THE REACTIONS OF SODIUM BOROHYDRIDE

WITH SIMPLE AND SUBSTITUTED AMIDES

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# INTRODUCTION

Although sodium borohydride was discovered in 1936 by Stock and Laudenklos (46), it was not characterized until 1947 (21). The first planned synthesis was carried out in 1948 by Schlesinger and coworkers (36). Since that time, sodium borohydride has been rather extensively studied as to methods of preparation, physical properties and chemical reactions.

A survey of the literature indicates the established and potential use of sodium borohydride as a reducing agent both for inorganic and for organic compounds. Most of the work done in the realm of organic reactions has involved the reduction of the carbonyl group as found in aldehydes, ketones, and acid chlorides. Reduction of amides has been accomplished with lithium aluminum hydride but the literature contains no record of reduction using sodium borohydride.

The purpose of this study was to investigate the reactions of sodium borohydride with urea and other simple and substituted amides as a class of weak organic acids.

# HISTORICAL

In 1936, Stock and Laudenklos (46) prepared a new compound from sodium amalgam and diborane and described it as sodium diborane. It was shown by Kasper (21) to have an identical diffraction pattern with that later reported by Soldate (44) for sodium borohydride.

## Preparation of Sodium Borohydride

One of the first methods for synthesizing sodium borohydride was worked out by Schlesinger and Brown (36). It was produced from a reaction between sodium hydride and trimethyl borate in two steps:

$$NaH + B(OCH_3)_3 = NaHB(OCH_3)_3$$

$$2 NaHB(OCH_3)_3 + B_2H_6 = 2 NaBH_4 + 2 B(OCH_3)_3$$
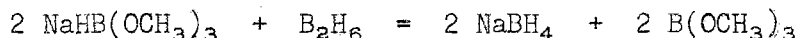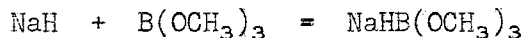
Schlesinger and Finholt (40) found that the trimethoxyborohydride disproportionates at high temperatures as follows:

$$4 NaHB(OCH_3)_3 = NaBH_4 + 3 NaB(OCH_3)_4$$
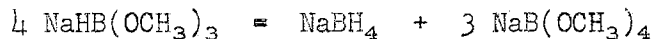
Continued heating under vacuum causes the tetramethoxyborohydride to undergo decomposition:

$$NaB(OCH_3)_4 = NaOCH_3 + B(OCH_3)_3$$
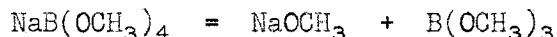
The sodium borohydride and sodium methoxide were separated by the use of isopropylamine or liquid ammonia, either of which dissolves the sodium borohydride but not the sodium methoxide.

A method for preparing sodium borohydride not requiring diborane involves a reaction between sodium hydride and trimethyl borate at high temperatures. The reaction is usually carried out in an autoclave (37).

$$4 NaH + B(OCH_3)_3 = NaBH_4 + 3 NaOCH_3$$

The reaction is rapid at 225-275° and produces sodium borohydride of 90-96% purity in a yield as high as 94%. Methyl borate may be replaced by either sodium trimethoxyborohydride or sodium tetramethoxyborohydride or by higher esters such as ethyl and n-butyl borate.

Treatment of metallic sodium with a mixture of hydrogen and methyl borate at high temperatures and under pressure produces sodium borohydride in relatively low yields (40).

$$4 \ Na \ + \ 2 \ H_2 \ + \ B(OCH_3)_3 \ = \ NaBH_4 \ + \ 3 \ NaOCH_3$$
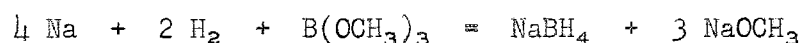
Sodium hydride and boric oxide undergo reaction to yield sodium borohydride (39).

$$4 \ NaH \ + \ 2 \ B_2O_3 \ = \ 3 \ NaBO_2 \ + \ NaBH_4$$

Yields of 60% were obtained at a high temperature. Difficulties involved in the preparation suggest that other methods are to be preferred.

## Physical Properties of Sodium Borohydride

Sodium borohydride is a white crystalline solid, very hygroscopic, but stable in dry air to 500°. It is extremely soluble in liquid ammonia and moderately soluble in several lower-molecular-weight amines and in pyridine. It is soluble in water, methanol, and ethanol but reacts with these solvents at room temperature.

Soldate (44) investigated the crystal structure of sodium borohydride using the X-ray powder method. He found that sodium borohydride exists as ionic crystals in which the unit cells contain four boron atoms and four sodium atoms, the arrangement in each borohydride ion being tetrahedral. Spectral absorption measurements have been made on sodium borohydride in various wavelength regions (16, 19, 31, 32).

The following thermodynamic properties at 25° have been determined:

Entropy = 25.024 cal./mole-deg. (6)

Entropy of formation = 51.58 cal./mole deg. (6)

Heat of formation = -43.83 ± 0.07 kcal./mole (12)

Free energy of formation = -28.45 kcal./mole (6)

Internal energy of hydrolysis = -66,760 cal./mole (5)

Heat of hydrolysis = -57.0 kcal./mole (35)

Density = 1.08 g./ml (12)

Specific heat = 0.55 ± 0.1 cal./g. deg. (12)

Heat of solution (0.07 molal) in isopropylamine = -7.6 kcal./mole (35)

Heat of solution (1 molal) in ammonia = -10 kcal./mole (35)

The heats of reactions of importance in the preparation of sodium boro-
hydride have also been calculated (35).

## Chemical Properties of Sodium Borohydride

The reactions of sodium borohydride have been extensively investi-
gated. They may be generally classified as to the type of reaction in-
volved.

Hydrolysis: Sodium borohydride reacts with water in the following
manner:

$$NaBH_4 + 2 H_2O = NaBO_2 + 4 H_2$$
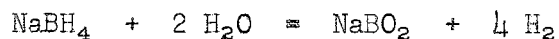
In cold water the reaction is very slow, allowing recrystallization of
the borohydride from water if desirable. In hot water, however, the
reaction is quite rapid. Hydrolysis occurs with great speed in acid
solution (38):

$$NaBH_4 + 3 H_2O + HCl = H_3BO_3 + NaCl + 4 H_2$$

This is the basis of a method for the determination of sodium borohy-
dride quantitatively.

The effect of pH on the evolution of hydrogen from sodium borohydride solutions has been studied (38). It was found that certain acidic substances such as oxalic acid, succinic acid, phosphorous pentoxide, aluminum chloride, and boric acid acted as accelerators. Salts of cobalt, nickel, iron, manganese, and copper act as accelerators of hydrolysis in sodium borohydride solutions (38).

Hydrogen is also obtained from a reaction between sodium borohydride and methanol:

$$NaBH_4 + 4\ CH_3OH = NaB(OCH_3)_4 + 4\ H_2$$

A further decomposition of the tetramethoxyborohydride to sodium methoxide and trimethyl borate occurs as mentioned in the section _Preparation of Sodium Borohydride_. Again the reaction is slow in cold solution, but becomes faster as the solution is warmed (41).

_Metathesis_: Sodium borohydride has found considerable use in the preparation of other borohydrides. Following are some other borohydrides and reactions for their preparation:

Aluminum borohydride (42)

$$AlCl_3 + 3\ NaBH_4 = Al(BH_4)_3 + 3\ NaCl$$

Lithium borohydride (42)

$$LiCl + NaBH_4 = LiBH_4 + NaCl$$
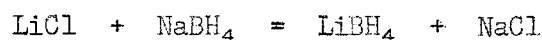
Potassium borohydride (3)

$$KOH + NaBH_4 = KBH_4 + NaOH$$

Rubidium borohydride (3)

$$RbOCH_3 + NaBH_4 = RbBH_4 + NaOCH_3$$

Cesium borohydride (3)

$$CsOCH_3 + NaBH_4 = CsBH_4 + NaOCH_3$$

Methylammonium borohydride (1)

$$CH_3NH_3Cl + NaBH_4 \text{ in } CH_3NH_2 = CH_3NH_3BH_4 + NaCl$$
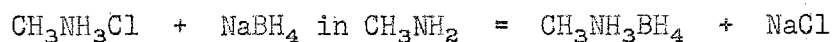
Hydrazinium borohydride (1)

$$N_2H_4 + N_2H_5HSO_4 + NaBH_4 = Na_2SO_4 + N_2H_5BH_4$$
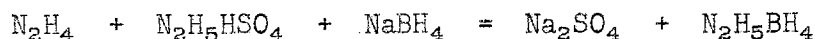
Guanidinium borohydride

$$H_2NC(NH_2)_2Cl + NaBH_4 = NaCl + H_2NC(NH_2)_2BH_4$$

Ammonium borohydride (1)

$$(NH_4)_2SO_4 + 2 NaBH_4 \text{ in liq. } NH_3 = Na_2SO_4 + 2 NH_4BH_4$$
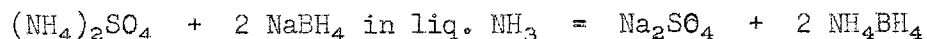
The ammonium borohydride thus formed is somewhat unstable and evolves hydrogen to yield polymeric $(BNH_6)_n$. The insolubility of sodium sulfate furnishes the driving force for the reaction. The same type of reaction seems to occur between sodium borohydride and ammonium chloride.

Reduction: Sodium borohydride has been found to act as a reducing agent in reactions involving both inorganic and organic compounds. It is somewhat less active than lithium borohydride or lithium aluminum hydride, excellent reducing agents.

Aqueous sodium borohydride is a good reducing agent to produce such elements as nickel, ruthenium, tellurium, and rhenium (36). Silver, bismuth, mercury, arsenic and antimony salts are reduced to the metal and nickel sulfate is reduced to nickel boride (36). Sodium borohydride has been used in aqueous solution for the reduction of iron (III) to iron (II). Thallium (III) is reduced in alkaline medium to thallium (I) and vanadium (V) as the sulfate is reduced in acid medium to vanadium (IV). Both of these reactions can be made the basis of methods of determinations of thallium and vanadium. Silver (I) in acid solution is quantitatively reduced to silver by the reagent. Manganese (VII) yields manganese (II), manganese (IV), and manganese (VI) in acid,

neutral, and basic solutions, respectively. In acid and neutral solutions chromium (VI) is reduced to chromium (III) but no reduction occurs in alkaline solution. Molybdenum (VI) is reduced to molybdenum (V) in acid or neutral solution (34). Sodium borohydride reacts with nickel chloride hexahydrate to yield a black precipitate containing 7.7% boron which is useful as a catalyst in place of Raney nickel (30). Schlesinger and Brown (35) have found that diborane is produced in quantitative proportions from the reaction between sodium borohydride and a boron halide such as boron trifluoride in the presence of an organic solvent such as ethyl ether, methyl ether, and 1,4-dioxane. Arsenates are reduced in acid solution to the arsenite, elementary arsenic, and arsine.

Sodium borohydride is a valuable reducing agent for organic compounds, since it may be used in aqueous or alcoholic solution depending on the solubility of the organic compound. Chaikin and Brown (7) have investigated the reduction of organic compounds and have found that sodium borohydride reduces aldehydes and ketones to the corresponding alcohols. Acid halides are reduced to primary alcohols. Carboxylic acids and anhydrides are reduced very slowly and esters and nitriles are virtually unaffected. Benzenediazonium chloride reacts rapidly to give poor yields of benzene, aniline, and phenylhydrazine. Table I contains some organic compounds reducible by sodium borohydride and their corresponding reduction products and yields as obtained by Chaikin and Brown. A general equation for the reduction of aldehydes and ketones may be written as:

$$4 \ R_2CO \ + \ NaBH_4 \ = \ NaB(OCHR_2)_4$$

$$NaB(OCHR_2)_4 \ + \ 2 \ NaOH \ + \ H_2O \ = \ Na_3BO_3 \ + \ 4 \ R_2CHOH$$
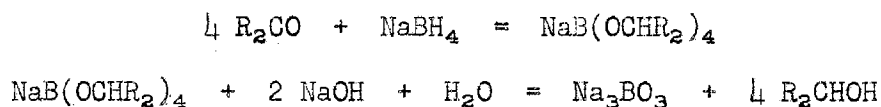
From Table I it may be seen that one of the outstanding features in the use of sodium borohydride as a reducing agent is its ability to preferentially reduce one group in the presence of another.

Sodium borohydride may be used for selective reduction of a carbonyl group at carbon number three to a hydroxyl group in a steroid molecule containing other reducible functional groups (18). Graber and Wendler (17) have found that oxo-steroids containing unsaturated C-N bonds are reduced by sodium borohydride to hydroxy-steroids. Examples of the selective reduction of di- and tri-ketones have also been reported in the steroid field (24, 29, 45). The method of preparing cholesterol from cholestenone, via its enol acetate, has now been extended to the synthesis of other important hydroxy steroids from keto steroids (11).

Lindberg and Misiorny (22) have used sodium borohydride to reduce carbohydrates as a method of quantitative analysis of such carbohydrates. Fission of a glycosidic linkage on prolonged treatment with sodium borohydrode has been observed (20).

