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The synthesis of phenyl carbamate (from urea, phenol, and a Lewis acid)

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THE SYNTHESIS OF PHENYL CARBAMATE
(from Urea, Phenol, and a Lewis Acid)

by

Michael W. Barrett

* * * * *

Submitted in partial fulfillment
of the requirements for
Honors in the Department of Chemistry

UNION COLLEGE

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ABSTRACT

BARRETT, MICHAEL The Synthesis of Phenyl Carbamate from Urea, Phenol, and a Lewis Acid.
Department of Chemistry, June 1986.

The synthesis of phenyl carbamate from urea, phenol, and a Lewis acid was attempted with varied results being observed. The proposed reaction mechanism involves an Acyl-2 type reaction with a nucleophilic attack on urea by phenol. The Lewis acid is present to add carbocation character to the urea and to further complex with by-products, thus driving the reaction to completion.

The solvents utilized were isopropyl alcohol, dichloromethane, and tetrahydrofuran. The reaction parameters were varied in an effort to successfully run a reaction which would follow the proposed reaction mechanism.

Phenyl carbamate was not isolated and what was observed of the reactions did not appear to follow the proposed mechanism. A white crystalline product was isolated and found to have both amide and aromatic character, but its identity remains unknown.

ACKNOWLEDGEMENT

I would like to thank
Dr. John R. Sowa
for the assistance and guidance
which made this project possible.

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BACKGROUND

The purpose of this research project is to examine the synthesis of phenyl carbamate (the phenyl ester of carbamic acid) utilizing a technique which involves the reacting together of phenol, urea and a Lewis acid in an appropriate solvent. The major goals of this project were to develop a consistent technique for running this reaction system, to examine the system as the reaction proceeds in an effort to better understand the reaction's mechanism, and finally, to maximize the reaction's utility by varying the reaction parameters (i.e. solvent, temperature, molar ratios, Lewis acid catalysts) in such a way as to give the greatest yields and the least difficulty in attaining these yields.

Carbamates, also known as the esters of carbamic acid or urethanes, have long been used as pesticides in agriculture, and also for such things as hypnotics for children and anaesthetics for animals. Carbamates are crystalline solids and are usually soluble in water, alcohol, and benzene. (see Sidgwick's Organic Chemistry of Nitrogen) Phenyl Carbamate is a white, crystalline solid which melts at 149-152°C and is soluble in hot water, ethanol, and diethyl ether. It is slightly soluble in isopropyl alcohol. As far as their

chemical behavior is concerned, carbamates participate in many of the same reactions as amides and esters.

Carbamates have been synthesized using many different reactions and methods, some of which are listed below:

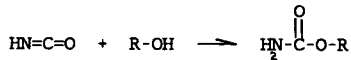
- 1.) by the action of ammonia or an amine on esters of carbonic acid or chloroformic acid.



- 2.) by the interaction of an alcohol and carbamyl chloride.



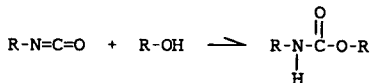
- 3.) from an alcohol and cyanic acid.



- 4.) from urea, by heating with an alcohol.



- 5.) from the reaction of an alcohol with an isocyanate (to give the N-substituted carbamate)

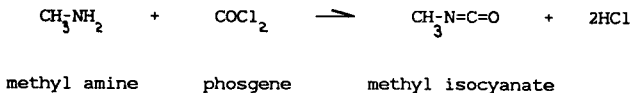


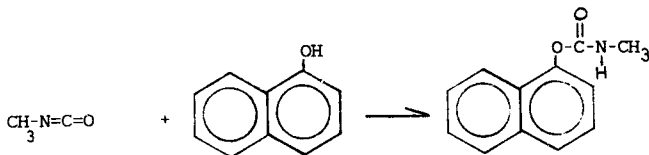
All of the above techniques have been used to prepare carbamates, but not all of them would be useful in the industrial preparation of carbamates. The one reaction that

has become an important industrial procedure for producing carbamates is the reaction of an alcohol with an isocyanate, this to give the N-substituted carbamate. This technique recently came under much criticism because of the dangerous nature of one of its reactants, the isocyanate.

It was methyl isocyanate which escaped from a storage tank at the Union Carbide India Ltd. facility in Bhopal, India, on December 3, 1984. A cloud of methyl isocyanate gas rolled through the city, hugging close to the ground, killing more than 2000 people and permanently injuring up to 10,000 more.

Union Carbide is one of the largest producers of carbamate pesticides and the Union Carbide India Ltd. plant was producing the pesticide with the tradename SEVIN (1-Napthyl-N-methylcarbamate). Union Carbide's production technique requires the use of methyl isocyanate as a precursor. This is a very reactive and toxic chemical, and it is responsible for the tragedy which occurred at Bhopal. The reaction involving methyl isocyanate which is used to produce SEVIN is shown below:





methyl isocyanate

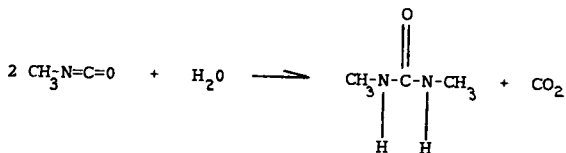
 α -Naphthol

SEVIN

Union Carbide has another reaction system that it can use to prepare SEVIN, and this system does not involve any methyl isocyanate. However, it is an economically sound plan to use the methyl isocyanate route since other companies are more than willing to purchase any spare methyl isocyanate from Union Carbide. What really happened at the Union Carbide India Ltd. plant is still a matter of debate, but a couple of explanations which deal with an understanding of the reactivity of isocyanates have received much support. (see C&EN, February 11, 1985)

