THE PREPARATION OF 2 HEPTANOL AND INVESTIGATIONS INTO METHODS FOR THE PREPARATION OF ALPHA NAPHTHYLISOCYANATE AS PRELIMINARY SYNTHESES FOR THE DETERMINATION OF THE PROPERTIES OF THE URETHANES OF FOUR ISOMERIC HEPTYL ALCOHOLS

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Introduction

For a great many years certain reagents have been investigated which will convert alcohols into solid substances. The melting points of these solid substances were then determined and as a consequence the alcohols under consideration could be detected. There have been several reagents proposed, the most satisfactory of which have been phenylisocyanate and alpha naphthylisocyanate, up to the present time. Particularly with the phenylisocyanate it has been noted that with certain of the higher alcohols, the greater the number of carbon atoms there was in the chain, the lower the melting point of the solid derivative obtained, so that when it was attempted to secure solid derivatives of certain of these six and seven carbon atom alcohols it was found impossible to get a substance which was a solid at ordinary temperatures, and which would serve as a convenient means for the detection of the alcohols in question. Only very recently has alpha naphthylisocyanate been proposed and it seems to be a very promising reagent judging from the small amount of work which has been done and from the success that has been attained.[1]

(1)"Alpha Naphthylisocyanate as a reagent for alcohols", V.T.Bickel and H.E.French, J.A.C.S., 48, 1111, Apr.(1926).

In connection with another research problem in the laboratory, it was desired to detect four heptyl alcohols, namely, 1 heptanol, 2 heptanol, 3 heptanol, and 4 heptanol. There were sufficient quantities of 3 heptanol and 4 heptanol accessible, ten grams of 1 heptanol were purchased from the Eastman Kodak Company, and it was found necessary to synthesize 2 heptanol as it could not be purchased at any of the leading dealers in organic chemicals. Alpha naphthylisocyanate is sold by the Eastman Company but the price is very high and as a sufficient quantity for this research would have cost quite a sum it was decided to try to find a satisfactory method for its preparation.

After the reagent and the alcohol had been prepared it was decided to convert the alcohols into the urethanes, purify them by recrystallization in ligroin, making a melting point determination of these urethanes, and finally subjecting each urethane to a nitrogen determination by the Kjeldahl method and comparing the nitrogen content found to that calculated from the formula of the particular urethane in question.

It was also decided to investigate other alcoholic derivatives if time permitted.

Preparation of 2 Heptanol

For the most convenient preparation of 2 Heptanol it is necessary to prepare normal amyl alcohol, and then from this alcohol to proceed by adding 2 additional carbon atoms, which is comparatively easy.

The price of n-amyl alcohol as quoted by Eastman is $28 per 100 grs., so it hardly seemed feasible to buy it. For this reason it was necessary to synthesize the n-amyl alcohol before proceeding to the addition of the two carbon atoms.

Normal amyl alcohol can be prepared by the reduction ethyl-n-valerate by hydrogen[2] but this means was not suitable because of the scarcity of the compound and the difficulty with which it is made. Organic Syntheses gives a very satisfactory method of preparing n-heptyl alcohol by the use of ethylene oxide.[3] This method was found to be applicable to the synthesis of n-amyl alcohol also, but no specific directions could be found for this particular synthesis. It was therefore necessary to study the conditions of this reaction and devise a means for obtaining n-amyl alcohol and at the same time obtaining a good yield.

(2)"Organic Chemical Reagents II", Roger Adams, O. Kamm, and C.S.Marvel, University of Illinois Bulletin, 6, pg. 54, October(1911).

(3)"Organic Syntheses", Vol. VI, page 54.

The following equations show the procedure which was followed for the synthesis of the alcohol (2 Heptanol).

