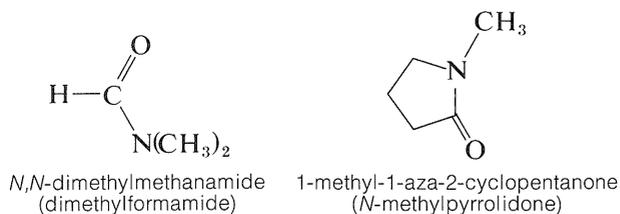


An important feature of the group is that it is *planar*—the carbon, oxygen, nitrogen, and the first atom of each of the R groups on carbon and nitrogen lie in the same plane. The C–N bond distance of 1.34 Å is intermediate between the typical single bond C–N distance of 1.47 Å and the double bond C=N distance of 1.24 Å. This and other evidence indicates that the amide group is a hybrid structure of the valence-bond forms **1a** and **1b**, with a stabilization energy of about 18 kcal mole⁻¹:

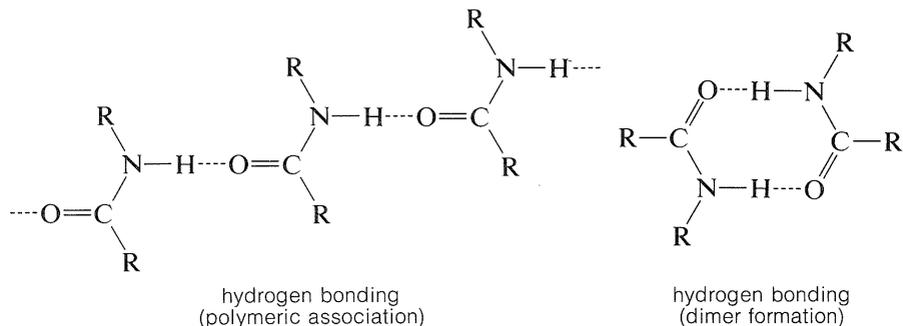


Coplanarity is required if the dipolar structure **1b** is to be significant. An appreciable dipole moment may be expected of amides and, in fact, simple amides have dipole moments in the range 3.7–3.8 debye. (For reference, the carbonyl group has a moment of about 2.7 debye, Section 16-1B.)

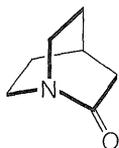
As a consequence of the polarity of the amide group, the lower-molecular-weight amides are relatively high-melting and water-soluble, as compared to esters, amines, alcohols, and the like. The few that are liquids, such as *N,N*-dimethylmethanamide and 1-methyl-1-aza-2-cyclopentanone, have excellent solvent properties for both polar and nonpolar substances. Therefore they are good solvents for displacement reactions of the S_N type (Table 8-5).



Another very important consequence of amide structure is the extensive molecular association of amides through hydrogen bonding. The relatively negative oxygens act as the hydrogen acceptors while N–H hydrogens serve as the hydrogen donors:



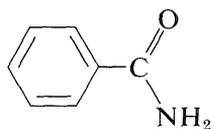
Exercise 24-1 Amides with structures like the following are difficult to prepare and are relatively unstable. Explain.



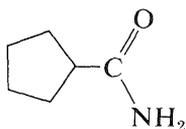
24-1B Nomenclature

The naming of amides is summarized in Section 7-7D. The points to remember are that they generally are named either as (i) *alkanamides*, in which the prefix *alkan(e)* is determined by the longest carbon chain that *includes* the

carbonyl group ($\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ is methanamide), or as (ii) substituted *carboxamides*, $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$, in which the name is completed by identifying the R substituent:

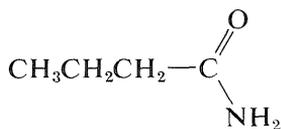


benzenecarboxamide
(benzamide)

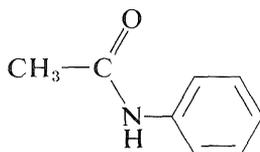


cyclopentanecarboxamide

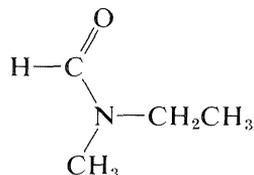
The degree of substitution on the amide nitrogen determines whether the amide is *primary*, RCONH_2 , *secondary*, RCONHR , or *tertiary*, RCONR_2 . When the amide is secondary or tertiary, the symbol *N* (for nitrogen) must precede the name of *each* different group attached to nitrogen:



butanamide
(primary)

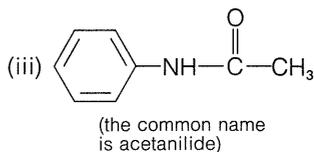
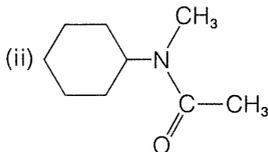
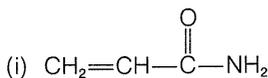


N-phenylethanamide
(secondary)



N-ethyl-*N*-methylmethanamide
(tertiary)

Exercise 24-2 a. Name each of the following compounds by the system described in this section:



b. Write a structure to represent each compound shown:

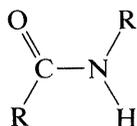
(i) *N*-ethylbenzenecarboxamide

(ii) *N*-cyclohexyl-2-methylpropanamide

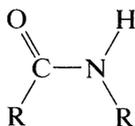
24-1C Infrared Spectra

Considerable information is available on the infrared spectra of amides. By way of example, the spectra of three typical amides with different degrees of substitution on nitrogen are shown in Figure 24-1.

A strong carbonyl absorption is evident in the spectra of all amides, although the frequency of absorption varies somewhat with the structure of the amide. Thus primary amides generally absorb near 1680 cm^{-1} , whereas secondary and tertiary amides absorb at slightly lower frequencies. The N—H stretching frequencies of amides are closely similar to those of amines and show shifts of 100 cm^{-1} to 200 cm^{-1} to lower frequencies as the result of hydrogen bonding. Primary amides have two N—H bands of medium intensity near 3500 cm^{-1} and 3400 cm^{-1} , whereas secondary amides, to a first approximation, have only one N—H band near 3440 cm^{-1} . However, a closer look reveals that the number, position, and intensity of the N—H bands of mono-substituted amides depend on the conformation of the amide, which can be either *cis* or *trans*:

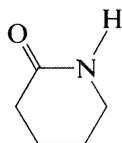


trans (or *E*)



cis (or *Z*)

Normally, the *trans* conformation is more stable than the *cis* conformation for primary amides. However, for cyclic amides (lactams), in which the ring size is small, the configuration is exclusively *cis*:



1-aza-2-cyclohexanone
(δ -valerolactam)

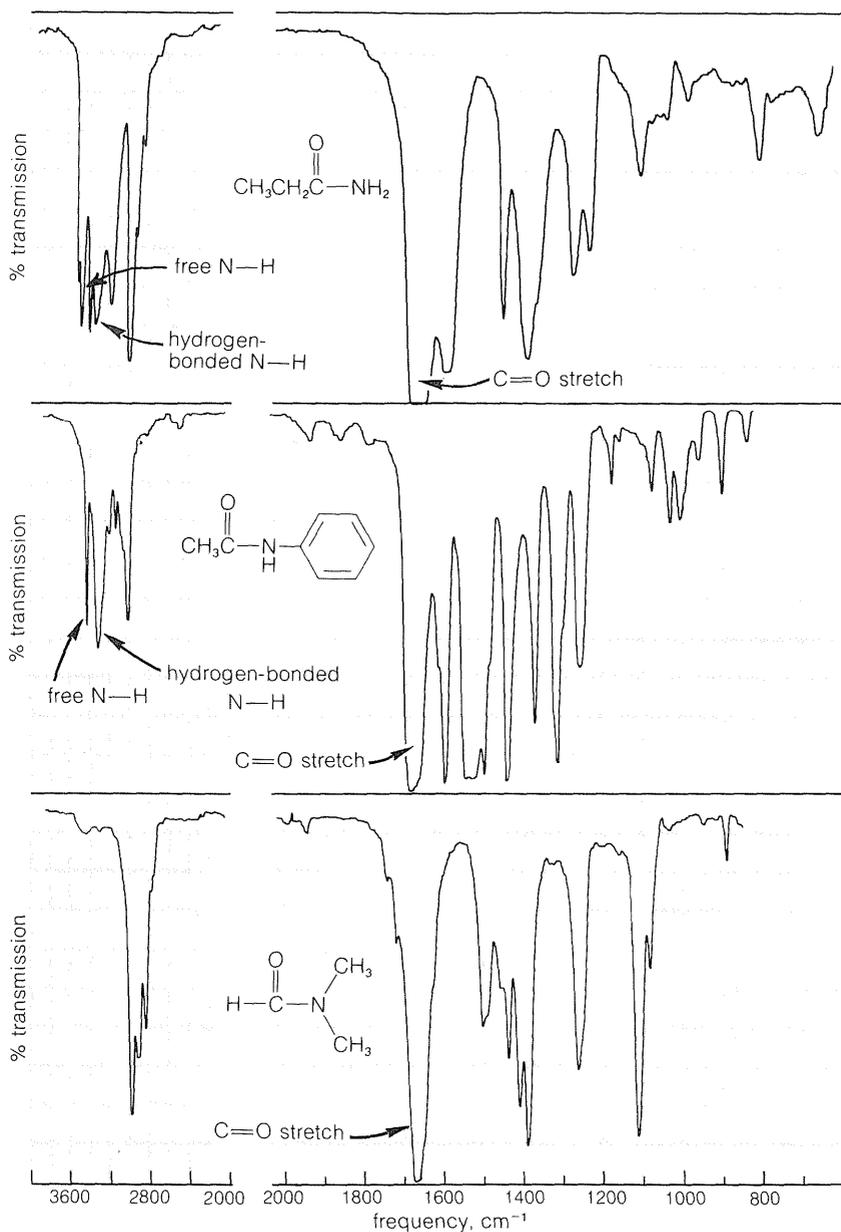


Figure 24-1 Infrared spectra of propanamide, *N*-phenylethanamide, and *N,N*-dimethylmethanamide in chloroform solution. Notice the appearance of both free NH bands (sharp, 3300–3500 cm^{-1}) and hydrogen-bonded NH bands (broad, 3100–3300 cm^{-1}) for primary and secondary amides.

24-1D NMR Spectra

The proton nmr resonances of the N—H protons of amides are different from any we have discussed so far. Generally, these will appear at room temperature as a broad singlet absorption, which may turn into a broad triplet at higher temperatures. A typical example is propanamide (Figure 24-2).

The broad N—H proton resonance is due to the special nuclear properties of ^{14}N , the predominant natural isotope of nitrogen. This is established beyond question by observation of the proton spectrum of an amide in which the ^{14}N is replaced by the ^{15}N isotope to give $\text{RCO}^{15}\text{NH}_2$. In this case the proton lines are sharp. The details of the phenomena that lead to the broad resonances of the N—H protons in amides are discussed elsewhere;¹ for our purposes it should suffice to note that the ^{14}N nucleus has much shorter lifetimes for its magnetic states than do protons, and the broad lines result from uncertainties in the lifetimes of the states associated with ^{14}N —H spin-spin coupling (Section 27-1). One should be prepared for absorptions of this character in amides and some other substances with N—H bonds that are not involved in rapid intermolecular proton exchanges. That similar behavior is not observed for the N—H resonances of aliphatic amines (see Figure 23-5) is the result of intermolecular proton exchanges, which, when sufficiently rapid, have the effect of averaging the magnetic effects of the ^{14}N atoms to zero:

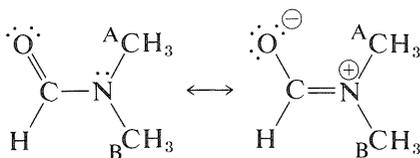


or



The situation here is analogous to that discussed previously for the splitting of the resonances of O—H protons of alcohols by protons on the α carbons (see Section 9-10I).

The nmr spectra of amides are revealing as to the structure of the amide group. For example, the spectrum of *N,N*-dimethylmethanamide shows *two* three-proton single resonances at 2.78 ppm and 2.95 ppm, which means that at ordinary temperatures the two methyl groups on nitrogen are not in the same molecular environment:



This is a consequence of the double-bond character of the C—N bond expected from valence-bond structures **1a** and **1b**, which leads to restricted rotation

¹J. D. Roberts, *Nuclear Magnetic Resonance, Applications to Organic Chemistry*, McGraw-Hill Book Co., New York, 1959, Chapter 5. Also see the nmr references at the end of Chapter 9 in this book.