Methyl isocyanate will react with water in an exothermic reaction to give 1,3-dimethylurea and carbon dioxide gas. This reaction will add heat to the system and also increase the pressure as the carbon dioxide gas is being produced. Therefore, one theory is that water got into the methyl isocyanate storage tank, starting this exothermic reaction. The reaction got out of control as more heat was generated and soon the pressure in the tank was high enough to blow the gas release valve to vent the gas. The hydrolysis reaction

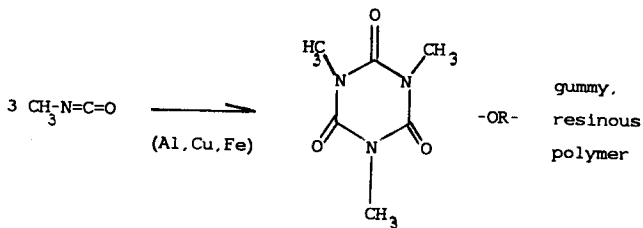
is seen below:



methyl isocyanate

1,3-dimethylurea

Another contamination reaction which could have occurred is the autoreaction of methyl isocyanate which could be catalyzed by a number of contaminants, including various metals and strong bases. This reaction would also be exothermic in nature, and tend to increase the temperature of the system, therefore increasing the pressure in the storage tank. The autoreaction is shown below:

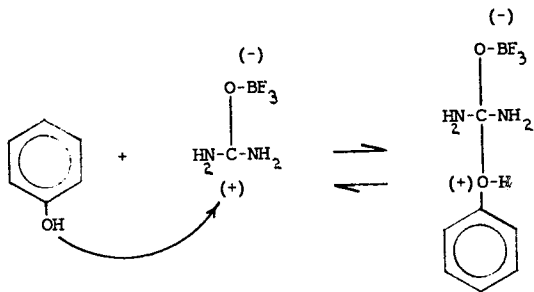
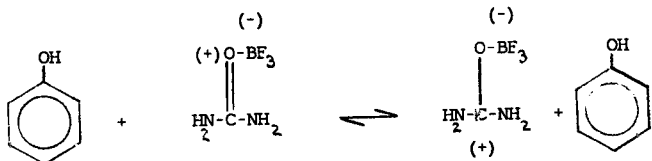
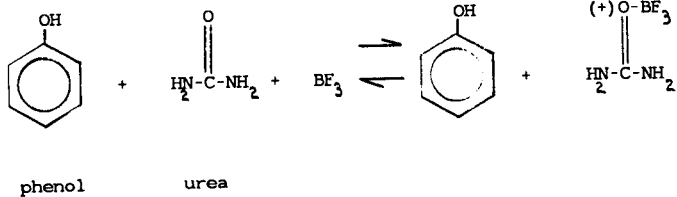


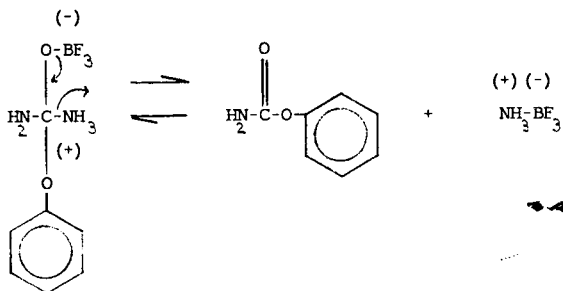
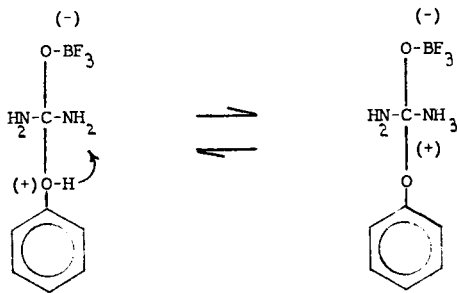
methyl isocyanate

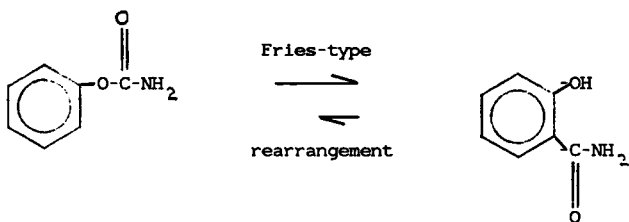
trimethyl isocyanate

The build up in pressure within the storage tank caused a release valve to blow. The gas should have then been neutralized by a vent gas scrubber using caustic soda, but the scrubber failed. The flare tower which would have burned the methyl isocyanate into harmless by-products was down for repairs, and the tank's refrigeration system was not functioning either. All of these malfunctions and safety oversights, coupled with the dangerous nature of methyl isocyanate, made for one of the worst chemical disasters in history.

