

THE ACTION OF VARIOUS REAGENTS
ON
SUBSTITUTED THIOUREAS.

By

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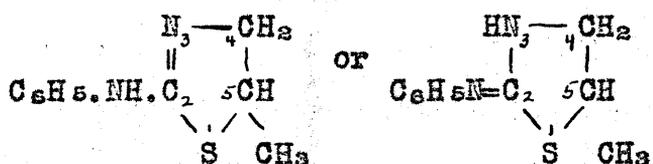
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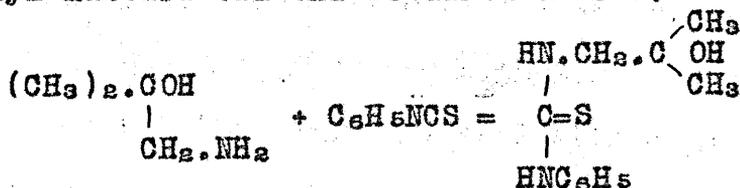
I wish to thank Dr. F. B. Dains for the direction of this work, and both Dr. Dains and Dr. Brewster for many helpful suggestions.

When 2 phenyl, 4 methyl thiazole was treated with methyl iodide, the compound which was obtained contained a methyl group in position 3, instead of being connected to the nitrogen of the anilido group. This, and similar experiments led Young and Crookes to adopt the above formula in preference to the configuration where the hydrogen atom is attached to the nitrogen outside of the ring.

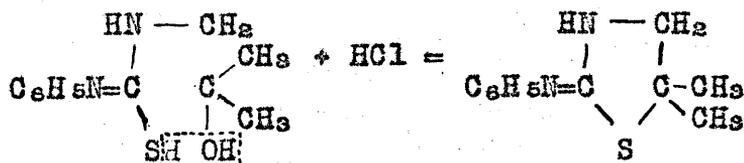


In the case of tri-substituted thioureas, the possibility of a mobile hydrogen is eliminated.

Dersin⁶ made amino di methyl carbinol which he treated with phenyl mustard oil and obtained a urea.



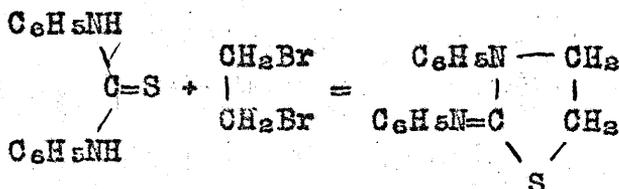
On heating the urea to 100° with hydrochloric acid, he obtained 2-phenyl, 5 di methyl thiazolidine.



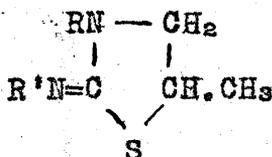
Dains, Brewster, Blair, and Thompson⁷ carried out analogous experiments using thioureas prepared from aryl amino ethanols and aryl mustard oils. They found that the use of acid was unnecessary to bring about ring closure, but that

when the mixture of the amino ethanol and mustard oil was heated to 110° a good yield of the thiazolidine was obtained. They also worked with aryl amino propanols, obtaining thiazenes.

Will⁸ was one of the pioneers in the preparation of thiazolidines. He heated molar quantities of thio-carbanilide and ethylene dibromide until no more hydrogen bromide came off, and dissolved the product obtained in hot water. The base was precipitated with weak alkali.



Any of the three methods can be used to make a thiazolidine of the general structure



with the methods of Gabriel and Dersin the position of R and R' groups are certain, since their relative positions depend on the reagents used. With the method of Will, the position of R and R' are not certain, and may be determined only by isolation of the products obtained in the reaction, the preparation of the product by one of the other methods and then proof that they are the same.

F. G. Stubbs made and isolated a number of thiazalidines

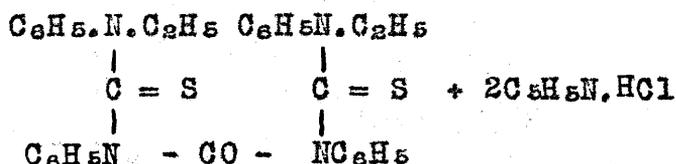
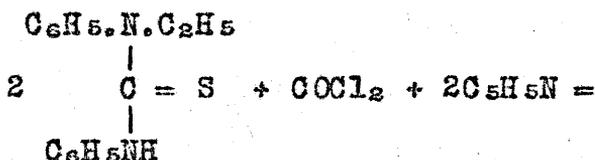
by both the methods of Will and Dersin.

Deninger¹⁰, Dixon¹¹ and Dains¹² have shown that the substituted thioureas and acid chlorides may react with the formation of an acyl derivative of the urea, a molecular addition product of the urea and acid chloride, or at elevated temperature with the production of a mustard oil and a substituted acid amide.

Dixon and Taylor¹³ have shown that alpha, beta di-phenyl, alpha methyl thiourea and benzoyl chloride form an addition product which readily loses hydrogen chloride yielding benzoyl di phenyl methyl thiourea, a stable compound not easily desulfurized.

Brewster⁴ obtained benzoyl derivatives by the treatment of allyl aryl thioureas with benzoyl chloride in the presence of pyridine. No thiazole was formed.

The same case of replacement was noticed in the case of di-phenyl ethyl thiourea and carbonyl chloride in the presence of pyridine.



The purpose of this work is to confirm and continue the

work outlined above by testing the effect of various reagents under varying conditions on substituted thioureas.

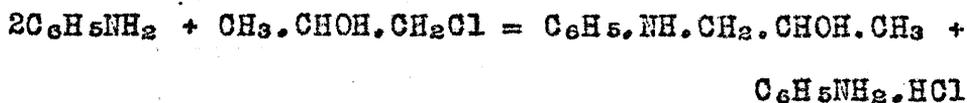
EXPERIMENTAL.

PREPARATION OF ALPHA-ANILIDO BETA PROPANOL.

The propanol was prepared from ninety-three grams of aniline and fifty-seven grams of eighty-nine percent propylene chlor hydrin, the solution of the chlor hydrin was prepared by salting out the technical forty per cent solution.

The two reagents were placed together in a round bottom flask and heated under a reflux condenser on an oil bath at 125° - 130° for eight hours. The mixture was then made alkaline with sodium hydroxide and steam distilled to remove the extra molecule of aniline that was added to take up the hydrogen chloride liberated in the reaction.

