

5. Traces of metallic impurities in either the tin or the acid may act as catalysts, with the result that hydrogen is evolved.

6. Most nitro compounds are reduced quantitatively to the amine by tin and hydrochloric acid.

### Questions

1. Write equations for the reactions in A, B, and C.
2. Was the dissolving in concentrated sulfuric acid due to a chemical change? Explain.
3. What is the function of ammonium nitrate?
4. What are the reduction products of nitrobenzene in an alkaline medium?
5. What is the reduction product of nitrobenzene in an acid medium?
6. What are the evidences of a chemical change with tin and hydrochloric acid?
7. Calculate  $\Delta H$  for a liquid-phase nitration from data on heats of formation and heats of combustion.
8. How does heat of dilution with water affect this value?

From: Principles & Practice in  
Organic Chemistry

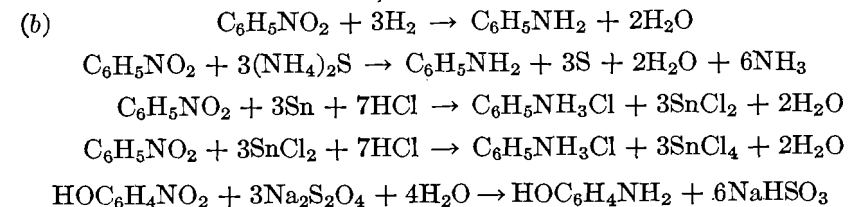
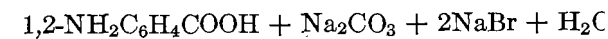
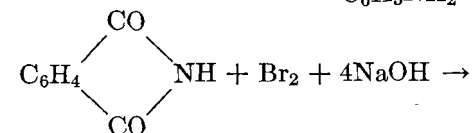
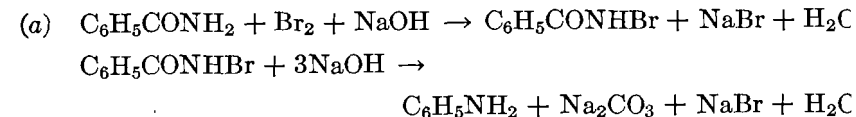
H. J. Lucas & D. Pressman

John Wiley & Sons, N.Y., 1949

## Chapter 33

### PRIMARY AROMATIC AMINES

Primary aromatic amines having the amino group on a side chain are prepared by methods used for aliphatic amines (Chapter 26). Nuclear primary amino groups are introduced mainly by (a) the Hofmann degradation of amides and (b) the reduction of nitro compounds:



**33.11 The Hofmann Degradation.** Method *a*, which is discussed in detail under 26.15, often is employed when reduction methods *b* are not applicable, as when side reactions, such as reduction of the wrong group, accompany or precede the desired reaction. The degradative method is especially useful in converting phthalic acid or its derivatives through the imide, to *o*-aminobenzoic acid or its derivatives.

**33.12 Reduction of Aromatic Nitro Compounds.** Method *b* is the usual method of preparing primary amines and may be carried out with a variety of reducing agents, as hydrogen, hydrogen sulfide, metals (iron, zinc, tin), or sodium hydrosulfite. The most commonly used reducing agent in beginning organic chemistry consists of tin and hydrochloric acid, as in Experiment 33-1, The Preparation of Aniline.

**33.13 Thermochemistry.** As noted under 26.13, the gas-phase hydrogenation of nitro compounds is very strongly exothermic (200

kcal.). Reduction under acid conditions with an active metal such as zinc, iron, or tin is even more strongly exothermic, since a strong acid reacts exothermically with these metals to give hydrogen and exothermically with the amines to give salts. Reduction with sodium hydrosulfite is strongly exothermic also. The gas-phase reduction with hydrogen sulfide is more exothermic than reduction with hydrogen since  $\Delta H$  of formation of hydrogen sulfide is positive. In general, control is necessary when reducing nitro compounds, because of the highly exothermic nature of the reaction.

**33.14 Rates.** In general, even in a homogeneous system reduction does not proceed rapidly at room temperature. Heating to about 50° especially if the system is heterogeneous usually is desirable. Rates often can be increased by adding alcohol to increase the solubility of the nitro compound. Homogeneous systems may be obtained in alcohol with stannous chloride or ammonium sulfide or in aqueous alcohol with sodium sulfide or sodium hydrosulfite. Because of the large heat effect, the rate must be controlled so that the reaction will not get out of hand.