What we wanted to do with our project was to produce a carbamate, in our case phenyl carbamate, by using very common chemicals as reactants in an open system. The essence of the reaction is the reacting of urea and phenol together in the presence of a Lewis acid. It is hoped that the Lewis acid will give the urea some carbocation characteristics, making it more susceptible to nucleophilic attack by phenol. The Lewis acid should also help by complexing with the released amino group, removing it to help make the reaction run to the right. The proposed reaction mechanism is diagrammed as follows:



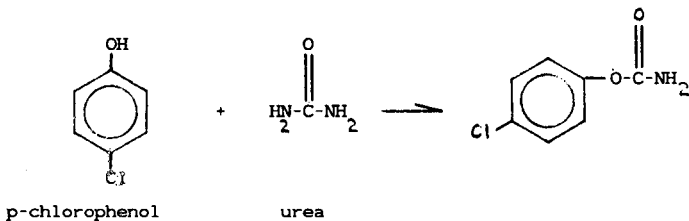




phenyl carbamate

salicylamide

Work of this nature was first carried out by Dr. John R. Sowa in the late Fifties. Reactions were run with p-chlorophenol and urea together without a catalyst, and the carbamate was formed directly.



p-chlorophenol

urea

Reactions were also run in an attempt to study our reaction system (urea, phenol, and a Lewis acid). The reaction would run as the proposed mechanism shows with ammonia boron trifluoride dropping out and the end result being salicylamide (after the Fries-type rearrangement). The yields which were being obtained were about 20% (if measuring the amount of salicylamide produced), with the limiting reagent being phenol. Lewis acid catalysts used included boron trifluoride and zinc chloride.

The result of the previous work showed an interesting reaction system which required further study in order to make the isolation of the carbamate product possible. The problems seemed to be mostly in the work-up of the reactions, since the system seemed to run basically as it had been outlined. Problems needing further study included:

- 1.) the protonation of urea by phenol.
- 2.) the effect of the ammonia boron trifluoride on the other reactants and products as it falls out of the solution.
- 3.) stopping the reaction before the Fries rearrangement occurs.
- 4.) maximizing yields by determining the best order of reagent addition, and using the optimum solvents for reaction and work-up.

It was these problems that we hoped to examine in our research into the proposed reaction mechanism.

EXPERIMENTAL

The attempts to produce the desired product, phenyl carbamate, were not limited to Lewis acid catalyzed reactions. Some early work was done in an effort to react phenol directly with urea, the intention being to produce phenyl carbamate which could then be analyzed and used to devise methods of detection. The first of these experiments involved simply heating different molar ratios of phenol and urea together and looking for some sort of reaction.

The first run consisted of combining 0.16 moles of phenol (15.1 g) directly with 0.08 moles of urea (4.8 g) in a large test tube. This tube was then heated to 120-130°C (the temperature did approach 160°C at one point). At these temperatures, all of the reactants had liquified, giving a clear, red-orange solution. The temperature was maintained at about 130°C for four hours, at which point the heat was turned off and the tube allowed to cool. During the four hour heating period, a wet piece of red litmus held over the mouth of the tube would turn blue, indicating the liberation of a basic gas.

By the following day, the reaction mixture had cooled and solidified. It was then extracted with ether using the Soxhlet extractor, leaving a white, crystalline solid with a

melting point of 132°C , this being urea. The ether was then extracted with five percent sodium hydroxide in an attempt to remove any phenol that was present. However, TLC plates run of the remaining ether solution after extraction with the 5% NaOH only showed the presence of phenol. After the TLC plates were run, the ether was distilled off under a vacuum. What was left was a dark, reddish liquid with a very strong phenolic odor. No crystals of any kind were seen to have formed.

Another experiment that was carried out in an attempt to produce phenyl carbamate was the reaction of urea with phenol in dimethyl sulfoxide. A reaction was attempted using 0.017 moles of urea (1.0 g) and 0.016 moles of phenol (1.5 g), along with enough DMSO to totally dissolve both solids, in a large test tube. This reaction mixture was heated to about 65°C and monitored for the next six days. It was monitored using the HPLC system, looking for new peaks that would indicate the presence of products from a reaction taking place. Although new peaks began appearing in the HPLC data, none were showing up in the position where phenyl carbamate would ordinarily be found.

A second attempt at this reaction was then carried out, increasing the temperature to about 120°C for a long period of time (about five to six days total). One of the samples tested did show a small peak in the area where phenyl carbamate would normally be found, but the small peak soon

disappeared. In order to test the stability of phenyl carbamate in hot DMSO, a small test was set up. In the test, 0.20 g of phenyl carbamate was dissolved in 4.0 mL of DMSO. This solution was then heated to a temperature of 120-160°C. As time passed, the phenyl carbamate peak on the HPLC data disappeared and a peak began to show in the position which is usually occupied by phenol. This would seem to indicate that the phenyl carbamate is not stable in hot DMSO so that if it was being formed in the reaction, it may be rearranging almost immediately.

The attempts at producing phenyl carbamate for analytical uses included a try at a synthesis technique which was devised by Bernard Loev and Minerva F. Kormendy (see *Journal of Organic Chemistry*, **28**, 3421, (1963)). Their synthesis involved the reaction of sodium cyanate, trifluoroacetic acid, and the appropriate alcohol to produce the desired carbamate. Many attempts were made at producing phenyl carbamate in this manner but none were successful. The method did work for t-butyl carbamate, but not for phenyl carbamate.