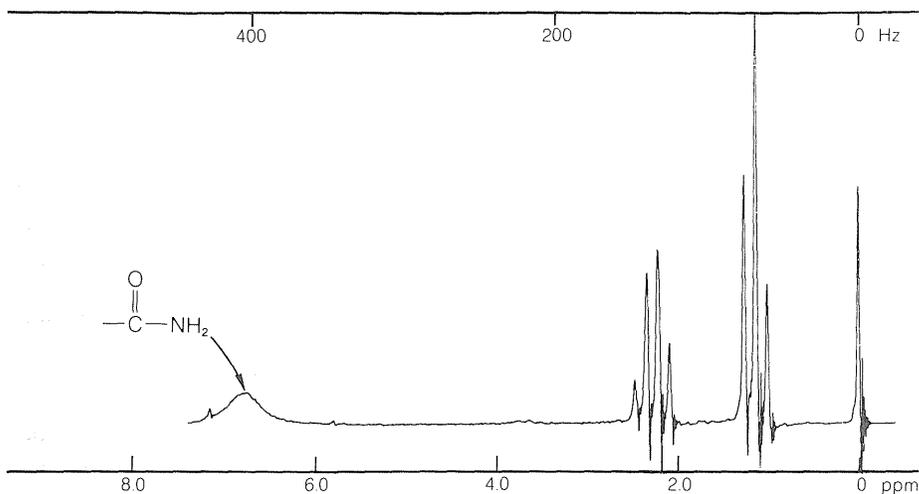
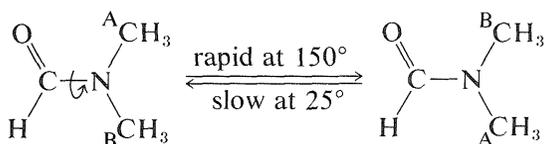


Figure 24-2 Proton nmr spectrum of propanamide, $\text{CH}_3\text{CH}_2\text{CONH}_2$, in chloroform solution (solvent not shown) at 60 MHz relative to TMS at 0.0 ppm

about this linkage. One of the methyl groups (A) has a different stereochemical relationship to the carbonyl group than the other methyl group (B). Groups A and B therefore will have different chemical shifts, provided that rotation about the C—N bond is slow. However, at 150° the two three-proton lines are found to coalesce to a single six-proton line, which means that at this temperature bond rotation is rapid enough to make the methyl groups essentially indistinguishable (see Section 9-10C):



Most amides do not rotate freely about the C—N bond. The barrier to this kind of rotation is about $19 \text{ kcal mole}^{-1}$, which is high enough for the non-equivalence of groups on nitrogen to be observable by spectral techniques, but not quite high enough to allow for actual physical separation of stable *E,Z* configurational isomers.

Exercise 24-3 Show how structures can be deduced for the two substances with the molecular formulas $\text{C}_5\text{H}_9\text{NO}_3$ and $\text{C}_{10}\text{H}_{13}\text{NO}$ from their infrared and nmr spectra, as given in Figure 24-3.

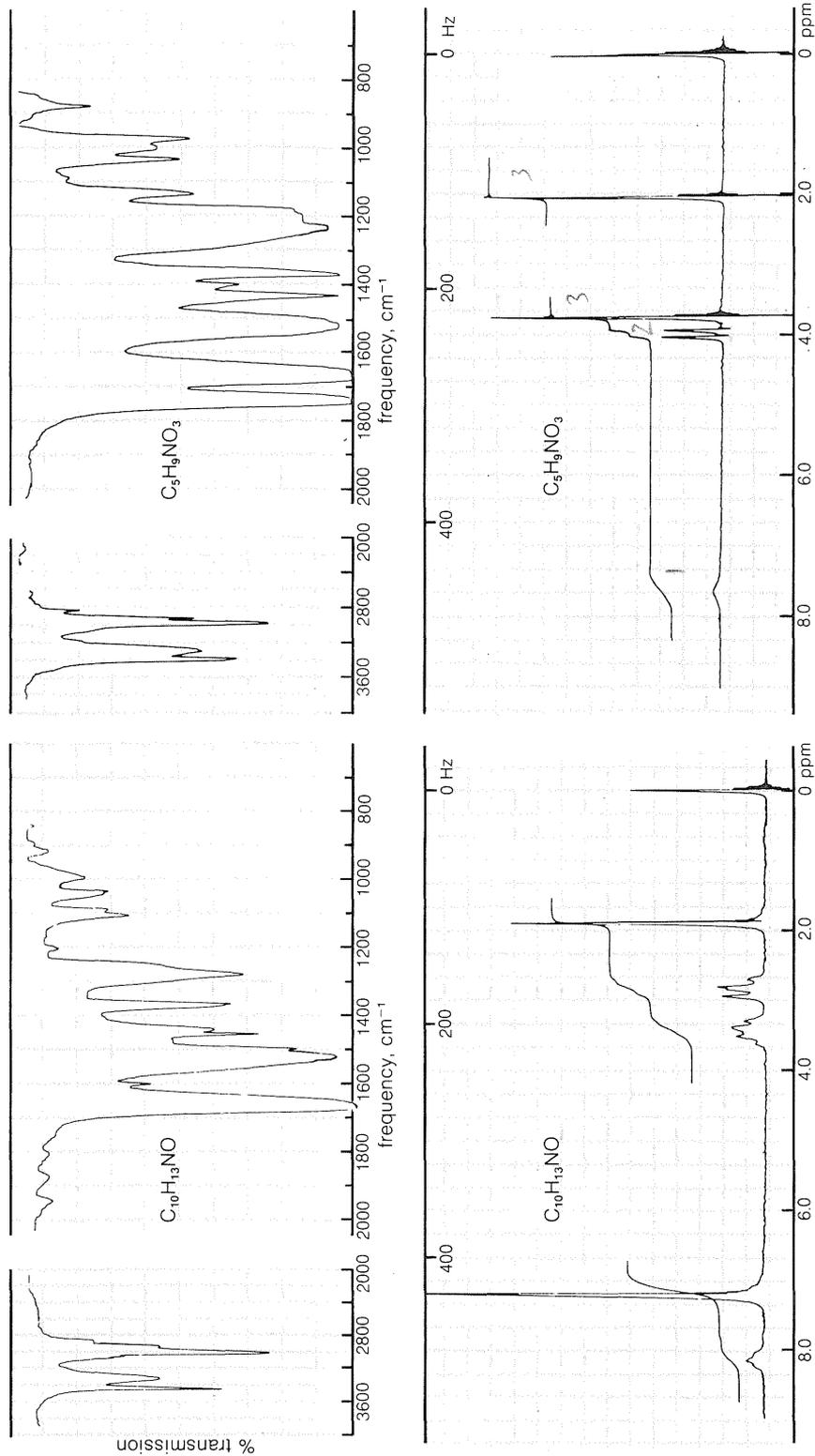


Figure 24-3 The infrared and proton nmr spectra of a substance C₁₀H₁₃NO and a substance C₅H₉NO₃ (see Exercise 24-3). The proton spectra were taken at 60 MHz with TMS as 0.0 ppm.

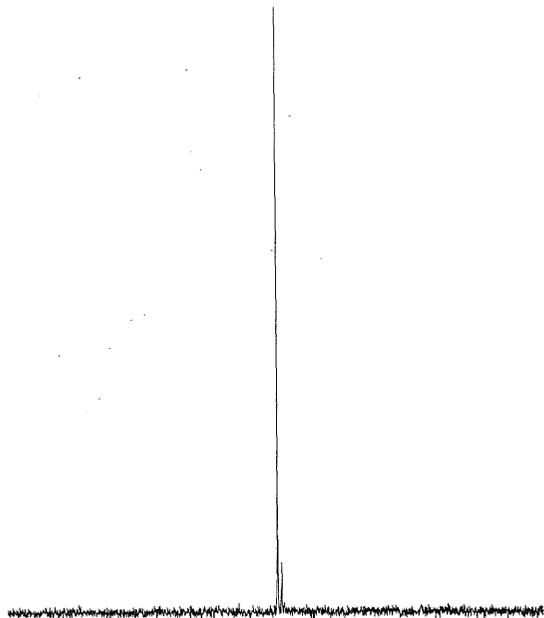


Figure 24-4 Natural-abundance ^{15}N spectrum of *N*-methylmethanamide, HCONHCH_3 , taken at 18.2 MHz with proton decoupling. The large and small peaks are separated by 2 ppm. See Exercise 24-5.

Exercise 24-4 Primary amides give a strong peak at m/e 44 in their mass spectra. Indicate the nature of this peak and suggest how it might be formed.

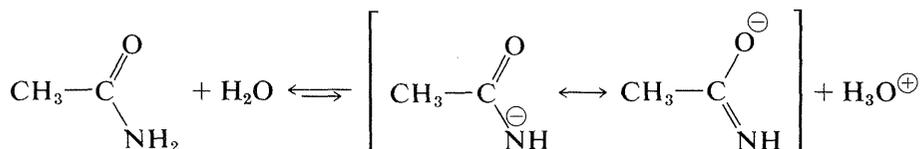
Exercise 24-5* a. The ^{15}N nmr spectrum *with proton decoupling* (Section 9-10I) of *N*-methylmethanamide (Figure 24-4) shows two closely spaced signals of unequal height. Explain how these peaks arise and what you would expect the spectrum to look like if it were taken at 150° .

b. The proton-decoupled ^{15}N spectra of lactams dissolved in CHCl_3 show only one peak when the ring size is 5, 6, 7, 8, 10, and 11, but two unequal peaks when the ring size is 9. Account for this behavior. (Review Section 12-7.)

24-2 AMIDES AS ACIDS AND BASES

24-2A Acidity

Amides with N–H bonds are weakly acidic, the usual K_a being about 10^{-16} :

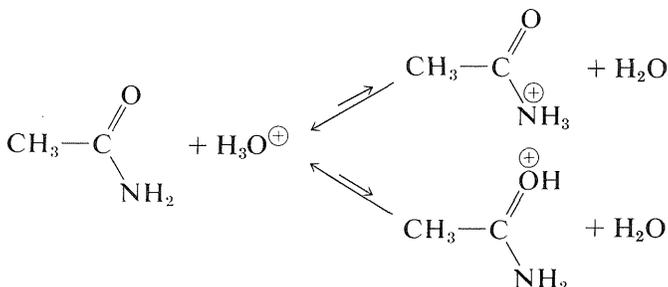


Nonetheless, amides clearly are far more acidic than ammonia ($K_a \sim 10^{-33}$), and this difference reflects a substantial degree of stabilization of the amide anion. However, amides still are very weak acids (about as weak as water) and, for practical purposes, are regarded as neutral compounds.

Where there are *two* carbonyl groups to stabilize the amide anion, as in the 1,2-benzenedicarboximide (phthalimide) anion (Section 18-10C), the acidity increases markedly and imides can be converted to their conjugate bases with concentrated aqueous hydroxide ion. We have seen how imide salts can be used for the synthesis of primary amines (**Gabriel synthesis**, Section 23-9D and Table 23-6).

24-2B Basicity

The degree of basicity of amides is very much less than that of aliphatic amines. For ethanamide, K_b is about 10^{-15} (K_a of the conjugate acid is ~ 10):



The proton can become attached either to nitrogen or to oxygen, and the choice between the assignments is not an easy one. Of course, nitrogen is intrinsically more basic than oxygen; but formation of the *N*-conjugate acid would cause loss of all the amide stabilization energy. Addition to oxygen actually is favored, but amides are too weakly basic for protonation to occur to any extent in water solution.

Exercise 24-6 Explain how the temperature variation of the proton nmr spectrum of *N,N*-dimethylmethanamide in strongly acidic solution might be used to decide whether amides accept a proton on nitrogen or oxygen. Review Section 24-1D.