Sodium borohydride has advantages over sodium dithionite in reducing diphosphopyridine nucleotide (DPN) whose light absorption at 340 millimicrons is employed in the determination of DPN (cozymase). Sodium borohydride shows no light absorption at 340 millimicrons and it is not necessary to remove excess reagent as it is in the case of sodium dithionite (25).

Adrenalone has been reduced to the adrenaline base in 98.3% yield with sodium borohydride (10).

The selective reduction of certain lactones has been accomplished with sodium borohydride (53, 54).

## Table I

Reductions of Organic Compounds with Sodium Borohydride

| Compound | Product | Yield, % |
|---|---|---|
| 2,5-Hexanedione | 2,5-Hexanediol | 86 |
| n-Butyraldehyde | 1-Butanol | 85 |
| Diacetyl | 2,3-Butanediol | 62 |
| Mesityl oxide | 4-Methyl-3-penten-2-ol | 77 |
| Methyl ethyl ketone | 2-Butanol | 87 |
| Anisaldehyde | Anisyl alcohol | 96 |
| Benzil | Hydrobenzoin | 89 |
| m-Hydroxybenzaldehyde | m-Hydroxybenzyl alcohol | 93 |
| m-Nitrobenzaldehyde | m-Nitrobenzyl alcohol | 82 |
| Benzoyl chloride | Benzyl alcohol | 76 |
| Cinnamoyl chloride | Hydrocinnamyl alcohol | 12 |
| n-Butyryl chloride | 1-Butanol | 81 |

Reduction of quaternary salts of heterocyclic bases gives N-alkyl-1,2-dihydro compounds (51, 52).

## Reduction of Amides

The classical reduction of carboxylic amides is accomplished with metallic sodium and alcohol. Primary amines and primary alcohols are obtained from such reactions depending on the conditions of the reaction. When the alcohol is produced the nitrogen is lost as ammonia (43).

Lithium aluminum hydride has been used to reduce simple or substituted amides to primary, secondary, or tertiary amines (8, 9, 13, 48, 49).

## Hydrogenolysis of Amides

Wittig and Hornberger (4) have successfully reduced unsaturated amides to unsaturated aldehydes. For example, they have reduced the N-$C_6H_5(CH=CH)_2CO$ derivative of carbazole with lithium borohydride or lithium aluminum hydride to $C_6H_5(CH=CH)_2CHO$.

A second method for the preparation of aldehydes consists of the reduction of N-methylanilides with lithium aluminum hydride (50). The yields reported are good, and the examples given include the methylanilides of aliphatic mono- and di-carboxylic acids, hydroxy- and halogeno-acids, aromatic mono- and di-carboxylic acids of the phthalic type, aromatic hydroxy-acids, and nicotinic acid. The reduction of both mono- and di-substituted amides in general, which may lead to amines, alcohols, or aldehydes, has also been carefully studied (26, 33).

The properties and reactions of sodium borohydride indicate its potential use. It shows promise in the generation of hydrogen where compressed gas is inconvenient or not available. At standard temperature and pressure 2.37 liters of hydrogen are liberated by 1 gram of the compound. It also shows potential use as a chemical reagent, especially for selective reduction.

# EXPERIMENTAL

## I. Reagents and Analytical Procedures

### Reagents

Sodium borohydride: Crude sodium borohydride (85-90%) was obtained from Metal Hydrides Incorporated. Recrystallization from liquid ammonia, isopropylamine, and cold water have been applied as methods for purification of the borohydride (4). Recrystallization from liquid ammonia was tried but did not yield a product of sufficient purity to be used in these studies. A more convenient method was developed by which the sodium borohydride was recrystallized from pyridine.

Crude sodium borohydride (20 grams) and anhydrous pyridine (500 ml.) were mixed and allowed to stand with frequent shaking for four hours. The pyridine solution was filtered by suction using a fine, fritted glass filter. The residue was washed with 100 milliliters of pyridine, and the wash solution combined with the original filtrate. The pyridine was then distilled from the filtrate until approximately 50 milliliters of solution remained. This distillation was accomplished with as little refluxing as possible. During the distillation, the solution usually developed an orange or red coloration which disappeared upon cooling. The solution which remained in the distillation flask was cooled and the sodium borohydride recrystallized. The sodium borohydride was filtered from the solution by suction using a fine, fritted glass filter. It was then placed in a drying pistol and dried at 15-25 mm. Hg and 100°, using a water aspirator with an attached drying tube to obtain the vacuum. The drying was completed in four hours.

During this time, the pistol was occasionally opened to remove pyridine which condensed in the cold end of the apparatus. After the drying was completed, the pistol was taken to a dry box. The pure sodium borohydride was removed and ground in a mortar to a fine powder. It was then placed in weighing bottles and these were stored in a desiccator. The purity was found to be 98% by measuring the hydrogen evolution of samples treated with aqueous acid.

A modification of this method was developed by Lindemann (23). The crude sodium borohydride was extracted with pyridine and the solution filtered as in the first method. The sodium borohydride was precipitated by adding diethyl ether until no more precipitate separated. The sodium borohydride was collected by filtration, dried, and bottled as in the first method.

Amides: The amides used in reactions with sodium borohydride, their melting points, and their sources are listed in Table II.

## Analytical Procedures

Determination of nitrogen: The micro gasometric Dumas method was used for all determinations of nitrogen (27). The method is applicable to any organic compound containing nitrogen in any form. The substance is oxidized in a closed system in an atmosphere of carbon dioxide; copper oxide is used as oxidizing agent, and metallic copper for the reduction of oxides of nitrogen to elementary nitrogen. To control the error due to the residual air in the carbon dioxide, which is determined separately in a blank determination, the combustion is carried out with a measured volume of carbon dioxide. The carbon dioxide used was obtained in a cylinder from Ideal Dri Ice Manufacturing Company, Ada, Oklahoma, as 99.99% carbon dioxide. The liberated nitrogen is collected

Table II

Amides Used In Reactions with Sodium Borohydride

| Compound | Melting point | Source |
|---|---|---|
| Acetamide | 79-80° | Baker and Adamson Company |
| Benzamide | 125-6° | Eastman Kodak Company |
| Benzenesulfonamide | 152-4° | Eastman Kodak Company |
| n-Butylurea | 95-6° | Eastman Kodak Company |
| Carbanilide | 241-2° | Eastman Kodak Company |
| Formamide | 2° | Eastman Kodak Company |
| N-Phenylurethan | 50-2° | Prepared in this laboratory |
| Sulfanilamide | 164-5° | Eastman Kodak Company |
| Thiourea | 176-8° | The Mathieson Company |
| Urea | 132° | Baker and Adamson Company |
| Urethan | 49-51° | Eastman Kodak Company |
| Uric acid | decomposes | Pfanstiehl Chemical Company |

quantitatively over 50% potassium hydroxide solution in a nitrometer. The permanent packing in the combustion tube was heated with an electric furnace and the temporary packing with a Tirrill burner.

Determination of carbon and hydrogen: The determination of carbon and hydrogen was made using micro techniques (28). A weighed amount of the organic compound was burned in a measured volume of oxygen under controlled pressure to yield quantitatively carbon dioxide from the carbon and water from the hydrogen, the amount of these combustion products being determined gravimetrically. The carbon dioxide was absorbed by Ascarite and the water by Anhydrone. The combustion tube was packed with a "combination band" type filling which is necessary for all substances containing nitrogen. The filling consists of alternating three layers of copper oxide and two layers of platinized asbestos, followed by silver wool and lead peroxide. A platinum wire gauze was placed at the begining of the filling. The lead peroxide required the inclusion of a heating mortar in the apparatus set-up.

Compounds containing boron have been analyzed by this method but it has been found that a higher combustion temperature is required (2). The samples were burned at temperatures between 850 and 900° obtained with an electrically heated wire coil. The permanent packing was heated by an electric furnace.

Determination of boron: Boron was usually determined quantitatively by titration as boric acid. With no mannitol present, boric acid is so weak that it is only partially neutralized at a pH of 7.6, but in the presence of sufficient mannitol it is completely neutralized at this pH (14). Samples analyzed were dissolved in hydrochloric acid solution and then boiled for five minutes prior to titration to

expel any carbon dioxide. The samples were cooled in an atmosphere of nitrogen and titrated, a Beckmann pH meter being used. The solutions were titrated to a pH of 8.0, mannitol was added, and the solutions again were titrated to this same pH. The alkali used for titrating was standardized against a known amount of boric acid in the same manner, so that the small amount neutralized up to pH 8.0 was taken care of in the standardization factor. Approximately three grams of mannitol was used per sample.

Determination of urea: The procedure followed for the determination of urea was basically the same as that developed by Fosse (15) in which urea is precipitated quantitatively with xanthydrol as dixanthylurea. The sample containing urea was dissolved in distilled water and warmed on the steam bath to remove any ammonia. The solution was cooled and made up to 200 milliliters volume. Five-milliliter aliquots were taken for analysis. To each aliquot was added five milliliters of glacial acetic acid. A sufficient volume of an alcoholic solution of xanthydrol to precipitate the urea was added in small amounts with stirring. Approximately four hours was allowed for precipitation. The dixanthylurea was filtered through a fritted Gooch crucible under vacuum and washed with five three-milliliter portions of ethyl alcohol. The crucible and contents was dried overnight at 50° and for an additional hour at 105°. They were allowed to cool in a desiccator and weighed.

As a comparison, a solution containing sufficient amount of urea, boric acid and sodium hydroxide to simulate the unknown solution was prepared. Analysis of this solution for urea was made in exactly the same manner as that for the unknown, and at the same time.

The xanthydrol solution was prepared by dissolving in alcohol as much as possible from crude xanthydrol and filtering out the undissolved solid.

Attempts to determine urea using the urease method of Van Slyke were unsuccessful.

Determination of sodium along with boron: The sodium and boron were determined from the residues left after carbon-hydrogen micro combustion analysis was complete. The assumption was made that such residues would contain no sodium carbonate but would be sodium metaborate. Comparison of results from the determination of boron by this method and by titration as boric acid was good.

Determination of ammonia: Ammonia was determined quantitatively by absorption in standard hydrochloric acid and back-titration with standard sodium hydroxide.

EXPERIMENTAL

II. Reactions

## Apparatus and General Procedures

All mixtures in which reactions resulted in any quantitative measurement were prepared in a dry box equipped with an analytical balance. All equipment was dried in an oven at 105° and stored either in a desiccator or in the dry box prior to use. The samples were exposed to the atmosphere only during the short time required to connect the reaction tube to the gas collection apparatus.

Figure 1 contains a diagram of the apparatus used to collect and measure any reaction gases. It also shows the source of ammonia, both liquid and gaseous. Figure 2 contains diagrams of the apparatus in which reactions in liquid ammonia and the majority of the reactions in gaseous ammonia or an initial air atmosphere were produced.

For reactions in liquid ammonia, the liquid was drawn from the tank into the storage Dewar bottle (Fig. 1) and from there into tube A (Fig. 2). Metallic sodium was added to remove traces of water which might be present in the liquid ammonia. Liquid ammonia was added to Dewar bottle B to surround tube B containing the reaction mixture. The reaction and collection apparatus were joined and ammonia was distilled from tube A to tube B where it was condensed under a slight pressure created by raising the variable mercury column in the collection apparatus. After solution of the reactants the liquid ammonia was removed from Dewar bottle B and the liquid ammonia in tube B allowed to