The first Lewis acid to be utilized in the examination of the proposed mechanism was zinc chloride. It was reacted with phenol and urea in two different solvents, isopropyl alcohol and tetrahydrofuran. The procedure used for these different solvents was basically the same, but all changes

will be noted.

Isopropyl alcohol was the solvent used in the first reactions catalyzed by zinc chloride. The isopropyl alcohol was distilled before its use, and the zinc chloride was taken from the shelf (it was not dried in a dessicator). The reaction was carried out by combining 0.5 moles of urea (30 g) with 0.5 moles of phenol in about 250-350 mL of isopropyl alcohol in a 500-mL, 3-necked, round-bottomed flask. This mixture was then stirred, using an electric stirrer, for about five minutes. The phenol went into solution but the urea did not. Instead, it remained a swirling, white cloud in the reaction flask. The zinc chloride was then added slowly to the flask, with a total of 0.1 moles (13.6 g) being added over the next hour. Addition of the zinc chloride caused the mixture to change from a white to a gray color, but the urea still did not dissolve. The reaction mixture was then heated to about 70°C, which caused the urea to go into solution, and the solution to take on a reddish-orange color. The solution was then heated and stirred for two and a half hours, at which point the apparatus was shut off and the solution allowed to cool overnight.

By the following day, a large amount of white solid with a melting point in the range of 40-60°C had fallen out of solution. However, it all went back into the solution when the heat was again applied along with the stirring. The solution was then heated to about 70°C and stirred for four

to five hours, but no obvious reaction could be seen to take place. Later, about six hours after the apparatus had again been shut down, examination of the reaction flask showed the formation of clumps of needle-like, clear crystals. These crystals were rather pink in color and melted from 120-144°C. An NMR of these crystals was taken and it did show a very small amount of aromatic character. However, its melting point was well below that of phenyl carbamate and its NMR did not show similar peaks.

As part of a follow-up analysis as to the results of the reaction, a 25 mL sample of the reaction solution had its isopropyl alcohol distilled off. This left a reddish-brown solid in the distillation flask. This solid was then extracted with ether in a Soxhlet extractor. A white solid remained, with a melting point of 115-120°C. This solid was most likely unreacted urea. The ether extract was then distilled in an attempt to isolate some sort of reaction product but the result was only a reddish-brown liquid. This liquid had a phenolic odor and TLC plates run versus phenol showed no reason to believe it to be anything else but phenol.

Another attempt at reacting phenol and urea together with zinc chloride in isopropyl alcohol was made, with some changes in the mole ratios and the procedure. In this reaction, 0.038 moles of urea (2.3 g) and 0.038 moles of phenol (3.6 g) were combined in about 30 mL of isopropyl alcohol in a 50-mL, 3-necked, round-bottomed flask. The

flask was fitted with a reflux tube and the solution was stirred by a magnetic stir bar. The reaction mixture was stirred and heated to about 70°C, at which point the urea went into solution. The solution at this point was an orange-brown color.

The addition of the zinc chloride was then begun, with 0.0077 moles of zinc chloride (1.1 g) being added over the next 15 minutes. Thus, the molar ratio of urea to zinc chloride and phenol to zinc chloride was five to one in this system. The temperature of the system was maintained at about 70°C for the next five days, with periodic checks of the reaction solution being made with the HPLC. The HPLC results showed no new products appearing in the reaction solution over the course of the reaction. A few small "peaks" were noticed, but none showed up clearly as new compounds.

After about twenty hours of heating and stirring, a brown colored solid began to crystallize at the liquid-air interface of the reaction system. These crystals were collected and dried, but a mass was not taken. After they had dried, a melting point was taken. The crystals melted or decomposed near 300°C. This information indicated that they were not any of the products which were expected. This was most likely some sort of zinc hydroxide or salt. Even after almost 150 hours, there was no sign of the formation of any new compounds, so the reaction was stopped.

The last attempt made at reacting phenol and urea

together with zinc chloride as the catalyst was run with tetrahydrofuran as the solvent. In this experiment, 0.125 moles of urea was added to about 175 mL of tetrahydrofuran in a 500-mL, three-necked, round-bottomed flask which was fitted with a reflux condenser and an electric stir apparatus. Next, 0.125 moles of zinc chloride was added to the urea in the THF. The whole mixture was then stirred and heated to about 50°C. When the urea and zinc chloride were both dissolved in the tetrahydrofuran, 0.125 moles of phenol was added to the flask. This solution was kept at about 50°C and stirred for the next one and a half to two hours, but no reaction seemed to be taking place. An NMR taken of the solution after the two hours showed no indication of any change in phenyl carbamate or salicylamide. The solution was distilled to remove the tetrahydrofuran and the final result was much unreacted phenol coating the sides of the distillation flask. A lot of some sort of zinc hydroxide or salt was also present. Perhaps the reaction would need more time, but nothing seemed to occur in the time period it was given.