24-3 SYNTHESIS OF AMIDES

24-3A From Carboxylic Acids

Formation of amides from carboxylic acid derivatives already has been discussed in some detail (Section 23-9A):

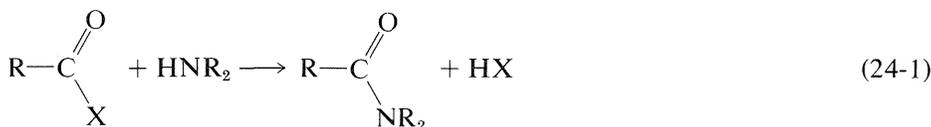
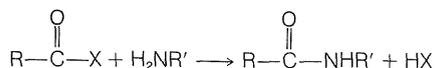
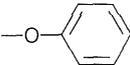
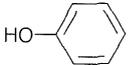
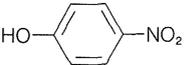
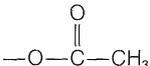
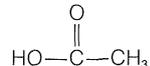
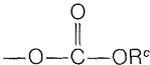


Table 24-1

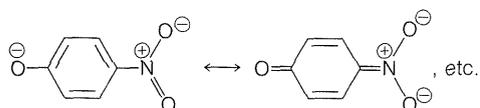
Derivatives and Reactivity of Carboxylic Acids Commonly Used in Amide Formation



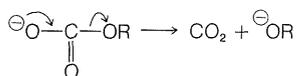
X	HX	pK _a of HX	Reactivity in amide formation
—OH	HOH	16	low ^a
—Cl	HCl	—6	good
—N ₃	HN ₃	3	good
—OCH ₂ CH ₃	HOCH ₂ CH ₃	16	low
		9.89	moderate
		7.15	good ^b
		4.75	moderate
	—	—	good ^c

^aAt ordinary temperatures, requires activation through a coupling agent (Section 23-9A), but on strong heating can give amide directly.

^bGood leaving group because of stabilization of the type



^cGood leaving group, possibly because of associated decomposition to more stable products

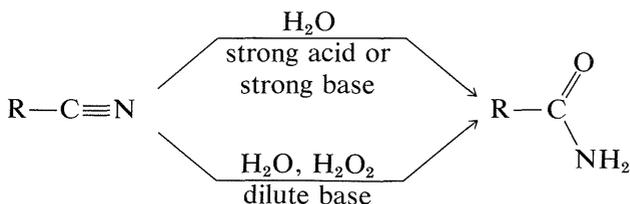


The ease of formation of amides by the reaction of Equation 24-1 depends a lot on the nature of the leaving group X. The characteristics of a good leaving group were discussed in Sections 8-7C and 8-7D in connection with S_N reactions, and similar considerations apply here. Some idea of the range of acid derivatives used in amide synthesis can be obtained from Table 24-1, which lists various RCOX compounds and the pK_a values of HX. As a reasonable rule of thumb, the stronger HX is as an acid, the better X is as a leaving group.

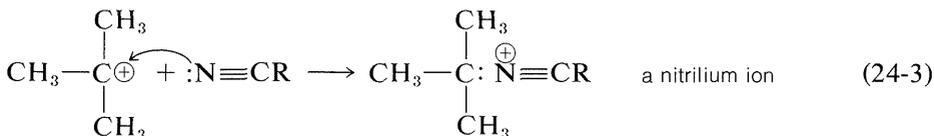
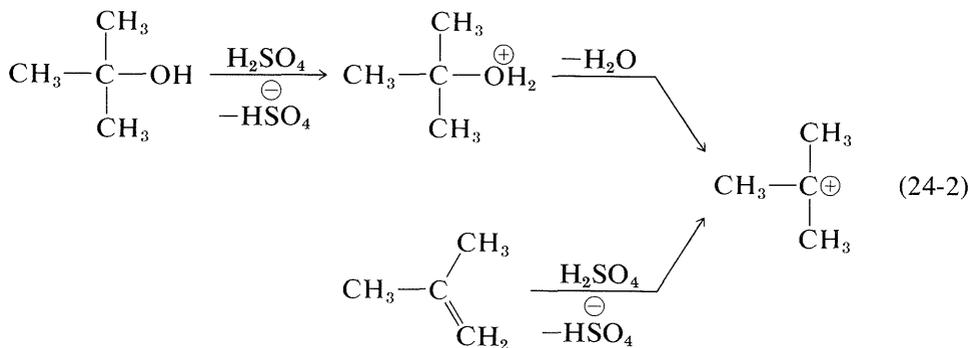
Amides generally are formed from acid chlorides, acid azides, acid anhydrides, and esters. It is not practical to prepare them directly from an amine and a carboxylic acid without strong heating or unless the reaction is coupled to a second reaction that “activates” the acid (see Exercise 15-25). Notice that esters of phenols are more reactive toward amines than esters of alcohols because phenols are stronger acids than alcohols.

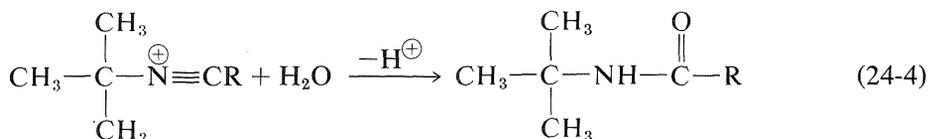
24-3B From Nitriles

The hydrolysis of nitriles is a satisfactory method for preparation of unsubstituted amides and is particularly convenient when hydrolysis is induced under mildly basic conditions by hydrogen peroxide (see Exercise 24-8):

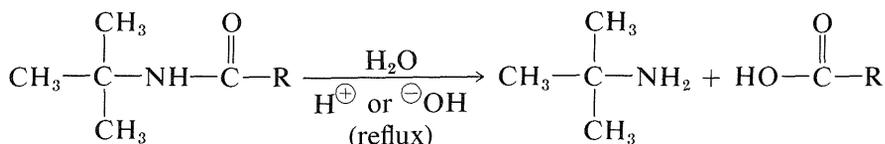


For the preparation of amides of the type R_3CNHCOR , which have a tertiary alkyl group bonded to nitrogen, the **Ritter reaction** of an alcohol or alkene with a nitrile or hydrogen cyanide is highly advantageous. This reaction involves formation of a carbocation by action of strong sulfuric acid on an alkene or an alcohol (Equation 24-2), combination of the carbocation with the unshared electrons on nitrogen of RCN : (Equation 24-3), and then addition of water (Equation 24-4). We use here the preparation of an *N-tert*-butylalkanamide as an example; $\text{RC}\equiv\text{N}$ can be an alkyl cyanide such as ethanenitrile or hydrogen cyanide itself:





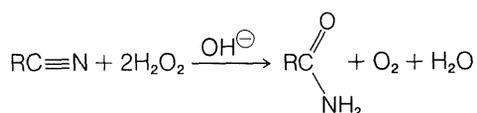
This reaction also is useful for the preparation of primary amines by hydrolysis of the amide. It is one of the relatively few practical methods for synthesizing amines with a tertiary alkyl group on the nitrogen:



Exercise 24-7 a. Draw the two important valence-bond structures for a nitrilium ion $[\text{RCNR}]^{\oplus}$ and write the steps involved in hydration of a nitrilium ion to an amide, RCNHR .

b. Would you expect *N*-methylethanamide to be formed from methanol and ethanenitrile in H_2SO_4 ? Explain.

Exercise 24-8 Nitriles are converted readily to amides with hydrogen peroxide in dilute sodium hydroxide solution. The reaction is



The rate equation is

$$v = k[\text{H}_2\text{O}_2][\text{OH}^{\ominus}][\text{RC}\equiv\text{N}]$$

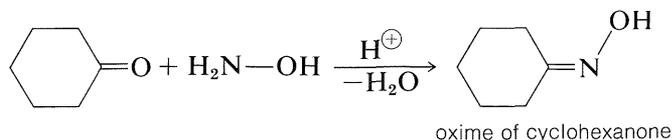
When hydrogen peroxide labeled with ^{18}O ($\text{H}_2^{18}\text{O}_2$) is used in ordinary water (H_2^{16}O), the resulting amide is labeled with ^{18}O ($\text{RC}^{18}\text{ONH}_2$).

Write a mechanism for this reaction that is consistent with *all* the experimental facts. Notice that hydrogen peroxide is a weak acid ($K_a \sim 10^{-12}$), and in the absence of hydrogen peroxide, dilute sodium hydroxide attacks nitriles very slowly.

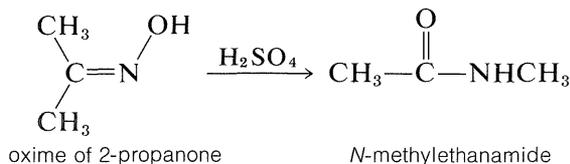
Exercise 24-9 Show how the following transformations could be achieved: $\text{C}_6\text{H}_5\text{-CH}_2\text{CO}_2\text{CH}_3 \longrightarrow \text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CH}_3)_2\text{OH} \longrightarrow \text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CH}_3)_2\text{NHCHO}$. Name the product by the system used in Section 24-1B.

24-3C The Beckmann Rearrangement of Oximes

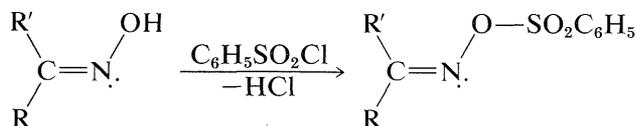
You may recall that ketones react with RNH_2 compounds to give products with a double bond to nitrogen, $\text{C}=\text{NR}$ (Section 16-4C). When the RNH_2 compound is azanol (hydroxylamine), $\text{HO}-\text{NH}_2$, the product is called a **ketoimine**, or oxime:



Oximes rearrange when heated with a strong acid, and this reaction provides a useful synthesis of amides:

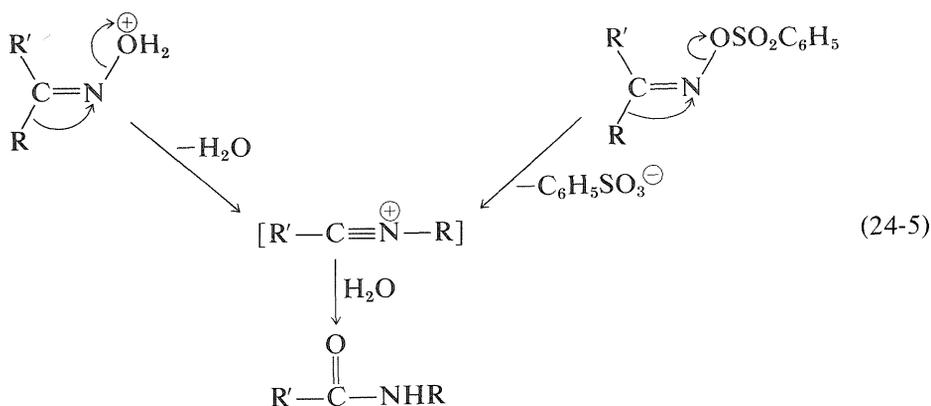


This intriguing reaction is known as the **Beckmann rearrangement**. It has been the subject of a number of mechanistic studies that have shown the acid or acid halide (PCl_5 , $\text{C}_6\text{H}_5\text{SO}_2\text{Cl}$) makes the hydroxyl group on nitrogen into a better leaving group by forming $-\text{OH}_2^+$ or ester intermediates:



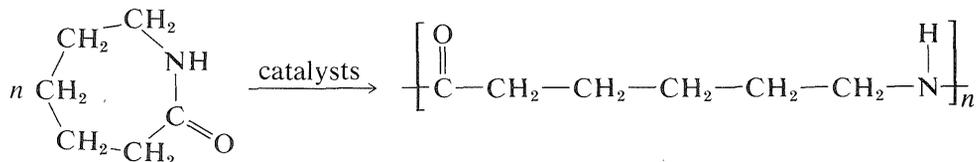
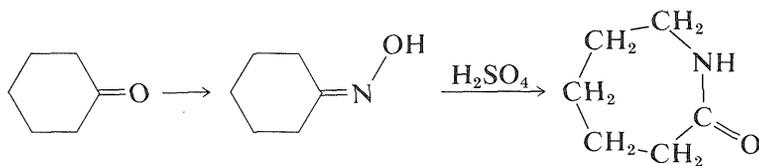
Thereafter, a rearrangement occurs resembling the reactions of carbocations (Sections 8-9B and 15-5E). When the cleavage of the $\text{N}-\text{O}$ bond occurs, the nitrogen atom would be left with only six valence electrons. However, as the bond breaks, a substituent R on the neighboring carbon moves with its bonding

electron pair to the developing positive nitrogen (Equation 24-5):



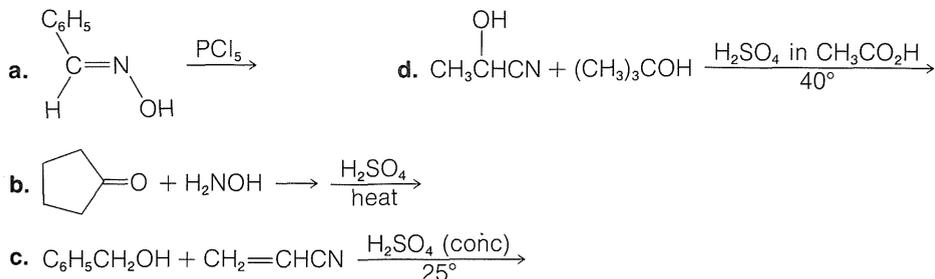
Oximes with R and R' as different groups exist as *E* and *Z* isomers (Section 19-7) and you will notice in Equation 24-5 that the group that migrates is the one that is *trans* to the leaving group. To some extent the Beckmann rearrangement is an internal $\text{S}_{\text{N}}2$ reaction with inversion at the nitrogen. Section 21-10F gives a theoretical treatment of this kind of reaction. The rearrangement product is a nitrilium ion, as in the Ritter reaction (Section 24-3B), which adds water to form the amide.