The oily residue in the flask was extracted with ether and dried over anhydrous potassium carbonate. The ether was distilled off and the oil was distilled in vacuo. The fraction boiling between 195° - 200° at 110 m.m. of mercury was collected. The product was a light yellow oil, almost colorless, that became red on standing.



Theoretical yield = 75 grams.

Actual yield = 52.5 "

Percentage yield = 70 ⁴⁰

PREPARATION OF PHENYL MUSTARD OIL

The phenyl mustard oil was prepared by the method of Dains, Brewster, and Olander¹⁴, using one hundred eight grams of carbon bisulfide, one hundred sixty grams of twenty-eight per cent ammonium hydroxide, one hundred twelve grams of aniline, and three hundred grams of copper sulfate.

Theoretical yield = 161 grams.

Actual yield = 100 grams.

Percentage yield = 62 grams. ^{70.?}

PREPARATION OF α -2 PROPANOL, α , β -DI PHENYL THIOUREA

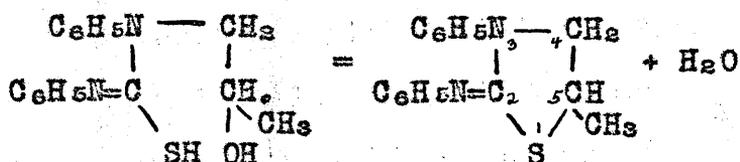
The thio urea was prepared from twenty-seven and two-tenths grams of alpha-anilido beta propanol and twenty grams of phenyl mustard oil.

The two reagents were placed together in a small flask. After a few hours, the mixture seemed to be thickening, and after standing twenty-four hours, it had become a very viscous gum. All attempts to obtain a pure crystalline product from ordinary solvents failed. The gum itself, after standing for two months showed indications of crystal formation, but a sample pure enough to obtain a melting point could not be obtained. The reaction was carried out in benzene solution, with hopes for a crystalline product, but only a gum was obtained.



ACTION OF HYDROCHLORIC ACID ON α -2 PROPANOL, α - β -DI PHENYL THIOUREA.

When alpha 2 propanol, alpha, beta-di phenyl thiourea is treated with concentrated hydrochloric acid, it undergoes ring closure with the formation of 2 phenyl imino, 3 phenyl, 5 methyl thiazolidine.



Five grams of the urea was dissolved in thirty-five cubic centimeters of alcohol. An equal volume of concentrated (sp. gr. 1.19) hydrochloric acid was added and the mixture was allowed to stand over night. The mixture was diluted with water until no more cloudiness occurred, and then filtered. The filtrate was neutralized with a solution of sodium hydroxide. The base that separated out on neutralization was recrystallized from alcohol. The thiazolidine separated in white needles that melted at 96°.

ANALYSIS:

Calculated for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{S}$: N = 10.45%

Found: N = 10.71; 10.62.

ANALYTICAL DATA:

Gunning-Arnold modified kjeldahl method.

Weight of sample	.2010 gms.	.2012 gms.
Volume of acid used by sample	15.06 c.c.	14.96 c.c.
1 c.c. of acid =	.0014293 grams nitrogen.	

Percentage of nitrogen in sample:

$$1. \frac{15.06 \times .0014293 \times 100}{.2010} = 10.71\%$$

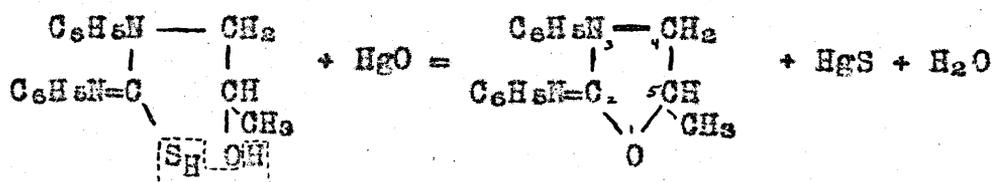
$$2. \frac{14.96 \times .0014293 \times 100}{.2012} = 10.62\%$$

REACTIONS OF THE THIOUREA

ACTION OF MERCURIC OXIDE ON

C-2 PROPANOL, C.β-DI PHENYL THIOUREA.

When alpha 2 propanol, alpha, beta-di phenyl thiourea is treated with mercuric oxide, the compound is desulfurized, and undergoes ring closure with the formation of 2 phenyl imino, 3 phenyl, 5 methyl oxazolidine. That desulfurization takes place before ring closure is shown by the fact the thiazolidine has no reaction with mercuric oxide.



Four and two-tenths grams of the thiourea was placed in a round bottom flask and dissolved in benzene. Four grams of mercuric oxide was added and the mixture heated under a reflux condenser on a water bath for four hours. The mercuric sulfide and unchanged oxide were allowed to settle and the supernatant liquid was decanted through a filter. The product was allowed to crystallize out of the benzene. The isolated compound was white needles melting at 64°.

Analysis:

Calculated for $C_{16}H_{16}ON_2$: N = 11.11%

Found: N = 11.07%; 10.92%.

Analytical Data

Gunning-Arnold Modified kjeldahl method.

	I	II
Weight of sample =	.2009 grams	.1993 grams
Vol. of acid used =	15.56 c.c.	15.22 c.c.
1 c.c. of acid =	.0014293 grams of N.	

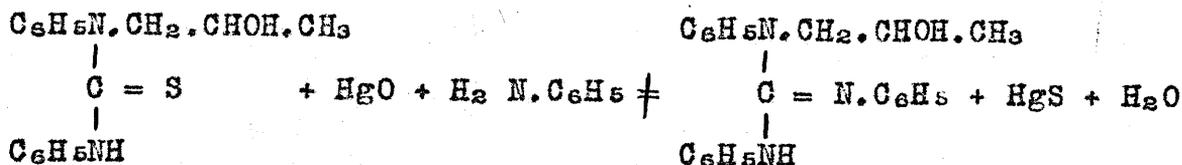
Percentage of nitrogen in sample:

$$1. \frac{15.56 \times .0014293 \times 100}{.2009} = 11.07\%$$

$$2. \frac{15.22 \times .0014293 \times 100}{.1993} = 10.92\%$$

ACTION OF MERCURIC OXIDE ON α -2 PROPANOL. α , β -DI PHENYL THIOUREA IN THE PRESENCE OF ANILINE.