Anhydrous

Ammonia

To Water
Absorber

Gas
Collec-
tion
Flask

To $O_2$ Supply

Combus-
tion
Pipette

To Mercury
Reservoir

100 ml. Gas
Buret with
Water Jacket

To Mercury
Reservoir

Variable
Mercury
Column

To water
Reservoir

To Mercury
Reservoir

Liq. $NH_3$ Storage
Dewar Bottle

To Water
Absorber
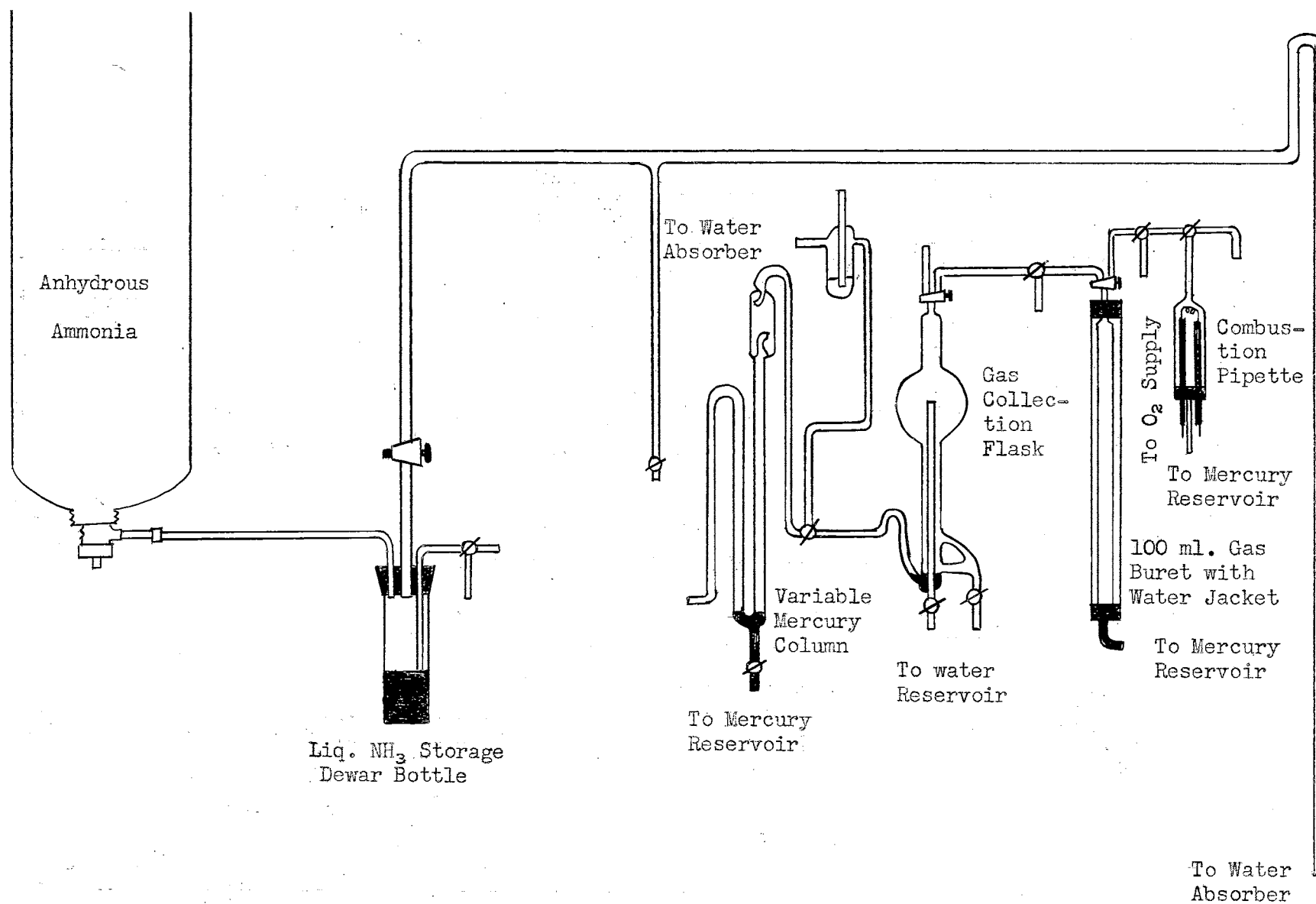
Fig. 1: Apparatus for the Generation and Measurement of Small Volumes of Gases

Internal Heaters

Liquid NH₃ →

Reaction Gases + NH₃ →

Gaseous NH₃

Gaseous NH₃

Reaction Gases + NH₃ →

Fritted Glass Tube

A          B

Test Tube 25 x 100 mm.
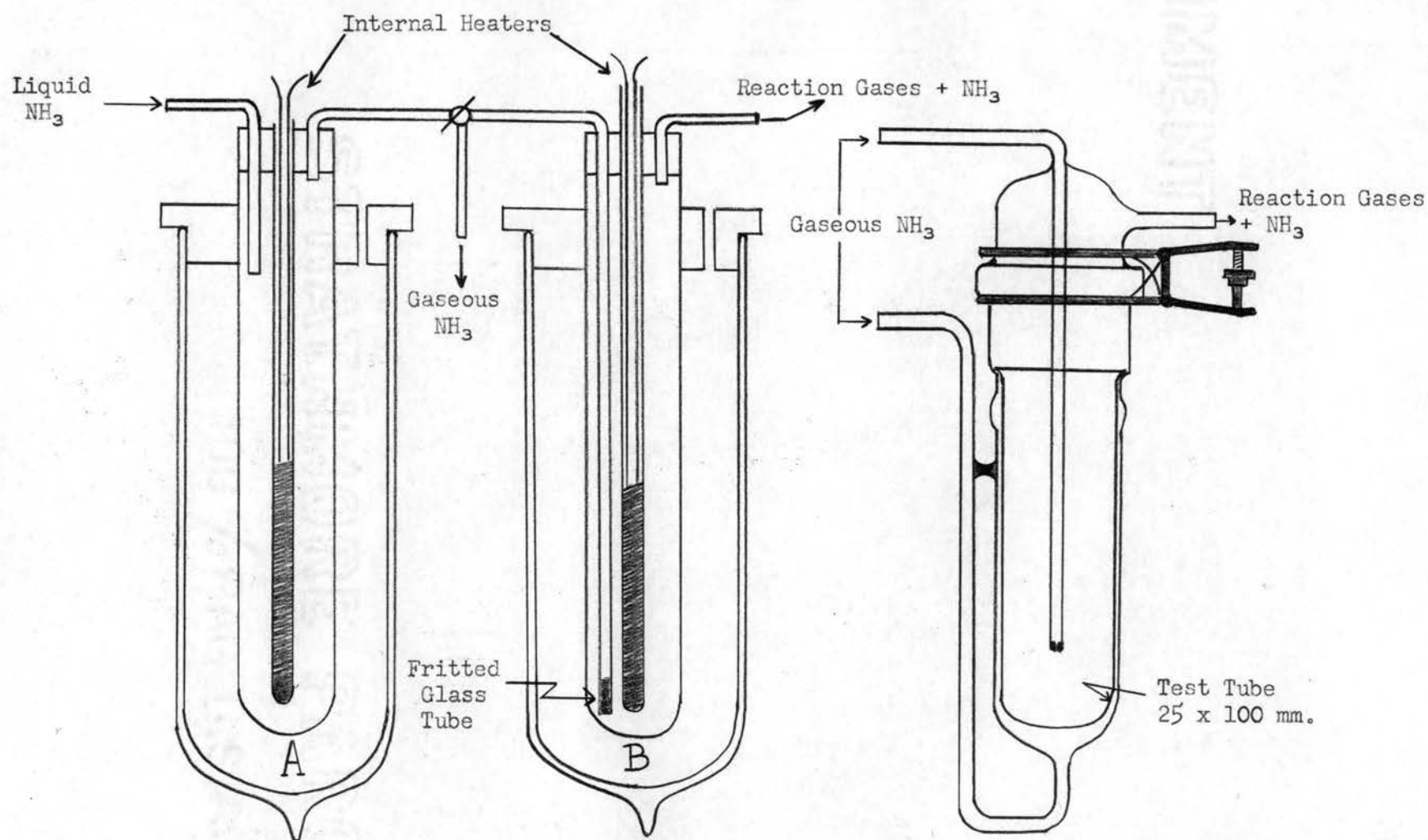
Clear Glass Dewar Thermos Bottles

Fig. 2: Apparatus for Reactions In Liquid and Gaseous Ammonia

evaporate through the collection apparatus. Subsequent heating of the sample was produced with an internal heater. Any gases produced by the reaction and not absorbed in the collection flask were subjected to combustion in the combustion pipette and the volumes of combustible, and noncombustible gases measured.

Reactions in an atmosphere of ammonia or air were carried out either in a test tube equipped with a two-hole rubber stopper and capillary glass tubing connected to the collection apparatus with Tygon tubing or in a 25 x 100 mm. test tube placed in the cell shown in Figure 2 and connected to the collection apparatus in the same manner. An oil bath was used to heat the reaction vessel. For reactions in an atmosphere of ammonia, the system was preflushed with ammonia until micro bubbles were obtained in the collection flask. The reaction was considered complete when micro bubbles were again obtained. The gases evolved by reactions in air were led directly into the collection flask without passing through the confining liquid in the gas collector and the system was flushed with nitrogen when the reaction was complete.

## Reaction of Urea with Sodium Borohydride

Numerous reactions involving urea and sodium borohydride were carried out for various reasons under a variety of conditions. Table III contains a summary of these reactions and may be used for comparisons.

Reaction in liquid ammonia: The reaction mixture of sodium borohydride ($1.70 \times 10^{-3}$ moles) and urea ($12.0 \times 10^{-3}$ moles) was dissolved in 20 milliliters of liquid ammonia, and the solution heated internally. When three milliliters of liquid remained, the heater was turned off. The reaction vessel and contents were allowed to reach room temperature. During this time, the volume of liquid was reduced to two milliliters

Table III

Reactions of Urea with Sodium Borohydride

| Reaction No.* | Mole Ratio Urea/NaBH$_4$ | Reaction Atmosphere | Reaction Temperature °C | Rate of Heating | Moles H$_2$ per mole NaBH$_4$ | Moles H$_2$ per mole NaBH$_4$ on Acidification |
|---|---|---|---|---|---|---|
| 1 | 1.0 | Air | 115-130 | Gradual | 2.41 | 1.72 |
| 2 | 2.0 | Air | 150 | | 3.21 | 0.17 |
| 3 | xs. urea | Air | 130 | Gradual | 3.78 | |
| 4 | xs. urea | Air | 130 | Slow | 3.44 | |
| 5 | 10.0 | Air | 133 | Rapid | 3.64 | |
| 6 | 5.0 | Air | 133 | Rapid | 3.77 | |
| 7 | 1.0 | Air | 133 | Rapid | 1.36 | 2.00 |
| 8 | 2.0 | Air | 135 | Rapid | 2.18 | 1.17 |
| 9 | 3.0 | Air | 150 | Rapid | 3.80 | 0.06 |
| 10 | 3.0 | Air | 135 | Rapid | 3.60 | |
| 11 | 3.0 | Air | 135 | Rapid | 3.77 | |
| 12 | 3.0 | Air | 150 | Rapid | 3.66 | |
| 13 | 3.0 | Air | 145 | Gradual | 3.52 | |
| 14 | xs. urea | | | Slow | 2.52 | |
| 15 | xs. urea | | | Rapid | 4.67 | |
| 16 | 3.0 | NH$_3$ | 135 | Rapid | 3.22 | |
| 17 | 2.5 | NH$_3$ | 132 | Rapid | 2.97 | |
| 18 | 3.0 | NH$_3$ | 135 | Rapid | 3.24 | |
| 19 | 3.5 | NH$_3$ | 140 | Rapid | 3.84 | |
| 20 | 4.0 | NH$_3$ | 135 | Rapid | 3.66 | |
| 21 | 3.0 | NH$_3$ | 120 | Very rapid | 3.87 | |
| 22 | 3.0 | NH$_3$ | 134 | Gradual | 5.00 | |
| 23 | 4.0 | NH$_3$ | 90-100 | Gradual | 3.68 | |
| 24 | 4.0 | NH$_3$ | 120 | Very rapid | 3.74 | |
| 25 | 3.0 | NH$_3$ | 120 | Very rapid | 3.73 | |
| 26 | 3.0 | NH$_3$ | 133 | Very rapid | 3.87 | |
| 27 | 3.0 | NH$_3$ | 140 | Very rapid | 3.74 | |
| 28 | xs. urea | Liq. NH$_3$ | | | 3.23 | |
| 29 | 1.66 | Liq. NH$_3$-air | 150 | | | |
| 30 | 1.66 | Liq. NH$_3$-NH$_3$ | 150 | Rapid | | |
| 31 | 1.66 | Liq. NH$_3$-air | 155 | Rapid | | |
| 32 | 1.66 | Liq. NH$_3$-air | 200 | Rapid | 1.07 | |
| 33 | 1.66 | Liq. NH$_3$-air | 200 | Rapid | 1.08 | |

* The Reaction No. indicates only the order in which the reactions

were produced.

but no gas other than ammonia was produced. The reaction vessel and contents were cooled to -64°. The ammonia solution, extremely viscous even at room temperature, became glass-like at -64°. The reaction vessel and contents were again allowed to reach room temperature. The heater was then turned on, producing an immediate evolution of gas. Heating was continued as long as gas was liberated. Ammonia was used to continuously flush the system. The gas was entirely combustible and and amounted to 3.23 moles of hydrogen per mole of sodium borohydride.

A similar qualitative procedure was followed omitting only the urea. A very small amount of hydrogen was obtained from a decomposition of the sodium borohydride.

Reaction in gaseous ammonia: The reaction mixture of sodium borohydride ($1.66 \times 10^{-3}$ moles) and urea ($4.99 \times 10^{-3}$ moles) was prepared in the dry box and the reactants ground together with a glass rod in a 25 x 100 mm. test tube. As the system was being preflushed with ammonia, the reactants became very wet. Foaming was evident at 45° and gas evolution began at 90°, accompanied by increased foaming. The temperature of the oil bath was raised to 133° and held there during most of the reaction. The hydrogen measured was equivalent to 3.22 moles of hydrogen per mole of sodium borohydride.

Reaction in air: The reaction mixture of sodium borohydride ($1.25 \times 10^{-3}$ moles) and an excess of urea was prepared as described earlier in a 25 x 100 mm. test tube. The oil bath was heated slowly. Foaming again began about 50° followed by gas evolution at 90°. Hydrogen measured was equivalent to 3.78 moles per mole of borohydride.

