




5-8-1953

Cyclization of W-tertiary Butyl Uramido Benzoic Acid

John R. Lovett

Follow this and additional works at: https://digitalcommons.ursinus.edu/chem_hon


 Part of the Chemistry Commons

[Click here to let us know how access to this document benefits you.](#)

CYCLIZATION OF ω -TERTIARY
BUTYL URAMIDO BENZOIC ACID

This paper is submitted to the faculty of Ursinus College
in partial fulfillment of requirements for departmental
honors in Chemistry.

Submitted:


John R. Lovett
Chemistry Department
Ursinus College
May 8th, 1953

Approved:



Acknowledgement

I wish to express my gratitude to those who helped me in the formation of this paper; particularly to Dr. Roger P. Staiger for his effort in providing me with the problem and for his help in the solving of it; to Dr. Russell D. Sturgis for his valuable advice and criticism; to Dr. Harold C. Beachell and Mr. Thrygve R. Meeker of the University of Delaware for their aid in obtaining and interpreting the infra-red spectrographs; and to Miss Kathleen J. Aeckerle for her help in the preparation of this paper.

Contents

I. Introduction

II. Synthesis of ω -Tertiary Butyl Uramido Benzoic Acid

- A. The Preparation of Tertiary Butyl Amine
- B. The Preparation of Isatoic Anhydride
- C. The Reaction of the Amine with Isatoic Anhydride
- D. Isolation and Purification of ω -Tertiary Butyl Uramido
Benzoic Acid

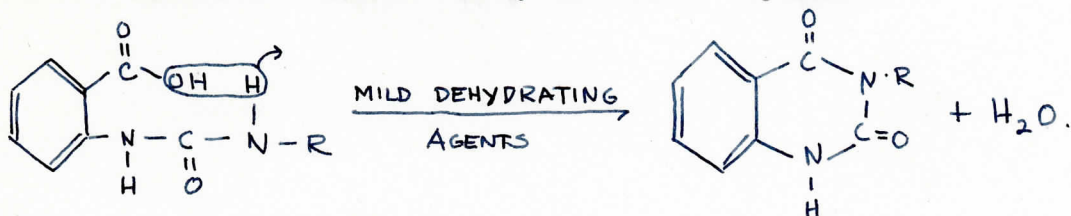
III. Cyclization of the Synthesized Product

- A. Procedure
- B. Apparatus
- C. Treatment
- D. Isolation, Purification, and Identification
 - 1. Solid in the Flask
 - 2. Liquid-Derivative in the Reaction Tubes

IV. Conclusions

I. Introduction

In most cases, ω -substituted uramido benzoic acids, when refluxed with mild dehydrating agents, undergo ring closure to form β -substituted benzoylene ureas.¹ Equation:



When ω -tertiary butyl uramido benzoic acid is treated in the same manner, however, the products of the reaction are a fine white crystalline precipitate and an unidentified gas. If the solid were the expected β -tertiary butyl benzoylene urea, purification would have yielded a compound with a melting point of approximately 160°C. - the purified crystalline product melted at 353°C.

The object of this paper is to investigate the cyclization of ω -tertiary butyl uramido benzoic acid and to establish the equation for the resulting reaction.

II. Synthesis of ω -Tertiary Butyl Uramido Benzoic Acid

This synthesis was accomplished in three steps. The first step involved the preparation of tertiary butyl amine; the second, the preparation of the isatoic anhydride; and the third,

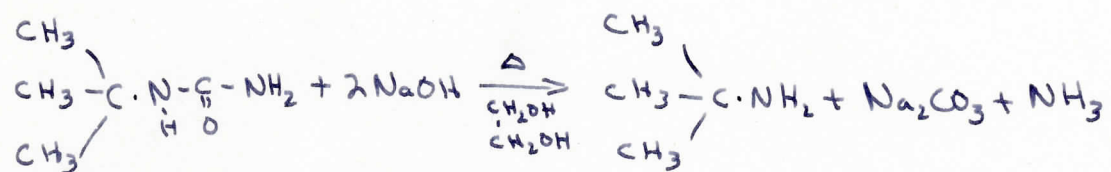
1. Doctoral dissertation, Roger P. Staiger, University of Pennsylvania, 1953.

the reaction of the amine with isatoic anhydride to form the ω -tertiary butyl uramido benzoic acid.