When alpha-2 propanol, alpha, beta-di phenyl urea is treated with mercuric oxide, it yields 2 phenyl imino, 3 phenyl, 5 methyl oxazolidine, but if aniline is present there is a possibility of obtaining a substituted guanidine according to the following equation:



Five grams of the urea, four grams of yellow mercuric oxide, and one and seven-tenths grams of aniline were used.

The urea was dissolved in alcohol and placed in a small

Erlenmeyer flask. The aniline and mercuric oxide were added and the mixture turbinated with a mechanical stirrer for 4 hours. The black sulfide was filtered off and the solution distilled with steam to remove any free aniline. The residual oil was treated with dilute hydrochloric acid and a part dissolved. The residue was a white crystalline mass. The mixture was filtered and the filtrate made alkaline with sodium carbonate. The precipitated base was recrystallized alcohol, giving white needles melting at 64° .

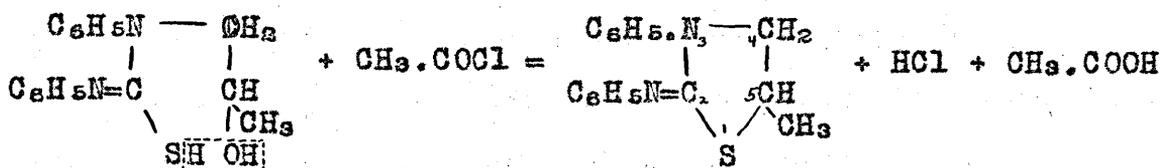
The crystalline residue, after treatment with HCl, was recrystallized from alcohol. White crystals melting with decomposition at 246° were obtained. This was proven to be the hydrochloric salt of the above base as follows: A portion of the crystals were dissolved in water. Sodium carbonate was added and a base was precipitated which, on recrystallization gave white needles melting at 64° . A mixture of the two bases obtained melted at 64° .

The base obtained by treatment of the thiourea with mercuric oxide in the absence of aniline melted at 64° , so a portion of this base was mixed with a portion of the base obtained by the action of mercuric oxide in the presence of aniline, and a melting point of the mixture taken. The mixture melted at 64° , so it is safe to assume that the aniline takes no part in the reaction, and that the 2 phenyl imino, 3 phenyl, 5 methyl oxazolidine is formed in each case.

ACTION OF ACETYL CHLORIDE ON α -2 PROPANOL. α - β DI PHENYL THIOUREA.

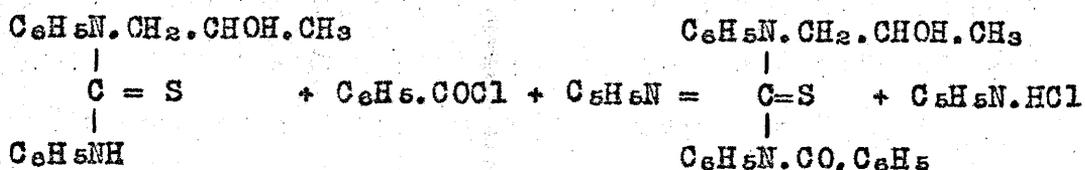
When alpha-2 propanol, alpha beta di phenyl thiourea is treated with acetyl chloride, there are two possibilities. The hydrogen of the beta position may be replaced by an acetyl group, or the compound may undergo ring closure as with hydrochloric acid.

Five grams of the thiourea were dissolved in benzene and placed in a round bottom flask. The mixture was refluxed on a water bath, the acetyl chloride slowly added, and the heating continued for several hours. The solution was poured into water and after thorough agitation the layers were separated. The benzene layer on evaporation left a small quantity of the original thiourea. The water layer was neutralized with sodium hydroxide and the precipitated base recrystallized from alcohol. White needles melting at 96° separated. A portion of this product was mixed with the 2 phenyl imino, 3 phenyl, 5 methyl thiazolidine obtained by treating the thiourea with hydrochloric acid, and a melting point of the mixture determined. The mixture melted at 96° . From this, we can conclude that ring closure took place and that the product was 2 phenyl imino, 3 phenyl, 5 methyl thiazolidine.



ACTION OF BENZOYL CHLORIDE ON α -2 PROPANOL.C. β -DI PHENYL THIOUREA IN THE PRESENCE OF PYRIDINE.

When benzoyl chloride acts on alpha-2 propanol, alpha, beta phenyl thiourea, there are two possibilities. The hydrogen of the beta position may be replaced by the benzoyl group, or ring closure may take place. The pyridine would take up any hydrochloric acid formed, and since it is a stronger base than the thiazolidine would tend to make the reaction go to the formation of the benzoyl derivative as follows:

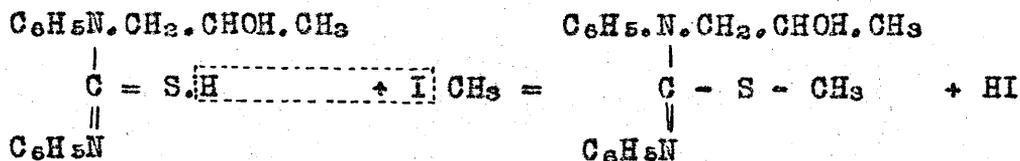


Ten grams of the thiourea was dissolved in pyridine. Ten grams (excess) of benzoyl chloride was added drop by drop with constant shaking. The color changed from a yellow to a wine color. The reaction caused an evolution of heat. A small quantity of alcohol was added to decompose any benzoyl chloride and the reaction mixture poured into water. The gum that appeared was filtered off and the filtrate made alkaline with sodium hydroxide. No base precipitated. Attempts were made to crystallize the gummy product from all ordinary solvents failed. After standing for two months, the gum showed signs of crystal formation, but a sample pure enough for analysis could not be obtained.

ACTION OF METHYL IODIDE ON α -2 PROPANOL.C. β DI PHENYL THIOUREA.

When alpha-2 propanol, alpha, beta di phenyl thiourea is

treated with methyl iodide a sulfur ether is formed according to the following reaction:



Five grams of the thiourea was dissolved in absolute methyl alcohol and the methyl iodide added. The mixture was refluxed on a water bath for four hours. Soon after the reaction started, the disagreeable odor of methyl sulfide was noticed. Methyl iodide was added from time to time to replace that lost in evaporation. The reaction mixture in the flask was treated with dilute hydrochloric acid but was only slightly soluble. Upon neutralization with sodium hydroxide, an oil separated. This, upon long standing, showed crystal formation, and upon washing with alcohol gave white crystals melting at $83^\circ - 84^\circ$. The perchlorate was a pinkish crystalline substance melting at $184 - 186^\circ$.

