CHAPTER
27

QUALITATIVE ORGANIC ANALYSIS

THE IDENTIFICATION OF UNKNOWNS

27.1-General Principles

The identification of organic compounds involves two different types of problems- (1) the recognition of a compound that is described in the literature and has been fully characterized and (2) the elucidation of the structure of a new compound. The experiments in this chapter deal with the former problem. Actually, the initial approach is much the same in both situations. Various physical and chemical properties are determined from which information is obtained about the structure of the compound in question.

The identification of a compound that is described in the literature is based upon the demonstration that the unknown posesses a large number of properties in common with those described for the compound in the literature. A sufficiently large number of properties must be utilized so the similarities cannot be attributed to coincidence. Those usually considered include general appearance, various physical constants, spectra of all kinds, solubilities in several solvents, chemical behavior, and physical constants of derivatives. A rigorous identification requires the demonstration that no known structure other that the one proposed for the unknown could have these same properties.

The identification is greatly facilitated if there is an authentic sample of the suspected compound available for direct comparison.[1] Then mixture melting points (section 7.4-2) and TLC experiments (section 9.4) will confirm the identification.

It is often possible to identify a compound by spectroscopic means alone (UV, IR, NMR, CMR; see Chapter 28). Each absorption band or peak in an infrared or nuclear magnetic resonance spectrum is the equivalent of one physical constant. However, the "classical" approach is used exclusively in these experiments[2] because it best illustrates the chemical behavior of organic compounds. The student should realize that today professional chemists make only limited use of these classical methods in actual identifications.

27.2 - Summary of Procedure

The analysis of an unknown involves the following steps, each of which is subsequently described in detail. They ordinarily should be undertaken in the order presented, but the general scheme is flexible and much is necessarily left to the judgement of the student.

1. Preliminary examination and ignition (Section 27.4).
2. Purification (Section 27.5).
3. Measurement of physical constants (Section 27.6).
4. Detection of elements present (Section 27.7).

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[1] You are free to make use of any compounds from the reagent shelves in the lab, or compounds you have previously synthesized, for this purpose. You should *not*, however, ask at the stockroom for compounds not on the reagent list, nor should you obtain them from other sources.

[2] Your instructor may let you make some limited use of spectroscopic methods if equipment is available. Surreptitious recording of spectra without your instructor's knowledge or permission is not allowed.

5. Classification by solubility (Section 27.8).
6. Chemical classification (Section 27.10) and examination of spectra (Chapter 28).
7. Examination of the tables for possibilities (Section 27.11).
8. Preparation of solid derivatives (Section 27.12).
9. Final identification and report of results (Section 27.13).

27.3 - Experimental Operations and General Techniques

During the course of the semester you will receive one or more unknowns to identify. As you carry out the various experimental operations a careful and complete record of all observations should be made in your laboratory notebook.

IMPORTANT! A very large number of reagents is necessary for qualitative organic analysis. Complete chaos results unless each reagent bottle is always left in its proper place. The bottles are numbered and lists are posted for the students' convenience. Instead of taking a reagent bottle to your desk to use, take your container to the reagent shelf and dispense the reagent there. Be sure to stopper the reagent bottles tightly after use. Hazardous reagents are stored in the hood and should be used in the hood.

Since many of the manipulations call for measurement of small quantities of liquids, it is convenient to prepare and calibrate in advance several capillary dropping tubes. To prepare two tubes, an approximately 25 cm length of 8 mm soft glass tubing is heated at its center over a Bunsen burner equipped with a wing top and then pulled apart. The capillary tip is cut off cleanly to a length of 5 to 6 cm from where the constriction begins. The other end is heated until it softens and then flattened squarely against a ceramic plate or a stone bench top, so it will accommodate a medicine dropper bulb. Calibrate the dropper by filling it with your unknown and expelling the liquid dropwise (count the drops) into a small flask which has been accurately weighed. From the weight of the liquid in the flask and the number of drops you can determine the weight of each drop. (Do not discard the unknown that you use for the calibration.)

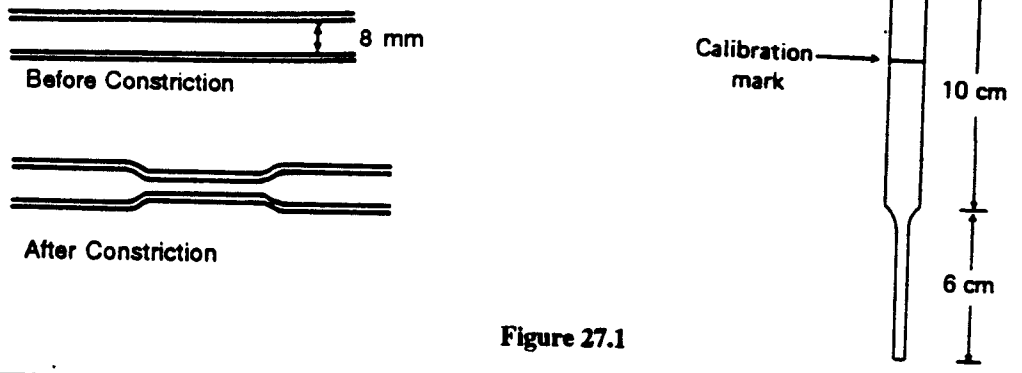

Figure 27.1

WARNING! Never insert your dropper (even though you know it is clean) into any of the reagent bottles. If you require a small amount of a reagent from a bottle which does not have a dropper in it, pour some of the liquid into a small test tube and fill your dropper from the test tube. Do not return any unused reagent to the bottle.

To estimate weights less than 1 gram of a *solid*, weigh out exactly 1 g and then subdivide it into tenths (100 mg) and one of the tenths into tenths again (10 mg).

IMPORTANT!

About the Conduct of Tests: In carrying out any qualitative test it is essential to know by actual observation what to expect in both a positive and a negative test. Therefore every test must be run on both a *control* (a compound expected to give a *positive* result) and a *blank* (a compound expected to give a *negative* result) either before or at the same time it is run on the unknown. Aside from showing what positive and negative tests look like, this practice alerts you immediately to contaminated or malfunctioning reagents.

27.4 - Preliminary Examination and Ignition Test

CAUTION! You must use special care in handling your unknown. At the outset you know nothing about the compound. Until you determine otherwise, you must assume that the compound may be hazardous. Do not get it on your hands. Do not breathe its vapors or dust. Do not spill it on the laboratory bench. Should it come into contact with your skin, wash thoroughly with soap and water.

Note the physical state and color of your unknown. Do *not* sniff your compound (see note above), but if you notice a distinctive odor, record that observation. Observe and make note of the physical state and color again *after* purifying your unknown.

For the ***ignition test*** place a few milligrams of the sample on the tip of a clean spatula or scoopula and bring to the edge of a Bunsen flame. Note if the compound is flammable and, if it is, note the nature of the flame. A luminous (yellow), sooty flame indicates a compound having a high carbon to hydrogen ratio (very likely aromatic). A luminous, but not very sooty, flame usually indicates an aliphatic hydrocarbon, a lower carbon to hydrogen ratio. As the oxygen content of the compound increases the flame becomes clearer (more blue). Heat any residue with a small flame, and finally ignite it strongly. (**Test Compounds:** Toluene, hexane, ethanol.)

If the original compound is a solid, in addition to observing if it is flammable and the nature of any flame,

(1) note if it melts and the manner of its melting,

(2) cautiously note the odor of any gases evolved, and

(3) note whether there is a non-carbonaceous residue.

A non-carbonaceous residue that cannot be burned away contains a metallic element, which indicates the original compound was probably a salt. (**Test Compounds:** Naphthalene, adipic acid, acetamide, sodium acetate.)

The melting point of a solid should be determined at this point for later comparison with that of the purified compound. The melting range gives some indication of the degree of purity.

Determination of the boiling point of a liquid (Siwoloboff Method, section **27.6**, or semi-micro method, section **2.3-4**, pp. 15-16) at this point will be helpful in deciding how to purify the liquid.

27.5-Purification

The compounds issued as unknowns have not been intentionally contaminated, but their purities are not guaranteed. A clear colorless liquid may or may not be pure, but a highly colored liquid certainly needs to be purified. A sharp melting point (narrow range) is an indication, but not proof, that a solid is fairly pure. Most of the unknowns are relatively inexpensive, practical grade, chemicals, and may need to be purified.

A solid ordinarily is purified by recrystallization from a suitable solvent (see Chapter 7). It will, of course, be necessary to find the recrystallization solvent by means of small scale trial recrystallizations using a variety of solvents until one is discovered that is satisfactory.

A liquid should be distilled at atmospheric pressure if it is stable at its boiling point.[3] Assemble a simple distillation apparatus but omit the condenser (as shown in Figure 27.2) and cool the receiver in an ice-water bath.[4] First, heat the distilling flask on a steam bath or with a hot-water bath. If the liquid does not boil, remove the steam bath and heat with a flame using a wire gauze.[5] If the liquid undergoes considerable darkening or shows other evidence of decomposition and no distillation has taken place, discontinue heating. If you choose to vacuum distill your liquid, set up the vacuum distillation apparatus shown in Figure 24.3 and follow the general directions in Chapter 4.

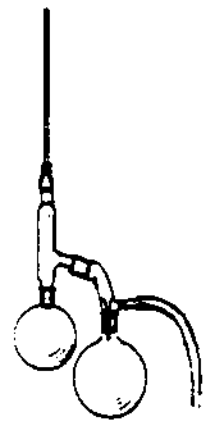

Figure 27.2

CAUTION! Never distil an unknown to dryness. Always leave some liquid in the distilling flask and do not overheat the residue. You have no way of knowing what explosive impurities might be present in the residue.

Record the temperature range over which the distillate is collected. If most of the material does not distil over a fairly narrow range, the various fractions should be redistilled separately.

Column chromatography (section 9.2) should be considered as a possible technique for purification of a solid that does not recrystallize satisfactorily. If a solid shows any tendency to sublime (you will notice when attempting to determine the melting point), it might be conveniently purified by sublimation (see your instructor for technique). A low melting solid may be purified by distillation.

27.6-Measurement of Physical Constants

After a solid unknown has been purified and thoroughly dried, determine its melting point. If the melting range is wide, first check to see if the compound is dry. If it is not dry, dry it and retake the melting point. If the compound is dry and still exhibits a wide melting point range, recrystallize the compound again. A melting point should also be determined for a liquid (by the macro method; see section 19.2), if it can be solidified by chilling it in an ice bath or an ice-salt bath.

An approximate boiling point has already been determined for a substance purified by distillation. For compounds boiling below 200° a more accurate boiling point can be determined by the **Siwoloboff Micro Method.** A micro boiling point tube is made by sealing one end of a 5mm glass tube and cutting off a piece 5 cm long. Two drops of the liquid is placed in the tube. A melting point capillary tube is sealed about 3 to 4 mm from the open end

[3] If you have done a preliminary boiling point determination (section 27.4), be guided by it. If your b.p. is below 85° use a steam bath or hot water bath. If the b.p. is above 100° you must heat with a flame using a wire gauze or with some alternative heat source.[5]

[4] Omission of the condenser from the distillation assembly is recommended for distillation of small quantities because it eliminates loss of material that ordinarily adheres to the inner surface of the condenser. The surface of the receiver, surrounded by ice water, substitutes for the condenser.

[5] Alternative sources of heating are a Glascol heating mantle, an oil bath, or a sand bath. These are more controlled sources of heat, but they are not always available in undergraduate laboratories.

and placed, open end down, in the larger tube (see Figure 27.3).[6] This tube is fastened to the thermometer with a rubber band or wire tie and heated in a Thiele tube. The temperature is raised until a rapid and continuous stream of bubbles issues from the small capillary and passes through the liquid. The flame is then removed and the bath allowed to cool. The temperature is noted at the instant bubbles cease to come out of the capillary and just before the liquid enters it. This temperature is the boiling point.

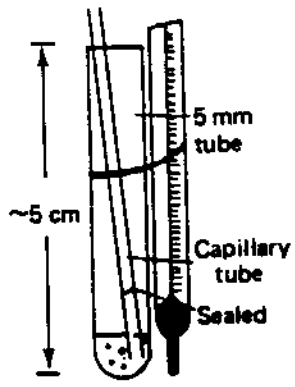

Figure 27.3 Micro Boiling Point Determination

Alternately, the boiling point can be determined by the ***semimicro method*** (section **2.3-4**). This method can be used for any liquid, but *must* be used with compounds boiling above 200°.

Other physical constants--specific gravity, index of refraction, molecular weight, optical rotation, *etc.*--may be measured if the necessary equipment is available. Consult references 5 or 6 at the end of this chapter for techniques of measurement.

Even if the specific gravity is not measured, it is useful to note whether a water insoluble substance is more dense or less dense that water. Make this observation when conducting the solubility tests (section **27.8**).

27.7-Detection of Elements Present

Assume that the compound contains carbon and hydrogen. Since there is no simple reliable test for oxygen, its presence or absence must be inferred from the compound's behavior in solubility and chemical classification tests.

Test for nitrogen and halogens using the sodium fusion procedure (**27.7-1**). Supplement this with the Beilstein test (**27.7-2**).

27.7-1. Sodium Fusion. Test for nitrogen and halogens. After fusion with metallic sodium, nitrogen and halogen in organic compounds are converted into cyanide and halide ions respectively. Detection of any of these ions in the resulting solution then constitutes a positive test for the constituent elements.

$$C_xH_yClBrI \xrightarrow{Na} CN^- + Cl^- + Br^- + I^-$$

> CAUTION! Some organic compounds react violently with molten sodium. Be certain that the test tube containing the fusion mixture is never pointed toward you or your classmates. Be certain that you are wearing your safety glasses.