(1) $C_3H_7OH + HBr \longrightarrow C_3H_7Br + HOH$ [4]

(2) $C_3H_7Br + Mg \xrightarrow{I_2} C_3H_7MgBr$ [5]

(3) $C_3H_7MgBr + CH_2\text{-}O\text{-}CH_2 \longrightarrow C_3H_7CH_2CH_2OMgBr$

(4) $C_3H_7CH_2CH_2OMgBr \xrightarrow{HOH} C_3H_7CH_2CH_2OH$

(5) $n\text{-}C_5H_{11}OH + HBr \longrightarrow n\text{-}C_5H_{11}Br + HOH$

(6) $n\text{-}C_5H_{11}Br + Mg \xrightarrow{I_2} n\text{-}C_5H_{11}MgBr$

(7) $n\text{-}C_5H_{11}MgBr + CH_3CHO \longrightarrow C_5H_{11}CH(OMgBr)CH_3$

(8) $C_5H_{11}CH(OMgBr)CH_3 \xrightarrow{H_2O} n\text{-}C_5H_{11}CHOHCH_3$

The reactions as represented by equations 1 and 2 are well worked out in the references given and no difficulty was experienced in obtaining good yields. However, the conditions for reactions represented by equations 3 and 4 had to be worked out as there was no data available which specifically furnished any information.

(4)"Organic Syntheses, Vol. I," page 6.

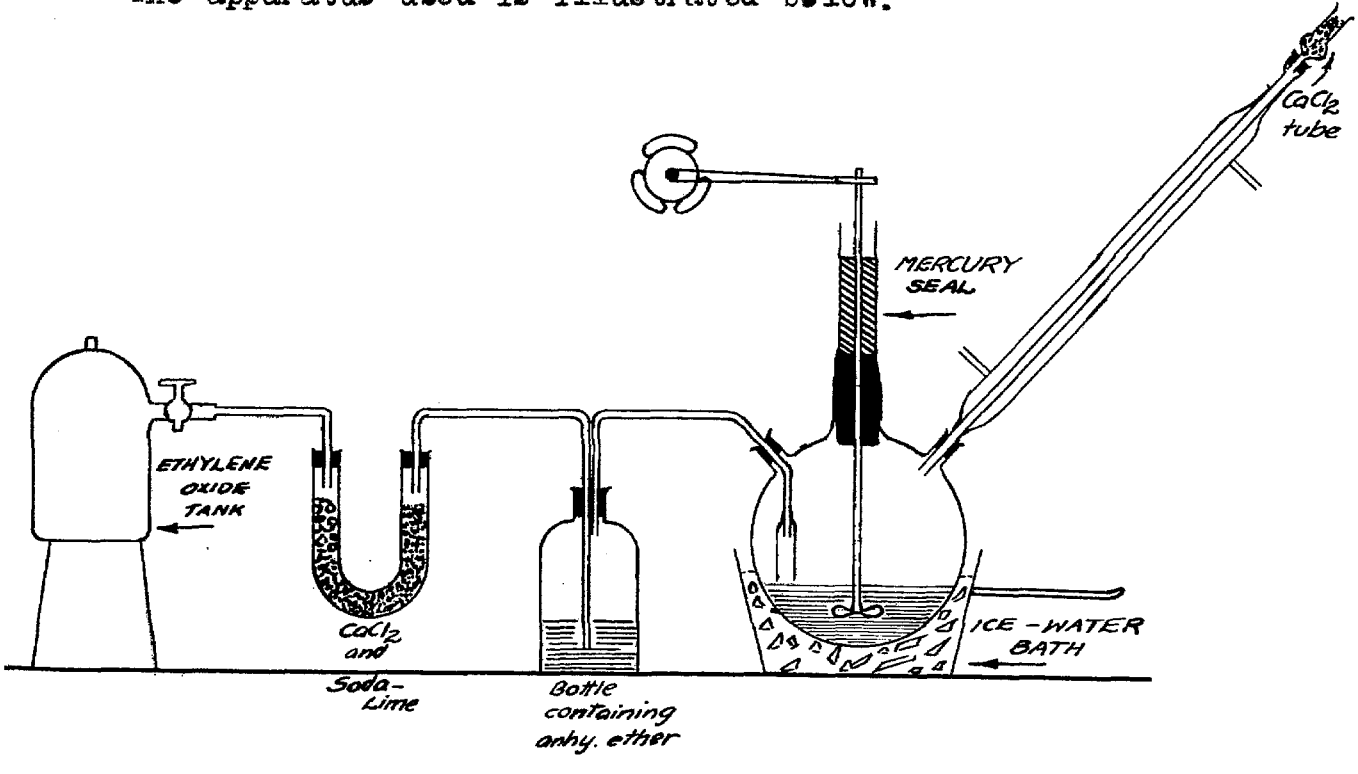
(5)"Organic Syntheses, Vol. VI ", page 54. (Conditions for successfully carrying out the Grignard reaction.)