Analysis of the Ether.

Calculated for $\text{C}_{17}\text{H}_{20}\text{ON}_2\text{S}$: N = 9.33%.

Found: N = 9.43; 9.65.

Analytical Data.

	I	II
Weight of Sample =	.1763 gms.	.1781 gms.
Vol. of acid used =	11.63 c.c.	12.02 c.c.
1 c.c. of acid =	.0014293 grams of N.	

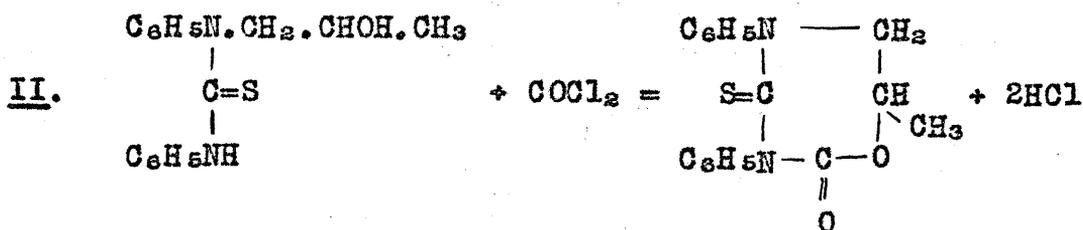
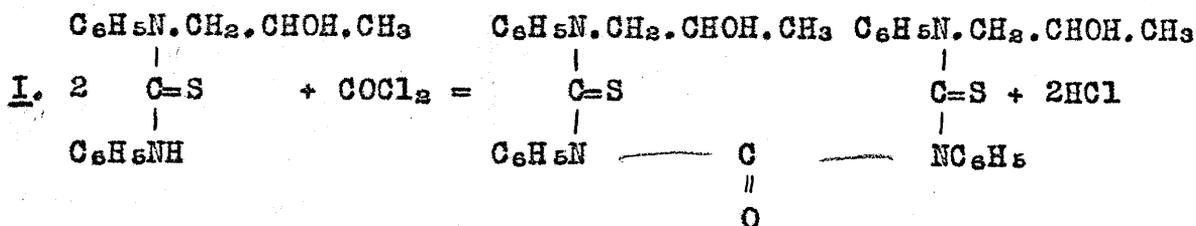
$$1. \frac{11.63 \times .0014293 \times 100}{.1763} = 9.43$$

$$2. \frac{12.02 \times .0014293 \times 100}{.1781} = 9.65$$

ACTION OF CARBONYL CHLORIDE ON α -2 PROPANOL.

C. β -PHENYL THIOUREA IN THE PRESENCE OF PYRIDINE.

With carbonyl chloride (phosgene) alpha-2 propanol, alpha, beta phenyl thiourea presents several possibilities. The possibility of ring closure with the formation of a thiazolidine is precluded by the addition of pyridine. Other possibilities may be illustrated by the following equations:



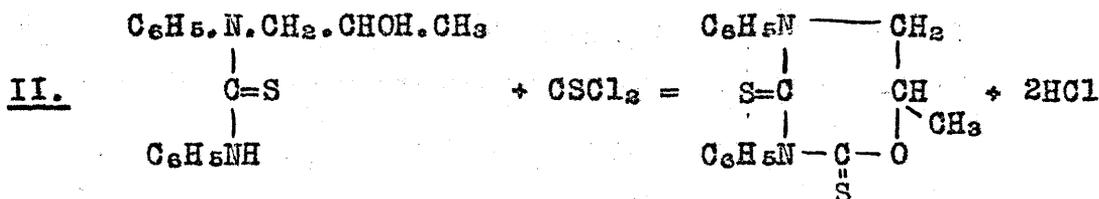
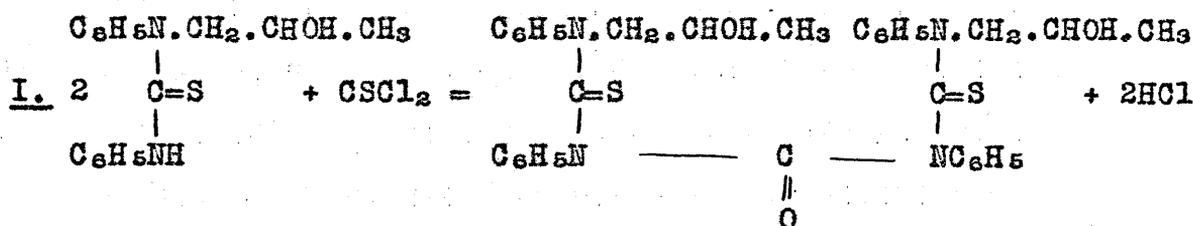
Ten grams of the urea was dissolved in fifty c.c.'s of benzene and to this solution three and a half grams of purified pyridine was added. A twenty per cent solution of phosgene in toluene was added in small portions. A red oil was thrown out of solution and considerable heat was given off. The phosgene was added until heat evolution ceased. The mixture was allowed to stand over night to rid itself of the phosgene. The benzene was poured off of the oily gum and was al-

lowed to evaporate. A small quantity of unchanged thiourea was left after evaporation. The gum was warmed with dilute hydrochloric acid and a portion was dissolved. The solution was filtered and made alkaline with sodium hydroxide. The precipitated base was allowed to crystallize from alcohol. White prism shaped crystals melting at 79° were formed. A qualitative test on this product showed the absence of sulfur. This shows that none of the possibilities shown above are realized, but that an entirely different reaction occurred.

ACTION OF THIOCARBONYL CHLORIDE ON α -2 PROPANOL.

α . β -DI PHENYL THIOUREA IN THE PRESENCE OF PYRIDINE.

As in the case of phosgene, thio carbonyl chloride or thiophosgene presents three possibilities, one of which, ring closure with the formation of a thiazolidine is precluded by the presence of pyridine. The other possibilities are shown by the following equations:



Five grams of the thiourea was dissolved in fifty c.c.'s of benzene and to this solution three and a half grams of py-

ridine was added. Thio phosgene in benzene solution was slowly added. A red oil was thrown out of solution and considerable heat was evolved. The thiophosgene was added until the evolution of heat ceased. The reaction mixture was allowed to stand over night to rid itself of the thiophosgene. The benzene was poured off and allowed to evaporate. A small quantity of a red gum that appeared to be the original thiourea was left after evaporation.