The second Lewis acid to be utilized in an attempt to carry out the proposed reaction was boron trifluoride. Since boron trifluoride is a gas at room temperature, it had to be introduced into the reaction system through a glass tube connected to a line running from its storage tank. Also, a method had to be devised to measure the amount of boron trifluoride that was being added to the system. This was

done by monitoring the change in the mass of the reaction system (flask, stir rod, stoppers, and reactants) as the boron trifluoride was being added. Since the system is basically closed, any increase in mass could be attributed to the added mass of the boron trifluoride which is being introduced. The experimental apparatus remained the same throughout the entire series of trials.

The first reactions that were run using boron trifluoride as the Lewis acid also used isopropyl alcohol as the solvent. In the first run using these conditions, 0.25 moles of urea (15 g) was added to 200 mL of isopropyl alcohol in the 500-mL reaction flask. The solution was stirred, and this caused the urea to dissolve. The boron trifluoride was then added as the solution was stirring. The addition of boron trifluoride caused the flask to grow warm, so it was cooled using an ice-bath. The boron trifluoride was added until 0.23 moles had entered the reaction system. The phenol (0.25 moles, 23.5 g) was then added slowly over the next 15 minutes. The temperature of the solution neither increased nor decreased significantly with the addition of the phenol. The solution was continued stirring for the next 45 minutes or so, at which point the stirring was stopped to wait for the next day. The reaction flask was then stored in the refrigerator overnight.

In an effort to monitor the progress of the reaction as time progressed, samples were taken to be checked using the HPLC. However, in the case of this reaction, no new peaks

were observed in the HPLC data. The solution was heated to about 65°C for nearly three and a half hours on the second day and this did not bring about any sign of reaction either. The solution grew a little darker in color (red-orange), but no precipitates could be seen forming. After many days of being left alone (no heat, no stirring), a very small amount of tiny crystals could be seen lying on the bottom of the flask. However, these were not examined further.

The next step was to try another run in isopropyl alcohol, but this time, the urea to boron trifluoride molar ratio would be kept at four to one. Therefore, 0.25 moles of urea (15 g) was added to 150 mL of isopropyl alcohol in the reaction flask. This mixture was then stirred as a total of 0.066 moles of boron trifluoride was added to the system. This time, the urea did not dissolve, but its appearance did seem to change. It no longer swirled in clumps, but was now a fine powder which took a long time to settle after the stirring was stopped.

The solution was allowed to stir for one-half hour, at which time 0.25 moles of phenol was added. The reaction system was kept in an ice-bath at this point in an effort to maintain the temperature near 0°C and hopefully keep the reaction under control. However, there was no evidence which pointed to any reaction occurring at all. The phenol went into solution, but the urea did not. Instead, it remained as a swirling, white solid in the flask.

The third and final attempt made at using boron

trifluoride as the catalyst along with isopropyl alcohol as the solvent involved a different approach. The idea of this experiment was to react urea with boron trifluoride in the hopes of producing a urea--boron trifluoride complex. This could then be reacted directly with phenol in an effort to produce the desired phenyl carbamate.

A 250-mL, 3-necked, round-bottomed flask was used now in the reaction system rather than a 500-mL flask. About 75 mL of isopropyl alcohol was placed in the reaction flask, and 0.125 moles of urea (7.50 g) was added to it. This was stirred while 0.156 moles of boron trifluoride (10.6 g) was added to the system. This time, the urea did go into solution as the boron trifluoride was being added. In an effort to concentrate any urea--boron trifluoride complex that might have been formed, the reaction solution was roto-vapped until it had become about half of its original volume. Next, 0.062 moles of phenol (5.8 g) was added to the urea--boron trifluoride solution. This solution was then stirred for about an hour, but no reaction was seen to occur. The following day, heat was added to the system in an effort to start the reaction. It was felt that as the reaction proceeded, ammonia boron trifluoride would drop out of the solution. However, this was not observed, nor did any other changes occur that would indicate some sort of reaction taking place.

The final Lewis acid type reactions to be run continued

to utilize boron trifluoride as the Lewis acid, but now used dichloromethane as the solvent. This was done because it was feared that the isopropyl alcohol was complexing with the boron trifluoride and preventing it from complexing with the urea. All of the reactions carried out using dichloromethane as the solvent used the previous reaction set-up, with a 250-mL, 3-necked, round-bottomed flask.

The reactions using dichloromethane as the solvent basically fall into three different categories based on the order of addition of the reactants. The first group that will be looked at has the phenol being added to the solvent first, followed by the boron trifluoride (at least a portion of it), and then the urea. The first reaction of this type which was run had 0.125 moles of phenol (11.75 g) added to about 50 mL of dichloromethane in the reaction system first. The phenol quickly dissolved as it was stirred, and then the addition of the boron trifluoride was begun. After about 0.053 moles of boron trifluoride (3.6 g) had been added to the solution, no more would seem to stay in the system. It was exiting out the top of the stir rod assembly as fast as it was being bubbled into the solution. At this point, the urea (0.125 moles, 7.50 g) was added to the solution. More boron trifluoride was then added until a total of 0.067 moles (4.6 g) had been reached. It should be noted here that the urea, which is actually insoluble in dichloromethane, went into solution almost immediately. Shortly after the addition of the urea, a white solid dropped out of the solution.

Boron trifluoride was still being added to the system after the solid had dropped out, but no change could be seen.