The following scheme was worked out for the preparation of n-amyl alcohol as represented by reaction 3.

Substances used: n-propyl bromide.....1.77 mols
Magnesium filings.....1.89 mols
Iodine.....small crystal
Ethylene oxide.....3.00 mols
Anhydrous ethyl ether..880 cu.cm.

In a previous trial it was attempted to make ethylene oxide by the action of a concentrated aqueous solution of NaOH on ethylene chlorhydrin but the yield of the gas was very low and its purity was questionable. A small cylinder of dry ethylene oxide was obtained from the Carbide and Carbon Chemicals Corp., New York, N.Y. at reasonable cost and this was employed in the synthesis to be described.

The apparatus used is illustrated below:



The required amount of magnesium filings were placed in the reaction flask along with a small crystal of iodine and 50 cc of a solution containing propyl bromide and anhydrous ethyl ether in the proportion of 3 moles of PrBr to 1 liter ether. After the reaction had started, noted by the refluxing of the ether, 220 cc more of anhydrous ether was added to the reaction flask and the remaining solution of the PrBr in ether was added in a small but steady stream until all had been added, the total time of addition being approximately two hours. After the completion of this stage in the process, ethylene oxide was added to the Grignard reagent in the reaction flask at the rate of about 500 cc per minute (standard conditions). It was not found advisable to allow the Grignard reagent to stand for any length of time before it was utilized as it crystallized out and the yield of n-amyl alcohol subsequently obtained was quite markedly lowered.

The ethylene oxide was then passed in at a constant rate until twice the theoretical had been added, the ether used as a wash bottle which contained some ethylene oxide dissolved was added to the reaction flask, and the mixture was then gently refluxed for 1 hour. The condensor was then set for downward distillation and about 300 cc of the ether was distilled off. As the ether distilled off, 330 cc of thiophene free benzene was added through a separatory funnel, the rate of add-

ition being controlled by the rate of distillation of the ether. When the temperature of the distilling vapors reached 60° C the condensor was again arranged for reflux.

The rearrangement reaction of the ethylene oxide addition product began at this point and great care was necessary to keep the reaction under control because if it becomes violent much of the product is lost and the yield is lowered about 50%. The stirring was kept up as long as the viscosity of the mixture permitted. It seemed quite important at this point to control the reaction, but not to stop it completely.[6] The refluxing of this benzene mixture was carried out for 1 hour when the rearrangement was apparently complete. The reaction flask contained a very viscous, gelatinous mass of light gray color possessing a strong odor of amyl alcohol.

After the mixture had cooled, a liter of ice water was slowly added, the reaction taking place represented by equation (4). This was an exothermic reaction and it was necessary to surround the reaction flask with an ice-water mixture. A heavy precipitate of $Mg(OH)_2$ resulted which was later decomposed by the addition of 6 N. sulphuric acid. If this precipitate was not dissolved it would occlude much of the product and the yield would be materially lowered.

(6)"Preparation of Iso-amyl alcohol" D.C. Maddy , private communication, University of Illinois.

The mixture in the reaction flask was then subjected to steam distillation, it being necessary to distill over three or four liters of liquid until the the distillate showed only one phase as it condensed. The oily layer containing the benzene and the n-amyl alcohol was separated from the aqueous phase, and the former was refluxed on a steam bath for 1 hour with 300 cc of a 20% NaOH solution in order to remove any n-propyl alcohol which might be present as an impurity.