A. The preparation of Tertiary Butyl Amine²

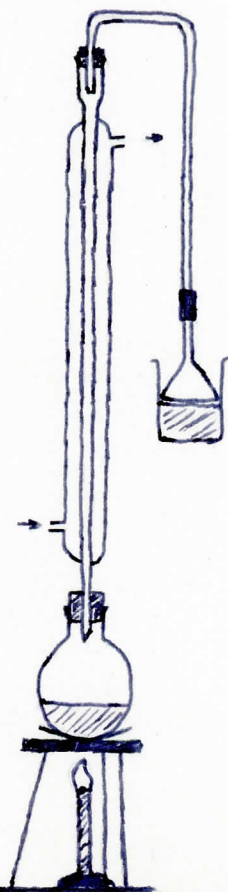
This amine was prepared by the hydrolysis of tertiary butyl urea.

Equation:



Apparatus:

Fig. A



2. Adams, Roger, et. al., Organic Syntheses, Vol., 29, p. 21.

Fig. B

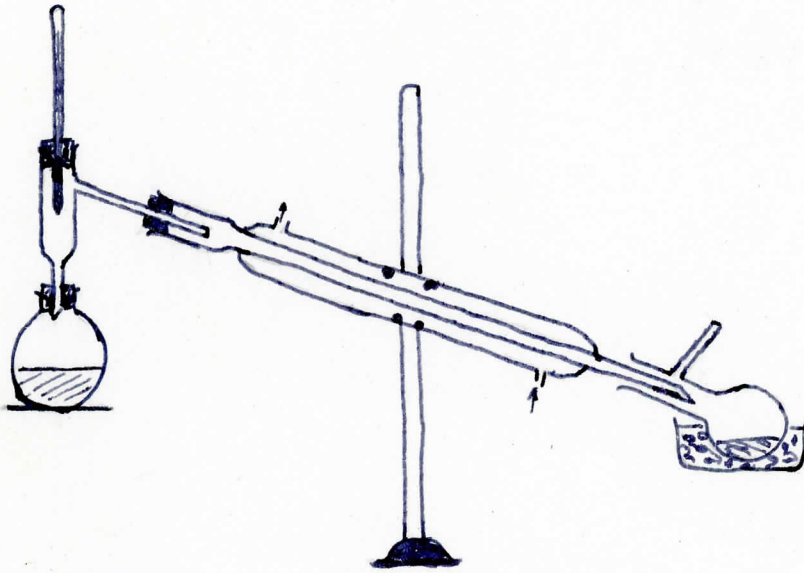
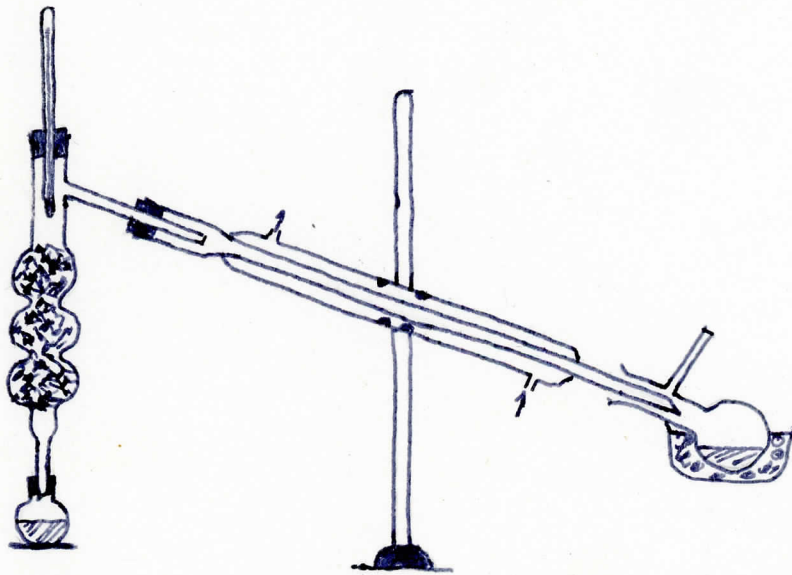


Fig. C



Procedure:

A one liter round bottom flask was charged with 60 grams (1.5 moles) of sodium hydroxide pellets and 75 c.c. of water. After the sodium hydroxide was completely dissolved in the water, 70 grams of tertiary butyl urea and 225 c.c. of ethylene glycol were added.