The white solid was filtered from the solution using suction filtration. Both the solid and filtrate were saved for further testing. The mass of the solid was never taken, but an NMR was. Two peaks showed in the aromatic region, one falling at 7.5 ppm and the other at 6.85 ppm. The peak at 7.5 integrated to 10 while the one at 6.85 integrated to 31. This spectra did not indicate that the solid was a the desired product, phenyl carbamate, so more reactions were run. An NMR taken of the filtrate showed absorptions in the aromatic region around 8.0 ppm. These peaks were somewhat scattered and seemed to be quite similar to those of salicylamide.

The above reaction was run again in the same manner, except this time 8.5 g of boron trifluoride was absorbed into the solution. However, the results were basically the same, with a white solid dropping out of the solution a few minutes after the urea had been added.

The final run that was done with the phenol being added to the dichloromethane first, followed by the boron trifluoride and then by the urea, gave very similar results to the first two trials. First, 0.125 moles of phenol was added to 80 mL of dichloromethane in the 250 mL reaction flask. This was started stirring and the phenol was quickly dissolved. The boron trifluoride was then started bubbling into the solution, but, after only about 2.0 g had been

added, no more seemed to be going into solution. At this point, 0.125 moles of urea (7.50 g) was added to the reaction system, and the boron trifluoride addition was resumed. Most of the urea dissolved very quickly, but a little remained clumped on the bottom. However, as more boron trifluoride was added, the urea could be seen dissolving away in the bottom of the flask. A total of 0.10 moles of boron trifluoride (7.10 g) was added to the system.

About five minutes after the urea had been added, a white solid dropped out of the solution all at once. This solid was then separated by suction filtration. The total mass of the solid collected was 18.12 g. This solid was then washed in ether, which caused a bubbling to occur as part of it was dissolved away. The ether solution was then filtered to give the final product, a white, fluffy, crystalline solid. When allowed to sit in a stoppered container overnight, the solid changed from a bright white to a tan color. A melting point was then taken and it melted around 70°C, but over a range starting around 60°C, pointing to its impurity. NMR spectra of the solid showed it to have two peaks in the aromatic region and basically no other peaks. An IR spectra that was made showed the presence of both an amino group (doublet near 3400 cm⁻¹) and the typical amide peak (seen around 1700 cm⁻¹). This spectral information seemed to point to the new solid being some sort of aromatic amide.

The next series of reactions to be looked at also

utilized boron trifluoride as the Lewis acid and dichloromethane as the solvent, but this time both the phenol and urea were started together in the reaction flask. The boron trifluoride was then added to them simultaneously and the results were observed.

The first of these reactions run started with 0.125 moles of urea (7.50 g) and phenol (11.75 g) in the reaction flask with about 175 mL of dichloromethane. The solution was stirred and the phenol went into solution almost immediately. The urea did not yet dissolve, remaining as a swirling, white solid in the flask. The boron trifluoride gas was then introduced into the solution, and a total of 0.11 moles (7.7 g) was added to the system. Again, the addition of boron trifluoride was stopped when it was exiting the system through the stir rod assembly nearly as quickly as it was being bubbled into the solution.

While the flask was being stirred, it was kept in a cold water bath to maintain a steady temperature. About five minutes after the last boron trifluoride had been added to the system, a white solid dropped out of the solution all at once. The solid was then scraped from the sides of the reaction flask and separated from the rest of the reaction solution by suction filtration. A total of 7.4 g of the unknown solid was collected. This solid had no well-defined melting point, melting in a range from 40-60°C.

This same sort of reaction was run again weeks later, and the results were very similar. The 0.125 moles of urea

(7.5 g) and of phenol (11.75 g) were placed in the reaction flask along with about 80 mL of dichloromethane. This initial reaction mixture was allowed to stir, and this stirring rapidly dissolved the phenol. The urea, however, did not dissolve even after rigorous stirring. The boron trifluoride was then added via the glass delivery tube, and a change could be seen taking place. The urea lost its usual granular appearance and became quite fluffy, clumping together on the bottom of the flask. The boron trifluoride continued to go into the reaction solution, not escaping out the top of the reaction system (through the stir rod assembly). As the boron trifluoride was added, the urea began to go into solution. It appeared to be bubbling a little as it dissolved. The layer around the urea took on a rather viscous, oily look. About five minutes after all of the urea had dissolved, a pinkish-white solid fell out of the solution and caked onto the sides of the flask. This was scraped off and collected, its total mass being about 23.4 g. The solid melted over the range of 55-67°C.

A final attempt was made using this same reaction procedure, with 0.125 moles of both phenol and urea, about 80 ml of dichloromethane, and a total of 0.09 moles of boron trifluoride. The phenol and urea were again started together, with the boron trifluoride being added as they stirred. After the 0.09 moles (5.8 g) of boron trifluoride had been added, the urea had dissolved and the solution would absorb no more. After about five minutes, a white solid

dropped out of the solution and was then collected by suction filtration. A total of 14.5 g of the unknown solid was collected, and it was then washed with ether. The ether dissolved some of the solid and what was left was 7.2 g of a white, crystalline unknown. This was then examined by taking both IR and NMR spectra. The NMR showed peaks in the aromatic region while the IR showed evidence of the presence of an amide. Some of the unwashed solid was also saved, along with the dichloromethane filtrate and the ether wash filtrate.