This mixture was then steam distilled and this time it was necessary to collect 3 liters before the condensate showed only 1 phase being distilled over. The oily layer was then separated from the aqueous phase and the former dried with anhydrous $CaCl_2$ for 12 hours. The $CaCl_2$ was then filtered out and the liquid was fractionated using a Hempel Column which was approximately 18in high. The distillate which came over below 85° C was benzene and water. The residue, after the distilling vapors had reached 85° C, was transferred to an ordinary distilling flask and the temperature was gently raised. At 137° C the distillate was collected until the temperature had reached 139° C, and this was retained as n-amyl alcohol, boiling point 138° C. Yield about 47% of the theoretical.

The n-amyl alcohol was then converted into the bromide by the use of HBr, sp. gr. 1.49.[7]

(7)"The Base-forming Property of Carbon", J.F.Norris, American Chemical Journal, 38, 627, July-Dec. (1907).

The n-amyl alcohol was treated with three times the theoretical quantity of HBr. The reaction was carried out with constant stirring, the HBr being admitted drop by drop and the temperature being kept approximately 65° C. A good yield of n-amyl bromide was obtained by this method.

The n-amyl bromide was then treated with Magnesium filings and the corresponding Grignard reagent prepared. This was done precisely as previously described under the amyl alcohol preparation.

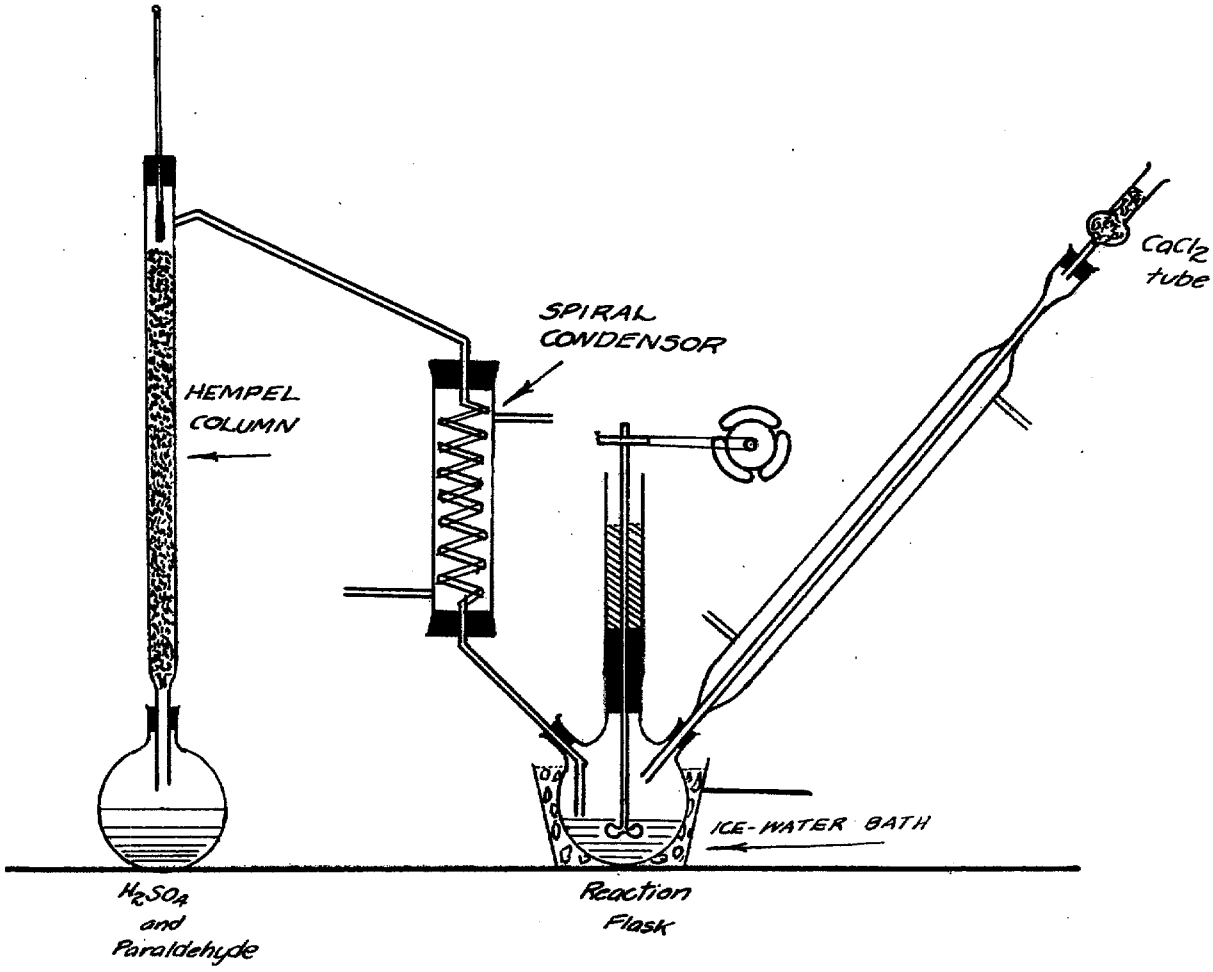
It was then necessary to devise a means of producing methyl aldehyde(acetaldehyde) by the depolymerization of paraldehyde. This was accomplished by treating 212.2 grams of paraldehyde with 10 cc 20% solution H_2SO_4.[8] The CH_3CHO was then led into the reaction flask containing the Grignard reagent. The flask was cooled by surrounding it with an ice-water bath.