A. Sodium Fusion. Place a cube of clean sodium approximately 2 to 3 mm on an edge in a small *soft glass* test tube. Support the test tube in a vertical position in a hole in the center of a wire gauze with a ceramic center resting on a metal ring. Place a small, *dry* beaker underneath to catch the contents should the test tube break

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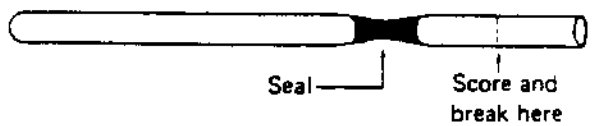
[6] The easiest way to seal a capillary 3 to 4 mm from one end is to heat a melting point tube in the tip of a very small Bunsen burner flame about one third of the way from the open end. When the glass is soft and begins to sag, remove it from the flame and twist it. Reheat the tube at the twist to be certain it has been sealed. Alternatively, the softened capillary can be pulled out slightly and then reheated at the constriction until it is sealed. Once the capillary has been sealed, score it about 3 to 4 mm from the seal (on the open end of the seal) and break it off.



prematurely.[7] Heat the bottom of the tube, very gradually at first, with a small flame until the sodium melts and sodium vapors rise about 1 cm in the tube. Remove the flame and immediately drop 10 to 20 mg of the compound directly onto the molten sodium. Take care not to let the compound run down the side of the test tube or it may volatilize (boil away) before it ever contacts the sodium.

Resume heating the test tube and add an additional 10 to 20 mg portion of the compound. Larger portions than the 10 to 20 mg specified above may be required if the compound is exceptionally volatile. However, if too much compound is used you may end up with a dark stock solution.

Heat the bottom of the tube to dull red and while the tube is very hot, cautiously immerse it in a small beaker containing 20 mL of deionized water. **CAUTION! There may be a vigorous reaction with water.** If the tube cracks but does not break on contact with the water, break out the bottom of the tube with a stirring rod. If the tube does not break or crack, reheat it and immerse it in water a second time. After the tube has broken, heat the contents of the beaker to boiling, stir, and then filter. Use the filtrate, which should be colorless, as the ***stock solution*** in the tests for nitrogen and the halogens described below. Test the stock solution with red litmus or pH paper to make certain it is strongly basic. If it is not basic, something went wrong in the fusion and it will have to be repeated.

Before carrying out the elemental analysis of an unknown compound, run through the fusion and the following tests on a known compound (e.g., *p*-chloroaniline or *p*-chloronitrobenzene), so you will know what positive tests look like. Tests are available for other elements such as sulfur and phosphorous.

B. Test for nitrogen. Place 1 mL of the stock solution in a test tube and add 2 drops of freshly prepared saturated iron(II) ammonium sulfate solution[8] and 2 drops of 30% potassium fluoride. A small amount of iron hydroxide which precipitates at this point is not a positive test for nitrogen.

Boil the solution gently for about 30 seconds and acidify it while it is hot by careful dropwise addition of 30% sulfuric acid until the precipitate of iron hydroxide just dissolves. Appearance of a deep blue precipitate of ferric ferrocyanide (Prussian blue) is a positive test for nitrogen.

A very small quantity of Prussian blue may appear only as a greenish solution. If in doubt as to whether there is actually a blue precipitate present, filter the mixture and wash the filter paper with a small amount of water. If Prussian blue is present, it will be revealed by the deep blue specks of color on the white filter paper.

The test for nitrogen sometimes fails, usually because of a poor fusion. Even with a good fusion some nitro compounds are not reduced to cyanide. The presence of nitrogen should never be ruled out entirely, therefore, until additional evidence has been accumulated.

C. Test for halogen. Acidify about 2 mL of the stock solution with 2M nitric acid and boil gently for three minutes to expel any hydrogen cyanide present. Do this even if a negative test for nitrogen was obtained. Failure to boil the solution long enough often results in a false halogen test.

Add a few drops of 10% aqueous silver nitrate solution to the test solution. A heavy precipitate indicates the presence of halogen. Silver chloride is white, silver bromide is pale yellow, and silver iodide is yellow. All the silver halides darken on exposure to light. A light clouding of the solution, often observed with tap water, is not a positive test.

If a silver halide precipitate is obtained, to confirm which of the halogens is present, acidify about 3 mL of the stock solution with dilute sulfuric acid and boil it for three minutes. Cool the solution, add 1 mL of CCl_4 and a drop of freshly prepared chlorine water (2 mL of Clorox acidified with 1 *M* sulfuric acid) and shake the mixture gently. Continue adding chlorine water drop by drop with shaking after each addition. A purple color in the carbon tetrachloride layer indicates iodine, a reddish brown color indicates bromine, and no color-change indicates chlorine.

[7] If the tube breaks or cracks *before* the fusion is complete, treat the mixture with 2 mL of ethanol and discard. If the tube cracks or breaks *after* the fusion is complete, place it and its contents in the beaker and break out the bottom of the tube with a stirring rod. Add 20 mL of distilled water to the material in the beaker. The unreacted sodium may react vigorously with the water, but there is so little of it the reaction will be over in seconds.

[8] Add a few crystals of iron(II) ammonium sulfate to 2 mL of water in a test tube and mix with a stirring rod. If the solid dissolves completely add additional quantities of the salt until no more can be dissolved. The solution deteriorates rapidly and must be used within a few minutes.

27.7-2. Beilstein test for halogens. This test depends upon the characteristic green color which cuprous, Cu(I), halides impart to a flame. The test is extremely sensitive. A small amount of a halogen-containing impurity could be responsible for a positive Beilstein test. Furthermore, some nitrogen-containing compounds may form cuprous cyanide, which also gives a greenish flame. Consequently a positive Beilstein test accompanied by a negative sodium fusion test should be regarded with suspicion. Run the test on a blank (toluene) and on a control (*p*-chlorotoluene), and if these give the expected results, run it immediately on the unknown.

To perform the test, wrap one end of a 5" length of copper wire around a pencil or small dowel or stick it into a cork (to use as a handle so you don't burn your fingers) and form a small loop at the other end of the wire. Hold the small loop of the wire in a Bunsen flame until the flame loses any green color present. Dip the loop into the material being tested and then heat it on the edge of a nonluminous flame (the blue part of a hot Bunsen flame). A green color indicates the presence of halogen.

27.8-Classification by Solubility

The first basis of classification consists of the solubility tests. For purposes of classification a substance will be considered soluble if 0.1 g dissolves in 3 mL of the test solvent. On the basis of the solubility tests the compound is assigned to one of the **Solubility Classes** as outlined in Table **27.1.**

An understanding of solubility effects is essential in interpreting the results of solubility tests.

A. Solubility in Water and Toluene. Polar functional groups promote water solubility and inhibit solubility in nonpolar solvents such as toluene. Hydrocarbon groups inhibit water solubility and promote solubility in nonpolar solvents.

Compounds consisting of one polar functional group with no more than about five carbon atoms are soluble in both water and toluene (solubility class H-1). Since six carbon atoms incorporated into a benzene ring have about the same effect on solubility as four aliphatic carbon atoms, aromatic compounds with up to seven carbon atoms may be soluble in water. Thus, 1-pentanamine and benzylamine have about the same solubility and are both classified H-1.

Compounds with more than one polar functional group tend to be highly water soluble, but are not soluble in toluene unless they possess several carbon atoms (usually at least two carbon atoms per polar group). For example, 1,2-ethanediol, 1,2-propanediol, 1,2,3-propanetriol (glycerol), sorbitol (6 OH groups, 6 carbon atoms) are all in class H-2, but 1,4-butanediol and butanedioic (succinic) acid are in class H-1.

Salts (e.g., $RCO_2^-Na^+$ and $RNH_3^+Cl^-$) are generally in class H-2. However, high molecular weight salts may not be water soluble and some may dissolve in nonpolar solvents.

B. Solubility in Dilute Sodium Hydroxide and Dilute Sodium Bicarbonate. Solubility in these aqueous bases depends on acidity. Compounds more acidic than water dissolve in dilute sodium hydroxide because they are converted into water soluble salts.

$$HA + OH^- \rightleftharpoons A^- + H_2O$$

Compounds more acidic than carbonic acid (pK_a ~7) are converted into water soluble salts by sodium bicarbonate.

$$HA + HCO_3^- \rightleftharpoons A^- + H_2CO_3 \longrightarrow CO_2 + H_2O$$

Most phenols, imides, and readily enolizable carbonyl compounds dissolve in dilute sodium hydroxide but not in bicarbonate and are, therefore, classified A-2. All carboxylic acids and those phenols with strongly electron-withdrawing substituents are strong enough acids to react with bicarbonate and are classified A-1. 2,4-Dinitrophenol (pK_a~4) dissolves readily in bicarbonate; *p*-nitrophenol (pK_a~7) lies on the borderline but dissolves slowly in bicarbonate.

C. Solubility in Dilute Hydrochloric Acid. Solubility in dilute aqueous acid depends on base strength. Most amines are strong enough bases to react with aqueous acid and belong to class B because they are converted into water soluble salts.

$$RNH_2 + H_3O^+ \rightleftharpoons RNH_3^+ + H_2O$$

The equilibrium lies to the right if the compound is more basic than water.

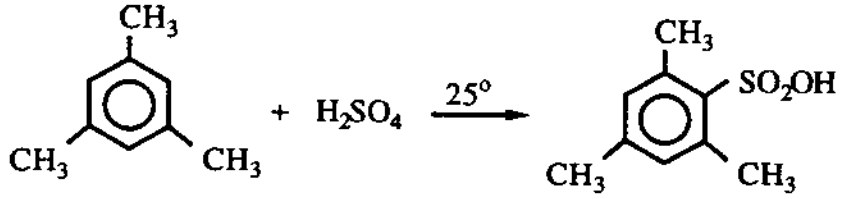
Aromatic amines with strongly electron-withdrawing substituents (e.g., *p*-nitroaniline, pK_b=13), and diarylamines (e.g., diphenylamine, pK_b=13) are too weakly basic to dissolve in aqueous acid and are in class M.

D. Solubility in Concentrated Sulfuric Acid. Compounds containing oxygen (*e.g.*, alcohols, ethers, aldehydes, ketones and esters) are generally strong enough bases to be converted into oxonium salts by concentrated sulfuric acid.

$$R_2O + H_2SO_4 \rightleftharpoons R_2OH^+ + HSO_4^-$$

Diaryl ethers are too weakly basic to react and constitute the major exception.

Some highly activated arenes dissolve in concentrated sulfuric acid because they undergo sulfonation with this reagent, producing a soluble sulfonic acid.



Alkenes dissolve in concentrated sulfuric acid because of addition to the double bond to form the soluble alkyl hydrogen sulfate.

The acid may cause polymerization, however, which would lead to an insoluble material.

Compounds containing nitrogen are not tested for solubility in concentrated sulfuric acid, since they are presumed to be soluble in the reagent, and are assigned to class M.

Conduct of the Solubility Tests

To determine the solubility of a substance in cold water treat 0.1 g of the compound (solids must be finely pulverized) with 3 mL of water at room temperature in a small test tube. Stopper the test tube and shake it vigorously. Do not heat it. Use a stirring rod to break up the solid if necessary. Allow the mixture to stand for several minutes with frequent shaking to give the compound enough time to dissolve. With liquid unknowns be certain to observe carefully whether two layers are present or not. Careful observation while gently shaking the mixture will help to distinguish the meniscus from a layer floating on top.

If the sample dissolves in water, test its solubility in toluene the same way using another sample (be certain the test tube is dry!).

If the sample is soluble in water but not in toluene, test the aqueous solution with red litmus paper. If the solution is basic (litmus paper turns blue), carry out Test #12 on the aqueous solution.

TEST COMPOUNDS: 2-propanol, acetic acid, ethyl acetate, sodium benzoate, anilinium chloride, *p*-toluidine.

If the compound is not soluble in water, test its solubility in exactly the same way in 2 M sodium hydroxide. If the compound is soluble in NaOH test its solubility in 1 M sodium bicarbonate. The reaction of solid acids with

sodium bicarbonate may be very slow. However, you may observe the solid floating up and down in the solution, often covered with small bubbles of CO_2. If the compound is insoluble in sodium hydroxide, test its solubility in 2 M hydrochloric acid.

TEST COMPOUNDS: *m*-methylphenol, *p*-nitrobenzoic acid, *p*-toluidine, *p*-nitrobenzamide.

If the sample is *insoluble* in all of the previous tests and *does not* contain nitrogen, test another portion of it in a dry test tube with concentrated sulfuric acid. Classify the compound as soluble in sulfuric acid (class N-1) if an obvious reaction takes place, e.g., the formation of a strongly colored solution, or the generation of much heat with or without a color change (but note that a trace impurity might also cause a color change).

TEST COMPOUNDS: benzaldehyde, ethyl benzoate, benzophenone, mesitylene, diphenylmethane, anthraquinone.

Table 27.1
Solubility Classification

<table>
<tr><th colspan="2">Soluble in Water</th><th colspan="6">Insoluble in Water</th></tr>
<tr><th>Soluble in Benzene TOLUENE</th><th>Insoluble in Benzene TOLUENE</th><th colspan="2">Soluble in dil. NaOH</th><th>Soluble in dil. HCl</th><th colspan="3">Insoluble in dil. NaOH and dil. HCl</th></tr>
<tr><td rowspan="2">Acids
Alcohols
Aldehydes
Amides
Amines
Esters
Ketones
Nitriles
Phenols</td><td rowspan="2">Acid Salts
Amine Salts
Polyamines
Polyhydric Alcohols
Polyprotic Acids
Some Amides</td><td>Soluble in $NaHCO_3$</td><td>Insoluble in $NaHCO_3$</td><td rowspan="2">Most amines
Guanidines
Ureas</td><td>Nitrogen Present</td><td colspan="2">Nitrogen Absent</td></tr>
<tr><td>Carboxylic Acids
Some Phenols</td><td>Most Phenols
Enols
Imides</td><td>Amides
Nitriles
Nitro Compounds[c]
Di- and Triaryl-amines
Neg-subst'd Arylamines</td><td>Soluble in H_2SO_4
Alcohols
Aldehydes
Some Aromatic Hydrocarbons
Esters
Ketones</td><td>Insoluble in H_2SO_4
Most Aromatic hydrocarbons
Halides</td></tr>
<tr><td>Class H-1[a]</td><td>Class H-2</td><td>Class A-1</td><td>Class A-2</td><td>Class B</td><td>Class M</td><td>Class N-1[b]</td><td>Class N-2</td></tr>
</table>

[a]The compounds listed for Class H-1 are generally monofunctional and contain no more than about five carbon atoms. However, six carbon atoms incorporated into a benzene ring has about the same effect on solubility as four carbon atoms in an aliphatic system. Thus, benzylamine and *n*-pentylamine have about the same solubility in water (both in Class H-1).