The oily gum in the flask was warmed with dilute hydrochloric acid. A part went into solution. This solution was filtered and the filtrate made alkaline with sodium hydroxide. The base that precipitated was recrystallized from alcohol. Pinkish prismatic crystals that melted at $84^{\circ} - 85^{\circ}$.

A portion of this product was mixed with a portion of the product obtained by the action of phosgene on the same thiourea, and a melting point of the mixture determined. It melted from $79^{\circ} - 85^{\circ}$.

The crystals obtained in this reaction were tested qualitatively for sulfur and none was found. This shows that none of the possibilities listed above were realized.

PREPARATION OF PARA TOLYL MUSTARD OIL.

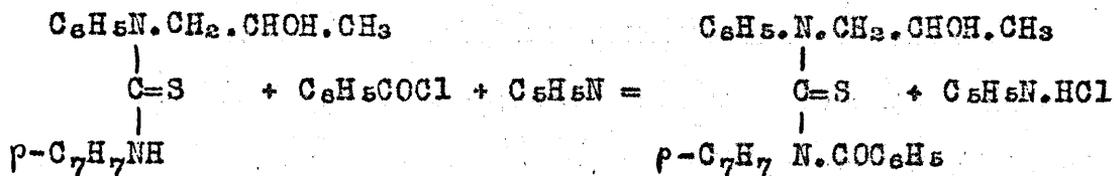
The para tolyl mustard oil was prepared by the method of Dains, Brewster, and Olander¹⁴ using one hundred eight grams of carbon bisulfide, one hundred sixty grams of 28% NH_4OH , one hundred twenty grams of para toluidine, and three hundred grams of copper sulfate.

lized with sodium hydroxide and the precipitated base recrystallized from alcohol. White needles, melting at 105° separated out. A portion of this product was mixed with the thiazolide obtained from the action of hydrochloric acid on this urea, and the melting point of the mixture determined. The mixture melted at 105°. We may therefore safely state that ring closure with the formation of 2-para tolyl imino, 3 phenyl, 5 methyl thiazolidine.

ACTION OF BENZOYL CHLORIDE ON α -2 PROPANOL, α PHENYL,

β PARA TOLYL THIOUREA IN THE PRESENCE OF PYRIDINE.

When benzoyl chloride acts on alpha-2 propanol, alpha phenyl, beta para tolyl thiourea, two possibilities present themselves. Ring closure with the formation of a thiazolidine might take place, but this is presumably precluded by the presence of pyridine. The other possibility is the replacement of the hydrogen of the beta group with the benzoyl group according to the following equation:



Five grams of the urea was dissolved in pyridine and five and a half grams of benzoyl chloride was added drop by drop with constant shaking. The color changed from a light yellow to a deep red, and a considerable quantity of heat was evolved. A small quantity of alcohol was added to decom-

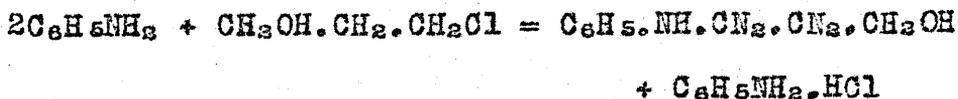
pose any unchanged benzoyl chloride. The reaction mixture was poured into water. The gum that precipitated out was filtered off and the filtrate made alkaline with sodium hydroxide. A faint cloudiness was the result. All attempts to crystallize the gum from all ordinary solvents failed.

PREPARATION OF α ANILIDO- γ PROPANOL.

The propanol was prepared from ninety-three grams of aniline and forty grams of tri-methylene chlorhydrin.

The two reagents were placed together in a round bottom flask and heated on an oil bath under a reflux condenser at 125° - 130° , for six hours. The mixture was made alkaline with sodium hydroxide and steam distilled to remove the mole of aniline that was added to take up the hydrogen chloride liberated in the reaction.

The oily residue in the flask was extracted with ether and dried over anhydrous sodium carbonate. The ether was distilled off and the oil was distilled in vacuo. The fraction boiling between 220° - 225° at 120 m.m. of mercury was collected. The product was a very light yellow oil that became red on standing.



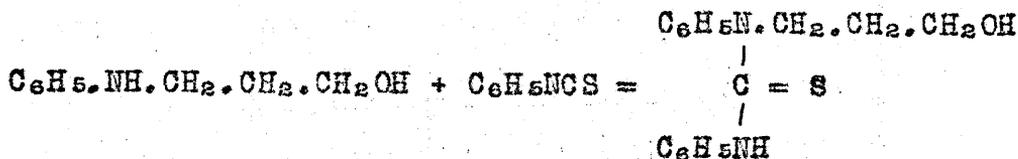
Theoretical yield = 73.4 grams.

Actual yield = 49.4 grams.

Percentage yield = 67.3 $\frac{8}{10}$

PREPARATION OF α -3 PROPANOL, α , β DI PHENYL THIOUREA.

The urea was prepared from ten grams of alpha anilido, gamma propanol and eight and nine-tenths grams of phenyl mustard oil.



The two reagents were placed together in a small flask. The mixture began spontaneously to warm up and soon became quite hot, and set to a mass of white crystals. This mass was recrystallized from alcohol and gave white needles melting at $127^\circ - 128^\circ$.

Analysis.

Calculated for $\text{C}_{16}\text{H}_{18}\text{ON}_2\text{S}$; N = 9.79%.

Found: N = 9.58; 9.49%.

Analytical Data.

	I	II
Weight of sample =	.2102 gms.	.2105 gms.

Vol. of Acid neutralized =	14.09 c.c.	13.98 c.c.
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1 c.c. of acid = .0014293 grams of N.

Percentage of nitrogen in sample:

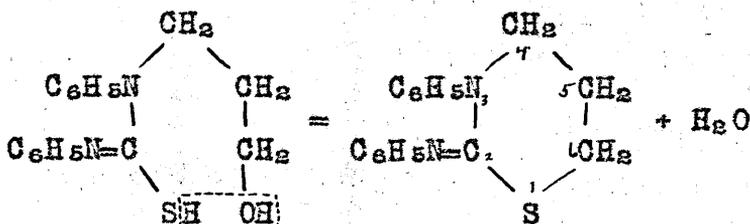
$$1. \frac{14.09 \times .0014293 \times 100}{.2102} = 9.58$$

$$2. \frac{13.98 \times .0014293 \times 100}{.2105} = 9.49$$

ACTION OF HYDROCHLORIC ACID ON α -3 PROPANOL,

.. α , β -DI PHENYL THIOUREA.