Reaction at low temperatures: Run 1: A reaction mixture of sodium borohydride ($3.32 \times 10^{-3}$ moles) and urea ($12.0 \times 10^{-3}$ moles) was

prepared in liquid ammonia and the ammonia allowed to evaporate. No heat was applied after the liquid ammonia had vaporized except in reaching room temperature. After all ammonia had apparently evaporated, liquid remained in the bottom and on the sides of the reaction tube. The residue was extracted with approximately 40 milliliters of anhydrous ethyl ether. All residual ether was evaporated from the reaction tube and the tube was stoppered and placed in the icebox over-night. Ammonia was then flushed through the vessel and 9.7 milliliters of hydrogen was collected.

Run 2: A mixture of urea and sodium borohydride (approximately 3/1 mole ratio) was prepared as described for reactions in air. The test tube was connected to a manometer and the apparatus placed in the icebox for approximately 16 hours. There was no apparent change in the manometer reading, indicating no gas evolution.

Optimum mole ratio: Reactions were run both in air and in an atmosphere of ammonia at varying mole ratios of urea to sodium borohydride. Five runs were made in air and four in ammonia, the mole ratio being varied from 1/1 to 10/1. A mole ratio of 3/1 appeared to be optimum and consequently most reactions between urea and sodium borohydride were carried out at this ratio.

Table IV contains the results of this study.

Reproducibility of reaction: Four runs were made in which all conditions except the maximum temperature were constant. (Table V). The runs were made in an ammonia atmosphere. The oil bath was pre-heated to the maximum temperature and the reaction vessel plunged in. The number of moles of hydrogen per mole of sodium borohydride obtained from each reaction varied only slightly.

Table IV

Optimum Mole Ratio for Urea-NaBH$_4$ Reactions

| Mole Ratio Urea/NaBH$_4$ | Reaction Atmosphere | Maximum Reaction Temperature* | Moles H$_2$ per Mole NaBH$_4$ |
|---|---|---|---|
| 1.0 | Air | 133° | 1.36 |
| 2.0 | Air | 135 | 2.18 |
| 3.0 | Air | 150 | 3.80 |
| 5.0 | Air | 133 | 3.77 |
| 10.0 | Air | 133 | 3.64 |
| 2.5 | NH$_3$ | 132 | 2.97 |
| 3.0 | NH$_3$ | 135 | 3.24 |
| 3.5 | NH$_3$ | 140 | 3.84 |
| 4.0 | NH$_3$ | 135 | 3.66 |

\* The rate of heating was rapid for each reaction.

Table V

Reproducibility of the Reaction of Urea with NaBH$_4$

| Mole Ratio Urea/NaBH$_4$ | Reaction Atmosphere | Maximum Reaction Temperature* | Moles H$_2$ per Mole NaBH$_4$ |
|---|---|---|---|
| 4.0 | NH$_3$ | 120° | 3.74 |
| 3.0 | NH$_3$ | 120 | 3.73 |
| 3.0 | NH$_3$ | 133 | 3.87 |
| 3.0 | NH$_3$ | 140 | 3.74 |

\* The rate of heating was rapid for each reaction.

<u>Rate of heating</u>: The rate of reaction did not seem to depend to any great extent upon the rate of heating except that the time required to complete the reaction varied inversely with the rate of heating and the maximum temperature. In a reaction in which the heating was gradual and the maximum temperature was 100°, more than nine hours were required to complete the reaction. In a second reaction in which the heating was rapid and the maximum temperature was 133°, the reaction was complete in fifteen minutes.

<u>Volatile products</u>: Carbon monoxide: Several runs were made in which the product gases were tested for the presence of carbon monoxide. The oxygen used for combustion in these runs was passed through a solution of barium hydroxide before entering the combustion pipette in order to remove traces of carbon dioxide found to be present in the oxygen. After combustion, the gases were measured, passed through freshly prepared barium hydroxide solution and remeasured. There was no evidence of the presence of carbon dioxide either by a decrease in volume of the gases or by a cloudiness in the barium hydroxide solution.

Boron: The reaction gases from a urea-borohydride reaction in air were passed through ten milliliters of water. The water solution was tested for the presence of boron using the common qualitative methyl borate test. The test was negative.

Ammonia: A reaction mixture containing sodium borohydride ($4.57 \times 10^{-3}$ moles) and urea ($4.57 \times 10^{-3}$ moles) was heated in dry air and the reaction gases were passed through 30 milliliters of 0.1023 N hydrochloric acid. Back-titration with 0.1014 N sodium hydroxide required 26.2 milliliters. The ammonia produced in this reaction was thus equivalent to approximately 0.1 mole per mole of urea in the original mixture.

Methanol: Run 1: A reaction mixture of sodium borohydride (0.1 gram) and urea (0.7 gram) was prepared in liquid ammonia, the liquid ammonia evaporated, and the mixture heated until evolution of gas was complete. The temperature was maintained at approximately 100°. Water was added to dissolve the residue and ten grams of chromic anhydride was added to convert any methanol to formaldehyde. The solution was distilled and about 20 milliliters of distillate was collected. Five milliliters of the distillate was added to 50 milliliters of milk and mixed well. Concentrated sulfuric acid was added slowly to form two layers. A violet coloration at the interface indicated the presence of formaldehyde and consequently methanol.

Run 2: A reaction mixture containing sodium borohydride (0.0167 gram) and urea (0.7 gram) was prepared in liquid ammonia and the liquid ammonia was evaporated until approximately five milliliters of the solution remained. The solution was extracted with anhydrous ether and the ether solution filtered through coarse filter paper. The solution was distilled and the distillate was collected and made up to 50 milliliters with anhydrous ether. Ten milliliters of the solution was tested for methanol as in Run 1. Again, a positive test was obtained. An attempt to determine the concentration of methanol in the solution by refractive index measurements was unsuccessful.

Reaction residue: The residue remaining after complete gas evolution by any of the previously described procedures was an almost white, nonhygroscopic solid. In reactions where the mole ratio of urea to sodium borohydride was three to one or greater, acidification yielded little or no additional hydrogen. For ratios less than three to one, acidification produced an amount of hydrogen bringing the total gas

evolution to between three and four moles of hydrogen per mole of boro-
hydride. (Table III).

Test for biuret: Dilute copper sulfate solution was added to an
alkaline solution of the urea-sodium borohydride residue. A positive
test for the presence of biuret was indicated by a violet coloration.

Test for sodium methoxide: A qualitative xanthate test on a urea-
sodium borohydride residue gave no evidence of the presence of sodium
methoxide.

Elemental analysis: A urea-borohydride residue was obtained by
reacting urea ($2.5 \times 10^{-3}$ moles) with sodium borohydride ($7.5 \times 10^{-3}$
moles) in a dry air atmosphere. The residue was powdered and samples
were taken for the analyses. The methods used for the determination
of carbon, hydrogen, and nitrogen have been described earlier. Boron
and sodium were determined on the assumption that the residue remain-
ing from the carbon and hydrogen analysis was sodium metaborate. The
hydrogen determination was relatively inaccurate while the nitrogen
value was much too low as shown in Table VI.

Table VI contains the results of analysis for carbon, hydrogen,
boron, sodium and nitrogen. The theoretical values are based on the
amount of the initial reactants less four moles of hydrogen.

A mixture of urea ($8.0 \times 10^{-3}$ moles) and sodium borohydride ($2.6
\times 10^{-3}$ moles) was prepared from liquid ammonia, the ammonia being re-
moved by evaporation and evacuation until the mixture appeared to be
dry. Two samples of this mixture were analyzed for nitrogen and yield-
ed 103% and 108% of the theoretical amount. The high results were as-
sumed to be due to ammonia held as an ammoniate. The residues from
reactions No. 26 and No. 27 (Table III) were found to contain 93.1%

and 92.6% respectively of the theoretical amount of nitrogen. These slightly low values could be accounted for by loss of ammonia from the original reaction mixture in forming biuret. The residues from reactions No. 3 and No. 4 were analyzed for boron by titrating it as boric acid and yielded 103% and 98.7% respectively.

Acetone extraction: Run 1: A urea-sodium borohydride residue was prepared by reacting sodium borohydride ($1.42 \times 10^{-2}$ moles) with urea ($4.26 \times 10^{-2}$ moles) in an ammonia atmosphere. Hydrogen evolution was not measured. The residue was extracted with 100 milliliters of C.P. acetone. The acetone upon filtration through filter paper and evaporation left an almost white solid. The nitrogen content of this extracted solid was 48% as compared with 46.7% for urea. Three additional extractions with 45 milliliters acetone each were made on the original residue. The residue extracted by the first 45 milliliters was rather dark in color, the second a lighter color, and the third very light. The amount of solid extracted decreased with each succeeding extraction. The initial acetone-soluble solid obtained was found to be only partially soluble in water. The water solution was centrifuged separating the water-insoluble fraction. This fraction had a brown color, was soluble in base but insoluble in acid, and did not melt up to 270°. On combustion it gave off a light gray smoke leaving a black residue. A qualitative test for boron was negative. Analysis indicated a nitrogen content of 35.4%. A water-soluble fraction was obtained on evaporation of the water. This fraction had a light yellow color, was insoluble in ether, and melted indistinctly between 88 and 98°. A qualitative test for boron was negative. Analysis for nitrogen in the acetone-insoluble fraction gave 26.5%.

Run 2: Urea (0.113 moles) and sodium borohydride (0.0376 moles) were mixed in an electrolytic beaker in an ammonia atmosphere until partial solution and adequate mixing occured. The beaker was heated in an oil bath until the reaction was complete. Extraction of the residue was performed over a period of four days using approximately 600 milliliters of C.P. acetone in 100 milliliter portions. After extraction, the first portion of acetone was evaporated to approximately 20 milliliters and then cooled in an ice bath. A white crystalline solid separated and was filtered off. This crystalline solid had the appearance of urea and melted between 132 and 134°. A mixed melting point produced the same melting point. The residue obtained on complete evaporation of the same portion of acetone was tan colored. An ether extraction was performed on this residue. Evaporation of the ether left a small amount of a light yellow, gummy substance. The ether-insoluble fraction was still tan colored. Extraction with water left a brown solid. Analysis of the acetone-insoluble residue indicated 9.19 and 9.33% boron and 18.1 and 18.5% nitrogen. Extraction was then repeated with 200 milliliters of C.P. acetone yielding a small amount of solid. Analysis of the acetone-insoluble fraction for boron as boric acid was repeated and found to give 9.38 and 9.34%. A 0.5-gram sample of the acetone-insoluble residue was placed in a distilling flask connected to a water-cooled condenser. Concentrated sodium hydroxide was added to the residue via a dropping funnel. Distillation was effected until ten milliliters of distillate was collected in a tube placed in an ice bath. The distillate gave a negative iodoform test. However, a voluminous black precipitate was formed on the addition of the iodine-potassium iodide solution to the basic test solution. The

precipitate dissolved on standing. Both a Tollens test and a qualitative test for boron were negative.

Table VII contains the results of elemental analysis of the acetone-insoluble fraction. The nitrogen content of this residue seemed to be too low. It was thought that perhaps all the nitrogen was not obtained by the Dumas method on the sample as it was. Consequently, a small sample was taken up in 6 N hydrochloric acid and subsequently evaporated to dryness. Allowance was made for the increase in sample weight due to this treatment. Analysis gave nitrogen equivalent to 17.6% on the bases of the sample before hydrolysis.

Extraction with liquid ammonia: Sodium borohydride ($1.38 \times 10^{-3}$ moles) and urea ($4.1 \times 10^{-3}$ moles) were reacted in an ammonia atmosphere at 120°. The hydrogen obtained was equivalent to 3.3 moles per mole of borohydride. The residue was extracted with three 15-milliliter portions of liquid ammonia, which was separated from the insoluble residue by forcing the solution through a frit under its own vapor pressure. The small amount of ammonia not removed by this procedure was evaporated by passing a stream of nitrogen over it. The residue was stored in a desiccator over concentrated sulfuric acid for 12 hours. Values obtained for the nitrogen content of the solid insoluble in liquid ammonia were 24.4 and 25.4%.