[b]Class N-1 can be further subdivided according to whether the compound dissolves in 85% phosphoric acid, in which case it probably contains no more than about nine carbon atoms.

[c]Includes compounds containing in addition to the nitro group any of the functional groups of class N-1 compounds.

27.9-Spectroscopic Analysis

If spectra (ir, nmr, cmr, uv or mass spectra) of your unknown compound are available, they should be examined carefully at this point (see Chapter 28). They will prove invaluable in guiding you to appropriate chemical tests or may, in fact, rule out the need for any chemical tests.

27.10-Chemical Classification Tests

27.10-1. Characteristics of chemical classification tests. A chemical reaction suitable as a test for a particular functional group should fulfill the following requirements:

1. The reaction should be capable of being carried out with simple equipment under normal laboratory conditions in relatively few operations and in a short time.

2. A physical change which can be easily and unequivocally detected should accompany the reaction. The physical change may be:

   a. Appearance of a new phase--gas, solid precipitate or oil;
   b. Disappearance of a phase--solubilization;
   c. Color change;
   d. Evolution of heat.

27.10-2. Selection of classification tests. A scheme is presented in Tables 27.2 through 27.9 for selecting appropriate chemical classification tests on the basis of the assignment of the compound to a solubility class. Descriptions of all the tests then follow. This scheme should be used only as a guide and should not be regarded as a rigid procedure. The student is urged to obtain as much confirmatory evidence as possible since occasional erroneous or misleading results may be obtained either in solubility or chemical classification tests.

27.10-3. Conduct of classification tests. Whenever you run a classification test for the first time, run at least one known compound (control) and a blank along with the unknown for comparison. Control compounds are suggested for each of the tests. Very little extra effort will be expended. Not only will this procedure demonstrate to you exactly what you are looking for in each test, but it will also alert you in the event that a reagent is spoiled or mislabelled. A sure way to receive a low lab grade is to thrust a test tube in front of your instructor with the question, "Is this a positive test for....?"

Caution must be exercised in the interpretation of the results of these tests. Compounds with the same functional groups can vary tremendously in reactivity because of steric effects and because of electronic effects due to substituents. The solubility of a compound in the reaction medium may also be an important factor in determining its responsiveness in a test.

Some tests may call for larger amounts of compound than you might be able to spare. If so, scale the test down.

Try to base your conclusions on an accumulation of as much evidence as possible so that it will not be necessary to place too much credence in the result of any single test.

If a test reaction produces a solid reaction product, it should, in most cases, be purified and used as a derivative. The tests where solid derivatives may be produced are starred (*).

Table 27.2

Class H-1: Compounds Soluble in Water and in Toluene

Acid to Litmus	Basic to Litmus	Neutral to Litmus	
		Nitrogen Present	Nitrogen Absent
Carboxylic Acids Phenols (a few) (Apply Tests for Classes A-1 and A-2, plus the $NaHCO_3$ Test #20)	Amines (Apply Class B Tests)	Nitriles Amides (Apply Class M Tests)	Alcohols Aldehydes Esters Ketones (Apply Class N-1 Tests)

Table 27.3

Class H-2: Compounds Soluble in Water but Insoluble in Toluene

Acid to Litmus		Basic to Litmus		Neutral to Litmus
Sodium Hydroxide Test #21		Hydrochloric Acid Test #12		Polyhydroxy Alcohols (Apply Class N-1 Tests)
Positive	Negative	Positive	Negative	
Amine Salts ($RNH_3^+ Cl^-$) (Apply Class B Tests)	Polyprotic Acids (Apply Class A-1 Tests, $NaHCO_3$ Test #20)	Salts of Carboxylic Acids ($RCO_2^- Na^+$) (Confirm with Ignition, Class A-1 Tests)	Amino alcohols Polyamines (Apply Class B Tests)	

Table 27.4

Class A-1: Compounds Soluble in 1 *M* NaOH and in 1 *M* $NaHCO_3$

Ferric Chloride Test #10	
Positive	Negative
Phenols (with electron withdrawing substituents) (Confirm with Class A-2 Tests)	Carboxylic Acids (Confirm with Esterification Test #9)

Table 27.5

Class A-2: Compounds Soluble in 2*M* NaOH but Insoluble in 2*M* $NaHCO_3$

Ferric Chloride Test #10 and Coupling Test #7		
Positive (Either or Both)		Both Negative
DNPH Test #8		Imides (Confirm with Saponification Test #18) (NOTE: Imides contain nitrogen)
Positive	Negative	
β-Keto Esters β-Diketones Phenolic Aldehydes Phenolic Ketones	Phenol (confirm with Bromine Test #5)	

Table 27.6
Class B: Compounds Soluble in 2*M* HCl

Benzenesulfonyl Chloride Test #3					
Product Soluble in KOH		Product Insoluble in KOH		Negative	
Nitrous Acid Test #16		Coupling Test #7		Nitrous Acid Test #16	
Red Dye	Gas	Positive	Negative	Positive	Negative
Primary Arylamines (confirm with Coupling Test #7)	Primary Alkylamines	Secondary Arylalkyl-amines	Secondary Dialkyl-amines	Tertiary Dialkylaryl-amines (Confirm with Coupling Test #7)	Tertiary Aliphatic Amines Heterocyclic Amines

Table 27.7

Class N-1: Compounds Soluble in Concentrated Sulfuric Acid

<table>
<tr><td colspan="6">DNPH Test #8</td></tr>
<tr><td colspan="3">Positive</td><td colspan="3">Negative</td></tr>
<tr><td colspan="3">Tollens' Test #22</td><td colspan="3">Chromic Acid Test #6</td></tr>
<tr><td colspan="2">Positive</td><td colspan="2">Negative</td><td>Positive</td><td colspan="2">Negative</td></tr>
<tr><td colspan="2">Aniline Test #2</td><td colspan="2">Iodoform Test #14</td><td rowspan="4">Primary and Secondary Alcohols (Confirm with Lucas Test #15, if bp < 150°)</td><td colspan="2">Hydroxamic Acid Test #13</td></tr>
<tr><td>Positive</td><td>Negative</td><td>Positive</td><td>Negative</td><td>Positive</td><td colspan="2">Negative</td></tr>
<tr><td rowspan="2">Aldehydes</td><td rowspan="2">α-hydroxy-ketones</td><td rowspan="2">Methyl Ketones</td><td rowspan="2">Other Ketones</td><td rowspan="2">Esters (Confirm with Saponi-fication Test #18</td><td colspan="2">Acetylation Test #1</td></tr>
<tr><td>Positive</td><td>Negative</td></tr>
<tr><td colspan="4"></td><td></td><td>Tertiary Alcohols (Confirm with Lucas Test #15, if bp < 150°)</td><td>Some Arenes (Confirm with Formaldehyde Test #11)</td></tr>
</table>

Table 27.8

Class N-2: Compounds Insoluble in Sulfuric Acid

<table>
<tr><td colspan="3">Halogen Present</td><td>Halogen Absent</td></tr>
<tr><td colspan="3">Silver Nitrate Test #19</td><td rowspan="3">Aromatic Hydro-carbons (Confirm with CH_2O Test #11; Test for unsaturation with Br_2 Test #4, MnO_4^- Test #17)</td></tr>
<tr><td>Immediate Positive</td><td>Positive After Heating</td><td>Negative</td></tr>
<tr><td>Benzylic Halides
Tertiary Alkyl Halides</td><td>Negatively Substituted Aryl Halides
Aralkyl Halides</td><td>Aryl Halides</td></tr>
</table>

Table 27.9

Class M: Neutral Water Insoluble Compounds Containing Nitrogen [a]

<table>
<tr><th colspan="3">Saponification Test #18</th></tr>
<tr><th>Positive</th><th colspan="2">Negative</th></tr>
<tr><td rowspan="3">Amides
Nitriles
(Confirm with Esterification Test #9)</td><td colspan="2">Coupling Test #7</td></tr>
<tr><td>Positive</td><td>Negative</td></tr>
<tr><td>Diarylamines
Triarylamines
Negatively Substituted Arylamines</td><td>Aryl Nitro Compounds</td></tr>
</table>

[a] Also apply tests for class N-1 to find compounds containing a nitro group plus another functional group.

27.10-4. Description of Classification Tests.

Test #1. Acetylation Test. This test for alcohols involves conversion of the alcohol into an acetate ester and then detection of the ester by means of the Hydroxamic Acid Test.

The function of the base, N,N-dimethylaniline, is to react with the HCl which would otherwise be liberated. In the absence of the base, tertiary alcohols react with acetyl chloride to give the corresponding alkyl chloride, but no ester.

Mix 0.1 mL of acetyl chloride with 0.2 mL of N,N-dimethylaniline. Add 0.2 g of the substance being tested. ***Caution! This reaction may be vigorous.*** *If heat is not evolved, heat the mixture in a water bath at 50° for 15 min. Cool the mixture, add a few grams of ice and 3 mL of concentrated ammonia, mix well and allow to settle. Remove the oil layer with a dropper, note its odor, and test it for ester by means of the Hydroxamic Acid Test (#13).*

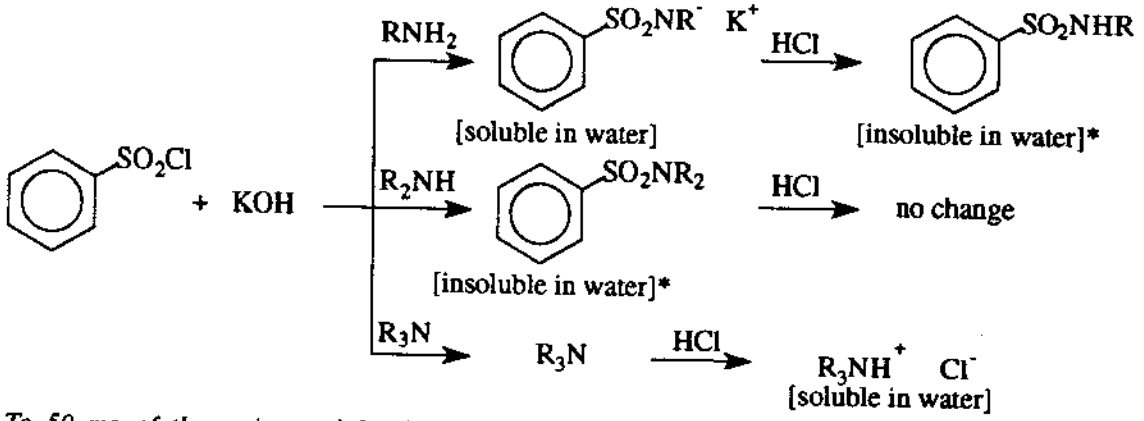
Test Compounds: ethanol, 2-propanol, benzyl alcohol

Test #2. Aniline Test. This test for aldehydes is based on the reaction of aldehydes (but not ketones) with aniline to form a Schiff base (anil) with elimination of water. The water produced is detected by its insolubility in the reaction mixture.

Using a dry test tube, dissolve 0.25 g of the compound (which must be free of water) in 0.25 mL of aniline. Stopper the test tube and gently shake. Aldehydes yield water (which appears as a cloudy emulsion) quite rapidly and with evolution of heat. Ketones do not react under these conditions.

Test Compounds: benzaldehyde, acetone

Test #3. Benzenesulfonyl Chloride (Hinsberg) Test.* This test depends upon the differences in behavior of primary, secondary, and tertiary amines toward benzenesulfonyl chloride in alkaline medium. Primary amines produce the water **soluble** potassium salt of a sulfonamide. Secondary amines produce a solid, water **insoluble** sulfonamide. Tertiary amines fail to react. The presence of the primary amine is confirmed by precipitation of sulfonamide from the solution of the potassium salt upon acidifcation. An unreacted tertiary amine is detected (unless it is water soluble) by its insolubility in the alkaline reaction mixture and its subsequent dissolution upon acidification. Unreacted benzenesulfonyl chloride may be mistaken for the sulfonamide of a secondary amine or may obscure it.



To 50 mg of the amine and 1 mL of 2 M potassium hydroxide in a test tube add 0.1 mL of benzenesulfonyl chloride. Stopper and shake the mixture vigorously, cooling it from time to time if it becomes very hot, until the odor of benzenesulfonyl chloride has disappeared. If the mixture is not strongly basic, add additional potassium hydroxide solution.

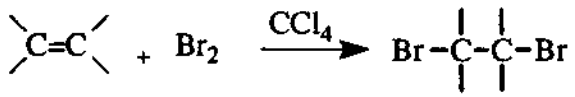
If the mixture has formed two phases, separate them and determine if the organic phase (solid or liquid) is soluble in 2 M hydrochloric acid. An unreacted tertiary amine should dissolve. A secondary amine should have produced a solid insoluble sulfonamide. Larger or cyclic primary amines form sulfonamides that may have low solublity in the basic medium and are thus partially insoluble; they remain insoluble in the hydrochloric acid, and may therefore be confused with the completely insoluble sulfonamides from secondary amines. To distinguish the two possibilities, acidify the original aqueous phase with 2 M hydrochloric acid to pH 4. The benzenesulfonamide of a primary amine, most of which remained in solution, will now precipitate.

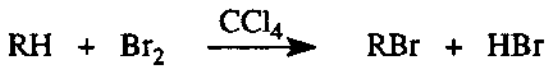
If the original mixture does not separate into two phases, a soluble salt of a benzenesulfonamide from a primary amine may be present. Acidify the solution to pH 4; a precipitate of the free sulfonamide confirms a primary amine.

**Any solid sulfonamide isolated should be purified and used as a derivative.*

Test Compounds: aniline, N-methylaniline, N,N-dimethylaniline, pyridine

Test #4 - Bromine in Carbon Tetrachloride Test. This test detects compounds which react with bromine, either by addition or substitution.

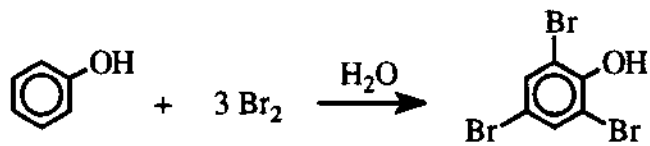




Dissolve 20 mg of the compound in 0.5 mL of carbon tetrachloride; add a solution of bromine in carbon tetrachloride (which is orange or yellow) drop by drop with shaking until the bromine color persists. Test for the presence of hydrogen bromide by blowing across the mouth of the tube (see section 13.3-1). If only a few drops of the bromine solution is decolorized, an unsaturated compound is probably not present.