When alpha-3 propanol, alpha, beta-di phenyl thiourea is treated with concentrated hydrochloric acid it undergoes ring closure with the formation of 2-phenyl imino, 3 phenyl thiazane.



Five grams of the thiourea was dissolved in thirty cubic centimeters of alcohol. An equal volume of concentrated (sp. gr. 1.19) hydrochloric acid was added and the mixture allowed to stand over night. The mixture was diluted with water until no more cloudiness appeared and then filtered. The filtrate was made alkaline with sodium hydroxide and the precipitated base recrystallized from alcohol. White needles melting at 142° separated.

Analysis.

Calculated for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{S}$: N = 10.46%

Found: N = 10.23; 10.30%

Analytical Data.

	I	II
Weight of sample =	.2001 gms.	.2000 gms.
Vol. of Acid used =	14.32 c.c.	14.41 c.c.
1 c.c. of acid =	.0014293 grams of N_2 .	
Percentage of nitrogen in sample:		

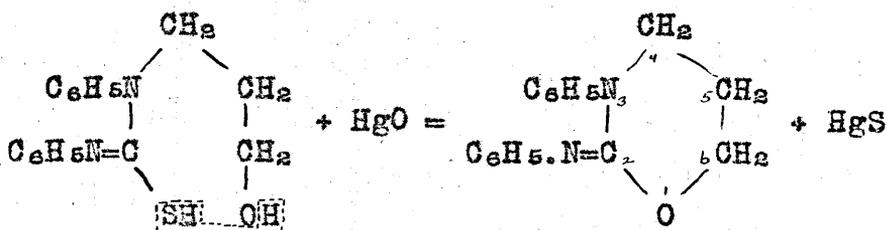
$$1. \frac{14.32 \times .0014293 \times 100}{.2001} = 10.23\%$$

$$1. \frac{14.41 \times .0014293 \times 100}{.2000} = 10.30\%$$

ACTION OF MERCURIC OXIDE ON α -3 PROPANOL,

α . β DI PHENYL THIOUREA.

When alpha-3 propanol, alpha, beta-di phenyl thiourea is treated with mercuric oxide, the compound is desulfurized and undergoes ring closure with the formation of 2-phenyl imino, 3-phenyl, oxazane.



Four and two-tenths grams of the urea was placed in a round bottom flask and dissolved in benzene. Four grams of mercuric oxide was added and the mixture heated under a reflux condenser on a water bath for four hours. The mercuric sulfide was allowed to settle and the supernatant liquid decanted through a filter. The product crystallized out of the benzene in white needles melting at 157° .

Analysis.

Calculated for $\text{C}_{16}\text{H}_{16}\text{ON}_2$: N = 11.11%

Found: N = 11.15; 11.37%

Analytical Data.

I	II
Weight of sample = .2071 gms.	.2063 grams.
Vol. of acid used = .16.16 c.c.	16.41 c.c.
1 c.c. of acid = .0014293 grams of N_2 .	

Percentage of nitrogen in sample:

$$1. \frac{16.16 \times .0014293 \times 100}{.2071} = 11.15\%$$

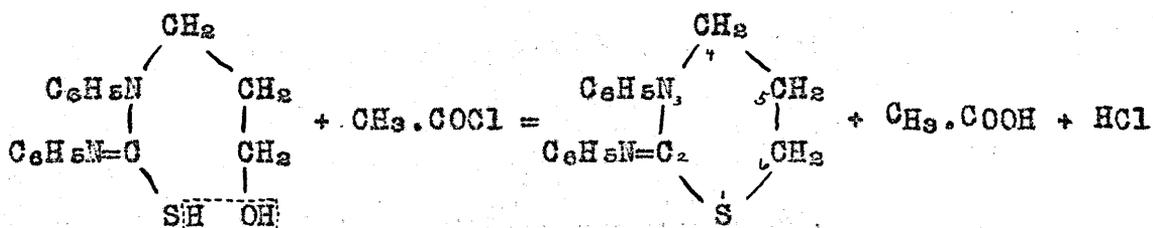
$$2. \frac{16.41 \times .0014293 \times 100}{.2063} = 11.37\%$$

ACTION OF ACETYL CHLORIDE ON α -3 PROPANOL.

α , β DI PHENYL THIOUREA.

When alpha-3 propanol, alpha, beta-di phenyl thiourea is treated with acetyl chloride, two possibilities present themselves. The hydrogen of the beta position may be replaced by the acetyl group, or the compound may undergo ring closure as with hydrochloric acid.

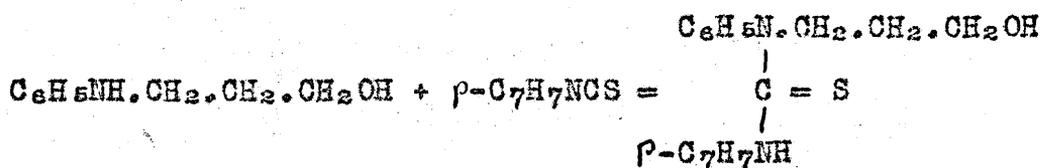
Five grams of the thiourea was dissolved in benzene and placed in a round bottom flask. The mixture was refluxed on water bath, acetyl chloride slowly added and heating continued for several hours. The solution was poured into water and after thorough agitation the two layers were separated. The benzene on evaporation contained a small portion of the original thiourea. The water layer was neutralized with sodium hydroxide and the precipitated base recrystallized from alcohol. The product separated as white needles melting at 141° - 142° . A portion of this sample was mixed with the thiazane prepared by the action of hydrochloric acid on the thiourea, and the melting point of the mixture determined. It melted at 141° - 142° . We can therefore assume safely that acetyl chlorides causes ring closure of the urea with the formation of 2 phenyl imino, 3 phenyl thiazane.



PREPARATION OF α -3 PROPANOL, α PHENYL.

β PARA TOLYL THIOUREA.

The urea was prepared from ten grams of alpha anilido, gamma propanol and nine and two-tenths grams of para tolyl mustard oil.



The two reagents were placed together in a small flask. The mixture began spontaneously to warm up and soon became quite hot, and set to a mass of white crystals. The mass was recrystallized from alcohol and gave white needles melting at $125^\circ - 126^\circ$.

Analysis.

Calculated for $\text{C}_{17}\text{H}_{20}\text{ON}_2\text{S}$: N = 9.34%

Found: N = 9.11; 9.05%.