The synthesis of aza-2-cycloheptanone (ϵ -caprolactam) by the Beckmann rearrangement of the oxime of cyclohexanone is of commercial importance because the lactam is an intermediate in the synthesis of a type of nylon (a polyamide called "nylon-6"²):



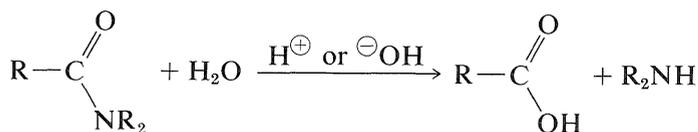
²The number 6 specifies the number of carbons in each monomer unit comprising the polyamide structure. By this code, nylon-6,6 is $(-\text{NH}(\text{CH}_2)_6\text{NHCO}(\text{CH}_2)_4\text{CO}-)_n$.

Exercise 24-10 Complete the following reactions to show the structures of the products formed:

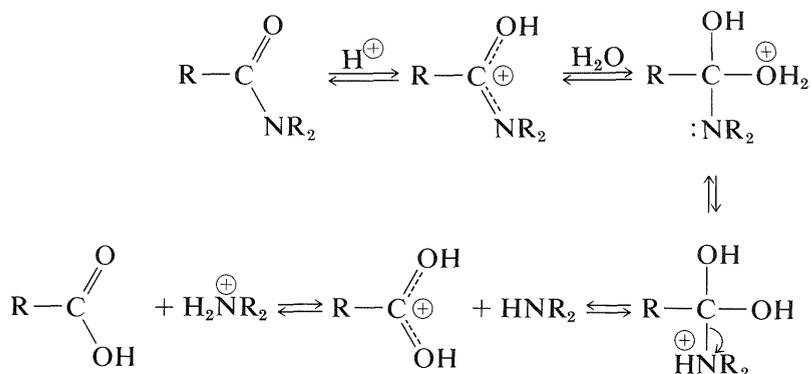


24-4 HYDROLYSIS OF AMIDES

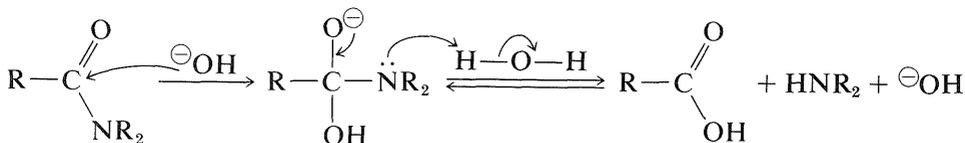
Generally, amides can be hydrolyzed in either acidic or basic solution. The mechanisms are much like those of ester hydrolysis (Section 18-7A), but the reactions are very much slower, a property of great biological importance (which we will discuss later):



As we have indicated in Section 23-12, amide hydrolysis can be an important route to amines. Hydrolysis under acidic conditions requires strong acids such as sulfuric or hydrochloric, and temperatures of about 100° for several hours. The mechanism involves protonation of the amide on oxygen followed by attack of water on the carbonyl carbon. The tetrahedral intermediate formed dissociates ultimately to the carboxylic acid and the ammonium salt:

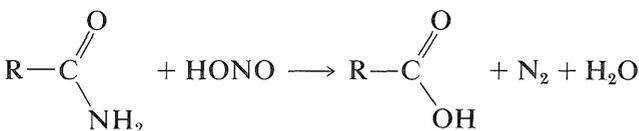


In alkaline hydrolysis the amide is heated with boiling aqueous sodium or potassium hydroxide. The nucleophilic hydroxide ion adds to the carbonyl carbon to form a tetrahedral intermediate, which, with the help of the aqueous solvent, expels the nitrogen as the free amine:

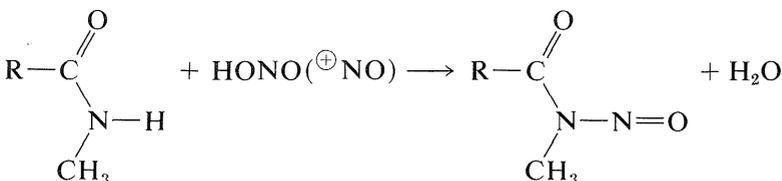


Biological amide hydrolysis, as in the hydrolysis of peptides and proteins, is catalyzed by the proteolytic enzymes. These reactions will be discussed in Chapter 25.

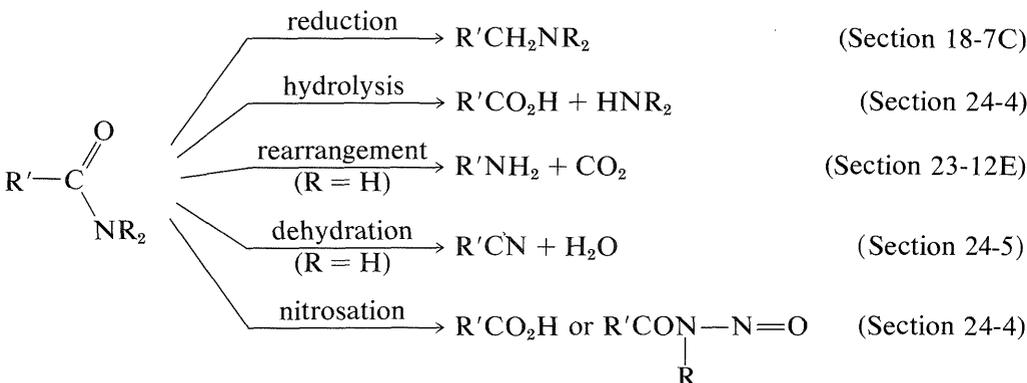
An indirect method of hydrolyzing some amides utilizes nitrous acid. Primary amides are converted easily to carboxylic acids by treatment with nitrous acid. These reactions are very similar to that which occurs between a primary amine and nitrous acid (Section 23-10):



Secondary amides give *N*-nitroso compounds with nitrous acid, whereas tertiary amides do not react:



A brief summary of important amide reactions follows:



Of the many other types of organonitrogen compounds known, the more important include

nitriles, $\text{R}-\text{C}\equiv\text{N}$	(Section 24-5)
isonitriles, $\text{R}-\text{N}=\text{C}$:	
nitro compounds, $\text{R}-\text{NO}_2$	(Section 24-6)
nitroso compounds, $\text{R}-\text{NO}$	(Section 24-6C)
nitrile oxides, $\text{R}-\overset{\oplus}{\text{C}}\equiv\overset{\ominus}{\text{N}}-\overset{\ominus}{\text{O}}$	} (Section 23-11B)
amine oxides, $\overset{\oplus}{\text{R}_3\text{N}}-\overset{\ominus}{\text{O}}$	
isocyanates, $\text{R}-\text{N}=\text{C}=\text{O}$	(Section 23-12E)
hydrazines, $\text{R}_2\text{N}-\text{NR}_2$	(Section 24-7A)
azo compounds, $\text{R}-\text{N}=\text{N}-\text{R}$	(Sections 23-10C and 24-7B)
diazo compounds, $\text{R}_2\overset{\oplus}{\text{C}}=\overset{\ominus}{\text{N}}=\overset{\ominus}{\text{N}}$	(Section 24-7C)
azides, $\text{R}-\overset{\oplus}{\text{N}}=\overset{\ominus}{\text{N}}=\overset{\ominus}{\text{N}}$	(Section 23-12E, Table 23-6, and Section 24-7D)
diazonium ions, $\text{R}-\overset{\oplus}{\text{N}}\equiv\text{N}$	(Section 23-10)
azoxy compounds, $\text{R}-\overset{\oplus}{\text{N}}(\overset{\ominus}{\text{O}})=\text{N}-\text{R}$	(Section 24-6C)

Although it is impractical to discuss all of these compounds in detail, we now will describe briefly several that have not been given much attention heretofore.

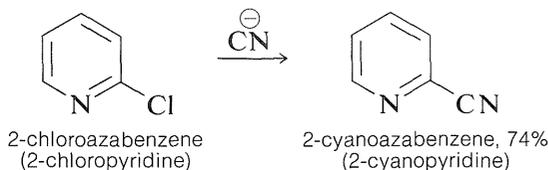
24-5 NITRILES

The carbon–nitrogen triple bond differs considerably from the carbon–carbon triple bond by being stronger (212 kcal mole⁻¹ vs. 200 kcal mole⁻¹) and much more polar. The degree of polarity of the carbon–nitrogen triple bond is indicated by the high dipole moment (4.0 D) of the simple nitriles (RCN), which corresponds to about 70% of the dipole moment expected if *one* of the bonds of the triple bond were fully ionic. With this knowledge it is not surprising that liquid nitriles have rather high dielectric constants compared to most organic liquids and are reasonably soluble in water. Ethanenitrile, CH₃CN, is in fact a good solvent for both polar and nonpolar solutes (Table 8-5).

Nitriles absorb with variable strength in the infrared in the region 2000 cm⁻¹ to 2300 cm⁻¹, due to stretching vibrations of the carbon–nitrogen triple bond.

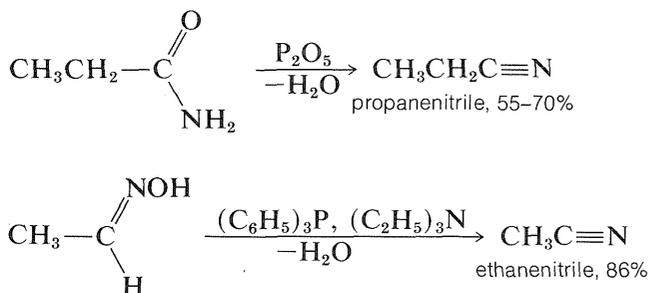
The **preparation of nitriles** by S_N2 reactions between alkyl halides and cyanide ion has been mentioned previously (Section 8-7F) and this is the

method of choice when the halide is available and reacts satisfactorily. Activated aryl or azaaryl halides similarly give nitriles with cyanide ion:



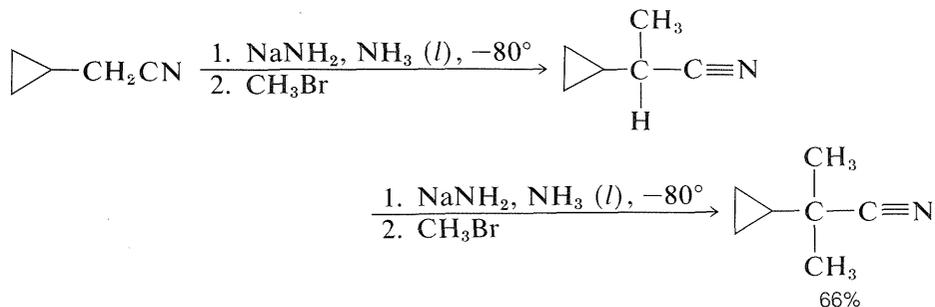
Another practical route to arenecarbonitriles involves the replacement of the diazonium group, $\text{—N}^{\oplus}\equiv\text{N}$, in arenediazonium ions with cuprous cyanide (Section 23-10B). Other useful syntheses involve cyanohydrin formation (Section 16-4A) and Michael addition to conjugated alkenones (Section 17-5B).

Nitriles also can be obtained by the dehydration of the corresponding amide or aldoxime. This is a widely used synthetic method and numerous dehydrating agents have been found to be effective:



The reactions of nitriles include reduction to amines and hydrolysis to acids. Both reactions have been discussed previously (Sections 18-7C and 18-7A).