Test Compounds: toluene, cyclohexene, cyclohexane

Test # 5 - Bromine Water Test. Phenols undergo bromination (usually in all unoccupied *ortho* and *para* positions) with bromine water.



Dissolve about 20 mg of the compound in 2 mL of water or, if not water soluble, in a mixture of ethanol and water. Add bromine water drop by drop until the bromine color is no longer discharged. If a solid precipitate is formed, it should be filtered off and purified for use as a derivative.

Test Compound: phenol

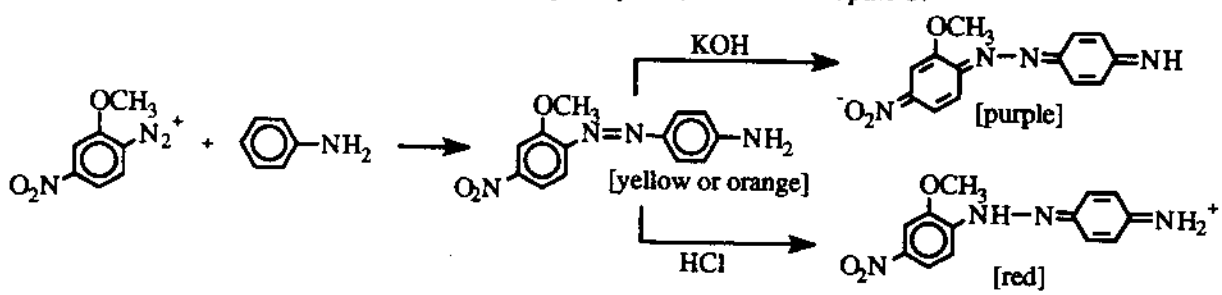
Test #6. Chromic Acid Test. This test for primary and secondary alcohols involves the oxidation of the alcohol with chromic acid and a concomitant reduction of the chromic acid to chromous ion. The reduction is easily detected by a color change from orange (chromic acid) to violet or dark green (chromous ion). The reaction mixture is subsequently treated with DPNH to convert any aldehyde or ketone formed in the oxidation to a 2,4–dinitrophenylhydrazone. The hydrazone can be collected and used as a derivative.

*Add 0.1 g or 0.1 mL of the compound to 0.3 mL of formic acid (CAUTION! **Avoid contact of formic acid with skin**) in a 6–inch test tube suspended in a beaker of water at room temperature. **Cautiously** add one mL of chromic acid (2 M in HOAc) to the alcohol–acid mixture. **The reaction may be very vigorous.** Remove the test tube from the bath and allow it to warm to 60°. When the chromic acid is completely reduced (the mixture is violet or dark green), cool the mixture, add 3 mL of DNPH solution, and then gradually add 3 mL of 2 M HCl. Filter the precipitate, wash it with 2 M HCl and then with water. Confirm that the precipitate is the hydrazone by treating a small bit of it with 1 mL of 2 M methanolic KOH (see DPNH Test #8). If there is sufficient precipitate, take a melting point and compare it with the melting points of the dinitrophenylhydrazones in Table 27.19.*

TEST COMPOUNDS: 1–butanol, 2–butanol

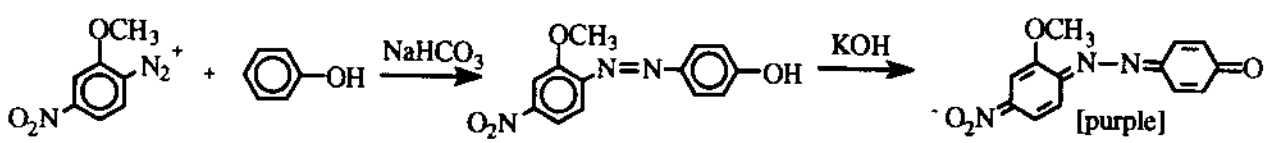
Test #7 – Coupling Test. A positive coupling test indicates that you have an aromatic amine or a phenol. However, the results of this test must always be taken with a grain of salt because the test reagent, a diazonium salt, sometimes does not react with a given aromatic amine or phenol, and sometimes gives bright colors with compounds that are **not** aromatic amines or phenols. This is definitely one instance where carrying out the test on a known compound **and** carrying out a blank test is an absolute necessity.

A. Dissolve 50 mg of 4–nitro–2–methoxybenzenediazonium naphthalene–1,5–disulfonate (Diazo Red B) in 5 mL of water and filter if any solid remains undissolved. Dissolve 30 mg or 1 drop of the compound being tested in 1 mL of methanol and add 1 mL of the Diazo Red B solution. Aromatic amines generally give intensely colored yellow or orange precipitates of azo compounds. If a colored precipitate forms, continue with part B below. If little or no precipitate forms, continue with part C.



B. Precipitate has formed in Part A. *Shake the reaction solution and divide it into two portions so some precipitate is in each test tube. Add 0.5 mL of 2 M methanolic KOH to one portion, and 0.5 mL of concentrated HCl to the other. Azo compounds derived from primary amines are converted to purple and red solutions respectively with KOH and HCl. Those derived from secondary and tertiary amines are unaffected by KOH but give red solutions with HCl. An intensely colored precipitate formed in the part A is usually good evidence for an aromatic amine (do not mistake a pale yellow or orange color for the intensely colored azo dye), but* ***the subsequent color changes with KOH and HCl are less reliable.***

C. No precipitate forms in Part A. Divide the reaction solution into two portions and add 0.5 mL of 1 M $NaHCO_3$ to one portion and 0.5 mL of 2 M methanolic KOH to the other portion. If a precipitate forms on the addition of $NaHCO_3$ this is a good indication that you have a phenol. Phenols usually do not react with the weakly electrophilic diazonium salt until a base ($NaHCO_3$ or KOH) is added to increase the concentration of the phenolate ion.

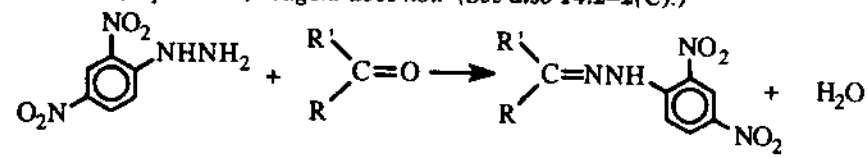


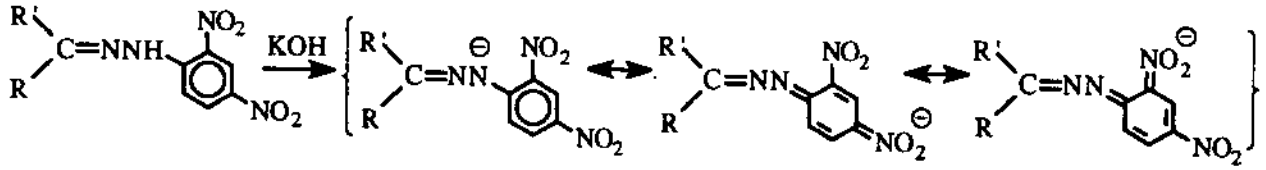
TEST COMPOUNDS: aniline, N–methylaniline, phenol

Test #8 – 2,4–Dinitrophenylhydrazine (DPNH) Test.* A positive DPNH test indicates the presence of a ketone or aldehyde.

Dissolve 30 mg or 1 drop of the compound in 1 mL of DPNH solution. Solids may be added as methanol solutions (30 mg solid in 1 mL of methanol). If no precipitate forms at once, cork the tube and allow it to stand (overnight, if necessary) or reflux for 15 minutes or longer. If a precipitate forms, collect it

by suction filtration for use as a derivative (see 27.12-5). Treat a small portion of the precipitate with 2 mL of 2 M methanolic KOH. 2,4–Dinitrophenylhydrazones give a stable, red, purple or blue color with KOH; unreacted DNPH (m.p. ~200°) reagent does not. (See also 14.2–2(C).)



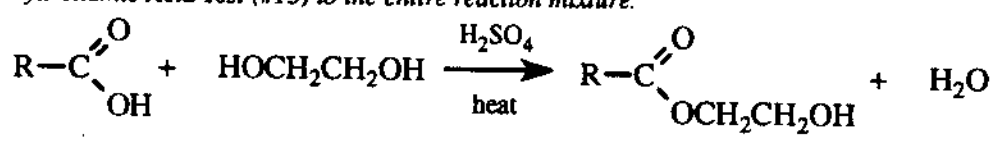


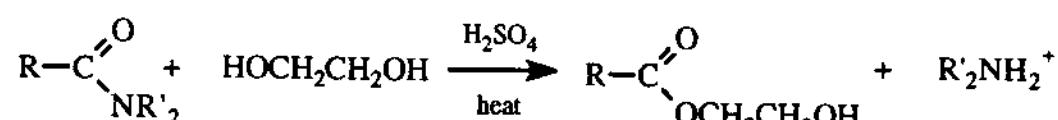
Saturated aldehydes and ketones generally give yellow derivatives; α,β–unsaturated and aromatic carbonyl compounds generally give orange or red derivatives. A false DPNH test may be obtained from an alcohol which has undergone air oxidation, especially after a long period of reflux.

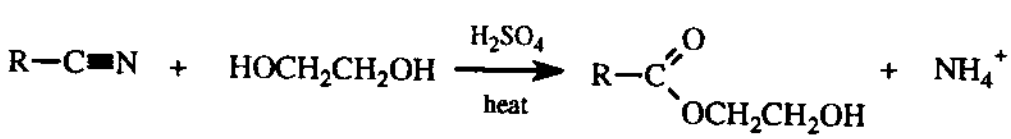
TEST COMPOUNDS: acetone, acetophenone, benzaldehyde

Test #9 – Esterification Test. This is a test for carboxylic acids, amides and nitriles. The acids, amides and nitriles are converted into monoesters of ethylene glycol, and the presence of ester is confirmed with the Hydroxamic Acid Test (Test #13).

Dissolve 30 mg or one drop of the compound in 0.5 mL of ethylene glycol and add 1 drop of concentrated sulfuric acid. Mix well and boil gently for 1 minute or longer, but avoid charring. Allow to cool and apply the Hydroxamic Acid Test (#13) to the entire reaction mixture.

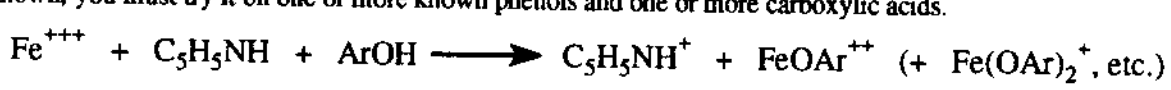






TEST COMPOUNDS: acetic acid, benzoic acid, acetamide, acetanilide, acetonitrile, benzonitrile

Test #10 – Ferric Chloride Test. This is a test for phenols and is used to distinguish phenols from carboxylic acids. However, the test reagent gives colors with a variety of compounds, so before trying this test on an unknown, you must try it on one or more known phenols and one or more carboxylic acids.



Mix 1 mL of chloroform with 0.5 mL of pyridine in a dry test tube, cool and divide the solution into two portions. Add 30 mg or 1 drop of the compound to one portion, then add methanolic ferric chloride

solution to both portions 1 drop at a time and compare the colors of the solutions. Phenols and enols give colors which include red, purple, brown and green.

TEST COMPOUNDS: phenol, *p*–methylphenol, acetic acid, benzoic acid

Test #11 – Formaldehyde–Sulfuric Acid Test. This test is for aromatic hydrocarbons. The formation of a deep–colored sludge (benzene, red; naphthalene, blue; phenanthrene, green) is a positive test. Aromatic compounds other than hydrocarbons may respond to the test provided that electron withdrawing substituents are not attached to the ring. The sludge is the result of acid catalyzed copolymerization of the aromatic ring with formaldehyde. The color probably arises from formation of diaryl– and triarylcarbocations through disproportionation.

Dissolve 30 mg or 1 drop of the compound in 0.5 mL of CCl_4, add 1 mL of concentrated H_2SO_4, agitate well, add one drop of 40% formaldehyde and agitate again.

TEST COMPOUNDS: benzene, toluene, naphthalene

Test #12 – Hydrochloric Acid Test. This test is used only on Class H–2 compounds that are basic to litmus paper. A positive test, the separation of a solid compound or the separation of a second liquid phase indicates that the unknown compound is a salt of a Class A–1 or A–2 compound.

$$RCO_2^- Na^+ + HCl \longrightarrow RCO_2H + NaCl$$

$$ArO^- Na^+ + HCl \longrightarrow ArOH + NaCl$$

Add 0.5 mL of 2 M HCl to 1.5 mL of an aqueous solution of the test compound. (Use the solution from the solubility test.) If a solid precipitates, collect it by suction filtration, dry and take a melting point. This may serve as one derivative of your unknown. If a second liquid phase separates, try and isolate this liquid and prepare a derivative from it. The development of a pungent odor (but no separate liquid or solid phase) suggests that the compound is the salt of a Class H–1 acid.

TEST COMPOUNDS: sodium benzoate, sodium *p*–nitrophenoxide

Test #13 – Hydroxamic Acid (HA) Test. This test is used to detect carboxylic acid esters but is applicable only to compounds which *do not* give an intense color with ferric chloride (see Test #10).

$$NH_2OH \xrightarrow{OH^-} NH_2O^- \xrightarrow{RCOOR'} RC(=O)NHO^- \xrightarrow{H^+} RC(=O)NHOH \xrightarrow{Fe^{+++}} (RC(=O)NHO)_3Fe$$

[purple]

Dissolve 30 mg or 1 drop of the compound (or the entire reaction mixture from Test #9) in 1 mL of hydroxylammonium chloride solution (1 M in methanol, containing methyl yellow and thymolphthalein indicators). Add 2 M methanolic KOH dropwise until the mixture just turns blue and then add 0.5 mL more. Mix well and pour one–half of the mixture into a second test tube. After a minute, add 2M methanolic HCl to one test tube until the solution just turns rose and then add a drop of 10% methanolic ferric chloride. If a deep purple color is obtained (a positive test), discard the material in the second test tube. If no deep purple color appears, reflux the material in the second test tube for 15 min., cool, add 0.5 mL more of the hydroxylammonium chloride reagent and proceed as with the first portion (Add methanolic HCl to rose color, then a drop of methanolic ferric chloride. Look for a purple color.).