A reflux apparatus as described in Figure A was set up. The mixture was refluxed gently for four hours. The tertiary butyl urea gradually dissolved and a gelatinous mass of sodium carbonate appeared in the flask. Any ammonia evolved was dissolved in the water contained in the beaker shown.

At the end of four hours, heating was discontinued and the mixture was allowed to cool to room temperature or lower. The reflux apparatus was replaced by the arrangement shown in Figure B, and the contents of the flask were distilled.

The fraction distilling in the temperature range 40° to 60° C. was collected in an ice-cooled receiver to prevent loss of product. The yield of crude amine was 35- 39 grams. The impure product was then dried by allowing 5- 7 grams of sodium hydroxide pellets to remain in contact with it for two hours.

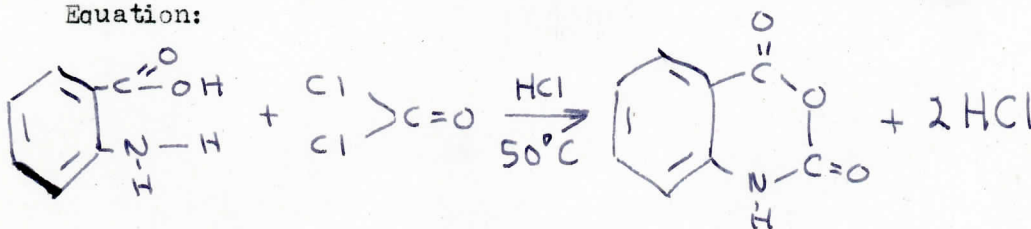
Further purification was accomplished by redistilling the amine from an apparatus similar to that shown in Figure C. The fraction distilling between 44° - 46° C. was collected, again in an ice-cooled receiver. The yield weighed from 31 to 34 grams. The pure product was a colorless liquid having the characteristic

amine odor of dead fish. Tertiary butyl amine has a density of 0.699 (20°C.) and an index of refraction of 1.3800 (20°C.).

Since three molar amine is used in the reaction, the pure amine was diluted to this molarity by adding the required amount of water, 34.5 c.c. of water for every 15.5 c.c. of pure amine.

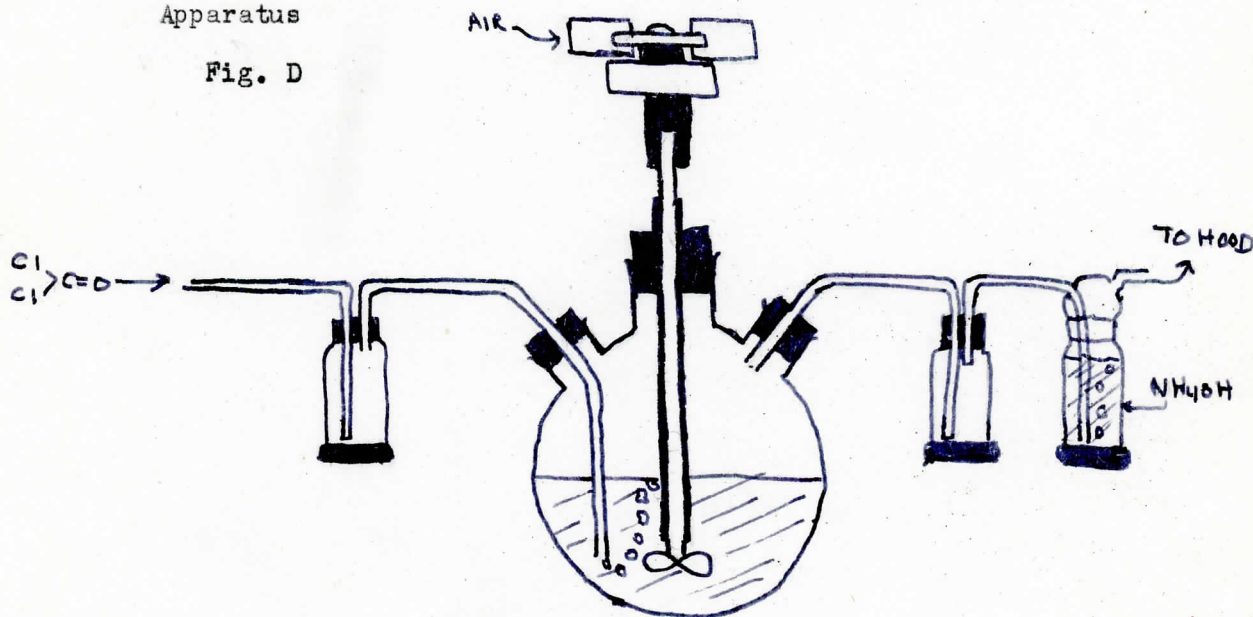
B. The Preparation of Isatoic Anhydride³