When the reducing agent is iron and water, it is necessary for iron chloride to be present. The mixture must be heated for some time. The iron chloride usually is obtained by adding a small amount of hydrochloric acid, about 5% of theoretical. The reaction is accelerated by the presence of ammonium chloride.

When the reducing agent is tin and hydrochloric acid, control is accomplished by adding the acid in portions to the reaction mixture, as in the usual reductions with tin and hydrochloric acid (Experiment 33-1). However, accumulation of acid, which happens when the temperature is too low, must be avoided because the reaction is liable to get out of control, and also because of side reactions. Thus the initial temperature must be such that the first portion of acid reacts almost completely before more is added, usually not below 50° to 70°. Of course, control can be accomplished by adding either tin or the nitro compound to the other two, but side reactions are most extensive when the acid concentration is high.

When sodium hydrosulfite is the reducing agent, it is added in portions if the resulting system is homogeneous, as in the reduction of *o*-nitrophenol (Experiment 33-2).

Direct hydrogenation takes place only in the presence of a catalyst. Catalysts that permit the reduction to proceed at ordinary temperature and pressure, such as platinum, palladium, and active forms of nickel, are easily poisoned by small amounts of impurities, especially sulfur compounds. Less active catalysts, for example metallic iron, are not

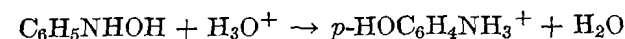
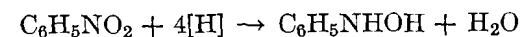
so easily poisoned, but higher temperatures and pressures are necessary. Agitation must be violent since one reactant is a gas and the catalyst is a solid.

**33.15 Completeness of Reaction.** If the nitro compound is insoluble in water, completion of reaction with an acidic reducing agent is indicated by the complete solution of the compound in water. Dilution may be necessary, in case the salt of the amine is not very soluble. If alcohol or some other organic solvent has been added to increase the solubility of the nitro compound, a test for completion often can be made by adding a few drops of the mixture to dilute aqueous acid, provided the amount of solvent is not too great. A cloudiness indicates that the reaction is not complete. Naturally, these tests are not valid if the nitro compound is soluble in water.

**33.16 Side Reactions.** The principal side reactions are: (1) formation of products of a reduction state intermediate between the nitro and amino states, (2) formation of aminophenols, (3) replacement of hydrogen by halogen, (4) replacement of halogen by hydrogen or other groups, and (5) formation of sulfamic acids.

The formation of secondary-reduction products, such as azoxybenzene, azobenzene, or hydrazobenzene, is prevalent in the reduction with metals under alkaline conditions. However, ammonium sulfide, sodium sulfide, and sodium hydrosulfite usually give the desired product.

The formation of aminophenols takes place in the reduction with a metal and acid and becomes more important as the concentration of the acid is increased since the reaction is acid-catalyzed. This takes place through a molecular rearrangement of the intermediate phenylhydroxylamine.

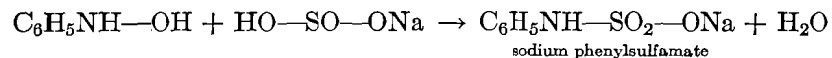


This type of reaction is possible whenever the *para* position is open. In order to keep the acid concentration low it is desirable that each portion of acid react before more is added. Thus, when the rate is low at room temperature, heating is desirable, or, if the system is heterogeneous, agitation must be carried out continuously.

Sometimes chlorine enters the ring when hydrochloric acid is present. Reduction of *o*-nitrotoluene with tin and hydrochloric acid gives a mixture of the desired amine and 2-amino-5-chlorotoluene. This type of side reaction often occurs with tin, stannous chloride, and zinc. Zinc is the worst offender. The product is usually dark colored also. If possible, some other acid, as for example sulfuric or acetic acid, should be used in place of hydrochloric acid.

Halogen atoms *ortho* to nitro groups may be replaced by hydrogen or rarely by other radicals. Stannous chloride and *o*-bromonitrobenzene give aniline, as well as *o*-bromoaniline. This type of reaction is liable to occur with tin, stannous chloride, and zinc; less likely with iron. Halogen atoms in general may be replaced by reduction with hydrogen and a palladium catalyst. Ammonium and sodium sulfides yield sulfur-containing amines with a nitro compound having a halogen or nitro group in the *ortho* position.