Hydrogens on the *alpha* carbons of nitriles are about as acidic as the hydrogens alpha to carbonyl groups; accordingly, it is possible to alkylate the α positions of nitriles through successive treatments with a strong base and with an alkyl halide as in the following example:



Exercise 24-11 Nitriles of the type RCH_2CN undergo a self-addition reaction analogous to the aldol addition in the presence of strong bases such as lithium amide. Hydrolysis of the initial reaction product with dilute acid yields a cyanoketone,

$\text{RCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{CN}}{\text{CH}}-\text{R}$. Show the steps that are involved in the mechanism of the overall reaction and outline a scheme for its use to synthesize large-ring ketones of the type $(\text{CH}_2)_n\text{C}=\text{O}$ from dinitriles of the type $\text{NC}(\text{CH}_2)_n\text{CN}$.

Exercise 24-12 Show how the following substances can be synthesized from the indicated starting materials:

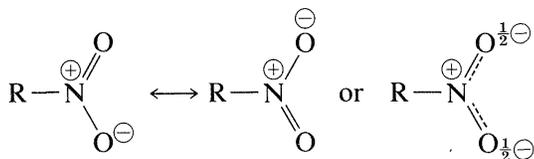
- $(\text{CH}_3)_3\text{CCN}$ from $(\text{CH}_3)_3\text{CCl}$ (two ways)
- $\text{CH}_3\text{CH}=\text{CHCN}$ from $\text{CH}_2=\text{CHCH}_2\text{Br}$
- $\text{CH}_2=\text{CHCO}_2\text{H}$ from CH_3CHO

Exercise 24-13 Propanedinitrile [malononitrile, $\text{CH}_2(\text{CN})_2$] reacts with tetracyanoethene in the presence of base to yield a compound of formula $\text{HC}_3(\text{CN})_5$, which is a monobasic acid of strength similar to sulfuric acid. What is the structure of this compound and why is it such a strong acid? Write a mechanism for the formation of the compound that is based in part on the Michael addition (Section 17-5B).

24-6 NITRO COMPOUNDS

24-6A Physical and Spectroscopic Properties

Nitro compounds are a very important class of nitrogen derivatives. The nitro group, $-\text{NO}_2$, like the carboxylate anion, is a hybrid of two equivalent resonance structures:



The hybrid structure has a full positive charge on nitrogen and a half-negative charge on each oxygen. This is in accord with the high dipole moments of nitro compounds, which fall between 3.5 D and 4.0 D, depending upon the nature of R. The polar character of the nitro group results in lower volatility of nitro compounds than ketones of about the same molecular weight; thus the

boiling point of nitromethane (MW 61) is 101°, whereas 2-propanone (MW 58) has a boiling point of 56°. Surprisingly, the water solubility is low; a saturated solution of nitromethane in water is less than 10% by weight, whereas 2-propanone is completely miscible with water.

Nitro groups of nitroalkanes can be identified by strong infrared bands at about 1550 cm⁻¹ and 1375 cm⁻¹, whereas the corresponding bands in the spectra of aromatic nitro compounds occur at slightly lower frequencies. A weak $n \rightarrow \pi^*$ transition occurs in the electronic spectra of nitroalkanes at around 270 nm; aromatic nitro compounds, such as nitrobenzene, have extended conjugation and absorb at longer wavelengths (~330 nm).

24-6B Preparation of Nitro Compounds

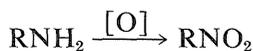
Nitro compounds can be prepared in a number of ways, including the direct substitution of hydrocarbons with nitric acid,



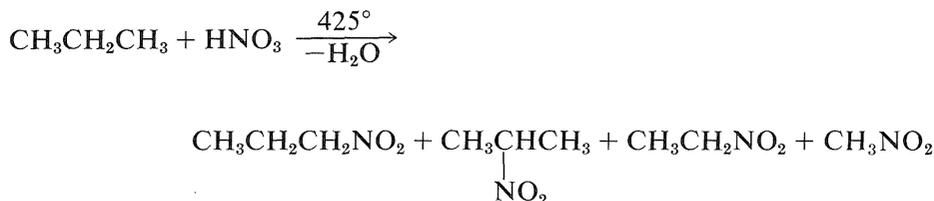
by displacement reactions with nitrite ions,



and by oxidation of primary amines,



Nitration of alkanes is successful only when conducted at high temperatures in the vapor phase. Mixtures of products are invariably obtained (Section 4-6):



In contrast, direct *nitration of aromatic compounds* such as benzene takes place readily in the liquid phase, as discussed in Section 22-4C.

Like other electrophilic substitutions, nitration of a *substituted* benzene, where the substituent is electron withdrawing (NO₂, CO₂H, CN, and so on; Table 22-6), generally produces the 1,3-isomer. To prepare the 1,4-isomer, less direct routes are necessary—the usual stratagem being to use benzene derivatives with substituent groups that produce the desired orientation on

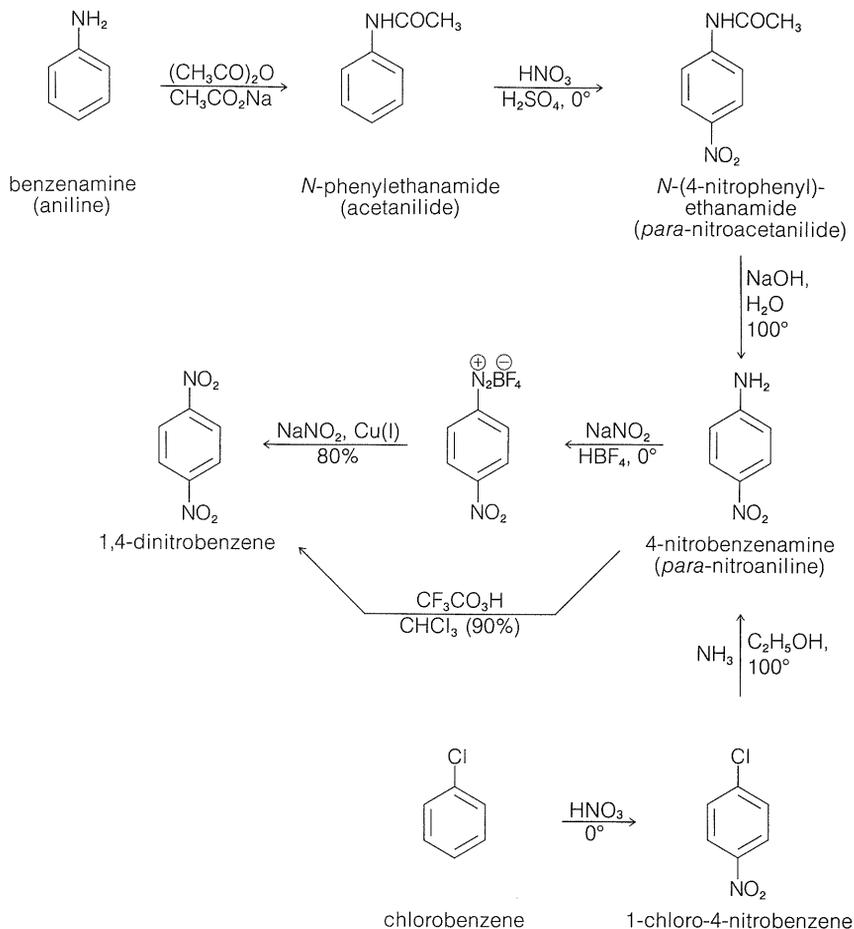
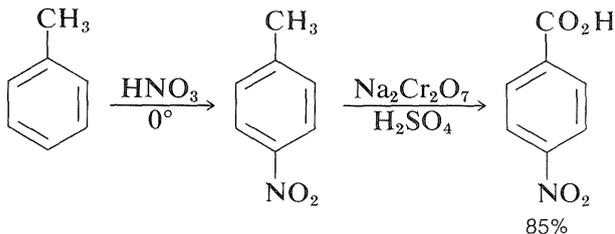


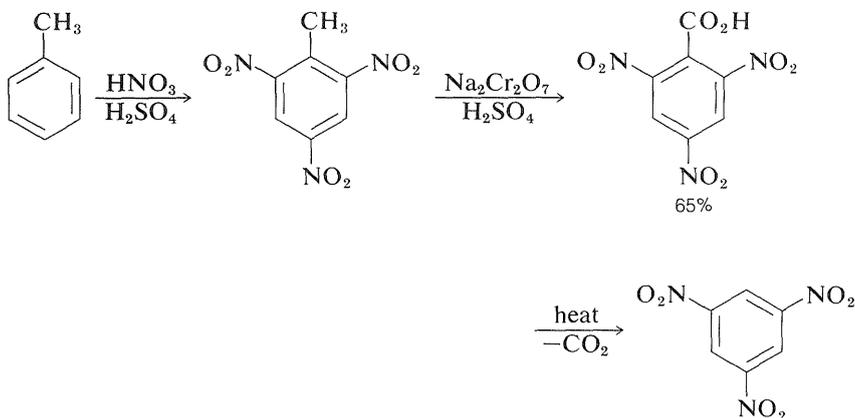
Figure 24-5 Synthetic routes to 1,4-dinitrobenzene

nitration and then to make the necessary modifications in these groups to produce the final product. Thus 1,4-dinitrobenzene cannot be obtained by nitration of nitrobenzene but can be prepared from benzenamine by the sequence shown in Figure 24-5. Benzenamine is converted to *N*-phenylethanamide (acetanilide) which on nitration yields the 1,4-isomer. Hydrolysis of the amide to 4-nitrobenzenamine and replacement of amino by nitro, using nitrite ion in the presence of cuprous salts, gives 1,4-dinitrobenzene (see Section 23-10B). Alternatively, the amino group of 4-nitrobenzenamine can be oxidized to a nitro group by trifluoroperoxyacetic acid. In these syntheses, *N*-phenylethanamide is nitrated in preference to benzenamine itself because, not only is benzenamine easily oxidized by nitric acid, but the nitration

reaction leads to extensive 3-substitution as the result of formation of phenylammonium ion. Another route to 4-nitrobenzenamine is to nitrate chlorobenzene and subsequently replace the chlorine by reaction with ammonia. The nitrations mentioned give mixtures of 2- and 4-isomers, but these usually are easy to separate by distillation or crystallization. The same approach can be used to synthesize 4-nitrobenzoic acid. The methyl group of methylbenzene directs nitration preferentially to the 4 position, and subsequent oxidation with chromic acid yields 4-nitrobenzoic acid:

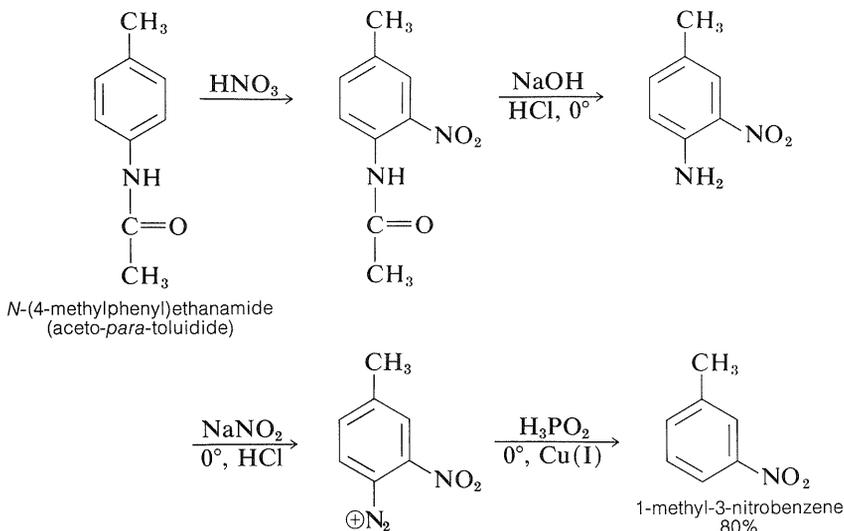


In some cases it may be necessary to have an activating group to facilitate substitution, which otherwise would be very difficult. The preparation of 1,3,5-trinitrobenzene provides a good example; direct substitution of 1,3-dinitrobenzene requires long heating with nitric acid in fuming sulfuric acid. However, methylbenzene is converted more readily to the trinitro derivative and this substance, on oxidation and decarboxylation (Section 18-4), yields 1,3,5-trinitrobenzene:



Acylamino groups also are useful activating groups and have the advantage that the amino groups obtained after hydrolysis of the acyl function can be removed from an aromatic ring by reduction of the corresponding diazonium salt with hypophosphorous acid, preferably in the presence of copper(I) ions.