The final variation of the phenol, urea, and boron trifluoride reaction run in dichloromethane started with urea alone in the solvent, and then had the boron trifluoride being bubbled in. Only after all of the boron trifluoride had been added was the phenol to be added. This order of addition led to some interesting results, and the consistent production of a few different solids.

The first run using this order of reactants started with 0.125 moles of urea (7.50 g) being added to about 75 mL of dichloromethane in the reaction flask. The boron trifluoride was then bubbled into this mixture (the urea had not dissolved) and the reaction system was stirred vigorously. This time, however, the urea did not bubble away and go into solution. Instead, it changed its appearance somewhat, clumping together a little more and taking on an almost fluffy white appearance. Another important fact to note is that the reaction system was not gaining in mass as the boron

trifluoride was being added. Instead, it lost a little mass, about 0.5 g. by the time the addition of boron trifluoride was completed. This might possibly be due to the dichloromethane evaporating through the poor seal in the stir rod assembly.

The white solid in the bottom of the flask was then separated by suction filtration and examined. The mass of the separated solid was 9.35 g, whereas the mass of the urea originally in the system was 7.50 g. This mass change indicated some sort of reaction and the presence of a new solid. In an attempt to dry the white solid, it was placed in a vacuum dessicator and a vacuum was applied. This led to the decomposition of the solid as it bubbled away and a clear liquid formed in the beaker below it. A sample of the liquid was collected for further study.

A second attempt was made at running the reaction in this manner, with the urea reacting with boron trifluoride first, and then introducing the phenol to the system. The procedure was practically the same, with 0.125 moles of urea (7.50 g) reacting with an undetermined amount of boron trifluoride (undetermined since there was no registered mass gain in the system). The white solid which resulted was again separated and massed, this time having a mass of 9.35 g. Thus, the results for two trials that were done in the same manner were identical. This solid that was collected also decomposed under the vacuum of the dessicator.

The final two attempts at this reaction utilized the

same procedure as the two initial attempts, but with slightly different results. In the first reaction, excess boron trifluoride was reacted with the 0.125 moles of urea (7.5 g) in about 75 mL of dichloromethane. The reaction system experiences an overall weight loss of almost 15 g, and the new solid has a mass of 14.8 g before being placed in a nitrogen filled glovebag, and 10.7 g after it had decomposed in the bag (the seal on the bag was suspect). The new solid underwent the same breakdown as the previous products had when exposed to air.

The results of the final run were very similar, though the reaction system only experienced a 4.4 g weight loss as the boron trifluoride was being added. The final mass of the solid was 10.12 g and it too broke down when exposed to air, but not nearly so much, since it was stored in a properly sealed nitrogen filled glovebag (with phosphorous pentoxide as the dessicant). Overall then, some sort of urea-boron trifluoride complex was produced with some regularity, and since it seems to have appeared in many of the other runs, it is very important to this reaction system.

RESULTS AND CONCLUSIONS

The first reactions that were run in an attempt to produce a quantity of phenyl carbamate for standard tests, consisted of trying to react phenol directly with urea. The reaction utilizing a 2:1 molar ratio of phenol to urea gave no recognizably new product. Phenol itself was the only substance which showed up consistently in attempts to determine the final contents of the reaction system. However, a basic gas was noted (using wet litmus paper) evolving from the reaction tube. This would seem to indicate some sort of reaction taking place, but again, no evidence of new compounds was found.

The second reaction of this type used a 1:5 ratio of phenol to urea however the results were essentially the same. A basic gas was evolved, but no new reaction products were isolated by extraction of the reaction mixture.

The reaction of urea and phenol together in dimethyl sulfoxide (DMSO) produced some different and interesting results, but no phenyl carbamate was isolated. HPLC chromatograms taken of the reaction solution over time showed the formation of different compounds, one even with a retention time similar to phenyl carbamate's. However, these

peaks changed with time indicating that the compounds being formed were fairly reactive or unstable in the DMSO.

In an effort to determine the stability of phenyl carbamate in DMSO, a five percent solution of phenyl carbamate in DMSO was made up and monitored while it was heated. The peak representing phenyl carbamate on the HPLC chromatogram disappeared over the course of an hour and a new peak appeared, with a retention time equal to that of phenol. Another check was run with phenol and phenyl carbamate heated together in DMSO. The result was the same, with the phenyl carbamate peak disappearing and the phenol peak growing stronger. This is evidence that even if the reaction of phenol and urea in DMSO was to work to give phenyl carbamate, the phenyl carbamate would have to be separated quickly to prevent its conversion to another product. It is also possible that the phenyl carbamate is being converted to salicylamide through the Fries rearrangement, a problem to be watched for in the Lewis acid reactions.

The results of the reactions utilizing zinc chloride as the Lewis acid catalyst varied, as did their procedures. The first reaction utilizing zinc chloride had a 1:5 molar ratio of zinc chloride to both urea and phenol. A small amount of large, clear, needle-like crystals was ultimately separated, but their identification was never completed. A small group of absorptions in the aromatic region of the NMR spectra of these crystals gave some hope that they were at least related

to the desired product but their melting point (120-124°C) was well below that of phenyl carbamate (149-152°C). The distillation of a portion of this trial's reaction solution showed the presence of urea and phenol, but no new compounds.