TEST COMPOUNDS: ethyl acetate, methyl benzoate

Test #14 – Iodoform Test. See **14.2–2(A).**

Test #15 – Lucas Test. This is a test to distinguish primary, secondary and tertiary alcohols from one another. This test is applicable **only** to alcohols which are soluble in the reagent, hence, to those having boiling points below 150°.

$$\underset{[2^o \text{ or } 3^o]}{R_3COH} + HCl \xrightarrow{ZnCl_2} R_3CCl + H_2O$$

To 0.1 mL of an alcohol, add 1 mL of Lucas reagent (zinc chloride dissolved in concentrated hydrochloric acid). Stopper the tube, shake, and allow it to stand. Note the time required for the formation of an insoluble layer or emulsion of alkyl chloride. If no emulsion or insoluble layer appears, add 1 to 2 mL of water.

Tertiary alcohols give the alkyl chloride at once, secondary alcohols after 5 to 10 minutes, and primary alcohols do not react. Allyl alcohol reacts rapidly with the Lucas Reagent, however, allyl chloride does not separate unless the mixture is diluted with water.

TEST COMPOUNDS: 1–butanol, 2–butanol, *t*–butyl alcohol

Test #16 – Nitrous Acid Test. This test is used to distinguish primary aliphatic amines from primary aromatic amines and will **also** distinguish tertiary aliphatic amines from tertiary aromatic amines.

Primary aliphatic amines give an immediate vigorous evolution of nitrogen (not to be confused with oxides of nitrogen arising from decomposition of nitrous acid; run a blank). Primary aromatic amines give a clear solution of the diazonium salt, which can be confirmed by running a coupling reaction with ß–naphthol which will give an intensely colored azo dye. Tertiary aliphatic amines do not give an obvious reaction with nitrous acid, but tertiary aromatic amines form green *p*–nitroso compounds whose hydrochlorides are yellow.

$$RNH_2 + HONO \longrightarrow ROH + N_2\uparrow + H_2O$$

$$ArNH_2 + HONO \longrightarrow ArN{\equiv}N \xrightarrow[OH^-]{OH} \left[\text{N=NAr, O}^- \leftrightarrow \text{N}^-\text{–NAr, O} \right]$$

[intense color]

$$\text{NR}_2 + HONO \longrightarrow \text{O=N, NR}_2$$

[green]

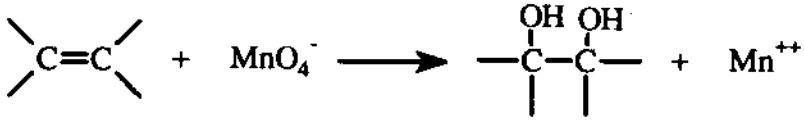
Cool a solution of about 50 mg of a ***primary amine*** *in 0.5 mL of 2 M hydrochloric acid to 0° and add a few drops of an aqueous solution of sodium nitrite. Look for the evolution of a gas. If no gas appears, add a few drops of the cooled solution to a solution of 50 mg of ß–naphthol in 3 mL of 2 M sodium hydroxide. Look for the formation of the azo dye.*

Cool a solution of about 50 mg of a ***tertiary amine*** *in 0.5 mL of 2 M hydrochloric acid to 0° and add a few drops of an aqueous solution of sodium nitrite. Add 2 M sodium hydroxide dropwise until the solution is basic. Look for the green p–nitroso compound.*

TEST COMPOUNDS: 1–pentanamine, aniline, N,N–dimethylaniline

Unsubstituted amides and ureas ($RCONH_2$ and $R'NHCONH_2$) also evolve nitrogen when treated with nitrous acid.

Test #17 – Potassium Permanganate Test. This is a test for carbon–carbon double or triple bonds. A positive test is one in which the purple color of the permanganate disappears and a dark brown precipitate of MnO_2 appears.



Dissolve 2 drops or 50 mg of the compound in 2 mL of methanol. Add a 2% solution of potassium permanganate drop by drop with shaking until the purple color persists. If there is doubt as to whether a significant reaction has occurred, run a blank using the same amounts of methanol and permanganate solution for comparison. See 13.3–2.

TEST COMPOUNDS: cyclohexene, toluene

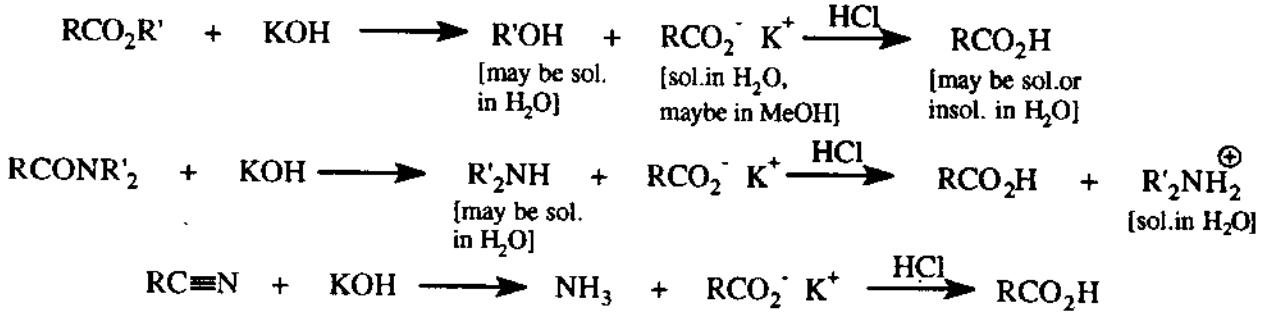
Test #18 – Saponification Test.* This is a test for esters, amides or nitriles. These three classes of compounds on heating with methanolic potassium hydroxide will undergo saponification to form salts of carboxylic acids. These salts are generally soluble in water but, in most cases, the free acid will precipitate when the solution is acidified. (Remember: Carboxylic acids with fewer than 4 carbons are infinitely water soluble.)

Esters also yield an alcohol or phenol on saponification and, depending on the alcohol, it may or may not be isolated using this procedure. If the resulting alcohol is insoluble in methanol or methanol–water, it will separate as a liquid or solid during this procedure. If it is a solid it can be used as a derivative. If it is a liquid it can be converted to a solid derivative (see Table **27.10**).

Unsubstituted amides and imides yield ammonia which may be detected by holding a wet piece of red litmus paper above the condenser. If the paper turns blue it indicates that a volatile base (NH_3) is being evolved from the reaction mixture. (This test is not always reliable. Hold a wet piece of red litmus paper over a refluxing solution of methanolic potassium hydroxide containing no unknown and see if you detect any color change.)

Substituted amides yield an amine on saponification which, if it is volatile, may turn the wet red litmus paper blue. If the amine is of sufficiently high molecular weight, it may be isolated as a separate phase (liquid or solid) at the conclusion of the saponification. If it is a solid it may be used as a derivative. If it is a liquid it may be converted to a solid derivative (see Tables **27.13** and **27.14**).

Nitriles, like unsubstituted amides, yield ammonia along with the carboxylic acid.



In a test tube or a small flask equipped with a reflux condenser add 1 mL of 2 M methanolic potassium hydroxide and 0.1 g or 3 drops of the test compound. Reflux for 1/2 hr or longer. Hold a piece of moist red litmus paper above the opening in the condenser from time to time during the reflux period. Cool the reaction mixture and note if a precipitate forms, if there is a second phase, or if there has been a change in odor. Dilute the reaction mixture with 2 mL of water. Note if the resulting mixture is clear, is cloudy, or

there is a precipitate.

If the solution is clear and the original substance was insoluble in water, it indicates that saponification has taken place. In this case, acidify the solution with 2 M HCl to pH 4 (at pH 4 Congo red indicator paper will turn from red to blue) and note whether an insoluble precipitate of a carboxylic acid appears. If a precipitate forms, collect it by suction filtration, dry it and take a melting point. If it is the carboxylic acid, it serves as one derivative.

If you suspect that an acid is present but little or no precipitate has formed, extract the acidified solution 2 times with diethyl ether, dry the ether solution with sodium sulfate and evaporate.

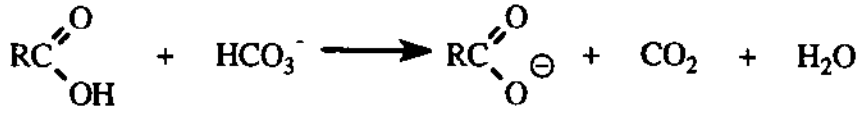
TEST COMPOUNDS: methyl benzoate, acetamide, acetanilide, benzonitrile

Test #19 – Silver Nitrate Test. This is a test applied to alkyl halides, and can also be applied to compounds suspected of being ionic halides, e.g., ammonium chlorides. Tertiary alkyl halides, allyl halides, and benzyl halides give an almost immediate precipitate, as do ionic halides. Secondary and primary halides give a precipitate more slowly, often not until the solution is heated. Vinyl and aryl halides are inert, except for aryl halides with electron withdrawing groups, e.g., nitro groups, *ortho* or *para* to the halogen. If a precipitate appears it should be treated with 2 *M* nitric acid; silver halides are insoluble in dilute nitric acid, but silver salts of most organic acids are soluble.

Add a drop of the halogen compound to 2 mL of alcoholic silver nitrate solution. If no reaction is observed after 5 minutes, heat the solution to boiling. If there is a precipitate, note its color. Add 2 drops of 2 M nitric acid and note whether the precipitate dissolves.

TEST COMPOUNDS: *t*–butyl chloride, 1–bromobutane, allyl chloride

Test #20 – Sodium Carbonate Test. This test is for Class H–1 or H–2 compounds suspected of being carboxylic acids. Water insoluble (Class A–1) acids will already have been tested with bicarbonate. The evolution of carbon dioxide indicates the unknown is a carboxylic acid or other acid stronger than carbonic acid.



To 50 mg or 0.1 mL of the unknown compound dissolved in the minimum amount of water add 0.5 mL of 1 M $NaHCO_3$. Look for gas bubbles.

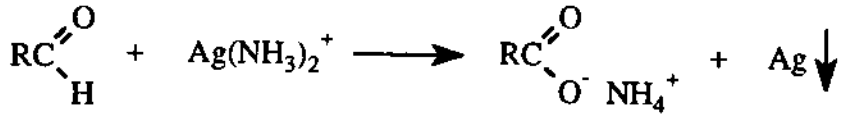
TEST COMPOUND: acetic acid

Test #21 – Sodium Hydroxide Test. This test is for Class H–2 compounds and will determine whether a compound is the salt of a water soluble or water insoluble amine. If the compound in question forms a precipitate or a second liquid phase on treatment with sodium hydroxide it is the salt of a Class B compound. If the compound remains in solution but you note the development of an ammonia–like odor or a fishy odor, this suggests the compound is a salt of a Class H–1 amine.

Dissolve 0.1 g of the compound in 1.5 mL of water and add 0.5 mL of 2 M NaOH. Note if a precipitate or a second liquid phase is formed. If no second phase forms, smell the solution and note, if any, the development of an ammonia–like odor or a fishy odor.

TEST COMPOUNDS: anilinium chloride, diethylammonium chloride

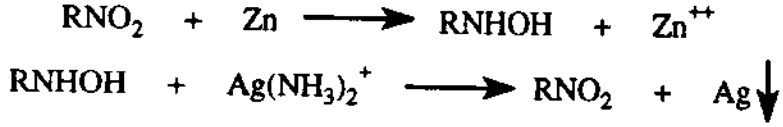
Test #22 – Tollens' Test. This is a test for aldehydes. If an aldehyde is present you will see a silver mirror form on the walls of the test tube. If the test tube is not completely clean, you will see a black precipitate of silver form rather than the mirror.



In a scrupulously clean test tube place 2 mL of aqueous silver nitrate solution and add a drop of dilute sodium hydroxide solution (a dirty white precipitate will form). Add a very dilute (about 2%) solution of ammonia drop by drop, with constant stirring or shaking, until the precipitate of silver oxide just dissolves. Add a drop of the compound being tested and stir once. (If the compound is a water insoluble solid, dissolve 10–20 mg in a minimal amount of methanol and add the methanol solution to the silver ammonium nitrate solution.) If no reaction takes place in the cold, the solution should be warmed slightly in a beaker of warm water. **Whether or not a positive test is obtained, the mixture should be flushed down the drain after a few minutes, since an explosive precipitate tends to form on standing.**

TEST COMPOUNDS: acetaldehyde, benzaldehyde, ethanol, acetic acid

Test #23 – Zinc Reduction Test. This is a test for nitro compounds. Under the conditions of the test zinc reduces nitro compounds to hydroxylamines (ArNHOH; see **21.1**), which in turn reduce silver ion in the Tollens' test.



Dissolve 0.1 mL or 20 mg of the compound in 2 mL of 50% ethanol; add 0.1 g of ammonium chloride and 0.1 g of zinc dust. Shake the mixture and heat to boiling. Allow the mixture to stand 5 minutes, filter and test the filtrate with Tollens' reagent. If a positive test is obtained, make certain that the original compound does not give a Tollens' test.

TEST COMPOUNDS: *p*–nitrotoluene, *p*–nitrobenzoic acid

27.11 – Examination of Tables. Consideration of Possible Structures

Once the nature of the unknown has been determined – that is, the functional group has been recognized or the fact established that the compound possesses no functional group – possible structures should be considered. For this purpose consult the tables in **27.14**. Look at the table for the class of compounds to which you believe your compound belongs, *e.g.*, alcohols (**Table 27.10**), carboxylic acids (**Table 27.17**), ketones (**Table 27.19**), etc., and consider as tentative possibilities all those compounds whose melting points or boiling points are within 15 degrees above or below the melting point or boiling point you measured for your unknown.

The tables should be examined carefully. The unknown might be one of the compounds listed in the columns of derivatives. For example, if your unknown is thought to be an amide, you must consider not only those amides listed in **Table 27.12** but also those listed as derivatives of amines in **Table 27.13** and those listed as derivatives of carboxylic acids in **Table 27.17**.

Salts of carboxylic acids and salts of amines must be considered as possibilities even if they are not separately listed. In general, salts are listed in the tables only when they possess reproducible melting points. Most salts do not.