The reaction of the acetaldehyde with the Grignard reagent proceeded with violence accompanied by a hissing sound and it was important to control the rate of admission of the acetaldehyde for this reason. No rearrangement reaction was necessary in this addition, so after the addition reaction had finished, an ice-water mixture was added to decompose the addition product, whereupon a heavy precipitate of $Mg(OH)_2$ came down. This was then dissolved with 6 N H_2SO_4. Two hundred cubic centimeters

(8)"On Aldol, Pantaerythrose and the action of Copper Acetate on the Hexoses", A.F.McLeod, American Chemical Journal, Vol. 37, 27, (1907).

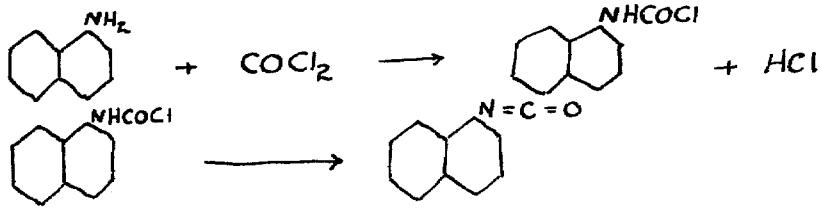
of benzene was then added in order to dissolve all of the 2 heptanol. The upper oily layer was then separated from the aqueous phase, dried with anhydrous $CaCl_2$ for 12 hours, and finally subjected to distillation the fraction boiling between 158° and 160° C being saved as the pure product. 2 heptanol boils at 159° C. 10 grams were obtained.

The apparatus used for this final proceedure is illustrated below.



Investigations into methods for the preparation of alpha naphthylisocyanate.

The most satisfactory method for preparing an isocyanate is by the use of phosgene, a gas at ordinary temperatures having a boiling point of 8° C. The reaction takes place as illustrated by the following equations.



It was therefore necessary to obtain phosgene or devise a satisfactory laboratory means of preparing it. Savell, Sayre and Company of Niagara Falls, N.Y., commercial fabricators of phosgene, were only able to supply the gas in 150 pound tanks as any smaller quantity would not meet shipping specifications for the product. They submitted, however, a laboratory method for the preparation of phosgene from CCl_4 and 45% fuming sulphuric acid. Consequently this method was investigated, and proved satisfactory. With a few revisions the proceedure is as follows.

The reaction runs quantitatively as follows;

$$H_2SO_4;SO_3 + CCl_4 \longrightarrow COCl_2 + 2ClSO_3H$$

Chlorsulphonic acid is also formed.