Equation:



Apparatus

Fig. D



Procedure:

One mole of anthranilic acid (137 grams) was dissolved in a mixture of 150 grams (125 c.c.) of concentrated hydrochloric acid and one liter of water. The solution was filtered into a

3. Clark, Robert C., "Isatoic Anhydride. I. Reaction With Primary and Secondary Amine and With Some Amides," The Journal of Organic Chemistry, Volume 9, No. 1, January, 1944.

three-liter, three-necked flask fitted with a sealed mechanical stirrer, an inlet tube reaching to the bottom of the flask, and an outlet tube connected to a safety flask, followed by a Drechsel absorber charged with ammonium hydroxide. The mixture was stirred mechanically and phosgene was passed through an empty safety bottle and then into the solution of anthranilic acid at such a rate (about two bubbles per second) that bubbles of gas escaped only slowly at the surface of the liquid (hood). The temperature rose, but was readily maintained near 50°C. by regulation of the rate at which the phosgene was introduced. The rate of absorption of phosgene was found to be increased as the rate of stirring was increased. Separation of isatoic anhydride began soon after the stream of phosgene was started. The process was continued during several (2 to 4) hours or until the absorption of phosgene was much decreased. The flask was disconnected and a stream of air bubbled through its contents to remove the phosgene. The white solid was collected, washed several times with cold water, and dried at 110°C. Yields from a number of runs ranged from 115 grams to 125 grams (71- 77%) of material melting at 240°- 243° C., pure enough for use. Further purification may be effected by crystallizations from 95% ethanol (30 c.c per gram) or from hot dioxane (10 c.c. per gram).

C. Reaction of the Amine with Isatoic Anhydride⁴

The reaction involved the dissolving of a suf-

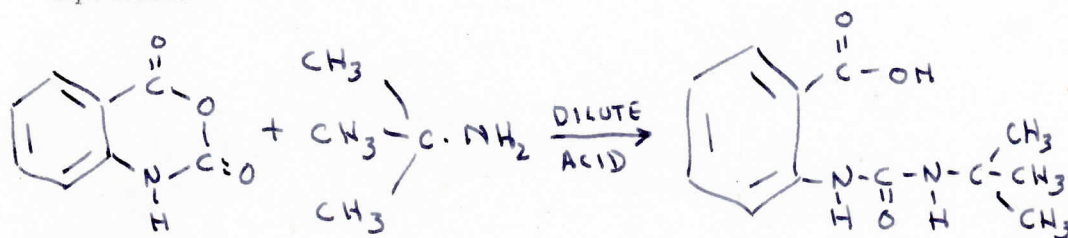
4. Staiger R. P., op. cit., pg. 26-28.

ficient amount of isatoic anhydride in the three molar tertiary butyl amine and the acidifying of the clear solution with cold dilute sulfuric acid.