Additional chemical tests may suggest themselves at this point to distinguish among some of the

possibilities. Otherwise, the preparation of derivatives is undertaken next.

27.12-Preparation of Derivatives

Final identification is achieved by the preparation of solid derivatives. Derivatives are required for confirmation even if the number of possibilities has already been narrowed down to one.

A derivative is any reaction product of the unknown that can be isolated in a pure state and for which at least one physical constant can be measured. Almost all useful derivatives for purposes of identification are solids because small quantities of solids can be easily purified and their melting points determined, whereas small quantities of liquids require specialized techniques for purification. An additional consideration is that melting points are more likely to show variations for closely related and isomeric compounds than are boiling points.

The student is urged to consider other possible derivatives either instead of or in addition to those found in the tables in **27.14**. The references listed at the end of this chapter should be consulted for additional information. Select derivatives whose melting points will clearly distinguish among the possibilities.

The directions given for the preparation of derivatives are necessarily generalized procedures applicable to a large number of compounds, but certain individual compounds may require modifications. Some experimentation may be necessary to find the right conditions to bring about some of the reactions.

Not infrequently a derivative expected to be a solid separates from a reaction mixture as a liquid or "oil." Sometimes the oil is a supercooled liquid, which, upon cooling and scratching of the inside walls of the flask eventually can be made to solidify. More often, unfortunately, the physical state is a result of the derivative being contaminated by a sufficient quantity of impurities to lower its freezing point below ice bath temperature.

Sometimes enough of these impurities can be dissolved out of the oil with an appropriate solvent to permit it to crystalize. The solvent chosen for this purpose should be one in which you expect the derivative to be partially but not highly soluble. If the reaction mixture is aqueous, a water-soluble solvent should be selected, if possible. The reagents from which the derivative was synthesized are likely contaminants, so a solvent known to dissolve them is desirable. The solvent recommended for recrystallization of the derivative would very likely be a good choice.

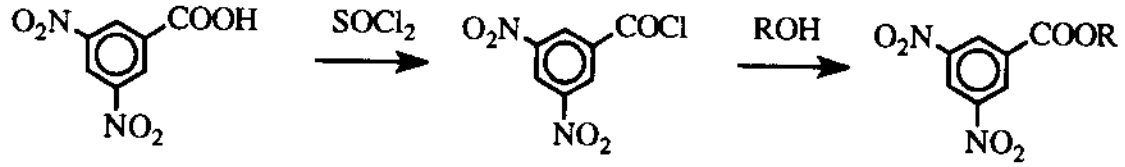
First try to solidify the oil by prolonged cooling in an ice bath and scratching the inside walls of the flask. If that procedure is not successful, decant as much as possible of the mother liquor from the oil and add a few drops of solvent. Triturate (mix or rub vigorously) the mixture with a stirring rod and cool it thoroughly. If the oil remains, repeat the process with the same or a different solvent.

Most derivatives require recrystallization before they exhibit the correct melting point. If the directions specify a recrystallization solvent, it should be tried first on a minute amount of the derivative, since the solvent specified may not be satisfactory in all cases. If none is specified or if the specified solvent is found unsatisfactory, find a solvent using the procedure described in section **7.3-1**.

Alcohols
(Table 27.10)

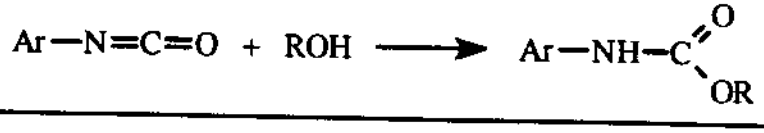
27.12-1. 3,5-Dinitrobenzoate esters. In a hood, heat a mixture of 1 g of 3,5-dinitrobenzoic acid,* 3 mL of thionyl chloride, and 1 drop of pyridine under reflux for 30 min or until all the acid has been in solution for 10 min. Distil off the excess thionyl chloride.

*If a freshly opened bottle of 3,5-dinitrobenzoyl chloride is available omit the preparation in this paragraph; add 1 mL of the alcohol to 1 g of the commercial 3,5-dinitrobenzoyl chloride and proceed as described in the second paragraph. If the commercial acid chloride is old or if its age is in doubt, do not use it, and prepare fresh 3,5-dinitrobenzoyl chloride as described here.



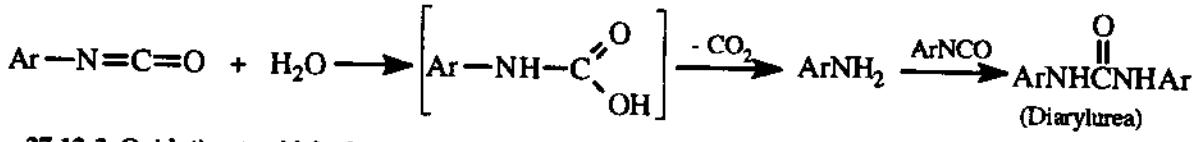
To the residue add 1 mL of the alcohol and reflux the mixture gently for 20 min (take care to prevent the entrance of moisture). Then add 5 to 10 mL of water and rub the product with a stirring rod to effect crystallization. Collect the precipitate by suction filtration, break up any large lumps and wash with 5 to 10 mL of 5% sodium carbonate solution. Recrystallize the ester from ethanol or ethanol and water.

27.12-2. Phenylurethans and α-naphthylurethans.



CAUTION! Isocyanates are lachrymators and should be used only in the fume hood.

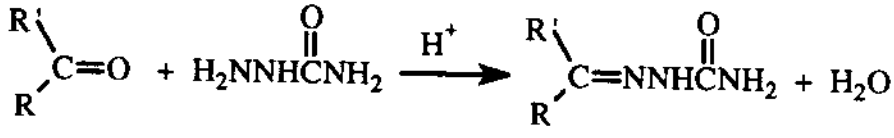
The exclusion of water is essential in this preparation. One gram of the anhydrous alcohol or phenol is placed in a test tube, and 0.5 mL of phenyl isocyanate or α-naphthyl isocyanate is added. If the reactant is a phenol, the reaction should be catalyzed by the addition of 2 to 3 drops of anhydrous pyridine or triethylamine. If a spontaneous reaction does not take place the solution should be warmed on the steam bath for 5 min. It is then cooled in a beaker of ice, and the sides of the tube are scratched with a glass rod in order to induce crystallization. The urethan is purified by dissolving it in 5 mL of petroleum ether or carbon tetrachloride, filtering the hot solution and cooling the filtrate in an ice bath. The resulting crystals are collected and dried. A sparingly soluble solid melting well above 200° is probably the diarylurea arising from reaction of the isocyanate with water.



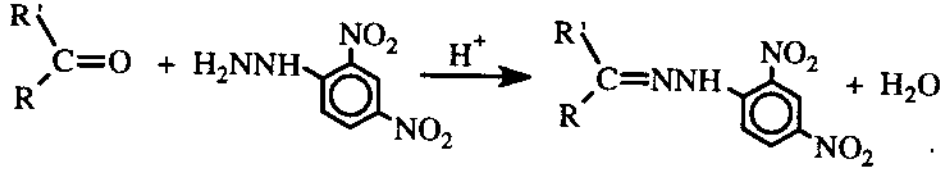
27.12-3. Oxidation to aldehyde or ketone. Conduct the chromic acid test (#6) on a larger scale, isolate the 2,4-dinitrophenylhydrazone derivative, and purify it by recrystallization from ethanol, ethanol and water, or ethyl acetate and ethanol. See also **14.2-1** for isolation of a ketone.

Aldehydes
(Table 27.11)

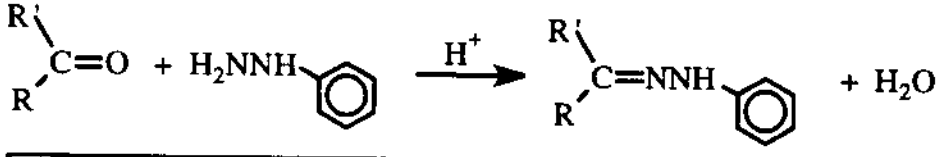
27.12-4. Semicarbazones. See **14.2-2(B)**.



27.12-5. 2,4-Dinitrophenylhydrazones. See **14.2-2(C)**. Recrystallize the derivative from ethanol, ethanol and water, or ethyl acetate and ethanol.



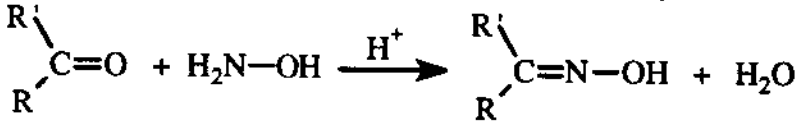
27.12-6. Phenylhydrazones.



CAUTION! Phenylhydrazine is a skin poison and must be handled with care.

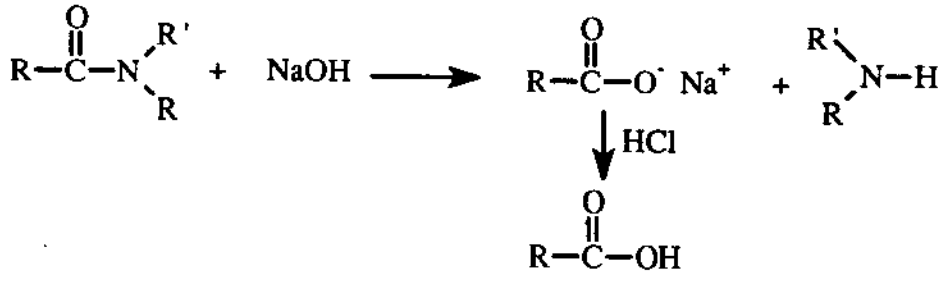
Dissolve 0.5 g of the aldehyde or ketone in 2 mL of ethanol, add water dropwise until the cloudiness just disappears on shaking. If too much water is added, a little alcohol should be added to clarify the solution. To this clear solution add 0.2 mL of pure phenylhydrazine. If the solution remains clear for several minutes, add a drop of acetic acid to catalyze the reaction, warm gently for a few minutes and then cool. Collect the phenylhydrazone by filtration and recrystallize it.

27.12-7. Oximes. Dissolve about 0.5 g of hydroxylamine hydrochloride in 3 mL of water; then add 2 mL of 10% sodium hydroxide solution and 0.2 g of the aldehyde or ketone. If the carbonyl compound is not water soluble, add just sufficient ethanol to the mixture to give a clear solution. Warm the mixture on the steam bath for 10 min and cool in an ice bath. In order to hasten crystallization, scratch the inside of the flask with a glass rod. Occasionally the addition of a few milliliters of distilled water will assist in causing the oxime to separate.



Amides
(Table 27.12)

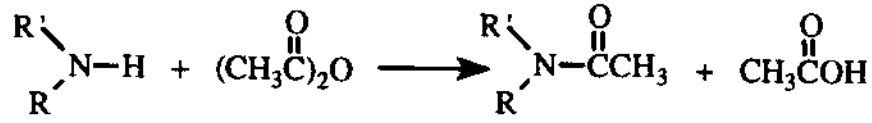
27.12-8. Hydrolysis. Amines and carboxylic acids. To 1 g of the amide add 25 mL of 10% sodium hydroxide. Reflux the mixture for 10 min or until the original material has disappeared. If the resulting amine is insoluble it may appear as an oil or as a solid. In the latter case collect it by filtration and either purify it to use as a derivative itself or else convert it into an amine derivative. If the amine appears as an oil, separate it by extraction with a small amount of benzene or distil it and then convert it to an amine derivative. After removal of the amine acidify the alkaline solution with hydrochloric acid to precipitate the carboxylic acid, which, if a solid, can also be used as a derivative.



If the amine is water soluble its presence will usually be revealed by a characteristic odor in the alkaline solution. It can be isolated as an acetyl, benzoyl, or benzenesulfonyl derivative by treating the solution or a portion of it directly with acetic anhydride, benzoyl chloride, or benzenesulfonyl chloride respectively.

Amines, Primary and Secondary
(Table 27.13)

27.12-9. Acetamides. Dissolve about 0.5 g of the amine in 25 mL of 5% hydrochloric acid. Add small portions of 5% sodium hydroxide until the mixture becomes cloudy; then remove the turbidity by adding 2 or 3 mL of 5% hydrochloric acid. Add a few chips of ice followed by 5 mL of acetic anhydride. Stir or swirl the mixture vigorously and add, in one portion, a previously prepared solution of 5g of sodium acetate in 5 mL of water. If the product does not crystallize, chill the mixture.

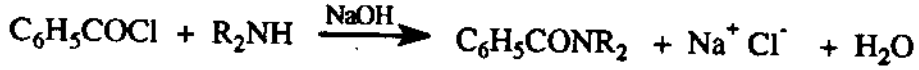


The procedure above is applicable only to class B amines. For water soluble amines mix the amine and acetic anhydride together without solvent, warm gently if solution does not occur, and rub the mixture with a stirring rod until it solidifies.

If neither of the procedures is successful, mix 0.5 g of the amine with 5 mL of acetic anhydride. Add 5 mL of acetyl chloride dropwise with cooling and shaking. Warm gently for a few minutes, cool, and *cautiously and very slowly* pour it into 10 mL of ice water with continual stirring. Collect the solid by suction filtration.

Acetamides can usually be recrystallized from alcohol and water, petroleum ether, or benzene and petroleum ether.

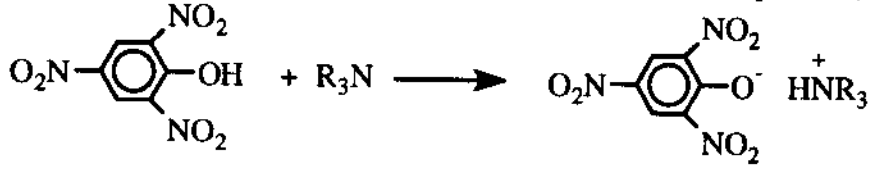
27.12-10. Benzamides. Shake a mixture of 0.5 g of the amine, 10 mL of 10% sodium hydroxide and 0.5 mL of benzoyl chloride with occasional cooling until crystallization of the amide is complete. Collect it by filtration, wash it, dry it, and recrystallize it from ethanol, ethanol and water, ethyl acetate and petroleum ether, or petroleum ether.