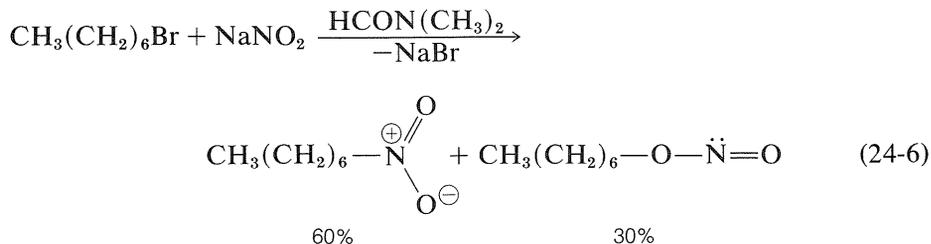
An example is the preparation of 1-methyl-3-nitrobenzene from *N*-(4-methylphenyl)ethanamide (aceto-*para*-toluidide):



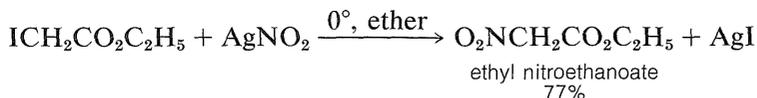
Exercise 24-14 Show how the following compounds may be synthesized from the indicated starting materials. (It may be necessary to review parts of Chapters 22 and 23 to work this exercise.)

- 1-methyl-3,5-dinitrobenzene from methylbenzene
- 1-methyl-2,6-dinitrobenzene from 4-methylbenzenesulfonic acid (notice that $\text{—SO}_3\text{H}$ can be removed by hydrolysis; Section 22-4G)
- 2,4-dinitrobenzenamine from chlorobenzene
- 1-chloro-3,5-dinitrobenzene from chlorobenzene
- 1,2,3-trinitrobenzene from 4-chlorobenzenesulfonic acid

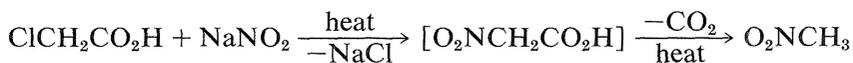
Routes to *aliphatic nitro compounds* include the reaction of an alkyl halide (of good $\text{S}_{\text{N}}2$ reactivity) with nitrite ion. Suitable solvents are methylsulfynylmethane [dimethyl sulfoxide, $(\text{CH}_3)_2\text{SO}$] and dimethylmethanamide (dimethylformamide). As will be seen from Equation 24-6, formation of the nitrite ester by O- instead of N-alkylation is a competing reaction:



Silver nitrite sometimes is used in preference to sodium nitrite, usually in diethyl ether as solvent:



Nitromethane can be prepared conveniently by the reaction



Displacement reactions with nitrite ion do not work well with aryl halides. However, displacement of the diazonium group is a practical route to nitroarenes (the **Sandmeyer reaction**), as described in Section 23-10B:

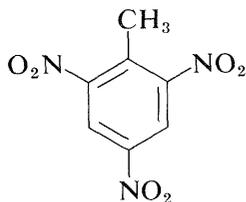


24-6C Reactions of Nitro Compounds

Nitro compounds are quite unstable in the thermodynamic sense; for example, the heat of decomposition of nitromethane, according to the following stoichiometry, is 67.4 kcal mole⁻¹.



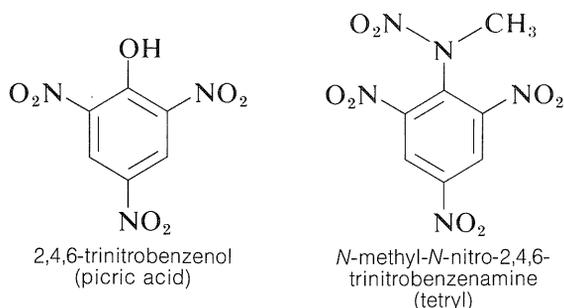
Advantage is taken of the considerable energies and rapid rates of reactions such as this in the commercial use of nitro compounds as explosives. With some nitro compounds, such as TNT, there is a further advantage of low shock sensitivity.



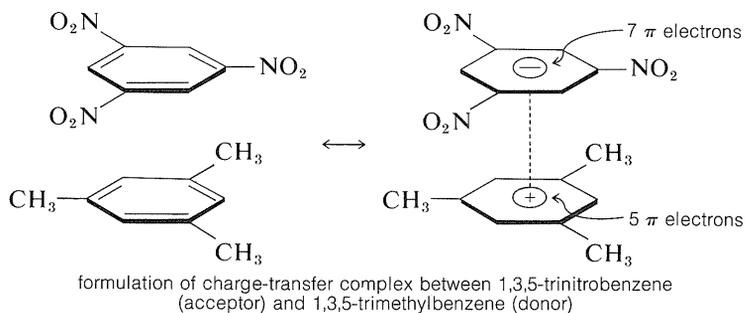
1-methyl-2,4,6-trinitrobenzene
(2,4,6-trinitrotoluene, TNT)

TNT is not detonated easily by simple impact and even burns without exploding. However, once detonation starts, decomposition is propagated rapidly. The characteristics of reasonable handling stability and high thermodynamic

potential make nitro compounds particularly useful. Other polynitro compounds that are useful as explosives include PETN (Section 17-3C), cyclonite (Section 16-4C), picric acid, and tetryl:



An important characteristic of aromatic polynitro compounds is their ability to form “charge-transfer” complexes with aromatic hydrocarbons, especially those that are substituted with alkyl groups. Complexes of 2,4,6-trinitrobenzenol (picric acid) and aromatic hydrocarbons often are crystalline solids, which are useful for the separation, purification, and identification of aromatic hydrocarbons. These substances are called “hydrocarbon picrates,” but the name is misleading because they are not actually salts. Furthermore, similar complexes are formed between aromatic hydrocarbons and trinitrobenzene, which demonstrates that the nitro groups rather than the hydroxyl group are essential to complex formation. The binding in these complexes resembles that in the π complexes of halogens with alkenes and benzene (Sections 22-4D and 10-3C) and results from attractive forces between electron-rich and electron-poor substances. The descriptive name—**charge-transfer complex**—suggests that the complex has VB structures involving transfer of an electron from the donor (electron-rich) molecule to the acceptor (electron-poor) molecule. The name π complex also is used because, usually at least, one component of the complex has a π -electron system. Charge-transfer or π complexes between polynitro compounds and aromatic hydrocarbons appear to give sandwich-type structures with the aromatic rings in parallel planes, although not necessarily centered exactly over one another:



Charge-transfer complexes are almost always more highly colored than their individual components. A spectacular example is benzene and tetracyano-

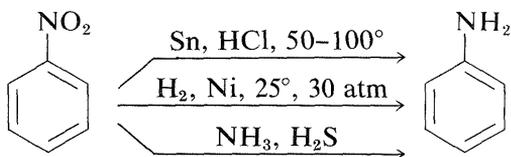
ethene, each of which separately is colorless, but which give a bright-orange complex when mixed. A shift toward longer wavelengths of absorption, relative to their components, is to be expected for charge-transfer complexes because of the enhanced possibility for stabilization of the excited state through electron delocalization involving both components.

Exercise 24-15 Tetracyanoethene in benzene forms an orange solution, but when this solution is mixed with a solution of anthracene in benzene, a brilliant blue-green color is produced, which fades rapidly; colorless crystals of a compound of composition $C_{14}H_{10} \cdot C_2(CN)_4$ then are deposited. Explain the color changes that occur and write a structure for the crystalline product.

Exercise 24-16 Would you expect the dipole moment measured for 1,3,5-trinitrobenzene in 1,3,5-trimethylbenzene solution to be the same as in tetrachloromethane solution? Explain.

Exercise 24-17 Anthracene (mp 217°) forms a red crystalline complex (mp 164°) with 1,3,5-trinitrobenzene (mp 121°). If you were to purify anthracene as this complex, how could you regenerate the anthracene free of trinitrobenzene?

Reduction of nitro compounds occurs readily with a variety of reducing agents and such reductions afford a particularly useful synthesis of aromatic amines (Section 23-12B):



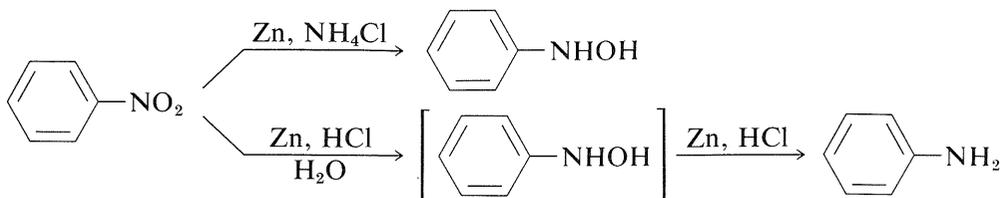
The reduction of a nitro compound to an amine requires six equivalents of reducing agent:



One would not expect such a reduction to occur in a single step. Indeed, reduction is stepwise and proceeds through a string of intermediates, which, with strong reducing agents in acid solution, have at most a transient existence. The intermediates formed successively from RNO_2 by increments of two equivalents of reducing agent are nitroso compounds, $R-N=O$, and *N*-substituted azanols (hydroxylamines), $RNHOH$:

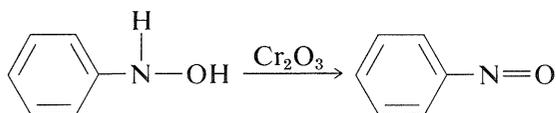


Thus *N*-aryl-substituted azanols can be obtained directly from the corresponding nitro compounds with zinc and ammonium chloride solution. However, zinc and hydrochloric acid gives the amine:

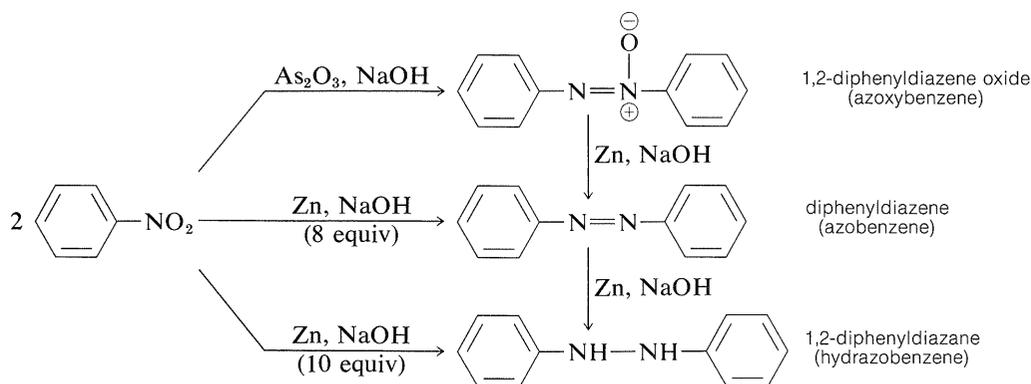


The difference between these reactions is in the reduction rates associated with the *acidity* of the solution. Ammonium chloride is a much weaker acid than HCl ; the pH of ammonium chloride solutions is around 6.

Oxidation of the *N*-arylanzols under controlled conditions yields nitroso compounds. This reaction is not unlike the oxidation of alcohols to ketones (Section 15-6B):



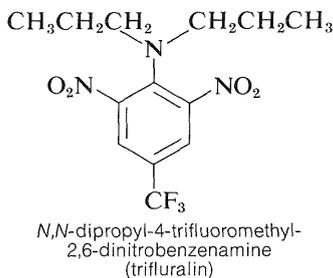
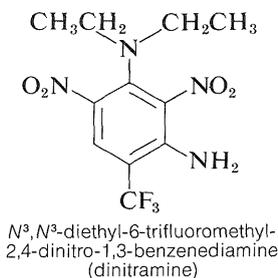
Reduction of aryl nitro compounds with less-powerful reducing agents, especially in alkaline media, gives what may appear to be a mysterious conglomerate of bimolecular reduction products. For example, with nitrobenzene,



All of these substances can be reduced to benzenamine with tin and hydrochloric acid. As a result, each could be, but not necessarily is, an intermediate in the reduction of nitro compounds to amines. Formation of the bimolecular reduction products is the result of base-induced reactions between nitroso compounds and azanols or amines and possibly further reduction of the initially produced substances (see Exercise 24-18).