The reaction or molar ratio is:

$$\frac{0.815 \text{ grams of isatoic anhydride}}{12.5 \text{ c.c. of } 3M \text{ tertiary butyl amine}} = \frac{1 \text{ mole}}{7.5 \text{ moles}}$$

Equation:



Apparatus:

The apparatus required in this step consisted of only a 500 c.c. beaker and two ice baths.

Procedure:

Using the above reaction ratio the appropriate amount of isatoic anhydride was added to the three molar tertiary butyl amine. When the anhydride was completely dissolved, the solution was diluted to four times its volume. Any precipitate was filtered off and the solution was placed in an ice-bath. Cold dilute sulfuric acid was then added slowly and the solution was stirred constantly.

D. Isolation and Purification of ω -Tertiary Butyl Uramido Benzoic Acid

A white precipitate formed when the solution was

acid to indicator. The precipitate was separated by suction filtration. Purification was accomplished by dissolving the product in hot ethyl alcohol and adding a small amount of norite. The filtered solution was then reprecipitated by the slow addition of ice cold water. The precipitate was again isolated by suction filtration. The purified product was a snow-white compound having a melting point of 165°C.

III. Cyclization of the Synthesized Product

A. Procedure

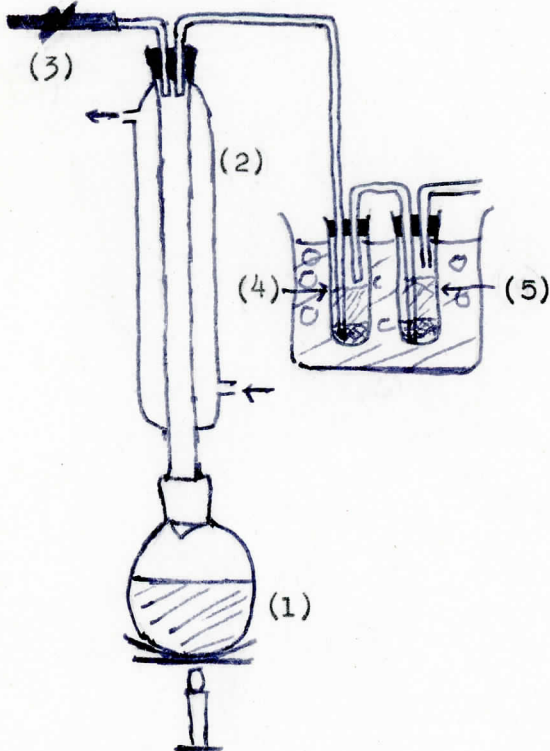
It was noted that a solid and a gas were produced when ω -tertiary butyl uramido benzoic acid was refluxed in dilute sulfuric acid. The composition of the solid was easily proven. Some problems arose in the identification of the gas. The major problem was to produce enough gas to make identification possible. The principle difficulty was the fact that only small amounts of the ω -tertiary butyl uramido benzoic acid could be prepared. The second problem of identifying this gas had to be looked at in another light. In deciding what reagent to use in converting the gas into an identifiable derivative, some assumption had to be made concerning the nature of this gas. After consideration of the possibilities provided by the reaction in question, it was decided that the gas was probably an unsaturated hydrocarbon. In view of the fact that relatively heavy, non-volatile liquids are

produced when bromine is used to saturate the double bond in gaseous alkenes,⁵ the method used here was to pass the gas into a bromine-water mixture.

B. Apparatus

For reasons already noted, the apparatus had to be kept as small as possible. It consisted of a 200 c.c. standard tapered round bottom flask (1) fitted with a reflux condenser (2). In the top of the condenser, a two holed rubber

Fig. E



stopper was placed containing two pieces of glass tubing which protruded slightly into the condenser. One of the two pieces was short and was provided with a piece of rubber tubing which could be clamped tightly shut. This acted as a pressure equalizer (3) to prevent the backing up of the contents of the reaction tubes when the flame was removed from beneath the flask. The other piece of tubing led to the

bottom of the first reaction tube (4). A second reaction tube (5)

5. Wertheim, E., Textbook of Organic Chemistry, New York, The Blakiston Company, 1951, p. 62.

was connected to the first and a final piece of tubing served as an outlet for the system. The reaction tubes were small test tubes. An ice bath (6) surrounded the reaction tubes to avoid loss of product.