27.12-11. Benzenesulfonamides. Carry out the procedure of the Hinsberg Test (#3) on a larger scale. Recrystallize the sulfonamide from 95% ethanol.

27.12-12. Phenylthioureas. Mix 1 mL each of the amine and phenyl isothiocyanate in a test tube and shake for 2 min. If no reaction occurs spontaneously, heat the mixture for 3 min over a small flame. The aliphatic amines usually react immediately whereas the aromatic amines require heating. Place the mixture in a beaker of ice until the mass solidifies. Powder the solid and wash it with ligroin and then with 50% ethanol to remove any excess of either reactant. Recrystallize the residue from 95% ethanol.

27.12-13. Picrates. Add a 0.3 to 0.5 g sample of a solid amine (primary, secondary, or tertiary) or aromatic hydrocarbon to 10 mL of 95% ethanol. (Liquids can be added directly to the picric acid solution). If solution is not complete, shake the mixture until saturated and filter it. Add this solution to 10 mL of a saturated solution of picric acid in 95% ethanol and heat to boiling. Allow the solution to cool slowly and remove the yellow crystals of the picrate by filtration. Wash the derivative with a little ether and dry it as quickly as possible. Determine the melting point immediately, since some picrates (especially those from hydrocarbons)



decompose on standing. In the melting point determination do not heat a picrate above 200°; some picrates explode at high temperatures. The picrate salts of amines are usually sufficiently stable to permit recrystallization from ethanol.

If crystallization of the picrate does not take place, try the same procedure again but with ether or chloroform solutions of the amine and picric acid.

27.12-14. Amine hydrochlorides. Treat 0.2 g of the amine with 1 mL of concentrated hydrochloric acid. Heat to boiling. If the amine does not dissolve add water dropwise until a clear solution results. Allow to cool and collect the precipitated salt.

$$R_3N + HCl \longrightarrow R_3NH^+ Cl^-$$

Amines, Tertiary
(Table 27.14)

27.12-15. Picrates. Use the procedure given for primary and secondary amines (**27.12-13**).

27.12-16. Amine hydrochlorides. Use the procedure given in **27.12-14**.

27.12-17. Quaternary methylammonium *p*-toluenesulfonates (methyl tosylates). Add 1 g of the amine to a solution of 2 g of methyl tosylate in 10 mL of dry benzene and boil 10 to 20 min. Recrystallize the product by dissolving it in the minimum amount of hot ethanol and adding ethyl acetate until crystallization starts. Cool thoroughly, filter, dry, and determine the melting point at once.

$$R_3N + CH_3{-}OTs \longrightarrow R_3NCH_3^+ OTs^-$$

27.12-18. Quaternary methylammonium iodides (methiodides). Warm a mixture of 0.5 g of the amine and 0.5 mL of methyl iodide over a steam bath for a few minutes. (CAUTION! Methyl iodide is very volatile.) Cool the mixture in an ice bath and scratch the inside of the test tube with a stirring rod, if necessary, to aid in crystallization. Recrystallize the product from absolute methanol, or ethyl acetate.

$$R_3N + CH_3I \longrightarrow R_3NCH_3^+ I^-$$

27.12-19. Tertiary ammonium *p*-toluenesulfonate (tosylate). Dissolve one gram of sodium *p*-toluenesulfonate in about 1 mL of water. Add 5 to 10 mL of 6 M HCl, 1.5 g of the amine, and enough water to bring all the material into solution at the boiling point. If the solution is not colorless, add decolorizing carbon, filter the hot solution, and cool. Filter the precipitated salt and recrystallize it from 1% acetic acid.

$$CH_3C_6H_4SO_3^- Na^+ + R_3N + HCl \longrightarrow CH_3C_6H_4SO_3^- R_3NH^+ + Na^+ Cl^-$$

Arenes
(Table 27.15)

27.12-20. Nitro derivatives. The conditions required for successful nitration of an aromatic ring vary considerably with the reactivity of the ring. It is recommended that the optimum conditions be found with very small-scale trial nitrations using a few drops of the unknown and a few drops each of sulfuric acid

> CAUTION! Special care should be employed in nitrating an unknown compound. Sometimes the reaction is violent. Carry out the reaction in the hood and be certain that the mouth of the reaction vessel is pointed away from everyone, including yourself.

and either concentrated or fuming nitric acid. It is best to try the mildest conditions first and then increase the severity of the conditions, if necessary, by changing to fuming nitric acid and using higher temperatures.

Whenever possible, specific directions for nitration of the suspected compound should be found in the literature (also see Chapter 20).

The following procedure yields mononitro derivatives from most simple alkyl- and monohalobenzenes.

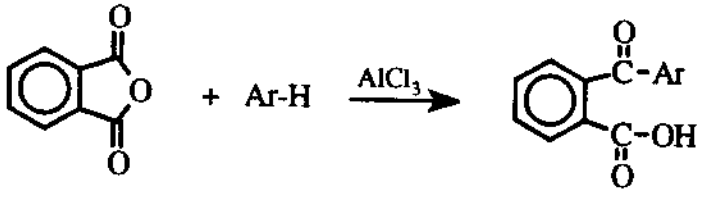
Add about 1 g of the compound to 4 mL of concentrated sulfuric acid. Mix well and add 4 mL of concentrated nitric acid drop by drop, and shake after each addition. Connect the flask to a reflux condenser and immerse the flask in a beaker of water kept at 45°. After 5 min pour the reaction mixture onto 25 g of ice and collect the precipitate on a filter. Recrystallize it from a mixture of ethanol and water.

To obtain dinitro derivatives from halobenzenes and trinitro derivatives from the more reactive arenes, substitute fuming nitric acid (EXTRA CAUTION!) for the concentrated nitric acid, increase the reaction temperature to that of the steam bath, and allow the reaction to run for 10 minutes or longer.

27.12-21. Aroylbenzoic acids. To a solution of 1 g of the *dry* aromatic hydrocarbon and 1.2 g of phthalic anhydride in 10 mL of dry carbon disulfide, add 2.4 g of anhydrous aluminum chloride. Heat the

> CAUTION! Carbon disulfide, used in this procedure, is extremely flammable and has a very low flash point. Its vapor is also poisonous. It should be kept away from open flames. The reaction must be conducted in the fume hood.

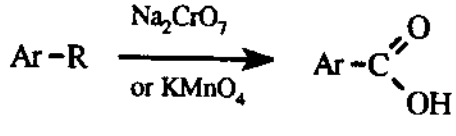
mixture under a reflux condenser in a hot water bath[10] for 30 min and cool. Decant the carbon disulfide layer and slowly add 10 mL of water and 10 mL of concentrated hydrochloric acid to the residue. Cool the mixture during this addition, if necessary, and shake it thoroughly afterwards. If the aroylbenzoic acid separates as a solid, immediately filter it and wash it with water.



If an oil separates, cool the mixture in an ice bath for some time and rub (triturate) with a glass rod. If the product remains oily, decant the supernatant liquid and wash the oil with cold water.

Boil the crude product, whether a solid or an oil, for 1 min with 30 mL of 6 M aqueous ammonia to which 0.1 g of Norite (decolorizing carbon) has been added. Filter the hot solution and cool the filtrate. Add 25 g of crushed ice and acidify with concentrated hydrochloric acid. Collect the aroylbenzoic acid by suction filtration and recrystallize it from aqueous ethanol. It may be necessary to allow the product to stand overnight while crystallization takes place.

27.12-22. Carboxylic acids by oxidation of a side chain.



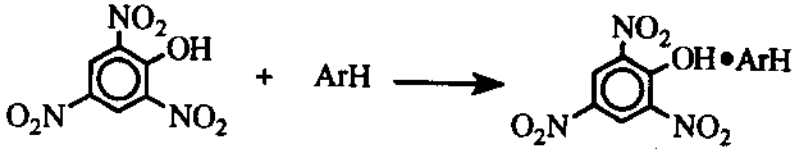
A. Sodium dichromate oxidation. Dissolve 2.5 g of sodium dichromate in 5 mL of water in a small round-bottom flask to which a reflux condenser has been attached. Add 1 g of the compound to be oxidized and

[10] Preheat the water to 60-70°, use water from the hot tap, or use a hot plate to warm the bath. DO NOT under any circumstances light a burner under the bath while the reaction mixture is immersed in it.

3.5 mL of concentrated sulfuric acid. Shake the mixture thoroughly and carefully heat it with a small flame until the reaction starts. Remove the flame and allow the reaction to proceed on its own. If it threatens to get out of control, cool the flask promptly in an ice bath. When the exothermic reaction has subsided, reflux the mixture for 1 to 2 hours. Pour it into 10 mL of water and collect the resulting precipitate by suction filtration. Transfer the solid to a small Erlenmeyer flask, and add 8 mL of 5% sulfuric acid, and heat the mixture on the steam bath for a few minutes while stirring it vigorously. Cool the mixture, filter it with suction, and wash the precipitate with two 5 mL portions of water. Dissolve the solid in the minimum amount (5 to 10 mL required) of 5% sodium hydroxide. Remove any insoluble material by filtration and pour the filtrate, with vigorous stirring, into 8 mL of 10% sulfuric acid. Collect the precipitate by suction filtration, wash it with water, and recrystallize it from ethanol or benzene.

B. Potassium permanganate oxidation. Add 1 g of the compound to 25 mL of water containing 4 g of potassium permanganate. Add 1 mL of 2 *M* sodium hydroxide and a few boiling stones. Heat the mixture on a hot plate with stirring under reflux until most of the purple color of the permanganate has disappeared (from 0.5 to 3 hr.; one hour should suffice). Filter the hot solution by vacuum filtration. Save the filter cake.[11] Cool the filtrate and add a little sodium bisulite to destroy excess permanganate.[12] Make sure that the solution is basic using indicator paper. Filter again if there are solids in the filtrate. Cool the filtrate in an ice bath and acidify it with 10% sulfuric acid. Then add an additional 5 mL of the acid.[13] Collect the precipitated acid by suction filtration, wash it thoroughly with water, air dry and take the melting point. If necessary, recrystallize the acid from ethanol or ethanol-water.

27.12-23. Picrates. Use the procedure given in **27.12-13.** Do not attempt to recrystallize the product, but determine the melting point immediately.



Aryl and Aralkyl Halides
(Table 27.16)

27.12-24. Nitro derivatives. See the procedure given in **27.12-20.**
27.12-25. Oxidation of a side chain. See the procedure given in **27.12-22.**

Carboxylic Acids
(Table 27.17)

27.12-26a. Anilides and *p*- toluidides. [Before preparing the acid chloride, prepare solutions of aniline and *p*-toluidine as described below].

Heat a mixture of 1 g of a carboxylic acid, 6 mL of thionyl chloride and three drops of dimethylformamide (DMF) for 20-30 min. Heating may be achieved with a very small, cool flame or with an electrical heater. **[WARNING: Add DMF before warming. Do not add DMF to the hot solution.]** The acid should be completely dissolved.

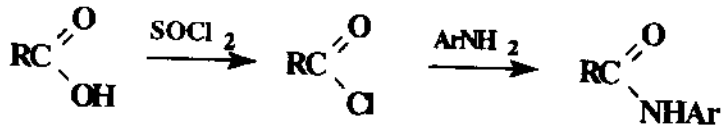
When the reaction of the acid and thionyl chloride is complete and the reaction mixture has cooled to room temperature, add 10 mL of dichloromethane. Divide the resulting solution in two and use half to prepare the anilide

[11] If little or no acid is isolated after acidification of the filtrate, triturate the filter cake with 15 mL of methanol. Filter the mixture and evaporate the filtrate in the hood. The residue from this extraction is unreacted starting material.

[12] Excess permanganate is present if the solution is still purple.

[13] If the acid fails to precipitate from the aqueous solution because of its water solubility, isolate it by extraction of the aqueous solution with ether.

and half to prepare the toluidide.



Anilide. Dissolve 1.5 mL of freshly distilled aniline[14] in 40 mL of dichloromethane in a 125 mL Erlenmeyer flask. Add 25 mL of a 25% aqueous NaOH solution to the Erlenmeyer.

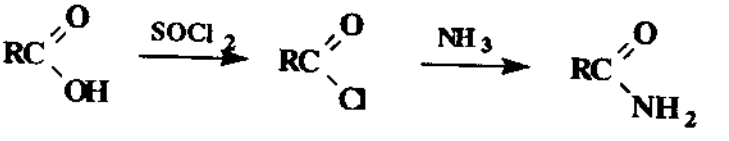
Add the acid chloride-dichloromethane mixture to the Erlenmeyer **dropwise** with vigorous stirring. A vigorous reaction will be observed on each addition of the acid chloride (much of the observed reaction is destruction of excess thionyl chloride). If the acid chloride is added too rapidly, the dichloromethane may boil. If this occurs, cool the reaction flask in an ice bath. If dichloromethane is lost through boiling or evaporation add more to make up for the loss. A precipitate or solid foam may appear in the reaction flask during the addition of the acid chloride.

After addition is complete, swirl the flask at room temperature until you obtain two clearly visible liquid phases. Usually any precipitate that forms during the acid chloride addition dissolves at this point. If the precipitate does not dissolve, add a little more water and a little more dichlormethane; if there is still some precipitate it should be collected by filtration and treated as if it could be the anilide derivative.

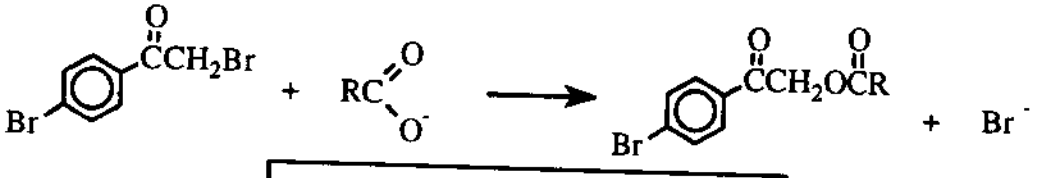
Transfer the two liquid phases to a separatory funnel and separate the two phases. Discard the basic aqueous phase. Wash the organic phase with 15 mL of 5% HCl and then with 15 mL of water. Evaporate the dichloromethane on a steambath (in the hood!) and recrystallize the residue from ethanol or ethanol-water.