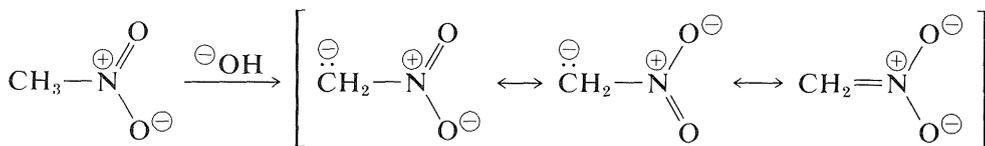
Exercise 24-18* Write the mechanistic steps to show how 1,2-diphenyldiazene oxide and 1,2-diphenyldiazene may be formed by base-induced condensation reactions of nitrosobenzene with *N*-phenylazanol and benzenamine, respectively. What product would you expect to be formed from nitrosobenzene and *N*-(4-chlorophenyl)azanol? Give your reasoning.

Several polynitrobenzene derivatives have important herbicidal uses. Examples are *N*³,*N*³-diethyl-6-trifluoromethyl-2,4-dinitro-1,3-benzenediamine and *N,N*-dipropyl-4-trifluoromethyl-2,6-dinitrobenzenamine:

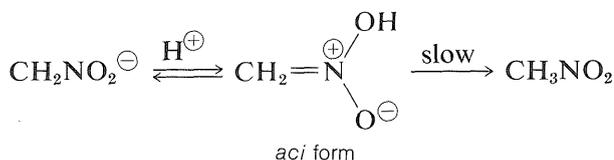


These substances when mixed with soil kill weed seedlings but not crop plants such as cotton, soybeans, and peanuts. The activity is high; normally only about 0.08 g meter⁻² is required for good weed control.

The most important reactions of *nitroalkanes* are those involving the α hydrogens of the primary and secondary compounds. For example, nitromethane is sufficiently acidic to dissolve in aqueous hydroxide solutions. The anion so produced has an electronic structure analogous to the nitrate anion:

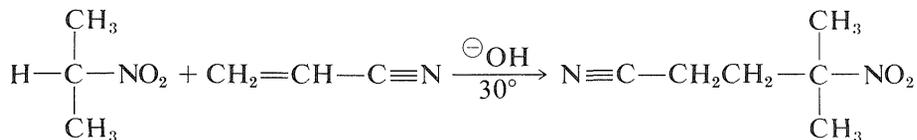
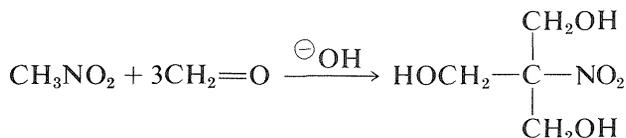
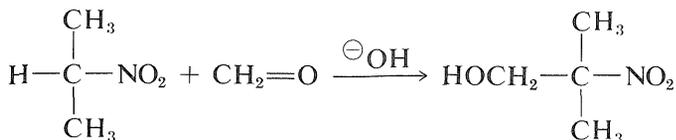


An interesting property of this ion is that when solutions of it are acidified, an unstable, rather strongly acidic isomer of nitromethane (called the *aci* form) is produced, which slowly reverts to the more stable nitro form:



Similar changes take place in the acidification of the enol salt of a carbonyl compound, the principal difference being the much longer life of the *aci*-nitro compound compared to that of an enol of a simple ketone (see Section 17-1B).

Primary and secondary nitro compounds undergo aldol additions and Michael additions with suitable carbonyl compounds and basic catalysts:



Unfortunately, alkylation reactions analogous to the base-catalyzed alkylation of carbonyl compounds generally are not useful for the synthesis of higher nitro compounds, because C-alkylation of the conjugate bases of primary nitro compounds is slower than O-alkylation.

Exercise 24-19 What kind of properties and reactions would you expect the double bond of nitroethene to have? Consider the ease of electrophilic and nucleophilic addition reactions as well as cycloadditions.

Exercise 24-20 Show how the following compounds can be prepared from the commercially available nitroalkanes obtained from the nitration of propane. (It may be desirable to review the material on aldol and Michael additions in Chapters 17 and 18.)

- | | |
|--|--|
| a. $\text{HOCH}_2\text{CH}_2\text{NO}_2$ | d. $\text{HOCH}_2\text{C}(\text{CH}_3)_2\text{NH}_2$ |
| b. $\text{CH}_2=\text{CHNO}_2$ | e. $(\text{N}\equiv\text{CCH}_2\text{CH}_2)_3\text{CNO}_2$ |
| c. $(\text{O}_2\text{NOCH}_2)_3\text{CNO}_2$ | f. $\text{H}_2\text{NCH}_2\text{CH}_2\text{C}(\text{CH}_3)_2\text{NH}_2$ |

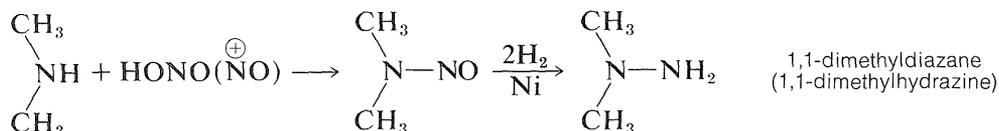
Exercise 24-21 Show how 2-methyl-2-nitropropane may be synthesized from (a) *tert*-butyl alcohol and (b) 2,2-dimethylpropanoic acid. (Review Sections 23-12E and 24-3B if necessary.)

24-7 SOME COMPOUNDS WITH N-N BONDS

Among the organic nitrogen compounds having nitrogen above the oxidation level of ammonia are a wide variety of substances with N-N bonds. We shall mention only a very few of the more important of these substances: hydrazines, azo and diazo compounds, and azides.

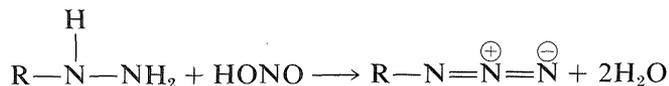
24-7A Hydrazines

Organic hydrazines or diazanes are substitution products of $\text{NH}_2\text{—NH}_2$ and have many properties similar to those of amines in being basic and forming acyl derivatives as well as undergoing alkylation and condensations with carbonyl compounds (Section 16-4C). Unsymmetrical hydrazines can be prepared by careful reduction of *N*-nitrosamines. 1,1-Dimethyldiazane is prepared in this way for use as a rocket fuel:

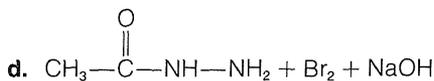
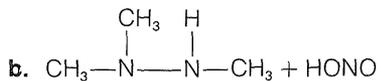
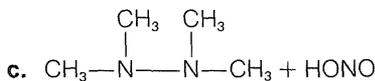
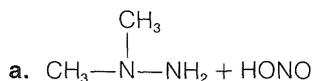


Aromatic hydrazines are best prepared by reduction of aromatic diazonium salts (Table 23-4).

Hydrazines of the type $\text{R—}\overset{\text{H}}{\text{N}}\text{—}\overset{\text{H}}{\text{N}}\text{—R}$ are easily oxidized to the corresponding azo compounds, R—N=N—R . With nitrous acid, monosubstituted hydrazines are converted to azides:



Exercise 24-22 Arguing on the basis of mechanistic principles and knowledge of related reactions, work out products that may be expected for the following reactions:



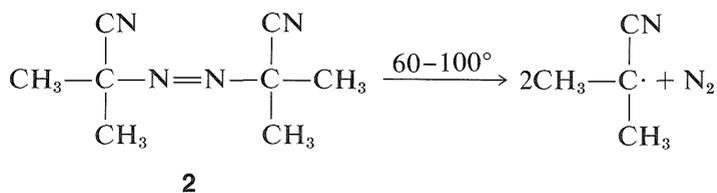
24-7B Azo Compounds

Azo or diazene compounds possess the $-\text{N}=\text{N}-$ grouping. Aliphatic azo compounds of the type $\text{R}-\text{N}=\text{N}-\text{H}$ appear to be highly unstable and decompose to $\text{R}-\text{H}$ and nitrogen. Derivatives of the type $\text{R}-\text{N}=\text{N}-\text{R}$ are much more stable and can be prepared as mentioned above by oxidation of the corresponding hydrazines. Aromatic azo compounds are available in considerable profusion from diazo coupling reactions (Section 23-10C) and are of commercial importance as dyes and coloring materials.

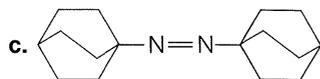
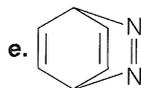
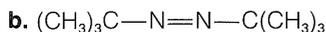
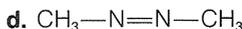
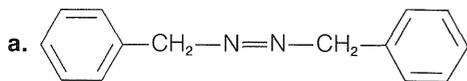
A prime characteristic of azo compounds is their tendency to decompose into organic free radicals and liberate nitrogen:



The ease of these reactions is usually a fairly reliable guide to the stabilities of the free radicals that result. For instance, it is found that dimethyldiazene (azomethane, $\text{CH}_3\text{N}=\text{NCH}_3$) is stable to about 400° , and diphenyldiazene (azobenzene, $\text{C}_6\text{H}_5\text{N}=\text{NC}_6\text{H}_5$) also is resistant to thermal decomposition; but, when the azo compound decomposes to radicals that have extra stability because of delocalization of the odd electron, the decomposition temperature is greatly reduced. Thus the azo compound, **2**, decomposes to radicals at moderate temperatures (60° to 100°), and for this reason is a very useful agent for generating radicals, such as those required for the initiation of polymerization of ethenyl compounds:



Exercise 24-23 Arrange the following azo substances in order of their expected rates of thermal decomposition to produce nitrogen. Give your reasoning.

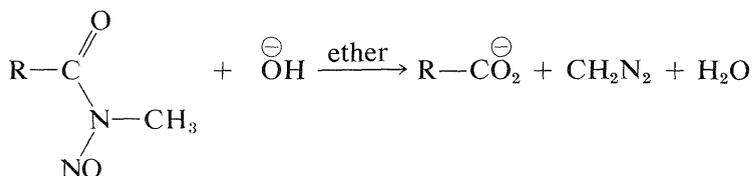


Exercise 24-24 Devise a synthesis (more than one step may be required) of **2** from 2-propanone, hydrazine, and hydrogen cyanide. What would you expect this substance to yield when heated in (a) a perfluorohydrocarbon solvent and (b) a solution of bromine in carbon tetrachloride?

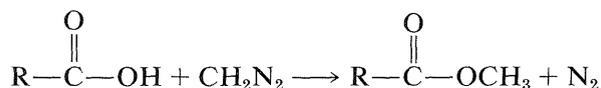
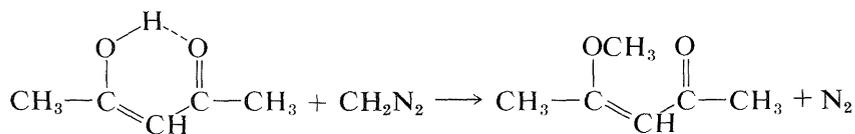
24-7C Diazo Compounds

The parent of the diazo compounds, diazomethane, $\text{CH}_2=\overset{\oplus}{\text{N}}=\overset{\ominus}{\text{N}}$, has been mentioned before in connection with ylide reactions for ring enlargement (Section 16-4A) and the preparation of methyl esters from acids (Table 18-7). It is one of the most versatile and useful reagents in organic chemistry, despite the fact that it is highly toxic, dangerously explosive, and cannot be stored without decomposition.