The second attempt at the reaction using zinc chloride as the catalyst with isopropyl alcohol as the solvent also utilized a 1:5 molar ratio of zinc chloride to urea and to phenol. In this reaction, a brown solid crystallized on the side of the flask. These brown crystals melted or decomposed somewhere above 300°C, so they were most likely some sort of compound containing the zinc (a zinc hydroxide or salt). Monitoring the reaction solution over time with the HPLC gave no evidence of any new compounds being formed.

The final attempt at carrying out the proposed Lewis acid reaction with zinc chloride used tetrahydrofuran (THF) as the solvent. In this reaction, zinc chloride was in a 1:1 molar ratio with both phenol and urea. After allowing the reaction system to go for about two hours, the THF was distilled off, leaving a mixture of solids. Some of the solid was unreacted phenol and urea, and much of the rest was probably a zinc oxide or salt. An NMR taken of the reaction solution showed no evidence of a change from phenol to phenyl carbamate or salicylamide at any time.

The change from using zinc chloride as the Lewis acid catalyst to using boron trifluoride gas met with similar success, but it did give some interesting results. One of

the attempts described in the experimental section notes that as boron trifluoride is being added to the urea in isopropyl alcohol, a change seems to come over the urea. This is accompanied by an increase in temperature of the solution, indicating that there is some sort of reaction taking place. The urea becomes a much more powdery solid, taking more time to settle out of the solution when the stirring is stopped. This could possibly indicate the formation of a urea--boron trifluoride complex, however, none of this solid was examined to determine if this was the case. The addition of phenol to this new solid in the isopropyl alcohol solution was not seen to cause any kind of reaction. Examination of the reaction solution gave no evidence of any new products, or of any reaction taking place at all.

Another of the attempts made using boron trifluoride as the Lewis acid catalyst in isopropyl alcohol showed some interesting results, with the urea going into solution as the boron trifluoride was being added. About half (35-40 mL) of the solution's isopropyl alcohol was then removed by evaporation, leaving what was hoped to be a more concentrated urea--boron trifluoride complex in solution in the isopropyl alcohol. Phenol was then added to this solution (1:2 molar ratio of phenol to urea) along with heat in an attempt to drive the reaction. However, no reaction was noted to have occurred. The interesting point about this reaction is the fact that 0.125 moles of urea dissolved with 0.16 moles of boron trifluoride in only 75 mL of isopropyl alcohol. But,

the urea--boron trifluoride complex was not observed dropping out of the solution, even when it was cooled, nor did the addition of phenol cause any sort of reaction. Therefore, this procedure was not effective.

The substitution of dichloromethane for isopropyl alcohol as the reaction solvent brought some new results, quite different from what had been seen before. The first result to be mentioned is the apparent production of some type of urea--boron trifluoride complex when boron trifluoride was bubbled into urea alone in dichloromethane. Two of the runs gave solids that had a total mass which would indicate four moles of urea combining with one mole of boron trifluoride. The resulting white solid bubbles and breaks down after prolonged exposure to air or being placed under a vacuum. Two other runs done in nearly the same manner, with the only difference being an excess of boron trifluoride being added (maybe 3 to 4 times as much as in the first two runs), gave solids with total mass values a little bit higher than the first two trials. However, these still pointed to a four to one molar ratio of urea to boron trifluoride. This is the ratio that Dr. F.J. Sowa predicts for his complex of urea and boron trifluoride in his U.S. Patent #2,960,733. However, his complex was found to be stable in air while this one decomposes unless it is kept very dry and is not placed under a vacuum.

The reactions of phenol, urea, and boron trifluoride

together in dichloromethane were all very similar in their behavior and in the products they gave. The crude solid product which consistently dropped out of the reaction solution after all of the reactants had been added and the urea dissolved, was filtered and then washed with ether. Washing with ether would cause a bubbling as some solid was dissolved. The solid which remained was very white and fluffy, but overnight it changed to a tan color. NMR and IR spectra showed it to be an aromatic compound with an amide group, but it has not yet been positively identified. It melts near 70°C , well below the melting point of the desired phenyl carbamate ($149-152^{\circ}\text{C}$), or, the anticipated by-product, salicylamide (140°C). It is soluble in both water and 95% ethyl alcohol, but obviously not in ether. Further work should be done on its identification in order to understand what reaction is going on.

THE NEXT STEP

The results of this research seem to show that the reaction mechanism may require a little more than just combining all of the reactants at once and letting it go. Instead, it would be beneficial to try to break the reaction up into parts, a certain sequence to be followed. One of the best ways to do this would be to form a urea--Lewis acid complex which could then be attacked by phenol.

Dr. F.J. Sowa patented a technique for synthesizing and isolating a variety of urea--boron trifluoride complexes in his U.S. Patent, #2,980,733. In his patent, Dr. Sowa claims to have produced and successfully isolated urea--boron trifluoride complexes with the ratios of urea to boron trifluoride being 4:1, 4:2, 4:3, and 4:4 (always four molecules of urea involved). If a stable complex of urea and boron trifluoride could be isolated, it could then be placed in an appropriate solvent with phenol and the desired reaction might very well run.

Once the reaction system can be made to run as it should, methods could be worked out to prevent the Fries rearrangement and isolate the desired product, phenyl carbamate.

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