## Reaction of n-Butylurea with Sodium Borohydride

Run 1: Sodium borohydride ($1.42 \times 10^{-3}$ moles) and n-butylurea ($11.6 \times 10^{-3}$ moles) were mixed together in a 25 x 100 mm. test tube and placed in the reaction cell (Fig. 2). A small cold trap was placed in the system between the cell and the collection apparatus and the

Table VI

Elemental Analysis of Urea-NaBH$_4$ Reaction Residue

| Sample No. | % Carbon Theo.* | Exp. | % Hydrogen Theo.* | Exp. | % Boron Theo.* | Exp. | % Sodium Theo.* | Exp. | % Nitrogen Theo.* | Exp. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 17.2 | 17.5 | 3.82 | 4.48 | 5.17 | 5.22 | 11.0 | 11.1 | 40.0 | 31.6 |
| 2 | 17.2 | 17.8 | 3.82 | 5.01 | 5.17 | 5.17 | 11.0 | 11.0 | 40.0 | 32.2 |
| 3 | 17.2 | 17.8 | 3.82 | 2.50 | 5.17 | 5.33 | 11.0 | 11.3 | 40.0 | 31.2 |

* Based on NaBH$_4$ + 3 NH$_2$CONH$_2$ - 4 H$_2$

Table VII

Elemental Analysis of Urea-NaBH$_4$ Reaction Residue

After Extraction with Acetone

| Sample No. | % Boron | % Nitrogen | % Carbon | % Hydrogen | % Sodium | % Oxygen* |
|---|---|---|---|---|---|---|
| 1 | 8.86 | 18.5 | 11.26 | 5.33 | 18.8 | 37.25 |
| 2 | 8.65 | 18.1 | 10.63 | 2.33 | 18.3 | 41.99 |
| 3 | | | 11.94 | 3.83 | | |
| Avg. | 8.75 | 18.3 | 11.28 | 3.83 | 18.5 | 39.34 |

* The percentage of oxygen was determined by difference

system was flushed with ammonia. The cell was heated rapidly in an oil bath. Considerable foaming began at 120° accompanied by gas evolution. The bath temperature was maintained between 130 and 140°. An amount of hydrogen equivalent to 3.72 moles per mole of sodium borohydride was measured by combustion. The cold trap collected a few drops of liquid with an odor suggesting an amine. The residue was acidified with 6 N hydrochloric acid but yielded no additional hydrogen.

Run 2: Sodium borohydride ($1.63 \times 10^{-3}$ moles) and n-butylurea ($12.9 \times 10^{-3}$ moles) were reacted in the same manner as in Run 1 except in an initially dry air atmosphere. The reaction began at 120° with a little less foaming than in Run 1. Three and three tenths moles of hydrogen were obtained per mole of sodium borohydride. Again the residue was acidified with no additional hydrogen evolution. A few droplets having an amine odor were collected in the cold trap.

Run 3: A large sample of n-butylurea (30 grams) was melted in a round-bottom flask with a side arm take-off midway between the bottom and neck. The temperature of the bath was raised to 130°. Sodium borohydride was added by means of a dropping funnel, so as to control foaming during the reaction. The volatile products were taken off through the side arm and into a cold trap. Sodium borohydride was added in small amounts until it appeared that all the n-butylurea had reacted. Approximately five milliliters of liquid were collected in the cold trap. The reaction also produced a considerable quantity of ammonia. The liquid had a boiling point of 77° and almost all of it distilled at that temperature. The index of refraction at room temperature was 1.391 which was identical with that of a known sample of n-butylamine, which also boiled at 77°. The yield was equal to 3.7 grams

or 0.05 moles of n-butylamine. Attempts to form sym. n-butylphenylurea or n-butylamine picrate failed. However, these same derivatives could not be obtained with a known sample of the amine.

A portion of the residue was treated with 6 N sodium hydroxide in which partial solubility was shown. Ether extraction of the sodium hydroxide solution yielded a yellow gummy substance plus a little brown granular solid. A second portion of the residue was extracted with acetone. An acetone-insoluble fraction was also insoluble in water. This fraction gave a positive test for boron, a negative test with nitrous acid, and did not melt at or below 360°. An acetone-soluble solid, almost white in appearance, melted between 69 and 73°. The residue before extraction with acetone contained 19.0% nitrogen. The acetone-insoluble residue after extraction contained 26.4% and the acetone-soluble solid contained 16.5%. A small quantity of water-insoluble solid was heated in a porcelain boat to 500°. A few drops of water was then evaporated and the boat heated to redness in the flame of a Fisher high temperature burner for 15 minutes. Several black particles still remained after this treatment.

Attempts were made to determine quantitative amounts both of n-butylamine and of ammonia liberated by this reaction but failed owing to the fact that n-butylurea itself decomposes and releases ammonia at the reaction temperatures.

Reaction of Carbanilide with Sodium Borohydride

Sodium borohydride ($3.62 \times 10^{-3}$ moles) and carbanilide ($23.9 \times 10^{-3}$ moles) were mixed together with a glass stirring rod and placed in the system and the system flushed with ammonia. The oil bath was

heated rapidly to 220° where reaction began and proceeded readily with very little foaming. Vapors condensed in the upper part of the cell and ran to the bottom. The cold trap collected only a little sublimed carbanilide carried over by the ammonia. Hydrogen was collected and determined by combustion to be equivalent to 0.91 moles per mole of sodium borohydride. The liquid collected in the bottom of the cell, approximately one milliliter, was distilled under vacuum and a liquid fraction was taken off at 48°. The liquid was characterized as aniline by preparing from it benzanilide with a melting point of 160-1° and acetanilide with a melting point of 111-3°.

## Reaction of Thiourea with Sodium Borohydride

A mixture of thiourea and sodium borohydride was prepared using a 1/1 mole ratio. The mixture was heated in a test tube placed in an oil bath. There was no evidence of reaction up to 160° where the reaction began suddenly and proceeded vigorously. The reaction gases were passed through a lead acetate solution. Lead sulfide was immediately precipitated and the odor of hydrogen sulfide was very apparent. The test tube was opened briefly and a piece of moist litmus held above the mouth indicated the presence of a volatile base presumed to be ammonia.

Sodium borohydride ($3.12 \times 10^{-3}$ moles) and thiourea ($3.80 \times 10^{-3}$ moles) were mixed together with a stirring rod. Three absorbers were introduced into the system. The first contained 25 milliliters of 0.1023 N hydrochloric acid to absorb the ammonia and the second and third each contained 25 milliliters of a cadmium chloride solution to absorb the hydrogen sulfide. It appeared that a non-absorbed gas was first evolved, followed shortly by hydrogen sulfide as indicated by a

cloudiness in the cadmium chloride solution. Reaction began at 157°
and the reaction temperature was maintained at 160° until the reaction
was complete. The precipitated cadmium sulfide was collected by fil-
tration using a fine fritted filtering crucible. It was dried, weigh-
ed, and found to be equivalent to $0.206 \times 10^{-3}$ moles of hydrogen sul-
fide. Nineteen milliliters of 0.1014 N sodium hydroxide was required
to back-titrate the acid solution and was equivalent to $0.63 \times 10^{-3}$
moles of ammonia. The hydrogen was collected and burned. It was e-
qual to $2.93 \times 10^{-3}$ moles of hydrogen. The residue when dissolved in
water evolved additional hydrogen which was measured and found equal
to $4.59 \times 10^{-3}$ moles of hydrogen. The solution containing the residue
was made up to 200 milliliters in a volumetric flask and 50 millili-
ters taken for a boron analysis. Ninety-three percent of the boron
originally present as sodium borohydride was recovered.

Reaction of Formamide with Sodium Borohydride

A sample of sodium borohydride ($2.52 \times 10^{-3}$ moles) was added to
a 25 x 250 mm. test tube equipped with a three-hole rubber stopper to
allow the insertion of a buret containing the formamide. A trap con-
taining ten milliliters of water was placed in the system and the sys-
tem flushed with ammonia. A vigorous foaming occurred immediately on
addition of formamide to the borohydride accompanied by a brisk but
not violent evolution of gas. No heat was applied for some time. The
first collection of gas amounting to approximately 75 milliliters was
made without heating the reaction mixture. Heat was applied slowly to
increase the rate of gas evolution but the rate increase was small.
The initial amount of amide added was 0.0283 moles. When the temperature

reached 150°, most of the amide had vaporized, and a brown decomposition product had formed. An additional 0.0914 moles of formamdie was added but produced very little additional gas. The total amount of hydrogen collected as determined by combustion was equivalent to 2.28 moles of hydrogen per mole of sodium borohydride. The water solution through which the gases were passed was evaporated to dryness, taken up in a little water and tested for the presence of boron. No boron was indicated.

## Reaction of Acetamide with Sodium Borohydride

Run 1: Sodium borohydride ($1.85 \times 10^{-3}$ moles) and acetamide (excess) were dissolved in liquid ammonia. No hydrogen was obtained during the evaporation of the ammonia. Heat was applied gradually by means of the internal heater and produced a slow evolution of gas. The temperature was increased slightly above the melting point of acetamide and maintained at this point until gas evolution ceased. The hydrogen obtained was equivalent to 3.04 moles per mole of sodium borohydride.

Run 2: Sodium borohydride ($1.29 \times 10^{-3}$ moles) and acetamide (excess) were prepared in a test tube equipped with a rubber stopper and reacted in an atmosphere of ammonia. When the temperature of the oil bath reached 45° the mixture melted and formed a cloudy solution. The reaction gases were passed through a little water to trap any transported boron compound. Soon after the reaction mixture melted, gas was evolved quite slowly. Increasing the temperature to 150° increased the rate only slightly. The hydrogen was collected and burned and found to be equivalent to 2.46 moles per mole of sodium borohydride. The

water solution through which the gases were passed was evaporated to about two milliliters. A test for boron on this solution was negative.

Run 3: Fifty grams of acetamide was introduced into a round-bottom flask with side-arm take-off. The sodium borohydride was added via a dropping funnel. Volatile products were passed through a cold trap maintained at -14°. The reaction temperature was maintained at 150° for six hours. Approximately 6.5 milliliters of liquid was collected in the cold trap. Considerable ammonia was also evolved during the reaction. The residue remaining was a greenish gel turning yellow-brown on cooling. The liquid obtained was distilled through a small fractionating column. Fraction 1 (three milliliters) boiling between 70 and 71° was taken off followed by Fraction 2 (two milliliters) boiling between 76 and 79°. Approximately one milliliter remained in the column and pot. Indices of refraction were measured at room temperature:

|  |  |
|---|---|
| Fraction 1 | 1.3492 |
| Fraction 2 | 1.3435 |
| Ethanol | 1.3513 |
| Acetonitrile | 1.3333 |
| Pot | 1.3493 |

Positive iodoform tests were obtained from samples of both fractions and the liquid remaining in the pot. A very positive test for the presence of nitrogen in Fraction 1 was obtained by sodium fusion. Sodium hydroxide was added to a sample of Fraction 1 in order to hydrolyze any nitrile present to the acid and the solution was refluxed for 30 minutes. Ammonia was liberated during this hydrolysis. Sulfuric acid was then added to form the ester from any acetonitrile and ethyl alcohol

initially present. The odor of ethyl acetate was very evident. On the basis of this evidence, it was concluded that both ethyl alcohol and acetonitrile are produced by the reaction between acetamide and sodium borohydride.

## Reaction of Benzamide with Sodium Borohydride

Run 1: A reaction mixture of sodium borohydride ($1.68 \times 10^{-3}$ moles) and benzamide ($10.2 \times 10^{-3}$ moles) was prepared for reaction in the cell in an ammonia atmosphere. The mixture was heated rapidly to 127° where melting and reaction began simultaneously. Excessive foaming accompanied the reaction at this temperature and may have carried some of the mixture out of heating range. When the reaction was apparently complete, the temperature was raised to 140°. The amount of hydrogen collected was equivalent to 2.1 moles per mole of sodium borohydride. The residue remaining was white and gave an odor suggesting the presence of an organic reaction product.

Run 2: Sodium borohydride ($0.97 \times 10^{-3}$ moles) and benzamide ($8.25 \times 10^{-3}$ moles) were reacted in the same manner as in Run 1 except that the foaming was controlled somewhat by submerging the cell in the oil bath a little at a time. The hydrogen measured from this reaction was equivalent to 2.5 moles per mole of borohydride.

Run 3: Approximately 25 grams of benzamide was placed in the side-arm round-bottom flask and heated to 140°. Sodium borohydride was added in small amounts through a dropping funnel until there was no further evidence of reaction. The volatile products were led into a cold trap. The flask was then heated to 187°. Considerable ammonia was evolved during the reaction and between three and four milliliters

of a liquid was collected in the cold trap. The liquid had a boiling

point between 187 and 189°. The yellow solid reaction residue was ex-

tracted with ether, which on evaporation left a liquid residue. This

was distilled and a fraction boiling between 190 and 192° was obtained.

A yellow solid remained in the distilling pot. Indices of refraction

were measured at room temperature:

| | |
|---|---|
| Benzonitrile | 1.5222 |
| Fraction boiling at 187-9° | 1.5236 |
| Fraction boiling at 190-2° | 1.5200 |

The two fractions were combined and a portion of the mixture was hy-

drolyzed with sodium hydroxide. A solid was obtained which melted at

119-21°. It was then concluded that benzonitrile was a product of

this reaction. A second portion was found to react to some extent

with acetyl chloride. The possible presence of traces of amine was

indicated by this reaction.


## Reaction of Benzenesulfonamide with Sodium Borohydride

Sodium borohydride ($1.51 \times 10^{-3}$ moles) and benzenesulfonamide

($6.5 \times 10^{-3}$ moles) were mixed and heated in the cell in an ammonia at-

mosphere. Heating was rapid to 145° where the evolution of gas began.

The reaction began slightly before the mixture showed signs of melting.