C. Treatment

About four grams of ω -tertiary butyl uramido benzoic acid were placed in the round bottom flask. Approximately 100 c.c. of 20% sulfuric acid were added. The reaction tubes were charged by the addition of 2c.c. of bromine and 10 c.c. of water to each. The apparatus was then arranged as previously described, and the pressure valve was closed.

The mixture was refluxed about six hours. The reaction could be assumed completed when the solid present in the flask became dispersed throughout the mixture rather than remaining on the surface of the dilute sulfuric acid. Further, upon cooling, the solid in the flask had a crystalline form different from the original ω -tertiary butyl uramido benzoic acid.

D. Isolation, Purification, and Identification

1. Solid in the Flask

The contents of the flask were cooled and the crystalline solid present was separated by suction filtration. The substance was purified by repeated recrystallizations from an alcohol-water mixture. The dried, purified solid had a melting point of 353°C . The melting point of benzoylene urea is 353°C .

More conclusive proof was obtained when infra-red spectrographs of portions of the compound prepared in the above manner and that of separately prepared benzoylene urea were found to be identical.

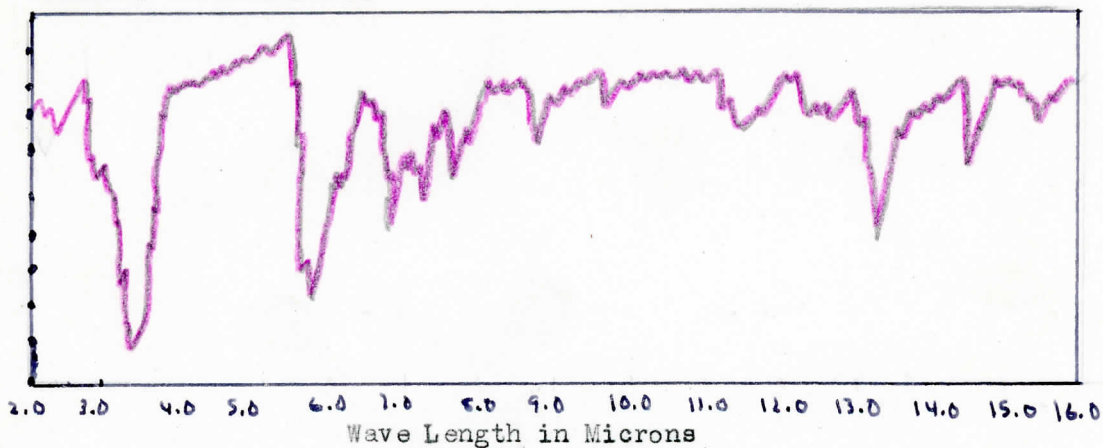


Figure F. Infra-red Spectrograph of Benzoylene Urea

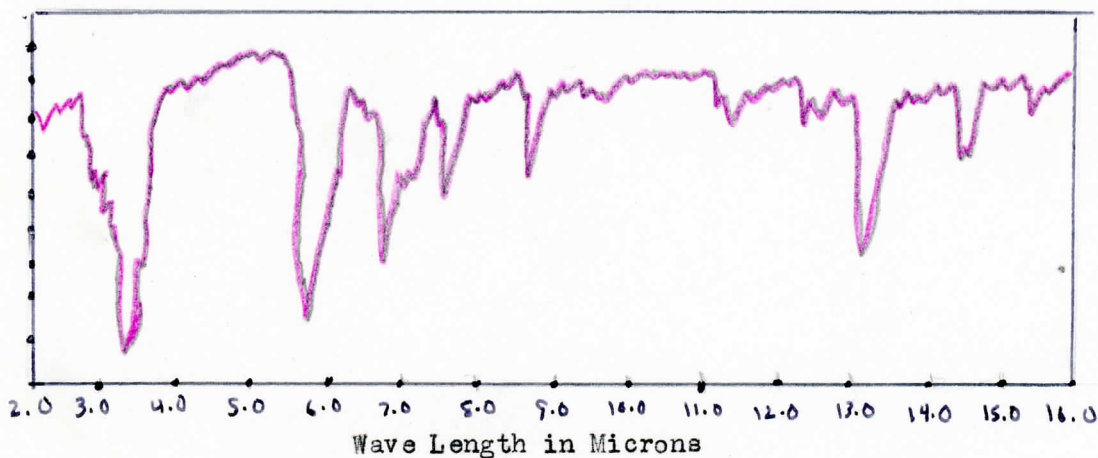


Figure G. Infra-red Spectrograph of the Solid in the Flask

The graphs illustrated in figure F and G of benzoylene

urea and the solid in the flask were determined with a Baird Associates Double Beam Infra-red Spectrophotometer using a mull of the sample in Nujol.

2. Liquid-Derivative in the Reaction Tubes

After the reaction had been carried to completion, the unreacted bromine in the reaction tubes was reduced by the addition of a saturated sodium bisulfite solution. The solution was then neutralized by the addition of sodium hydroxide. The heavy liquid in the bottom of the reaction tubes was the compound to be identified.