A side reaction that accompanies reduction with sodium hydrosulfite is the formation of a sulfamic acid, probably by a reaction of the intermediate hydroxylamine with sodium bisulfite:



Many sulfamic acids and their salts are soluble in water, and thus material is lost unless the sulfamic acid is hydrolyzed by heating with water. In order to minimize this side reaction the reduction should be carried out as rapidly as possible, as in Experiment 33-2, The Preparation of *o*-Aminophenol.

**33.17 Comparison and Recovery.** Direct hydrogenation offers the least complication in recovery. For purification, often removal of the catalyst by filtration suffices, before distilling off any solvent.

When ammonium sulfide is the reducing agent, recovery of the amine is comparatively simple, for the excess of reactant can be decomposed merely by heating, thus leaving behind water, the amine, and sulfur, the last of which results from the decomposition of the polysulfide. The sulfur is finely divided, but usually it changes to a more compact form on heating.

Volatile amines often are separated from reaction mixtures by steam distillation. This procedure is indicated when solvent extraction is impractical, as for example in mixtures containing insoluble solids, such as iron oxide and tin hydroxides, which are present respectively after reduction with iron and tin (or stannous chloride). It is necessary to add an amount of strong base which is an excess over any acid added during the reduction operation. If the amount of strong base is insufficient to neutralize the acid, the unneutralized acid will be distributed between the weak bases present, which are the desired amine and the metallic oxide. This hinders the recovery of the amine. Actually an excess of base usually is added, for it is desirable to decrease the amount of solid by dissolving the tin hydroxides.

Solvent extraction of an amine from a reaction mixture is possible only if the mixture is neutral or basic and is not practical if insoluble

compounds are present. However, oftentimes troublesome emulsions are encountered. The solvent should be low boiling, for example ethyl ether. Extraction is more convenient than steam distillation and is feasible when the reducing agent is metallic zinc or sodium hydrosulfite.

Sometimes solvent extraction of the aqueous portion of the distillate in steam distillation is desirable, as in Experiment 33-1, The Preparation of Aniline. In case alcohol or some other water-soluble solvent had been added for the purpose of increasing the solubility of the original nitro compound, it should be removed by distillation or evaporation from the acidic reaction mixture before the base is added.

Crystallization of a solid amine or of an amine salt often is possible if the other reaction products can be kept in solution, as for example when the reducing agent is metallic zinc or tin, stannous chloride or sodium hydrosulfite. In Experiment 33-2, *o*-aminophenol crystallizes from an aqueous solution containing sodium bisulfite. Sulfates of amines usually are not soluble in water; hydrochlorides, though much more soluble, often separate well when an excess of hydrochloric acid is added.

Oxidation of amines takes place slowly on exposure to air, producing a dark color. This takes place most readily with the most reactive amines, less readily with less reactive amines, for example nitranilines, and least readily with the salts of the amines. Thus the reaction with a given amine is accelerated under basic and retarded under acidic conditions. Darkening involves some loss which however is not great since the oxidation products usually are intensely colored. Distillation of volatile amines is the best method of purification, because the colored compounds have much higher molecular weights. Darkening is especially troublesome in Experiment 33-2, the Preparation of *o*-Aminophenol.

### Experiment 33-1 Preparation of Aniline

In a 1-liter round-bottomed flask provided with an air condenser (Note 1) place 0.20 mole of nitrobenzene (*Caution:* Notes 2 and 3) and 0.4 g. at. wt. of mossy tin. Measure sufficient technical concentrated hydrochloric acid (Note 4) to furnish about 25% excess over the amount required theoretically. Add 10 ml. Agitate carefully, so as not to break the flask, and *essentially continuously*. The mixture should become warm at once. If it does not, apply heat. Add the rest of the acid, at first in 10-ml. portions and later in larger portions. Agitate *essentially continuously* throughout the addition of the acid. Be sure that most of each portion of acid has reacted before adding the next

(Note 5). Moderate cooling may be advisable if the liquid boils. Finally heat on a steam bath, shaking frequently, until the nitrobenzene has reacted completely (Notes 6 and 7). More acid may be added, in case the amount seems to be insufficient. After reduction is complete, let the mixture cool. A double salt of anilium chloride and stannic chloride,  $C_6H_5NH_3Cl \cdot SnCl_4$ , may crystallize.

Assemble an apparatus for steam distillation, so that the 1-liter flask can be attached to it (refer to Chapter 10). Dissolve in 200 ml. of water an amount of sodium hydroxide that is a good excess, 20% or more, over the amount of hydrochloric acid added. Add this, cold, with thorough agitation, to the reaction mixture, also cold, cooling moderately if the liquid boils. Steam distil. At first a two-phase distillate is obtained; later a single-phase distillate. Collect enough of this, *ca.* 200 ml., to be sure that practically all aniline has distilled (Note 8). Add solid sodium chloride to the distillate in amount sufficient to produce a half-saturated solution (Note 9).