Foaming was very slight but the reaction was very vigorous as indicat-

ed by the rapid evolution of gas. The gas was measured as hydrogen

and was equivalent to 2.8 moles per mole of sodium borohydride.


## Reaction of Urethan with Sodium Borohydride

Sodium borohydride ($0.93 \times 10^{-3}$ moles) and urethan ($11.0 \times 10^{-3}$

moles) were mixed and placed in the cell. The cell was placed in the
system and the system flushed with ammonia. The mixture was heated to
45° where the urethan melted, forming an apparent solution of sodium
borohydride in the urethan. The temperature was raised to 90° where
an evolution of gas began and proceeded at a moderate rate. There was
no visible foaming. The temperature was raised to 110° and maintained
at that point until the reaction was complete. During the reaction
urethan refluxed in the reaction tube. Hydrogen obtained was equiva-
lent to 2.94 moles per mole of sodium borohydride. Six normal hydro-
chloric acid was added to the residue. Gas evolution occurred with
the initial addition of the acid. Less than one milliliter of the gas
was found to be combustible.

## Reaction of N-Phenylurethan with Sodium Borohydride

The N-phenylurethan was prepared by synthesis from anhydrous eth-
anol and phenylisocyanate and recrystallized from petroleum ether.
Sodium borohydride ($1.22 \times 10^{-3}$ moles) and N-phenylurethan ($16.6 \times
10^{-3}$ moles) were prepared for reaction in the same manner as for ure-
than. The mixture melted at 50°. Reaction began at this temperature
as indicated by gas evolution. The temperature was maintained at 110°
during the course of the reaction, which proceeded considerably more
slowly than the reaction between urethan and sodium borohydride. The
hydrogen liberated was equivalent to 1.62 moles per mole of borohy-
dride. Acidification of the residue yielded no additional hydrogen.

A reaction in air gave a residual odor indicating the presence of
some product other than the initial reactants. No attempt was made to
isolate reduction products in this reaction.

Reaction of Sulfanilamide with Sodium Borohydride

Run 1:  Sodium borohydride ($0.98 \times 10^{-3}$ moles) and sulfanilamide ($8.9 \times 10^{-3}$ moles) were mixed and placed in the cell.  A cold trap was placed in the system and the entire system flushed with ammonia.  A very slow evolution of gas began when the bath temperature reached 120° but did not become appreciable until the mixture began to melt at 165°. No excessive foaming was encountered.  Nothing was collected in the trap.  The hydrogen was equivalent to 2.86 moles per mole of borohydride.

Run 2:  A mixture of sodium borohydride ($1.40 \times 10^{-3}$ moles) and sulfanilamide ($6.72 \times 10^{-3}$ moles) was prepared for reaction in an initially dry air atmosphere as a comparison with the reaction in an atmosphere of ammonia.  The mixture was heated in the cell to 170° where decomposition of the sulfanilamide occurred as shown by charring.  The gas evolved was not collected.

Reaction of Uric Acid with Sodium Borohydride

Uric acid and sodium borohydride were mixed together in a test tube and heated in an air atmosphere to 270° without evidence of reaction.  The addition of water produced a very rapid evolution of hydrogen.

Reaction of Urea with Sodium Borohydride in the Presence of 2-Heptanone

Twenty grams of urea was placed in a round-bottom flask with side-arm take-off leading into a cold trap.  Twenty milliliters of 2-heptanone was added and quickly absorbed by the urea.  The flask was heated to 135° but the urea showed no signs of melting at this temperature and

gave no evidence of reacting when a little sodium borohydride was added from a dropping funnel. The temperature was raised to 147° where some liquid appeared and a reaction began. The separation into solid and liquid phases was soon complete and the reaction became quite vigorous as indicated by a rapid evolution of gas. Ammonia was liberated either as a result of a reaction between urea and sodium borohydride or from decomposition of the urea. No liquid was collected in the cold trap. The residue was a yellow-white gummy solid. Attempts to recover 2-heptanol from the reaction mixture were inconclusive.

## Reaction of Benzoic Acid with Sodium Borohydride

Twenty-five grams of benzoic acid were melted and the liquid was raised to 125°. Approximately three grams of sodium borohydride were added in small quantities. Each addition produced an immediate and rapid gas evolution. Continued addition of sodium borohydride converted the liquid benzoic acid to a white solid. No reaction products were isolated but the reaction residue gave an odor different from the odor characteristic of benzoic acid and sodium borohydride.

# DISCUSSION

The reaction of urea with sodium borohydride was more extensively studied than any other of the reactions under investigation. It does not appear to be a simple one-step reaction. This is indicated by a certain amount of variation in hydrogen evolution along with the presence of other reaction products. The reaction is, however, reproducible under unvarying reaction conditions. Temperature seems to affect only the rate of reaction and not the course providing the temperature is maintained below that at which urea is converted to biuret. Great differences are not noted in varying the atmosphere in which the reaction is produced. A small error is probably introduced when the reactants are dissolved in liquid ammonia prior to reaction owing to the decomposition of ammonium borohydride which is formed when liquid ammonia solutions of sodium borohydride are evaporated to dryness (20). Only traces of methyl alcohol and small amounts of ammonia were produced by the reaction of urea and sodium borohydride, as contrasted with appreciable amounts of hydrogen sulfide and ammonia liberated by the reaction of thiourea with sodium borohydride. This is probably due to the comparative stability of the urea molecule toward reduction.

Elemental analysis of the urea-borohydride residue indicated little loss of boron or carbon during the reaction. On this basis it was concluded that no volatile boron compounds are formed. Extraction of the residue with acetone left a white solid which did not melt below 250°. Elemental analysis of this solid yielded the ratio of elements equivalent

to one molecule of sodium metaborate plus one molecule of urea. From a reaction mixture made up from three moles of urea per mole of boro-hydride, two moles of urea are recoverable as such on hydrolysis of the residue.

The reaction between urea and sodium borohydride produces a large amount of hydrogen and a small amount of methyl alcohol and ammonia. Reactions between lithium borohydride or lithium aluminum hydride and certain organic compounds produce no hydrogen but good yields of re-duction products. Hydrolysis is not required to obtain the products of reaction between sodium borohydride and the amides whereas for re-actions involving lithium borohydride or lithium aluminum hydride hy-drolysis is almost always necessary. The mechanism for the reaction between urea and sodium borohydride must therefore be fundamentally different than for reactions involving lithium borohydride or lithium aluminum hydride. The reaction may thus form a complex as follows:

$$(3n + 4)\ H_2NCONH_2 + (n + 1)\ NaBH_4 \longrightarrow$$

$$\text{COMPLEX} + (4n + 4)\ H_2 \qquad \text{Eq. 1}$$
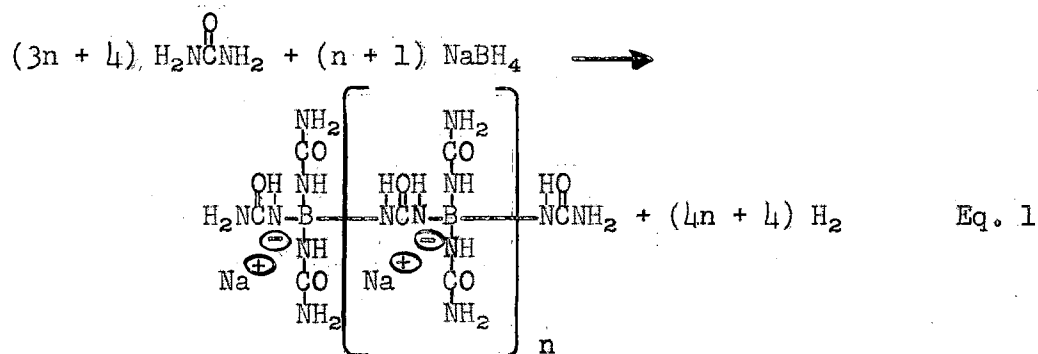
This complex could subsequently be partially hydrolyzed:

$$\text{COMPLEX} + (2n + 2)\ H_2O \longrightarrow (2n + 3)\ H_2NCONH_2 + (n + 1)\ H_2NCN{-}BOH \qquad \text{Eq. 2}$$
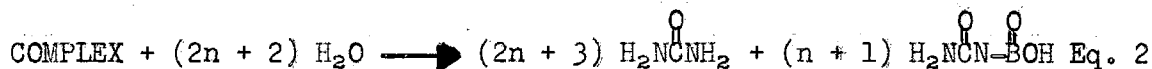
The enol form of urea could also form a complex

$$(3n + 4)HN{=}\underset{\underset{H}{\overset{O}{|}}}{C}NH_2 + (n + 1)NaBH_4 \longrightarrow$$

$$H_2N\underset{HN}{\overset{}{C}}{-}O{-}B \left[ {-}NCN{-}B \right]_n {-}NCNH_2 + (4n + 4)H_2$$
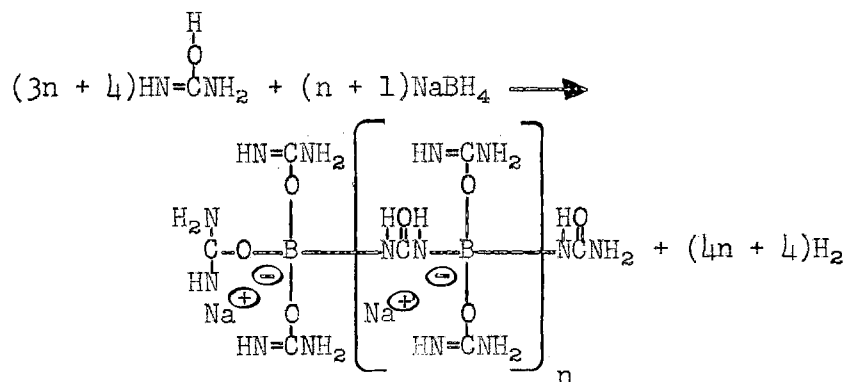
Hydrolysis would give back the same products as derived from the keto form. In these mechanisms it appears that one molecule of urea is held rather tightly by the boron while two molecules are held less tightly. Four moles of hydrogen are obtained by this mechanism as compared with an average of 3.7 produced from urea and sodium borohydride when the ratio was above three moles of urea per mole of borohydride. Production of free hydrogen by this mechanism is not a reduction reaction.

Formation of the oxygen-boron bond has been assumed in the mechanism of the reaction between sodium borohydride and acetone (17). This mechanism is as follows:

$$NaBH_4 + 4\ CH_3\overset{O}{\overset{\|}{C}}CH_3 \longrightarrow \left[ \cdots \right] Na^+ \xrightarrow{H_2O} 4\ CH_3\underset{H}{\overset{\overset{H}{\overset{|}{O}}}{C}}CH_3$$
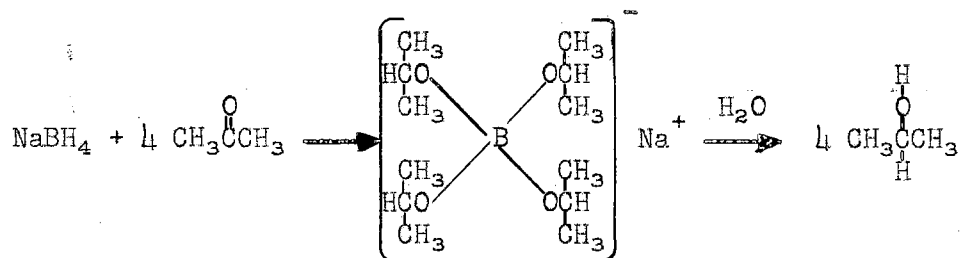
The alcohol was obtained only by hydrolysis.

The complex on the right side of equation 2 is a combination of atoms equivalent to one molecule of urea and one molecule of sodium metaborate. In the case of acetone extraction, the acetone, although C.P., may have contained traces of water sufficient to cause hydrolysis.

Extraction of a urea-borohydride residue with liquid ammonia, in which

urea is soluble and sodium metaborate is insoluble, left a solid with

a nitrogen content of twenty-five percent. This may be compared with

nitrogen contents of twenty-six and eighteen percent for the solids left

after acetone extraction of the urea-borohydride residues from two runs.

The theoretical percentage of nitrogen in one molecule of urea plus one

molecule of sodium metaborate is 22.4. The slightly high experimental

values may possibly be due to the formation of a complex with ammonia.

The nitrogen in each case was determined by the Dumas method.