Analytical Data.

	I	II
Weight of sample =	.2015 gms.	.2017 gms.
Vol. of acid used =	12.85 c.c.	12.77 c.c.
1 c.c. of acid =	.0014293 grams of N_2 .	

Percentage of nitrogen in sample:

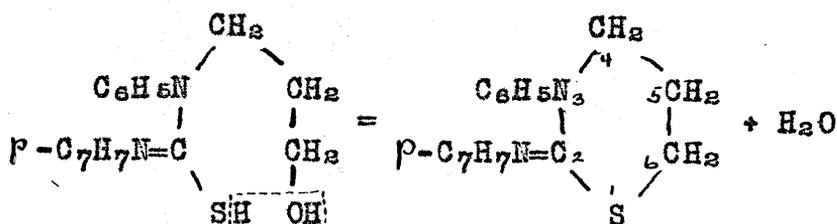
$$1. \frac{12.85 \times .0014293 \times 100}{.2015} = 9.11\%$$

$$2. \frac{12.77 \times .0014293 \times 100}{.2017} = 9.05\%$$

ACTION OF HYDROCHLORIC ACID ON α -3 PROPANOL,

α PHENYL, β PARA TOLYL THIOUREA.

When alpha-3 propanol, alpha phenyl, beta para tolyl thiourea is treated with concentrated hydrochloric acid, it undergoes ring closure with the formation of 2 para tolyl imino, 3 phenyl thiazane.



Five grams of the thiourea was dissolved in thirty cubic centimeters of alcohol. An equal volume of concentrated (sp. gr. 1.19) hydrochloric acid was added and the mixture allowed to stand over night. The mixture was diluted with water until no more cloudiness appeared and then filtered. The filtrate was made alkaline with sodium hydroxide and the precipitated base recrystallized from alcohol. White needles melting at 97° separated.

Analysis:

Calculated for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{S}$: N = 9.93%.

Found: N = 9.71; 9.53%.

Analytical Data.

I	II
Weight of sample = .2113 gms.	.2026 gms.
Vol. of Acid used = 14.35 c.c.	13.51 c.c.
1 c.c. of acid = .0014293 grams of N.	

Percentage of nitrogen in sample.

$$1. \frac{14.35 \times .0014293 \times 100}{.2113} = 9.71\%$$

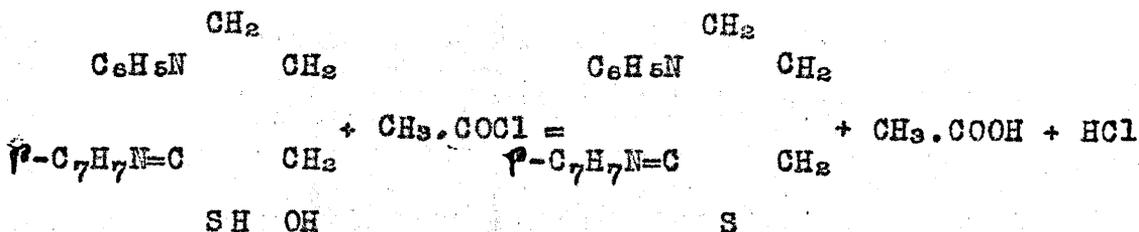
$$2. \frac{13.51 \times .0014293 \times 100}{.2026} = 9.53\%$$

ACTION OF ACETYL CHLORIDE ON α -3 PROPANOL, α PHENYL, β PARA TOLYL THIOUREA.

When alpha-3 propanol, alpha phenyl, beta para tolyl thiourea is treated with acetyl chloride, two possibilities present themselves. The hydrogen of the beta position may be replaced by the acetyl group, or the compound may undergo ring closure as when treated with hydrochloric acid.

Five grams of the urea was dissolved in benzene and placed in a round bottom flask. The mixture was refluxed on a water bath, acetyl chloride slowly added, and heating continued for several hours. The solution was poured into water and after thorough shaking the layers were separated. The benzene layer on evaporation left a small quantity of the original thiourea. The water layer was made alkaline with sodium hydroxide and the precipitated base crystallized from alcohol. White needles melting at 96° separated. A small portion of the sample was mixed with a portion of

the thiazane prepared by treatment of the urea with hydrochloric acid and the melting point of the mixture determined. It melted at 96° - 97° . We can, therefore, safely assume that ring closure took place with the formation of 2 para tolyl imino, 3 phenyl thiazane.



PREPARATION OF α -2, 4 DI METHYL PHENYL AMINO, β PROPANOL.

The propanol was prepared from seventy-three grams of 1, 2, 4 xylidene and twenty-two and a half grams of an eighty-nine per cent solution of propylene chlorhydrin.

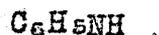
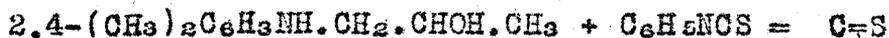
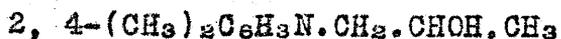


The two reagents were placed together in a round bottom flask and heated under a reflux condenser on an oil bath at 125° - 130° for six hours. The mixture was then made alkaline with sodium hydroxide and steam distilled to remove the extra mole of xylidine. The residue in the flask after steam distillation was extracted with ether. The ether solution was dried over anhydrous potassium carbonate, the ether distilled off, and the oily residue distilled in vacuo. The fraction boiling between 220° and 225° at 70 m.m. of mercury was collected. The distillate set to an oil mass of crystals, which on purification melted at 130° .

PREPARATION OF α -2 PROPANOL, α -2, 4 XYLIL,

β PHENYL THIOUREA.

The thiourea was prepared from ten grams of alpha-2, 4 di methyl phenyl amino, beta propanol and eight and a half grams of phenyl mustard oil.

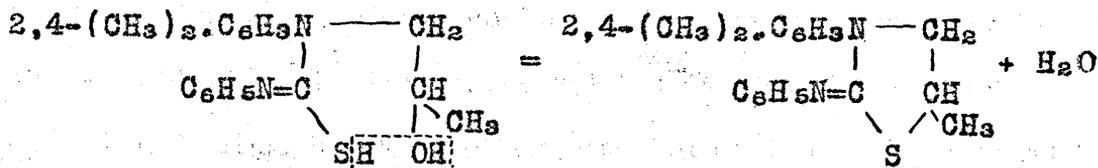


The two reagents were placed together in a small flask. The mixture seemed to have thickened after a few hours and after standing twenty-four hours had become a thick viscous gum, that could not be crystallized from ordinary solvents.