Extract three times with ethyl ether, using a total of 200 to 400 ml. (refer to Chapter 6). Dry the ether with a suitable drying agent (refer to Tables 12-2 and 12-3). Strip off the ether, using a flask of proper capacity to hold adequately the expected amount of product (refer to Subsection 9.15), heating by means of a water bath at a relatively low temperature, *ca.* 50° until most of the ether has been removed (*Caution:* See Experiment 22-1, Notes 1 and 4). Finally, above 100°, use a shorter condenser. Collect the desired product in a 5° range near the boiling point of aniline, taking cuts if much material distils ahead of this, and refractionating in systematic fashion. Calculate the percentage yield (Note 10).

### Notes

1. Refer to Subsection 7.21 in regard to air condensers.
2. Both nitrobenzene and aniline are poisons; avoid breathing the vapor and spilling the liquids on the skin.
3. This procedure serves to prepare other amino compounds that can be steam-distilled, for example the toluidines.
4. Technical hydrochloric acid may be 20° Be. or 22° Be., 32% or 35% acid, respectively. The acid need not be pure.
5. See discussion on the effect of a higher concentration of acid.
6. No drops of nitrobenzene should be visible, and a clear solution should result when a few drops of the liquid are added to about 5 ml. of distilled water.
7. If there is any doubt about this, the mixture can be steam-distilled at this point. If any nitrobenzene is present, the distillation is continued until the distillate is clear.
8. Aniline is slightly soluble in water.
9. Refer to Subsection 6.12, Salting Out.
10. The correct boiling point is 184.5°. The yield is 90%

### Questions

1. How much of the tin is in the stannous form after all the metallic tin has dissolved and reduction has been completed?
2. Why not keep the reaction mixture cold while adding the hydrochloric acid?
3. What side reaction may become important if the concentration of the acid is high?
4. What precipitate is formed when the sodium hydroxide is added to the reaction mixture?
5. Why should the amount of base added be sufficient to neutralize all the original acid?
6. Why is an excess of base desirable?
7. Why is an inorganic salt added to the distillate?
8. Why not extract the alkaline reaction mixture with ether?
9. Does the mixture of steam and aniline vapor come over above or below the boiling point of water?
10. What determines the ratio of the weight of water to aniline at the beginning of the steam distillation?
11. What other reagent could be used for the reduction of nitrobenzene?
12. What is the main impurity in the final product?
13. How can it be removed?

### Experiment 33-2 Preparation of *o*-Aminophenol (Notes 1 and 2)

In a 500-ml. conical flask place 0.10 mole of *o*-nitrophenol, 50 ml. of water, and 0.12 mole of sodium hydroxide. Heat until the solids have dissolved (about 60°). Weigh out three portions of sodium hydrosulfite (Note 3), of which two are each one-half the theoretical amount and the third corresponds to a 20% excess, based on 100% purity. Have ready also a warm solution (*ca.* 50°) of 0.08 mole of sodium hydroxide in 25 ml. of water. To the red solution at about 60° add one half the theoretical amount of sodium hydrosulfite gradually over a period of about 0.5 to 1 minute, cooling the solution moderately in case the contents begin to boil (Notes 4 and 5). Agitate continuously to promote rapid solution of the solid. Add the second portion of sodium hydroxide solution (Note 6) and then sodium hydrosulfite, as before, until the theoretical amount has been added. Then with the slurry of liquid and solid at 60° to 70°, add 25 ml. of alcohol, washing down any material near the top of the flask (Note 7). Any decided yellow color and any reddish particles of *o*-nitrophenol should disappear, thus indicating the completion of the reduction. If any remains, add more hydrosulfite in small portions until there is no more reaction. The reduction should be carried out in 3 to 5 minutes. The final reaction mixture should be only slightly colored; otherwise, the yield is low.

At once add about 175 ml. of alcohol (Note 8) to the still warm liquid (50° to 60°), cool quickly to about 20°, and agitate for 2 or 3 minutes to aid crystallization of salts still in solution (Note 9). Filter through a *clean* Buechner funnel, avoiding needless suction of air through the filter cake (Note 10). Discard this after washing with 50 to 100 ml. of warm alcohol, in 2 or 3 portions (refer to 5.42).