A second mechanism for the evolution of hydrogen involving boron-

nitrogen bonds may be set up in the following manner:

$$NaBH_4 + 4\ H_2N\overset{O}{\overset{\|}{C}}NH_2 \longrightarrow \left[ \begin{matrix} H_2N\overset{O}{\overset{\|}{C}}NH & HN\overset{O}{\overset{\|}{C}}NH_2 \\ & B & \\ H_2N\underset{O}{\underset{\|}{C}}NH & HN\underset{O}{\underset{\|}{C}}NH_2 \end{matrix} \right]^{--} Na^+ + 4\ H_2$$
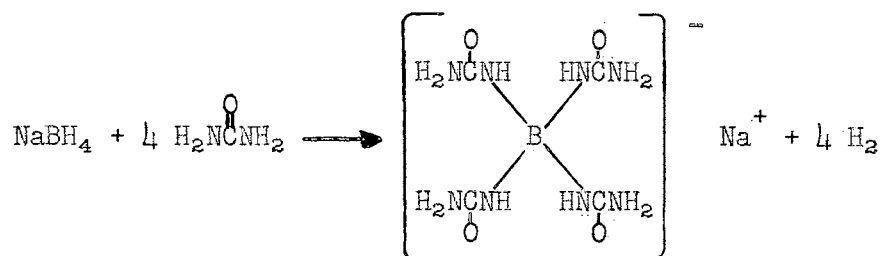
The enol form of the urea could be substituted so that a -B-O-C- link-

age is formed. As in the case of the first mechanism this mechanism

does not involve reduction.

A third possibility for producing free hydrogen without reduction

involves the formation of double bonds between the boron and a nitro-

gen from each of two molecules of urea. The mechanism is

$$NaBH_4 + 2\ H_2N\overset{O}{\overset{\|}{C}}NH_2 \longrightarrow \left[ H_2N\overset{O}{\overset{\|}{C}}N\!=\!\!=\!B\!=\!\!=\!N\overset{O}{\overset{\|}{C}}NH_2 \right]^{-} Na^+ + 4\ H_2$$
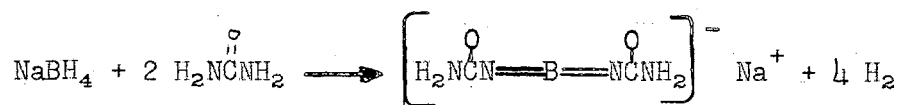
The mechanism for the formation of ammonia and methyl alcohol by

reduction of urea with sodium borohydride may be postulated as follows:

$$\left[\begin{array}{c} H \\ H\overset{|}{B}H \\ H \end{array}\right]^{-} + \underset{NH_2}{\overset{NH_2}{OC}} \longrightarrow \left[\begin{array}{c} \textcircled{H} \quad \boxed{NH_2} \\ HB{-}O{-}CH \\ H \qquad NH_2 \end{array}\right]^{-} \longrightarrow \left[\begin{array}{c} NH_2 \quad H \\ HB{-}O{-}CH \\ H \qquad NH_2 \end{array}\right]^{-}$$

$$\left[\begin{array}{c} NH_2 \quad H \\ HB{-}O{-}CH \\ H \qquad NH_2 \end{array}\right]^{-} + H_2N\overset{O}{\overset{\|}{C}}\underset{H}{NH} \longrightarrow \left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad\qquad H \\ HB{-}O{-}CH \\ H \qquad NH_2 \end{array}\right]^{-} + NH_3$$
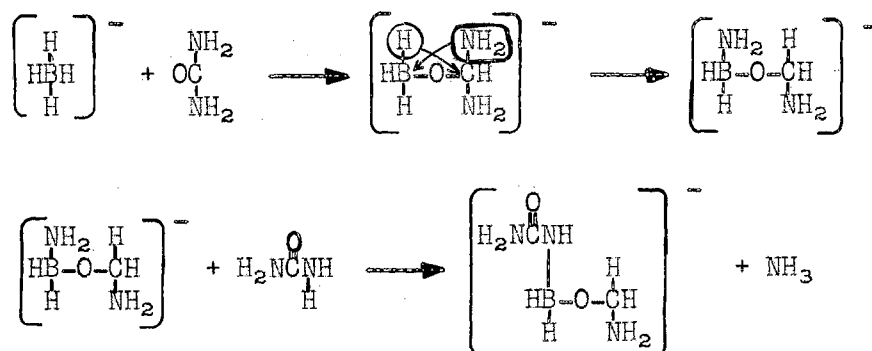
This reaction involves solvolysis of the urea-borohydride complex with excess urea. Repeating the hydrogen-transfer and solvolysis steps forms another molecule of ammonia:

$$\left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad\quad H \\ HB{-}O{-}CH \\ H \qquad NH_2 \end{array}\right]^{-} \longrightarrow \left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad\quad H \\ HB{-}O{-}CH \\ NH_2 \quad H \end{array}\right]^{-} \overset{H_2N\overset{O}{\overset{\|}{C}}NH_2}{\longrightarrow} \left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad\quad H \\ HB{-}O{-}CH \\ \overset{|}{O} \quad H \\ H_2N\overset{\|}{\underset{O}{C}}NH \end{array}\right]^{-} + NH_3$$
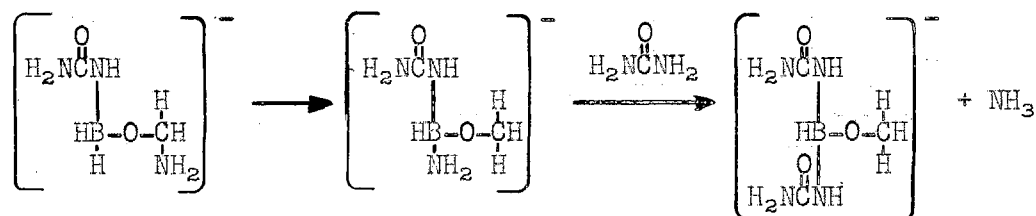
This leaves the $-OCH_3$ radical attached to the boron and available for solvolysis to methyl alcohol:

$$\left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad\quad H \\ HB{-}O{-}CH \\ \qquad\quad H \\ H_2N\overset{\|}{\underset{O}{C}}NH \end{array}\right]^{-} + H_2N\overset{O}{\overset{\|}{C}}NH_2 \longrightarrow \left[\begin{array}{c} H_2N\overset{O}{\overset{\|}{C}}NH \\ \qquad HO \\ HB{-}\overset{\|}{C}NH_2 \\ H_2N\overset{\|}{\underset{O}{C}}NH \end{array}\right]^{-} + CH_3OH$$
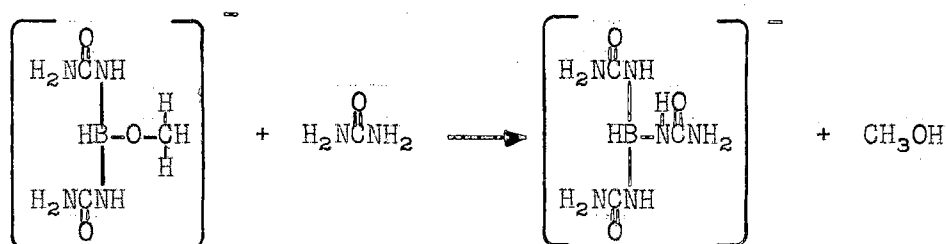
Presence of this final complex in the liquid ammonia-insoluble fraction of the urea-borohydride residue would account for the high nitrogen values obtained from analysis of the residue.

The idea of solvolysis seems reasonable from a consideration of the fact that amides are simultaneously acidic and reducible. Their weak acid function substitutes for the action of water and eliminates

the need for hydrolysis.  Similarly benzoic acid was found to react
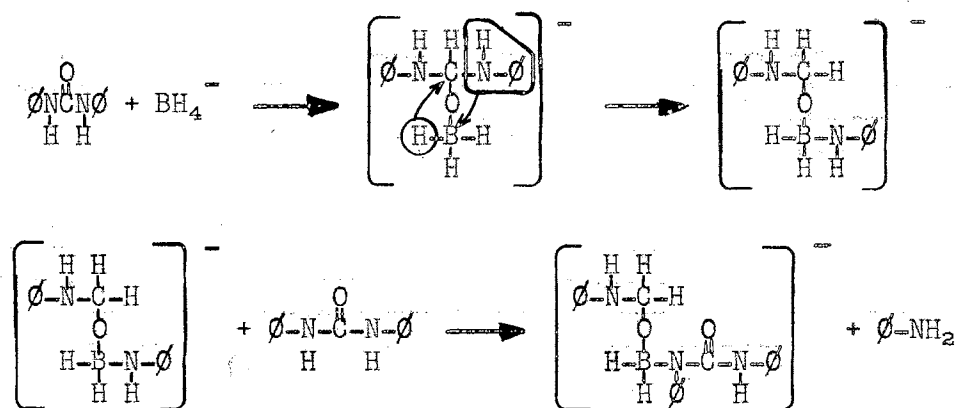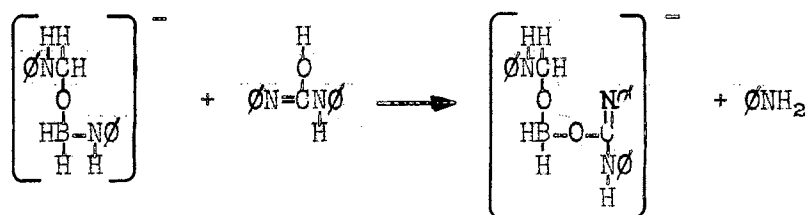with sodium borohydride, near the melting point of the benzoic acid,
to yield hydrogen and other undetermined products without hydrolysis.

Aniline was found to be produced by the reaction of carbanilide
with sodium borohydride.  The mechanism for such a reduction, which is
obviously similar to that of urea, may be postulated as follows:

$$\phi N\overset{O}{\overset{\|}{C}}N\phi + BH_4^- \longrightarrow \left[\begin{array}{c} H\ H\ H \\ \phi-N-C-N-\phi \\ O \\ H-B-H \\ H \end{array}\right]^- \longrightarrow \left[\begin{array}{c} H\ H \\ \phi-N-C-H \\ O \\ H-B-N-\phi \\ H\ H \end{array}\right]^-$$

$$\left[\begin{array}{c} H\ H \\ \phi-N-C-H \\ O \\ H-B-N-\phi \\ H\ H \end{array}\right]^- + \phi-N-\overset{O}{\overset{\|}{C}}-N-\phi \longrightarrow \left[\begin{array}{c} H\ H \\ \phi-N-C-H \\ O\qquad O \\ H-B-N-C-N-\phi \\ H\ \phi\qquad H \end{array}\right]^- + \phi-NH_2$$

This mechanism is similar to that for ammonia evolution and involves
the migration of the hydrogen atom to the carbonyl carbon and the split-
ing of the nitrogen-carbon bond, the nitrogen then migrating to form a
boron-nitrogen bond.  The complex thus formed can be broken up by sol-
volysis with another molecule of carbanilide.  The carbanilide could
give up a hydrogen atom to the anilino radical and displace aniline
from the complex.  The displacement could also proceed via the enol
form of carbanilide as follows:

$$\left[\begin{array}{c} HH \\ \phi N C H \\ O \\ HB-N\phi \\ H\ H \end{array}\right]^- + \overset{H}{\overset{|}{\underset{H}{\phi N=C N\phi}}} \longrightarrow \left[\begin{array}{c} HH \\ \phi N C H \\ O\qquad N\phi \\ HB-O-C \\ H\qquad N\phi \\ H \end{array}\right]^- + \phi NH_2$$

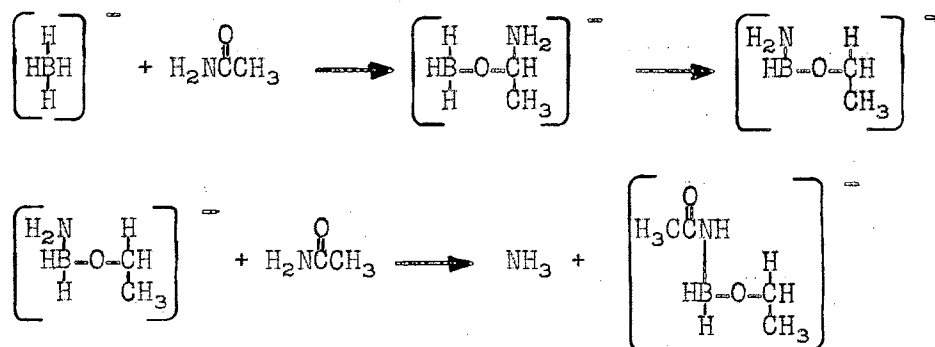The reaction of carbanilide and sodium borohydride produced hydrogen

equivalent to 0.9 moles per mole of borohydride and aniline equivalent to 1.5 moles per mole of borohydride charged to the reaction. This indicates that the formation of reduction products is accompanied by a decrease in the amount of available hydrogen. This competition between the production of hydrogen and of reduction products is shown by all reactions investigated.

Similar mechanisms may be proposed for the production of n-butyl-amine from the reaction of n-butylurea with sodium borohydride.