The acid, as indicated by the equation, should be 45% "free" SO_3. This acid is solid at ordinary room temperatures, and is not a regular article of commerce, but

may be made by mixing commercial 60% oleum with 26%. It is very important that the acid be as close as possible to the given strength.

A portion of CCl_4 is weighed out and placed in a fairly good size round-bottom, three-necked flask to which are connected a 40in reflux condensor, a 150° C thermometer, and a dropping funnel the top of which is fitted with a $CaCl_2$ tube. From the condensor the gas is conducted to 1 liter flasks placed in series containing benzene or toluene and the whole flask immersed in an ice-salt-water bath. This is to dissolve the phosgene as it comes over. The number of flasks in series depends on the rate and quantity of gas that is to be adsorbed. The temperature of the CCl_4 is raised to reflux, the temperature being determined by the thermometer which is under the surface of the liquid. A very small portion of the oleum is added cautiously, and a vigorous evolution of gas follows, although sometimes the evolution of the gas is slow to start. Great care should be taken to avoid a sudden and violent evolution. This suddenness is only observed the first time as after a body of chlorsulphonic acid has formed the reaction is always smooth, so for this reason a little of the chlorsulphonic acid is saved after a run with which to start the next run.

Until the reaction becomes smooth, the temperature should be allowed to drop, and heat is applied cautiously. After this the temperature should be brought back close to 80° C and the oleum added in a small stream thru the dropping funnel. A separatory funnel was used which was provided with a heating element of nickel-chrome wire in order to hold the temperature approximately 50° C at which temperatute the oleum is a liquid. The speed of the reaction is regulated by the rate of addition of the acid. After oleum has been added equivalent to CCl_4, another charge of CCl_4 is inserted, and the precess continued. This addition should be done with great care as quite a fluxuation of pressure within the flask takes place.

During the addition of oleum, the temperature should be maintained at 80° C. This is important. When no more reflux of CCl_4 takes place, even at 85° C, and the theory of oleum has been added, the charge of CCl_4 is repeated, and the proceedure carried out as before.

The gas evolved should be thoroughly refluxed to remove all possible CCl_4 vapors. The gas can not be washed through water as the phosgene is hydrolyzed. Impurities in the CCl_4 are said to result in the possible presence in the gas of Cl_2, CS_2, COS, and SO_2.

The concentration of the fuming sulphuric acid is

determined most accurately by a direct titration method. A small sample if the fuming acid is transferred to a small weighing bottle, the top tightly fitted on, and the sample weighed. A large weighing bottle is then secured and a small amount of distilled water placed in the bottom. The small weighing bottle is then inserted in this water, the top of the small weighing bottle removed carefully, and the top of the large weighing bottle inserted immediately. This is allowed to stand for several hours during which time the fuming vapors collect in the distilled water and with careful shaking the two liquid portions can be shaken and mixed without excessive evolution of heat. The liquid sample is then diluted with more distilled water and titrated with standard NaOH solution using phenolphthalein as the indicator.

Chlorsulphonic acid may be removed from the flask if it gets too full, and the generation continued indefinitely. It is necessary to handle chlorsulphonic acid with great care, as it reacts with water with the utmost violence. At the same time it gives off a little dissolved phosgene, so that disposing of it is an unpleasant task.

The alpha naphthylamine which was used was commercial grade possessing a dark red coloration due to contact with the air. This substance was purified by

distilling the substance under reduced pressure. A white solid was obtained which was quite pure alpha naphthylamine. This was dissolved immediately in benzene.

In the first preparation, the phosgene was led directly into flask containg the benzene solution of alpha naphthylamine[9]. The reaction expected has been previously given. However, a solid reddish-brown substance came down which was insoluble in benzene, water, but which turned green in the presence of conc. H_2SO_4. This residue was treated with aliquot parts of benzene in order to extract any alpha naphthylisocyanate which was present as it is soluble in this liquid. This benzene solution was then distilled under reduced pressure, but there was no trace of any alpha naphthylisocyanate which is an oil of straw-yellow color, boiling at 269° C (760 mm), and is a liquid at ordinary temperatures. It was then assumed that it would be necessary to have phosgene in solution in excess at all times during the reaction with the alpha naphthylisocyanate.