***p*-Toluidide.** Dissolve 1.2 g of p-toluidine in 40 mL of dichloromethane in a 125 mL Erlenmeyer flask and add 25 mL of a 25% aqueous NaOH solution. Prepare the *p*-toluidide using the same procedure described above for the anilide.

27.12-26b. Amides. Heat 1 g of the carboxylic acid under reflux with 5 mL of thionyl chloride 15-30 min. Pour the mixture cautiously into 15 mL of ice cold concentrated ammonia. Collect the solid precipitate by suction filtration and wash it with a small volume of ice cold water. If purification is necessary, water or water-ethanol may be used as recrystallization solvents.



27.12-27a. *p*-Bromophenacyl esters.



CAUTION! α-Haloketones are lachrymators.

Place 1 g of the acid and 5 mL of water in a small flask and carefully neutralize with 2 M sodium hydroxide. Add additional amounts of the acid until the solution is just acid to litmus. (Alternatively, if the sodium salt is available, dissolve 1 g of it in 5 to 10 mL of water; if the resulting solution is alkaline, add 1 or 2 drops of dilute

[14] Use a simple distillation apparatus, omitting the condenser, to distill a small amount of aniline, b.p. 184°, shortly before you need it.

hydrochloric acid.) Add a solution of 1 g of *p*-bromophenacyl bromide (2,4'-dibromoacetophenone) in 10 mL of 95% ethanol and reflux the mixture for 1 hr (or 2 hr for a dicarboxylic acid). If a solid separates during the refluxing, add a few more milliliters of ethanol. Allow the solution to cool and filter the precipitated ester. Recrystallize it from ethanol.

27.12-27b. Neutralization Equivalent. Accurately (3 significant fig.)[15] weigh two samples of about 0.1 g each of the acid and dissolve each in 25 to 50 mL standard NaOH (ca 0.1-0.2 *N*) accurately delivered from a burette. If necessary, warm the mixtures to dissolve the compound completely. Add a few drops of phenolphthalein indicator solution. Titrate the solutions with standardized (ca. 0.1 *N*) HCl solution. Calculate the neutralization equivalent (N.E.) according to the equation.

$$\text{N.E.} = \frac{\text{Wt. of sample (g) x 1000}}{\text{meq of NaOH - meq of HCl}}$$

$$\text{meq of HCl} = \text{Vol. of HCl (mL)} \times \text{Normality of HCl}$$

$$\text{meq of NaOH} = \text{Vol. of NaOH (mL)} \times \text{Normality of NaOH}$$

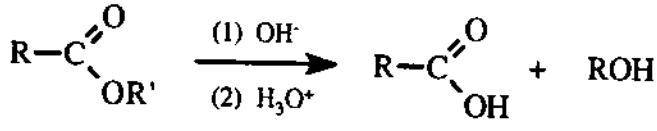
Duplicate determinations should agree with each other within ca 0.5%. The titrations should be performed on a control compound *(i.e.,* a **known** carboxylic acid) before attempting the unknown. If back titration is necessary (*i.e.,* if the endpoint has been exceeded) the meq of additional NaOH should be added to the originally entered value for meq of NaOH. In order to give an accurate neutralization equivalent, the substance titrated must be pure and anhydrous. If the value obtained for the neutralization equivalent does not agree with the theoretical value within less than 1% the compound should be further purified and/or dried.

The molecular weight is N.E. multiplied by the number of acidic groups in the molecule.

Water insoluble carboxylic acids may be recovered from the titrations by acidifying the solutions with a few mL of concentrated sulfuric acid or by extraction with diethyl ether.

Esters
(Table 27.18)

27.12-28. Hydrolysis



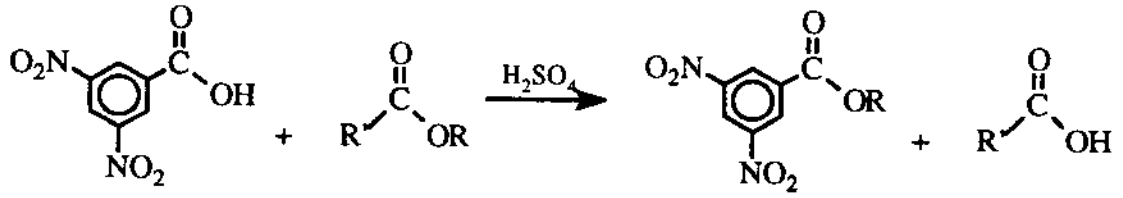
A. Hydrolysis in methanolic potassium hydroxide. If an insoluble acid was detected in the saponification test (#18), repeat the test on a larger scale, isolate, and purify the acid. If the ester is an aryl ester, the corresponding phenol will be precipitated.

B. Hydrolysis in aqueous sodium hydroxide. Reflux a mixture of 1 g of ester and 10 mL of 5% aqueous sodium hydroxide until the reaction mixture becomes homogeneous or until the characteristic ester odor disappears. About 1 to 2 hr is required. Cool the reaction mixture and acidify with phosphoric acid. Filter the precipitated acid, wash it with water, and recrystallize.

27.12-29. 3,5-Dinitrobenzoates. Heat a mixture of 2 mL or 2 g of the ester, 1.5 g of 3,5-dinitrobenzoic acid, and 2 drops of sulfuric acid in an oil bath maintained at 150°, stirring frequently. If the acid dissolves in the liquid within 15 minutes, continue heating for 30 min. Otherwise heat the mixture for a total of at least 1 hr. Cool the reaction mixture and dissolve it in 25 mL of ether. Wash the ether solution with two 15 mL portions of 5% sodium carbonate solution (CAUTION! Considerable pressure may develop as the acids liberate carbon dioxide from the carbonate). Then wash the ether solution with 10 mL water and evaporate the ether. Dissolve the residue, which may be an oil or a solid, in 5 mL of ethanol and heat to boiling. Filter the solution, if necessary, and add water to

[15] If a balance is available that permits estimation of weight to only two significant figures, the uncertainty in the neutralization equivalent is approximately 10%.

the hot filtrate to incipient cloudiness. Cool the mixture and filter the resulting crystals. Recrystallize, if necessary, from ethanol or aqueous ethanol.



Ketones
(Table 27.19)

27.12-30. Semicarbazones. See **14.2-2(B)**.
27.12-31. 2,4-Dinitrophenylhydrazones. See **14.2-2(C)**.
27.27.12-33. Oximes. See **27.12-7**.

Nitriles
(Table 27.20)

27.12-34. Hydrolysis.

$$R{-}C{\equiv}N + H_2SO_4 + 2\,H_2O \longrightarrow R{-}COOH + NH_4^+\ HSO_4^-$$

$$R{-}C{\equiv}N + KOH + H_2O \longrightarrow R{-}COO^-\ K^+ + NH_3$$

A. Acid hydrolysis. Gently reflux a mixture of 1 g of the nitrile, 8 mL of 85% phosphoric acid and 2 mL of 75% sulfuric acid for 1 hr. Cool the mixture and pour it onto a few grams of crushed ice. Collect the precipitate by suction filtration. Purify it by dissolving in a few milliliters of 5% sodium hydroxide, filtering off any insoluble material (which may be the corresponding amide and might constitute another useful derivative), and acidifying the filtrate with hydrochloric acid.

If the acid is sufficiently water soluble so that it does not precipitate out, extract the aqueous solution with ether, evaporate the ether, and isolate the acid from the residue.

B. Basic hydrolysis. Reflux a mixture of 1 g of the nitrile, 4 g of potassium hydroxide, and 8 g of ethylene glycol for 1 hr. Dilute the mixture with 10 mL of water, cool, and add 15 mL of ether. After shaking the mixture and separating the layers, acidify the aqueous layer with hydrochloric acid and isolate the product as in part A above.

Nitro Compounds
(Table 27.21)

27.12-35. Nitro derivatives. See **27.12-20**.
27.12-36. Oxidation of a side chain. See **27.12-22**.
27.12-37. Reduction to amine. See also **Chapter 21**. Place 1 g of the nitro compound, 2 g of granulated tin, and 5 mL of ethanol in a small flask connected to a reflux condenser. Add 20 mL of 10% hydrochloric acid in small portions, with vigorous shaking after each addition. Then heat the mixture on the steam bath for 10 min. Decant the hot solution into 10 mL of water and add 40% sodium hydroxide until the precipitate of tin hydroxide dissolves. Extract the mixture with two 20 mL portions of ether. Dry the ether extract and remove the solvent.

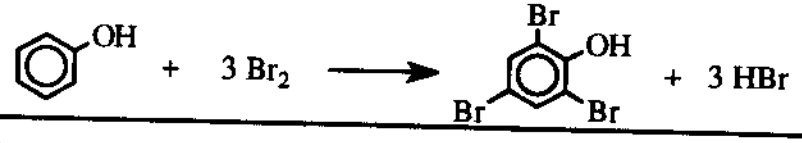
If the residue is a solid, recrystallize it and determine the melting point. Convert the residue, whether liquid or

solid, into one or more of the derivatives described in **27.12-9** through **27.12-14**.

Phenols
(Table 27.22)

27.12-38. Phenylurethans and α-naphthylurethans. See **27.12-2.**

27.12-39. Bromo derivatives.

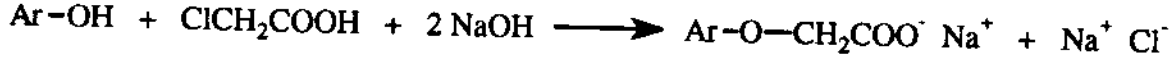


> **CAUTION!** Pure bromine is extremely hazardous. Handle it only in the hood. Do not let it come into contact with the skin. Bromine burns should be washed with large quantities of water then soaked in 10% sodium thiosulfate.

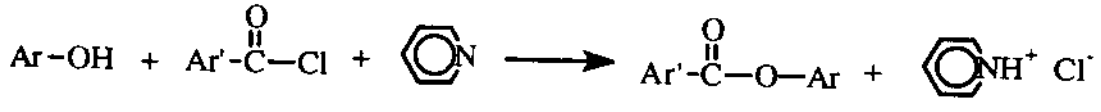
A. Bromination in aqueous solution. Slowly add the prepared bromine water solution (3 g of potassium bromide and 2 g of bromine in 20 mL of water), with shaking, to a solution of 0.2 g of the phenol dissolved or suspended in 4 mL of 50% aqueous methanol *only until a persistent yellow color has been imparted* to the reaction mixture. Add 6 to 8 mL of cold water and shake the mixture vigorously. Remove the precipitated solid by suction filtration, wash it with a dilute solution of sodium bisulfite, and then with water. Recrystallize it from ethanol or aqueous ethanol.

B. Bromination in chloroform. To a solution of 0.2 g of the phenol in 10 mL of chloroform slowly add a 2% solution of bromine in chloroform until the yellow color of the reagent is imparted to the reaction mixture. Evaporate the chloroform in the hood and purify the residue as in part A above.

27.12-40. Aryloxyacetic acids. To a mixture of 1 g of the phenol and 5 mL of 33% aqueous sodium hydroxide add 1.5 g of chloroacetic acid. Shake the mixture thoroughly and add up to 5 mL of water to dissolve any sodium salt which may have crystallized. Immerse the reaction vessel in a beaker of boiling water for 1 hr. Cool the solution, dilute it with 10 to 15 mL of water, and acidify to pH 4 with 5% hydrochloric acid. Extract the mixture with two 25 mL portions of ether and wash the combined ether extracts with 10 mL of cold water. Then extract the ether solution with 25 mL of 5% sodium carbonate. Acidify the sodium carbonate extract with dilute hydrochloric acid. Collect the aryloxyacetic acid on a filter and recrystallize it from hot water.



27.12-41. Benzoates, 4-nitrobenzoates, and 3,5-dinitrobenzoates. Dissolve 1 g of the phenol and 1 g of the aroyl chloride (benzoyl chloride, 4-nitrobenzoyl chloride, or 3,5-dinitrobenzoyl chloride[16]) in 20 mL of pyridine. Reflux the mixture gently for 1 hr, cool, and add 25 mL of water and about 1 mL of sulfuric acid. Mix well and collect the resulting crystals by suction filtration. Suspend the crystals in 25 mL of dilute sodium hydroxide and shake well to dissolve any carboxylic acid. Then filter the crystals, wash thoroughly with water, and recrystallize from ethanol or aqueous ethanol.



[16] If 4-nitrobenzoyl or 3,5-dinitrobenzoyl chloride is unavailable, it may be prepared as described in the first paragraph of **27.12-1**.

27.13-Final Identification and Report of Results

From the characteristics of the unknown observed in the various tests and from the melting points of the derivatives, it should now be possible to assign the structure without question. If there is still doubt, additional tests should be run or additional derivatives prepared until the identification is certain.

In addition to the complete record of your results in your notebook a summary should be submitted on one of the report forms (several of them are in the appendix). It is important to include all of your experimental results, both positive and negative. Part of your grade will depend upon the thoroughness and accuracy of your report.

27.14-Tables of Compounds and Derivatives

Compounds are listed in the order of increasing boiling points for liquids and increasing melting points for solids.

For economy of space only the upper temperature (rounded to the nearest degree) of a melting point or boiling point range is given. The student should be aware that an experimentally determined melting or boiling point is usually a range between two temperatures. A melting point reported in the original literature as, 136-137.4° appears in these tables as 137.

Where two values for a melting point are separated by a semicolon(;), different values are found in the original literature. Small differences may reflect different methods for measuring the melting point, differences in thermometer calibrations, or differences in degree of purity. Occasionally, by crystallization from different solvents, a compound is obtained in different crystalline modifications having different melting points. Many reactions for derivative formation lead to mixtures of stereoisomers. For example, the hydrazone derivatives of aldehydes or unsymmetrical ketones can exist as either *cis* or *trans* isomers. Different stereoisomers (or mixtures having different compositions) may be crystallized under different conditions. In any event, the first value listed for the melting point is the more likely to be reproduced.

Where two values for a melting point of a derivative are separated by a slash mark (/), there are two functional groups capable of reaction. The first melting point listed is for the derivative formed by reaction of one of the functional groups; the second is for the derivative formed by reaction of both of the functional groups. The latter is usually isolated.

If decomposition accompanies melting, the temperature is followed by d. If sublimation accompanies melting, the temperature is followed by s.

The tables appear on pages 158-169 in the laboratory manual (2nd edition).