When acetamide or benzamide was used, a nitrile was formed along with an alcohol and traces of an amine. At first glance, the formation of a nitrile seemed to be a dehydration reaction. Since sodium boro-hydride has not been found to be a strong dehydrating agent, a tenta-tive mechanism may be set up for the formation of a nitrile from acet-amide involving an enolization as follows:

$$BH_4^- + H_3CC=NH \longrightarrow H_2 + \left[H_3B-O-CCH_3\right]^- \longrightarrow \left[H_3BOH\right]^- + N\equiv CCH_3$$
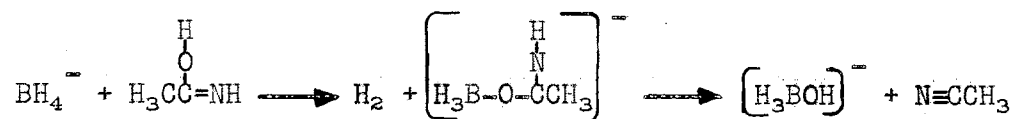
Since ethanol along with ammonia was also formed in the reaction, an-other series of reactions is proposed as follows:

$$\left[HBH\right]^- + H_2NCCH_3 \longrightarrow \left[HB-O-CH\right]^- \longrightarrow \left[HB-O-CH\right]^-$$

$$\left[HB-O-CH\right]^- + H_2NCCH_3 \longrightarrow NH_3 + \left[\begin{matrix}H_3CCNH\\HB-O-CH\end{matrix}\right]^-$$

Solvolysis of the complex thus formed would produce the alcohol. These same mechanisms may be applied to the formation of nitrile and ammonia

from benzamide and **sodium** borohydride.

Acetonitrile and ethyl alcohol were obtained from the reaction of acetamide with sodium borohydride in eighteen percent total yield based on the formation of one mole of either of these two products per mole of acetamide charged to the reaction. Of this yield, about one-fourth was estimated to be acetonitrile through measurements of index of refraction. In the case of benzamide, however, nearly all of the 19.1 percent yield proved to be benzonitrile; the remainder was tentatively identified as benzylamine. Again, the hydrogen obtainable per mole of borohydride was considerably less than was obtained from reactions of urea with sodium borohydride.
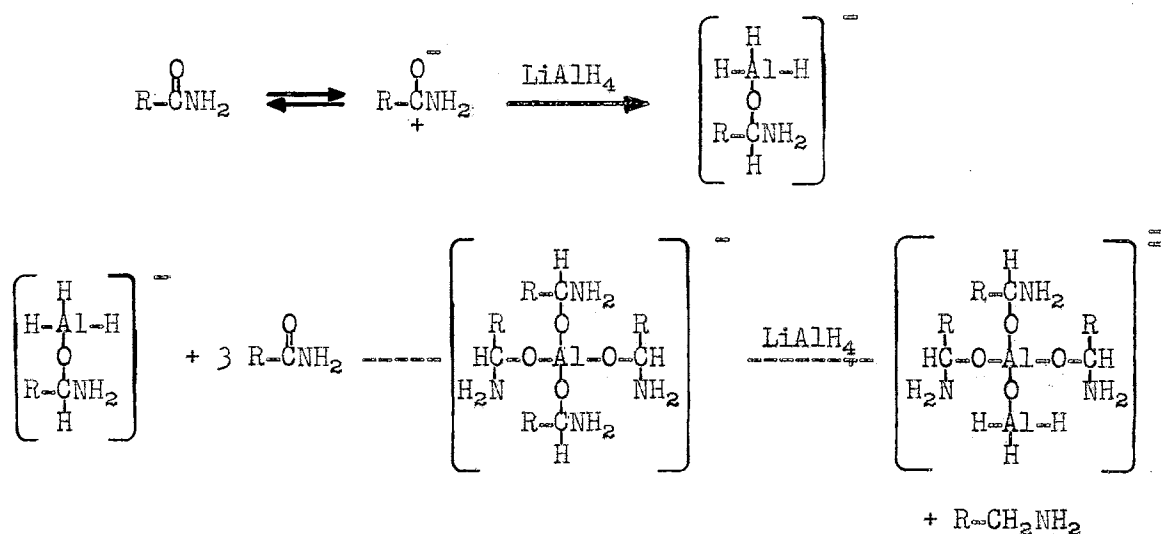
Varying the groups to which the amide group is attached or replacing the carbon atom in the amide group with a sulfur atom apparently does not change the general nature of the reaction. This is shown by the behavior of the sulfonamides and urethans with sodium borohydride. The lower yield of hydrogen in each case as compared to the urea-borohydride reaction indicates that considerable reduction also takes place in these reactions.

Uric acid, an easily enolizable amide, failed to release hydrogen from sodium borohydride. This fact seems to favor the formation of a boron-nitrogen bond over that of a boron-oxygen-carbon bonding for the release of hydrogen. However, uric acid undergoes decomposition at a relatively high temperature before reaching a melting point. The fact that seemingly a threshold temperature must be reached before reaction occurs may be of importance in this case.
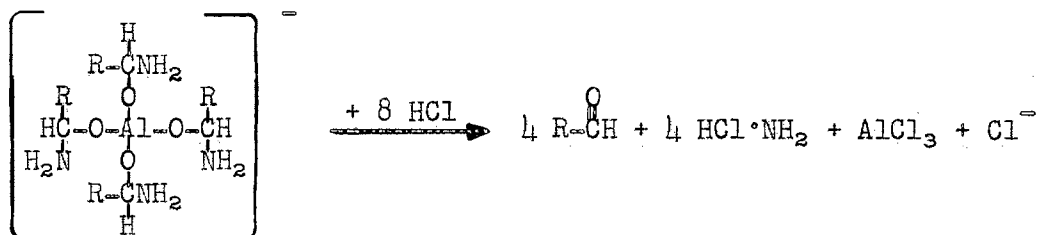
Heretofore, reduction of most organic compounds with sodium borohydride has involved hydrolysis to form the reduction products. Although

hydrolysis is not necessary in these reactions, the mechanisms may be the same due to solvolysis. Whether these mechanisms and that suggested by Schlesinger for the reduction of acetone with sodium borohydride are the same or not, the case for the formation of complexes through the same type of bonding is considerably strengthened.

Weygand (50) has proposed a mechanism whereby certain amides may be reduced with lithium aluminum hydride to corresponding amines without hydrolysis. For example, acetamide may be reduced to ethylamine by the following mechanism:

$$R-\overset{O}{\overset{\|}{C}}NH_2 \rightleftharpoons R-\overset{\overset{-}{O}}{\underset{+}{C}}NH_2 \xrightarrow{LiAlH_4} \left[ \begin{array}{c} H \\ H-\overset{|}{Al}-H \\ \overset{|}{O} \\ R-\overset{|}{C}NH_2 \\ \overset{|}{H} \end{array} \right]^{-}$$

$$\left[ \begin{array}{c} H \\ H-\overset{|}{Al}-H \\ \overset{|}{O} \\ R-\overset{|}{C}NH_2 \\ \overset{|}{H} \end{array} \right]^{-} + 3\ R-\overset{O}{\overset{\|}{C}}NH_2 \dashrightarrow \left[ \begin{array}{c} H \\ R-\overset{|}{C}NH_2 \\ R\ \ \ \ O\ \ \ \ R \\ H\overset{|}{C}-O-\overset{|}{Al}-O-\overset{|}{C}H \\ H_2N\ \ \ \ O\ \ \ \ NH_2 \\ R-\overset{|}{C}NH_2 \\ \overset{|}{H} \end{array} \right]^{-} \xrightarrow{LiAlH_4} \left[ \begin{array}{c} H \\ R-\overset{|}{C}NH_2 \\ R\ \ \ \ O\ \ \ \ R \\ H\overset{|}{C}-O-\overset{|}{Al}-O-\overset{|}{C}H \\ H_2N\ \ \ \ O\ \ \ \ NH_2 \\ H-\overset{|}{Al}-H \\ \overset{|}{H} \end{array} \right]^{=}$$

$$+ R-CH_2NH_2$$

On the other hand, Weygand found that acid hydrolysis of the lithium aluminum hydride-amide complex led to the formation of aldehydes:

$$\left[ \begin{array}{c} H \\ R-\overset{|}{C}NH_2 \\ R\ \ \ \ O\ \ \ \ R \\ H\overset{|}{C}-O-\overset{|}{Al}-O-\overset{|}{C}H \\ H_2N\ \ \ \ O\ \ \ \ NH_2 \\ R-\overset{|}{C}NH_2 \\ \overset{|}{H} \end{array} \right]^{-} \xrightarrow{+\ 8\ HCl} 4\ R-\overset{O}{\overset{\|}{C}}H + 4\ HCl\cdot NH_2 + AlCl_3 + Cl^{-}$$

In neither case was hydrogen evolved during the reaction. Good

yields of the reduction products were obtained in these reactions.

Reduction of acetamide with sodium borohydride follows some different course of reaction than the reduction with lithium aluminum hydride. This is evident from the production of ethyl alcohol and acetonitrile along with an appreciable evolution of hydrogen. It seems reasonable, then, to assume that the reaction mechanism is also different and of the type suggested. The production of benzylamine, found in trace amounts from the reaction of benzamide with sodium borohydride, could however follow such a mechanism.

It must be pointed out that hydrolysis is unnecessary in the production of the amines, nitriles, and alcohols obtained when sodium borohydride is the reducing agent; but solvolysis by excess amide is believed to occur instead.

Table VIII contains a comparison of the several amide-borohydride reactions studied. The amount of hydrogen obtained in these reactions seems to be an inverse indication of the extent to which other products are formed in the reaction. Thus, more reduction products and less hydrogen were obtained from thiourea than urea. For carbanilide, even less hydrogen but a comparatively large yield of aniline was obtained. The same comparison may be made for acetamide, benzamide, and to a lesser extent, n-butylurea. Considerable reduction might be expected for N-phenylurethan, and moderate reduction for formamide, urethan, benzenesulfonamide, and sulfanilamide. Whether this analogy is sound or not is a problem requiring additional work.

From this study, two factors appear to be important in determining the ease with which reaction occurs between amides and sodium borohydride. The reactions appear to depend to some extent on a threshold

## Table VIII

### Reactions of Sodium Borohydride with Amides

| Amide | M.P. of amide, °C | Minimum reaction temp., °C | Moles $H_2$ per mole $NaBH_4$ | Products |
|---|---|---|---|---|
| Urea | 132 | 90 | 3.7 | $CH_3OH$, $NH_3$ |
| Thiourea | 176-8 | 160 | 1.0 | $H_2S$, $NH_3$ |
| n-Butylurea | 95-6 | 120 | 3.5 | n-$C_4H_9NH_2$, $NH_3$ |
| Carbanilide | 241-2 | 220 | 0.9 | $C_6H_5NH_2$ |
| Formamide | 2 | 25 | 2.3 | |
| Acetamide | 79-80 | 45 | 2.8 | $C_2H_5OH$, $NH_3$, $CH_3CN$ |
| Benzamide | 125-6 | 127 | 2.3 | $C_6H_5CN$, $C_6H_5CH_2NH_2$, $NH_3$ |
| Benzenesulfonamide | 152-4 | 145 | 2.8 | |
| Sulfanilamide | 164-5 | 120 | 2.9 | |
| Urethan | 49-51 | 90 | 3.0 | |
| N-Phenylurethan | 50-2 | 50 | 1.6 | |

temperature which may be directly related to the amide. Increased solubility of the sodium borohydride in the amide also appears to enhance the ease of reaction.

It should be noted that the reduction of aldehydes, ketones, and acid chlorides with sodium borohydride and lithium aluminum hydride yields no hydrogen. Products of these reductions, the corresponding alcohols, are obtained only by hydrolysis. The reduction of amides with sodium borohydride, however, involves two competing reactions: one, the liberation of hydrogen; and two, the production of alcohols, nitriles, or amines. Again, it appears that the competition between the production of hydrogen and other reaction products results from the fact that amides are weakly acidic and reducible.

Compounds which are both acidic and reducible should follow the pattern set up by amides. Thus sodium borohydride should reduce organic acids to aldehydes at relatively high temperatures and in the absence of water by the mechanism of solvolysis. Excess acid would in effect hydrolyze the intermediate adduct formed by reducing action of sodium borohydride on the acid. The reaction of benzoic acid with sodium borohydride producing hydrogen and some other reaction product tends to support this conclusion.

Mechanisms proposed for the formation of the various reduction products from the amides studied of course need more substantiating evidence furnished by continued study before being completely accepted.

# SUMMARY

The reactions studied in this investigation involved the reductions of amides with sodium borohydride.

There are, in general, two predictable and competing reactions. One results in the production of hydrogen. The other results in the formation of other reaction products. The extent to which one is favored over the other depends on the nature of the amide involved.

Urea, a compound relatively stable toward reducing agents, shows very little tendency to form reduction products. For mole ratios of urea/NaBH$_4$ cf 3/1 or greater, approximately four moles of hydrogen per mole of sodium borohydride were obtained from the reaction. Very small yields of methyl alcohol and ammonia were also obtained.

Other amides yielded varying lesser relative amounts of hydrogen and increasing amounts of such products as alcohols, nitriles, amines, hydrogen sulfide, and ammonia, according to the favored reaction for each amide. The reaction products were obtained without hydrolysis. However, the mechanism is believed to be one of solvolysis. Reductions of some amides with lithium aluminum hydride have involved a similar mechanism of solvolysis (50).

Mechanisms have been proposed for the formation of the reaction products.

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