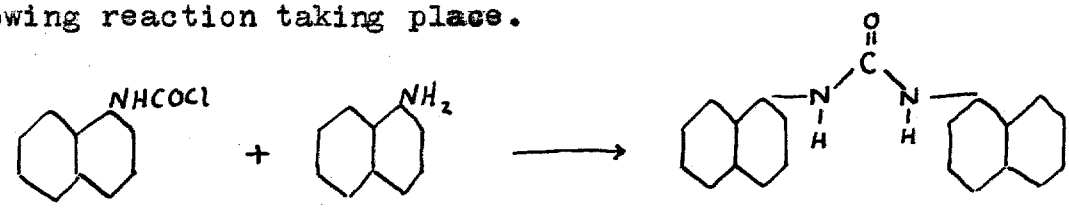
A new preparation was then commenced. This time the phosgene was not led directly into the the benzene solution of alpha naphthylamine, but was collected in a solution of benzene. The solution of benzene was cooled to such a temperarure that the phosgene was liquified, about 0° C. The benzene solution of the phosgene and the benzene solution of the alpha naphthylamine were then mixed. Heat was immediately evolved and it was necessary to cool the reaction flasks with an ice-water

mixture. However, the same dark-reddish-brown precipitate came down. This precipitate was washed thoroughly with benzene, this was united with the liquid remaining in the reaction flasks, and the combined solution subjected to distillation. Again no trace except possibly a few drops of alpha naphthylisocyanate was observed although during the reaction phosgene was present in excess. The extracted solutions all possessed the odor of phosgene. The mixed solutions in benzene of phosgene and alpha naphthylamine were allowed to stand in contact with each other for 3 days in order to insure that a reaction would take place if time was the important controlling factor. During the fore part of the distillation some phosgene was evolved. This was collected in some pure ethyl alcohol, converting the same to ethyl chlorcarbonate, evolving a considerable amount of heat. The ethyl chlorcarbonate was recovered by fractionation.

If time had permitted, a new system would have been tried, namely, that of converting the phosgene into ethyl chlorcarbonate, treating alpha naphthylamine with this substance forming the urethane, and then subjecting the urethane to the action of P_2O_5, whereupon alpha naphthylisocyanate would have resulted. This seemed to be the most promising method of preparation in light of

(9)"Sur les carbimides aromatiques", M. Henri Vittenet, Bulletin de la Societe Chimique, XXI, 957, (1899).

of the previous investigations.[10] The residue remaining after the reaction of the two benzene solutions was exactly similar to that obtained in the first run although phosgene was present in excess, but time prevented an investigation to establish its identity. It was possibly dinaphthyl urea which could have formed due to following reaction taking place.



(10) "Alpha and beta naphthyl urethanes", Neuberg and Kansky, Biochem. Zeitschrift, 20, 445, (1909).

Although this research problem seemed at the start perfectly straight-forward a great many obstacles were encountered particularly in the preparations which were carried out. Several of these preparations had to be completly worked out. This work has been done with the aim in view to solve all of these details as the work progressed and to fully understand the reasons underlying all steps.

The work has progressed to a stage where it can very easily be continued, the only really difficult task being to prepare alpha naphthylisocyanate, and the best method of attack for this work has been mentioned in the foregoing pages.

Acknowledgment.

The author wishes to express to Professor H.J. Lucas his sincere gratitude for his constant advice and help throughout the course of this work.

Summary

Alpha naphthylisocyanate seems to be the most promising reagent for the detection of alcohols at the present time.

2 heptanol was prepared, and in the course of this preparation, a good method was devised for the preparation of n-amyl alcohol.

A method was devised for the laboratory preparation of phosgene.

It was discovered that the reaction of a benzene solution of alpha naphthylamine and a benzene solution of phosgene will not react to form alpha naphthylisocyanate as the literature describes.[11]

(11) "Preparation of alpha naphthylisocyanate", Die Methoden der organischen Chemie, Besonderer Teil, Abt. 2, pg. 750.