Add 100 ml. of water to the combined filtrates, and distil (Note 11), so as to remove alcohol and leave only water. The final volume should not be less than 150 ml. (Note 12). Add a pinch of sodium hydrosulfite during the distillation if the liquid darkens. If cloudy, filter hot into a beaker; if clear transfer to the beaker, and cool rapidly in an ice pack. Stir until cooled to about 4°, collect on a small clean Buechner or Hirsch funnel, and wash well with a small amount (5 ml.) of water. Dry quickly and *completely* by pressing between absorbent paper or onto porous tile of excellent absorbing properties, removing the solid to another dry surface after one has become wet (Note 2). Obtain a second less pure crop from the filtrate, as before, after evaporating (in a flask) to about 50 ml. After each crop is thoroughly dry, take the melting point, and calculate the percentage yield (Note 13).

### Notes

1. The preparation of *o*-aminophenol by the usual methods of reduction is not satisfactory. In order to obtain satisfactory results with sodium hydrosulfite it is essential that the reduction be carried out rapidly, in 5 minutes or less, and that exposure to air be a minimum. To facilitate operations have all materials and apparatus ready before starting. The experiment should be completed in 1 to 1.5 hour.

2. Dry solid *o*-aminophenol is relatively stable toward oxygen. However, in aqueous solution it is oxidized to colored products by air. Oxidation is especially rapid under alkaline conditions. The moist solid turns dark on exposure to air.

3. Sodium hydrosulfite (sodium dithionite,  $\text{Na}_2\text{S}_2\text{O}_4$ ) deteriorates on standing, owing to oxidation by the air. The technical product, usually 94% pure, is satisfactory. The 20% excess usually is sufficient.

4. *o*-Nitrophenol is volatile with steam.

5. If the temperature of the reaction mixture does not increase markedly, the hydrosulfite is unsatisfactory.

6. The solution should not become alkaline (Note 2). Only one-half the base is added at the start because of this fact and also because the sodium salt of *o*-nitrophenol separates. If more than 0.2 mole of sodium hydroxide is taken altogether, a second liquid phase may form when the alcohol is added later.

7. The last portion of the nitrophenol reacts much more rapidly after the addition of the alcohol, because of the better solvent action of the alcohol. If more than 25 ml. of alcohol is added, some sodium hydrosulfite may be thrown out of solution along with the sulfite.

8. If preferred, methanol may replace ethanol.

9. Solubilities of *o*-aminophenol, grams per 100 g. of solvent, are: in water, 1.7 at 0°, 3.0 at 80°, and 7.1 at 100°; in ethyl alcohol, 4.3 at 0°. The addition of alcohol decreases the solubility of inorganic salts and increases the solubility of *o*-aminophenol.

10. Contact with the air (see Note 2) is minimized by using a funnel just large enough to hold the solid, by regulating the suction carefully, and by frequent pressing of the filter cake.

11. Distillation is preferred to evaporation, in order to prevent access of air.

12. As the alcohol is driven out of the solution, the solubility of *o*-aminophenol decreases, and that of the sodium salt present increases (Question 8).

13. The melting point of carefully purified *o*-aminophenol is 177° (cor.) when introduced into the hot bath. It decomposes below this temperature. Usual figures range between 170° and 174°. Yield, 55%.

### Questions

1. What is the reaction between oxygen and sodium hydrosulfite in aqueous solution?

2. What are the inorganic salts that separate when alcohol is added?

3. What other reducing agents are employed for reducing organic nitro compounds?

4. Why does *o*-nitrophenol separate as the reaction proceeds?

5. Why does *o*-nitrophenol distil with steam, whereas *p*-nitrophenol does not?

6. What is the function of the sodium hydroxide?

7. Why does the addition of a small amount of alcohol aid the reaction?

8. Calculate the amount of boiling water necessary to dissolve 0.1 mole of *o*-aminophenol.

9. What is a possible oxidation product of *o*-aminophenol?

10. Is *o*-aminophenol more easily oxidized than aniline? than phenol?

11. What are the main impurities in the final product?

### Experiment 33-3 Properties of Aromatic Amines

A SOLUBILITY. Test the solubility in water of aniline (or a toluidine) and of sulfanilic acid by shaking about 1 g. of the amine with 5 ml. of water. Add to the resulting mixture from a dropper 1 to 2 ml. of 6 *N* hydrochloric acid. To acidified contents add 3 to 5 ml. of 6 *N* sodium hydroxide.