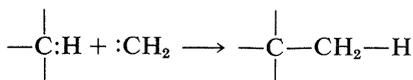
Diazomethane is an intensely yellow gas, bp -23° , which customarily is prepared and used in diethyl ether or dichloromethane solution. It can be synthesized in a number of ways, the most useful of which employs the action of base on an *N*-nitroso-*N*-methylamide:



As a methylating agent of reasonably acidic substances, diazomethane has nearly ideal properties. It can be used in organic solvents; reacts very rapidly without need for a catalyst (except with alcohols, which do require an acid catalyst); the coproduct is nitrogen which offers no separation problem; it gives essentially quantitative yields; and it acts as its own indicator to show when reaction is complete. With enols, it gives O-alkylation:



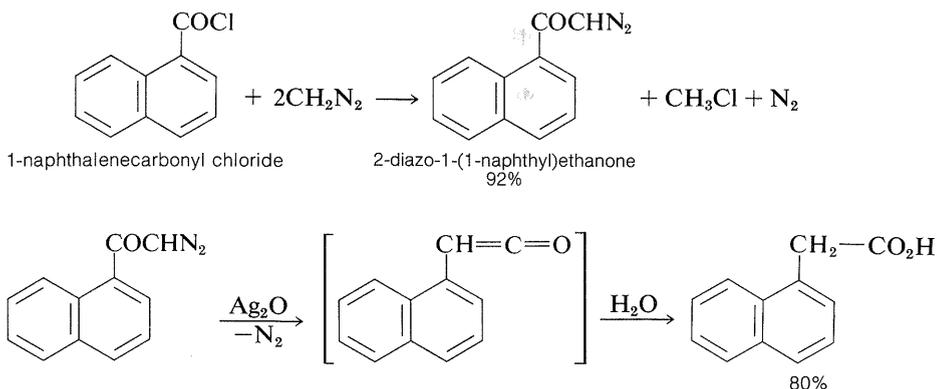
Besides being a methylating agent, diazomethane also is a source of $:CH_2$ when irradiated with light. The carbene formed in this way is highly reactive and even will react with the electrons of a carbon-hydrogen bond to "insert" the carbon of the carbene between carbon and hydrogen. This transforms $-C-H$ to $-C-CH_3$:



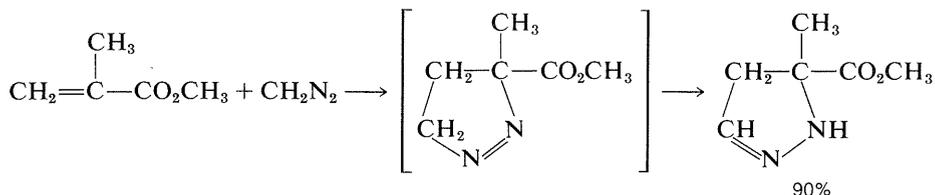
This $:CH_2$ species is one of the most reactive reagents known in organic chemistry.

Diazomethane undergoes a wealth of other unusual reactions. Besides those already mentioned are the following two examples:

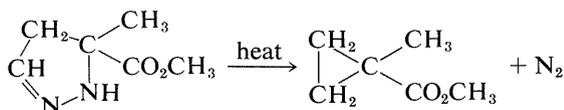
Arndt-Eistert synthesis ($-COCl \longrightarrow -CH_2CO_2H$, Section 16-4A)



Pyrazoline formation ([2 + 3] cycloaddition)

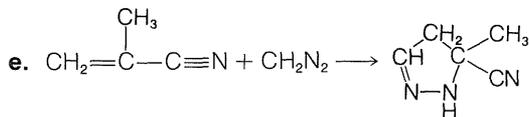
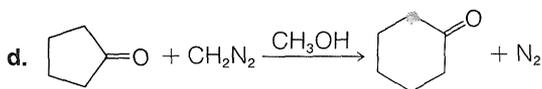
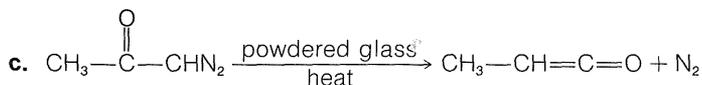
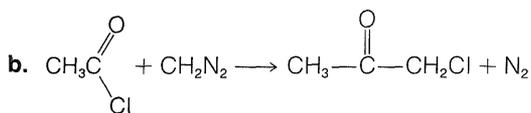
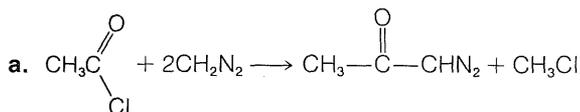


The Arndt-Eistert synthesis is useful for converting an acid to the next higher member of the series. Pyrazolines are important intermediates for the preparation of cyclopropanes:



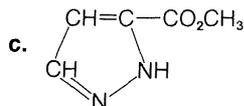
Exercise 24-25 Write the important resonance structures that contribute to the resonance hybrid of diazomethane and show how these can be used to rationalize the formation of methyl ethanoate from diazomethane and ethanoic acid.

Exercise 24-26* Write reasonable mechanisms based on analogy for the following reactions:



Exercise 24-27 Show how the following substances might be made by syntheses based on diazomethane reactions.

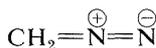
- a. hexanedioic acid (from butanedioic acid)
b. 2,2-dimethylcyclopropanone (see Section 17-11)



Diazomethane originally was believed to possess the three-membered 1,2-diazacyclopropene ring structure, but this concept was disproved by electron-diffraction studies, which showed the linear structure to be correct:



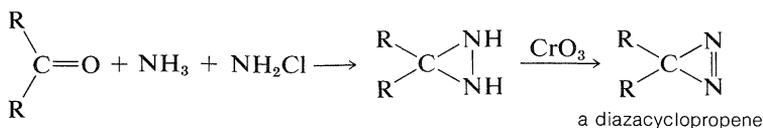
1,2-diazacyclopropene



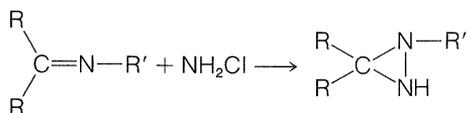
diazomethane

Recently, a variety of authentic 1,2-diazacyclopropenes (sometimes called *diazirines*) have been prepared, and these have been found to have very different properties from the diazoalkanes. The simple 1,2-diazacyclopropenes are colorless and do not react with dilute acids, bases, or even bromine. The

syntheses of these substances are relatively simple. One of several possible routes follows:



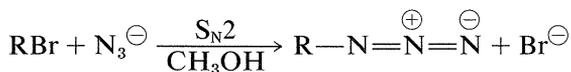
Exercise 24-28* Knowing that ketones and hydrazine react to give hydrazones, show how the combination of ketone, NH_3 , and NH_2Cl can react to give diazacyclopropanes. In working out a mechanism, start with the fact that the following reaction occurs in good yield:



Exercise 24-29* Explain why 1,2-diazacyclopropane reacts with acids much more slowly than does diazomethane.

24-7D Azides

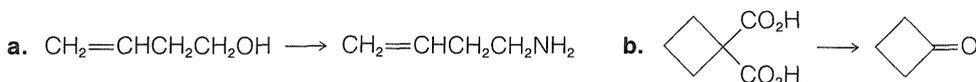
Organic azides can be prepared from hydrazines and nitrous acid (Section 24-7A) and by the reaction of sodium azide with acyl halides or with alkyl halides having good $\text{S}_{\text{N}}2$ reactivity:



The lower-molecular-weight organic azides often are unpredictably explosive and are best handled in solution.

The use of acyl azides in the preparation of amines by the Curtius rearrangement has been discussed previously (Section 23-12E). Alkyl azides can be reduced readily by lithium aluminum hydride to amines and, if a pure primary amine is desired, the sequence halide \longrightarrow azide \longrightarrow amine may give as good or better results than does the Gabriel synthesis (Section 23-9D).

Exercise 24-30 Show how the following transformations may be achieved with the aid of azide derivatives:



Additional Reading

I. T. Miller and H. D. Springall, *Sidgwick's Organic Chemistry of Nitrogen*, 3rd ed., The Clarendon Press, Oxford, 1966.

L. G. Donaruma and W. Z. Heldt, "The Beckmann Rearrangement," *Organic Reactions* **11**, 1 (1960).

Supplementary Exercises

24-31 Suggest a route for the synthesis of each of the following compounds from the indicated starting material:

- 2-methylpropanenitrile from 2-methylpropanal
- $(\text{CH}_3\text{CO}_2\text{CH}_2)_3\text{C}-\text{NO}_2$ from nitromethane
- N-tert*-butylbenzenecarboxamide from benzenecarbonitrile (benzonitrile)

24-32 a. Make a chart of the mp, bp, and solubilities in water, ether, dilute acid, and dilute base of each of the following compounds:

octanamine	<i>N,N</i> -dimethylethanamide
<i>N</i> -butylbutanamine	<i>N,N</i> -dipropylpropanamine
1-nitrobutane	2-nitro-2-methylbutane

b. Outline a practical procedure for separation of an equimolar mixture of each of the compounds in Part a into the *pure components*. Notice that selective reactions are *not* suitable unless the reaction product can be reconverted to the starting material. Fractional distillation will not be accepted here as a practical means of separation of compounds that have boiling points less than 25° apart.

24-33 For each of the following pairs of compounds give a chemical test, preferably a test-tube reaction, that will distinguish between the two compounds:

- $(\text{CH}_3)_3\text{CNH}_2$ and $(\text{CH}_3)_2\text{NC}_2\text{H}_5$
- $\text{CH}_3\text{CH}_2\text{NO}_2$ and CH_3CONH_2

- c. $\text{CH}_3\text{CH}_2\text{C}\equiv\text{N}$ and $\text{HC}\equiv\overset{\oplus}{\text{C}}-\overset{\ominus}{\text{C}}\text{H}_2\text{NH}_2$
- d. $\text{CH}_3\text{CH}_2\text{NHCl}$ and $\text{CH}_3\text{CH}_2\text{NH}_3\text{Cl}$
- e. $\text{CH}_3\text{NHCOCH}_3$ and $\text{CH}_3\text{NHCO}_2\text{CH}_3$
- f. $\text{CH}_3\text{OCH}_2\text{CH}_2\text{NH}_2$ and $\text{CH}_3\text{NHCH}_2\text{CH}_2\text{OH}$
- g. $\text{CH}_3\text{CH}_2\text{CONH}_2$ and $\text{CH}_3\text{OCH}_2\text{CH}_2\text{NH}_2$

24-34 Explain how you would use spectroscopic means to distinguish between the compound pairs in Exercise 24-33. Be specific about what you would expect to observe.

24-35 Using spectroscopic methods, how could you distinguish one isomer from the other in the following pairs? Be specific about what you would expect to observe in each case.

- 2-methylbenzenamine and *N*-methylbenzenamine
- propanamide and *N,N*-dimethylmethanamide
- nitroethane and ethyl nitrite
- 3-oxobutanenitrile and 2-butanamide

24-36 Compound *A* of molecular formula $\text{C}_6\text{H}_{12}\text{N}_2\text{O}_2$ (which can be obtained resolved into chiral forms) is insoluble in dilute acid and dilute base, but reacts with aqueous nitrous acid to give compound *B* of formula $\text{C}_6\text{H}_{10}\text{O}_4$, which readily loses water on heating to give *C*, $\text{C}_6\text{H}_8\text{O}_3$. Compound *A* reacts with a solution of bromine and sodium hydroxide in water to give *D*, $\text{C}_4\text{H}_{12}\text{N}_2$, which on treatment with nitrous acid in the presence of perchloric acid gives 2-butanone. Write structures showing configurations for compounds *A*, *B*, *C*, and *D* and equations for all the reactions involved.

24-37 How would you synthesize the following compounds from the indicated starting materials? Write equations for the reactions involved and indicate the reaction conditions.

- phenylnitroethanoic acid from ethyl phenylethanoate
- 3-phenylpropanoic acid from phenylethanoic acid

24-38 Show by equations how each of the following substances might be synthesized from the indicated materials. Specify reagents and approximate reaction conditions. Assume that any isomers formed are separable.

- N*-phenylethanamide from benzene
- 1,2-dinitrobenzene from *N*-phenylethanamide
- 4-nitro-1-nitrosobenzene from *N*-phenylethanamide
- 1,3,5-trideuteriobenzene from *N*-phenylethanamide
- 2,4-dinitrophenyldiazane (2,4-dinitrophenylhydrazine) from benzene

24-39 For each of the following pairs of compounds give a chemical test, preferably a test-tube reaction, that will distinguish the two compounds. Write a structural formula for each compound and equations for the reactions involved.

- 1-methyl-3-nitrobenzene and phenylnitromethane

- b. 1-methyl-4-nitrobenzene and benzenecarboxamide
- c. benzenamine and cyclohexanamine
- d. *N*-methylbenzenamine and 4-methylbenzenamine
- e. *N*-nitroso-*N*-methylbenzenamine and 4-nitroso-*N*-methylbenzenamine

24-40 Show how the following substances may be synthesized from benzene, nitrobenzene, and halogenated or alkylbenzenes, using the reactions discussed in this chapter and in Chapters 22 and 23.

- a. 3-nitrobenzenamine
- b. 1-bromo-4-nitrosobenzene
- c. 2-methyl-5-nitrobenzenamine
- d. 1-(4-bromophenyl)-2-(4-chlorophenyl)diazane
- e. phenyl-(4-nitrophenyl)diazene
- f. 1-phenyl-2-(4-methylphenyl)diazene 1-oxide