Because of the small amount of product (about 0.5 c.c.), purification was difficult. The liquid was dried by placing it in a small test tube containing a chip of anhydrous calcium chloride. Repeated dryings were necessary.

A micro-distillation was performed on the dried liquid. The redistilled compound was colorless and fairly dense.

Three micro boiling points were taken on both the purified liquid and a control (benzene). The average reading for benzene was 81° C. or one degree greater than the recorded boiling point. The average reading for the unknown compound was 151° C. or two degrees greater than the recorded boiling point of isobutylene dibromide (B. P. 149° C.).

The refractive index of the remainder of the purified liquid was 1.5110 (25° C.). The refractive index of isobutylene dibromide is 1.5119 (20° C.).

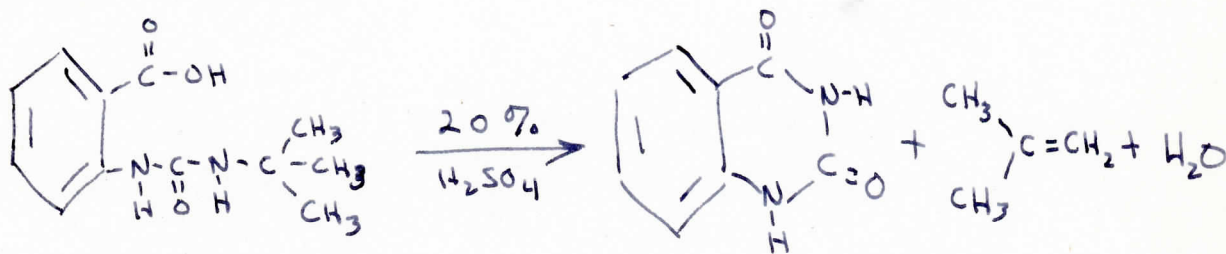
IV. Conclusions

From the foregoing results, the following conclusions have been reached:

(1) that the solid product of the reaction in question was benzoylene urea. Comparison of the melting-points and infrared spectrographs of the product in the flask and benzoylene urea show that these two compounds are identical.

(2) that the liquid derivative produced in the reaction tubes was isobutylene dibromide and that therefore the gas evolved in the reaction in question was isobutylene. To support this conclusion, the similarity of the physical constants of the unknown liquid and those of isobutylene dibromide is cited. No other possible bromide derivative has physical characteristics which compare favorably with these constants.

In view of these conclusions, ω -tertiary butyl uramido benzoic acid, when refluxed with dilute sulfuric acid, reacts in the following manner:



Instead of ring closure occurring to yield β -tertiary butyl benzoylene urea, isobutylene is cleaved and ring closure occurs with the formation of unsubstituted benzoylene urea.