B ACETYLATION. To 0.1 g. (2 or 3 drops) of aniline, or of some other aromatic amine, add 4 to 5 drops of good acetic anhydride (Note 1), and heat to *ca.* 100° for a few minutes. Add 2 or 3 ml. of water to remove the acetic acid, stir well, remove the water with a dropper, and repeat. A solid should remain. Crystallize this from hot water (Note 2). Determine the melting point.

Repeat with an unknown amine, which may be obtained from the instructor.

C HINSBERG TEST. Shake 2 to 3 drops of aniline, *N*-methylaniline, and *N,N*-dimethylaniline separately with 6 to 9 drops of benzenesulfonyl chloride, 4 to 5 ml. of water, and 2 ml. of 3 *N* sodium hydroxide, until the benzenesulfonyl chloride has reacted. Add hydrochloric acid in excess. Note the difference in behavior.

D BROMINATION. Obtain a clear aqueous solution of aniline by shaking about 0.5 ml. with 10 ml. of water and filtering through filter paper previously wet with water. Add bromine *water* to the filtrate until there is an excess and then a few crystals of sodium bisulfite to remove excess bromine.

E OXIDATION. Separately test the effect of chromic acid mixture (refer to 25.14) and of aqueous permanganate on aniline (use 1 or 2 drops) and on *o*-aminophenol. Test the effect of silver nitrate and of ammoniacal silver nitrate (Note 3) on these two amines.

### Notes

1. This deteriorates rapidly when exposed to moisture in the air.
2. The hydrolysis of acetanilide by hot water although slow becomes fairly rapid in strong acid.
3. The ammoniacal silver solution should not be kept. (See Experiment 25-5, Note 3.)

### Questions

1. Explain the solubility behavior of amino compounds in A.
2. Why is it desirable to remove acetic acid before crystallizing in B?
3. Do you think the product you obtained in B is pure?
4. Why is a test like this of value?
5. Compare the behavior of the three amines in the Hinsberg test. How do you account for the differences?
6. What other aromatic compound have you brominated?
7. Did it brominate as easily as aniline? Explain.
8. How do benzene and aniline compare in ease of oxidation?
9. Write equations for the reactions in B, C and D.
10. What is an approximate value of  $\Delta H$  for the rearrangement of phenylhydroxylamine to *p*-aminophenol?
11. According to the data of Table 1-4, can ferrous ion reduce nitrobenzene in 1 *N* hydrochloric acid? in 0.001 *N* hydrochloric acid? Refer also to 38.11.

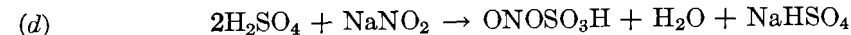
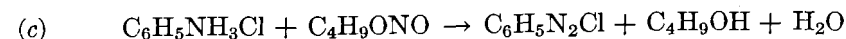
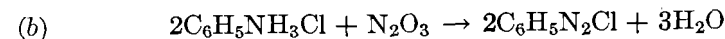
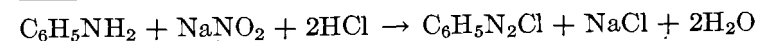
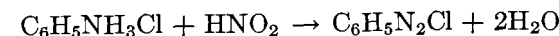
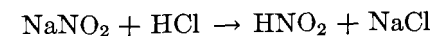
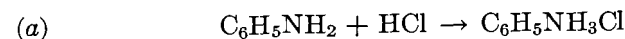
## Chapter 34

### AROMATIC DIAZONIUM COMPOUNDS

The diazonium compounds are very important in the aromatic series because they undergo a large variety of replacement reactions and also couple with a large number of amines and phenols to produce azo dyes.

#### SECTION 34.1 PREPARATION OF DIAZONIUM COMPOUNDS

Diazonium salts may be prepared by the action of (a) an acid on an aqueous solution of sodium nitrite and an amine salt, (b) nitrous anhydride on an amine salt, (c) butyl (or amyl) nitrite on an alcoholic solution of an amine salt in the presence of a trace of strong acid, or on an acetic acid solution of the amine, (d) nitrosyl sulfuric acid on an amine (or amine sulfate):



Method *a* is used with amines which diazotize easily and when isolation of the diazonium salt is not necessary. This is the usual method, for generally the subsequent reaction of the diazonium salt is carried out in aqueous solution. Methods *b* and *c* are useful mainly in the preparation of dry diazonium salts or when it is desirable to carry out the reaction in the absence of water. Method *d* is useful when the amine cannot be diazotized by the other methods.