An ELEMENTARY LABORATORY EXPERIMENT INVOLVING *the* HOFMANN REARRANGEMENT

THE PREPARATION OF METHYLAMINE HYDROCHLORIDE FROM ACETAMIDE BY MEANS OF CALCIUM HYPOCHLORITE

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THE well-known Hofmann reaction by which an amide, in the presence of chlorine or bromine and an alkali, is converted into a primary amine with one less carbon atom, is of considerable interest in organic chemistry. The reaction may be used in going "down series," and it serves as a laboratory method for the preparation of a primary aliphatic amine. The reaction is of interest also because it involves a molecular rearrangement.

The Hofmann reaction is often illustrated in the laboratory by the preparation of methylamine hydrochloride from acetamide. It has been our experience, however, that when this experiment is carried out with bromine and alkali according to the directions given in many laboratory manuals, a considerable portion of the product consists of ammonium chloride.

In this paper directions are given for the preparation of methylamine hydrochloride from acetamide using commercial calcium hypochlorite* and sodium hydroxide. The product obtained with these reagents is contaminated with only a small amount of ammonium

* The Mathieson Alkali Works, Niagara Falls, N. Y., manufacture calcium hypochlorite under the trade name of "H.T.H."

chloride, and this can be removed by treatment with aqueous alkali as described below.

In this experiment, acetamide is first converted into *N*-chloroacetamide, which, in the presence of alkali, eliminates hydrogen chloride and undergoes rearrangement to form methylisocyanate. Hydrolysis of the latter gives methylamine which is isolated as the hydrochloride. It should be pointed out that the elimination of hydrogen chloride from *N*-chloroacetamide in the presence of alkali, actually consists of the removal of the hydrogen as a proton to form the alkali salt of *N*-chloroacetamide; the chloride ion is apparently released from the anion of this salt. The complete transformation may be represented by the following equations.

$$2CH_3CONH_2 + Ca(OCl)_2 \longrightarrow 2CH_3CONHCl + Ca(OH)_2$$
$$2CH_3CONHCl + Ca(OH)_2 \longrightarrow (CH_3CONCl)_2Ca^{++} + 2H_2O$$
$$(CH_3CONCl)_2Ca^{++} + 2NaOH \longrightarrow 2(CH_3CONCl)^-Na^+ + Ca(OH)_2$$
$$\downarrow \text{heat}$$
$$2CH_3N{=}C{=}O \xleftarrow{\text{rearrangement}} 2CH_3CON + 2NaCl$$
$$\text{HOH} \downarrow \quad 4(\text{NaOH})$$
$$2CH_3NH_2 + 2Na_2CO_3$$
$$2CH_3NH_2 + 2HCl \longrightarrow 2(CH_3NH_3)^+Cl^-$$

Preparation of Methylamine Hydrochloride.—The apparatus for this experiment should be set up before any materials are mixed.

A 500-cc. distilling flask is fitted with a two-hole stopper carrying a thermometer and an inlet tube for air. The bulb of the thermometer should dip below the surface of the liquid, and the air tube should reach almost to the bottom of the flask. The distilling flask is attached to a condenser bearing an adapter. Two 250-cc. Erlenmeyer flasks containing 35 cc. each of 6 *N* HCl are placed in series as receivers. The first is fitted with a two-hole stopper. A glass tube attached to the adapter should dip below the surface of the HCl in the first receiver. The second receiver is connected to the first by means of another glass tube leading from above the acid solution in the first receiver to below the acid in the second.

To 16.4 g. of "H.T.H." in an Erlenmeyer flask is added 50 cc. of water, and the mixture shaken until practically homogeneous. A small amount of material will remain undissolved. The solution is cooled to about 0° in an ice-bath and 10 g. of crushed ice added.

The distilling flask is disconnected, and a cold solution of 10 g. of acetamide in 20 cc. of water poured into it. With the distilling flask immersed in an ice-bath, 100 g. of crushed ice is first added to the solution, followed by the addition of the *cold* "H.T.H." solution in three or four small portions with shaking after each addition. The temperature of the mixture should not rise above 0°. More ice may be added to the reaction mixture if necessary. If the mixture should warm to more than 10° (due to insufficient cooling), it should be discarded and the experiment repeated.

The flask is allowed to remain in the ice-bath for five to ten minutes. At the expiration of this time the flask is fitted to the condenser and a solution of 24 g. of NaOH in 40 cc. of water at room temperature is added. The stopper is immediately replaced, and a current of air passed through the mixture during the remainder of the manipulations. The current of air should be sufficient to produce thorough mixing of the contents of the flask and to prevent bumping, yet not strong enough to cause much loss of the methylamine from the receivers.

By heating the flask the temperature of the mixture is raised rapidly to about 60°. Between 65° and 75° the *N*-chloroacetamide decomposes with liberation of considerable heat, which, if not controlled, is likely to cause the contents of the distilling flask to bump over into the condenser. Consequently, the temperature is increased carefully from 60° to 65° and the flame removed. From this point the temperature will increase without the application of external heat. The current of air passing through the mixture is regulated so that it is just sufficient to prevent bumping. If the temperature rises to 80° the flask is cooled in a bath of crushed ice and water. The temperature is held between 70° and 80° for five to ten minutes, or until heat is no longer spontaneously generated.

The contents of the distilling flask are then heated to boiling and distilled until 75 to 100 cc. of distillate has been collected. The contents of the two receivers are combined, placed in a large evaporating dish, and evaporated over a wire gauze until the volume of the solution is about 15 cc. The dish is then transferred to a water bath and the contents evaporated to dryness.

The solid residue consists of methylamine hydrochloride together with a small amount of ammonium chloride. This product may be crystallized directly from absolute alcohol, in which case, the yield should be about seventy per cent. of the theoretical amount. It is recommended, however, that the crude product be purified according to the following procedure. The crude product is transferred to a casserole and dissolved in 15 cc. of water. Ten cc. of 7.5 per cent. sodium hydroxide is added and the solution heated to gentle boiling over a small flame. Since methylamine is a stronger base than ammonia, the latter, which is preferentially liberated from its hydrochloride, will be driven off with only a slight loss of methylamine. The casserole is kept in constant motion and the heating continued until all the water has evaporated and dense white fumes appear. A portion of the methylamine hydrochloride will be in the fused state. The flame is removed and the mass stirred while cooling. If the residue does not completely solidify when cold it is heated further. The residue is finely pulverized, transferred to a 250-cc. Erlenmeyer flask, and refluxed a few minutes with 125 cc. of absolute alcohol. A small amount of solid (NaCl) will remain undissolved. The solution is filtered through a steam funnel into a 250-cc. Erlenmeyer flask. The latter is connected by means of a bent glass tube to a condenser and the

alcohol distilled off until crystals begin to form in the hot liquid. The solution is then allowed to cool to room temperature and is finally cooled in an ice-bath. The crystals are filtered with suction, washed with 10 cc. of absolute alcohol, and dried on a watch glass set on a hot steam coil. The yield of methylamine hydrochloride should be about fifty-five per cent. of the theoretical amount, melting at 228–230°.

The use of air in this experiment serves to agitate the mixture and prevent it from bumping. If desired, a mercury-sealed mechanical stirrer may be used for this purpose and the air omitted. In this case one receiver will be sufficient. A short-stem funnel is fitted to the adapter, the larger end of the funnel dipping about 0.5 cm. below hydrochloric acid contained in a beaker. By using a mechanical stirrer the reaction may be carried out on a larger scale with no essential modification in procedure.