ACTION OF HYDROCHLORIC ACID ON α -2 PROPANOL,

α -2, 4 XYLYL, β PHENYL THIOUREA.

When alpha-2 propanol, alpha-2, 4 xylyl, beta phenyl thiourea is treated with hydrochloric acid, ring closure results with the formation of 2-phenyl imino, 3-2, 4 xylyl 5 methyl thiazolidine.



Five grams of the thiourea was dissolved in thirty cubic centimeters of alcohol and an equal volume of concentrated (sp. gr. 1.19) hydrochloric acid added. The mixture was allowed to stand over night. It was then diluted until no more cloudiness appeared, filtered, and the filtrate made alkaline with sodium hydroxide. The base that precipitated was crystallized from alcohol and separated as white needles

benzene solution decanted through a filter. The product was allowed to crystallize from the benzene and separated as white cubes melting at 107° .

Analysis.

Calculated for $C_{18}H_{20}ON_2$: N = 10.77%

Found: N = 10.52%; 10.63%.

Analytical Data.

Weight of sample = .2018 gms. .2019 gms.

Vol. of Acid used = 14.85 c.c. 15.02 c.c.

1 c.c. of Acid = .0014293 grams of N_2 .

Percentage of nitrogen in sample:

$$1. \frac{14.85 \times .0014293 \times 100}{.2018} = 10.52\%$$

$$2. \frac{15.02 \times .0014293 \times 100}{.2019} = 10.63\%$$

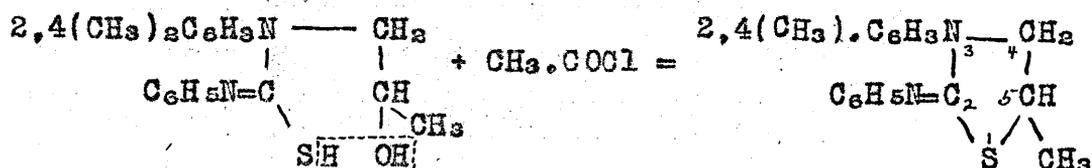
ACTION OF ACETYL CHLORIDE ON α -2 PROPANOL,

α -2,4 XYLYL, β PHENYL THIOUREA.

When acetyl chloride acts upon alpha-2 propanol, alpha 2, 4 xylyl, beta phenyl thiourea, two possibilities present themselves. The hydrogen of the beta position may be replaced by the acetyl group or ring closure with the formation of a thiazolidine may result.

Five grams of the thiourea was dissolved in benzene and placed in a round bottom flask. The mixture was refluxed on a water bath, the acetyl chloride slowly added, and heating continued for several hours. The mixture was poured

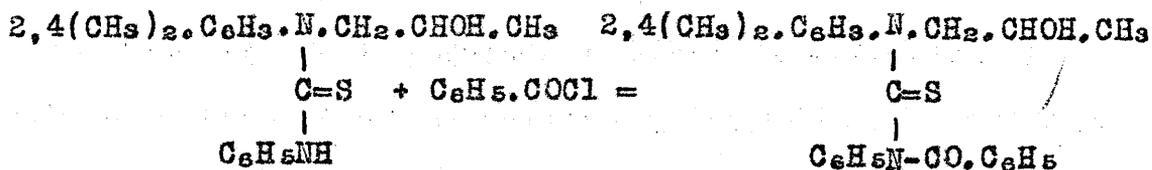
into water and after thorough agitation the two layers were separated. The benzene layer on evaporation left a trace of the original thiourea. The water layer was made alkaline with sodium hydroxide and the base that separated crystallized from alcohol. White needles melting at 118° separated. A portion of this sample was mixed with a portion of the thiazolidine obtained by the action of hydrochloric acid on the thiourea, and the melting point of the mixture determined. It melted at $118^{\circ} - 120^{\circ}$. We can safely assume that acetyl chloride causes ring closure with the formation of 2-phenyl imino, 3-2,4 xyllyl, 5 methyl thiazolidine.



ACTION OF BENZOYL CHLORIDE ON α -2 PROPANOL, α -2,4 XYLIL.

β -PHENYL THIOUREA IN THE PRESENCE OF PYRIDINE.

When benzoyl chloride acts on alpha-2 propanol, alpha-2, 4 xyllyl, beta phenyl thiourea, there are two possible reactions. Ring closure may result with the formation of a thiazolidine, but this is precluded by the presence of pyridine; and the hydrogen of the beta position may be replaced by a benzoyl group according to the following equation:

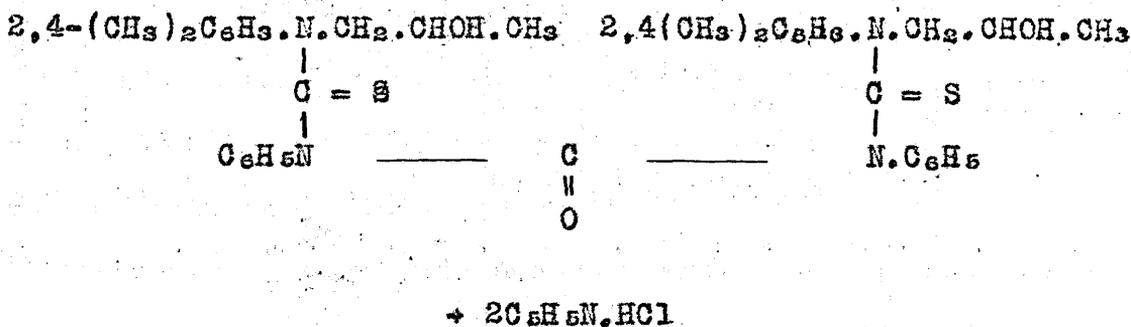
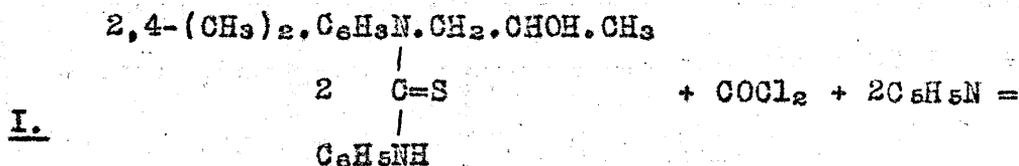


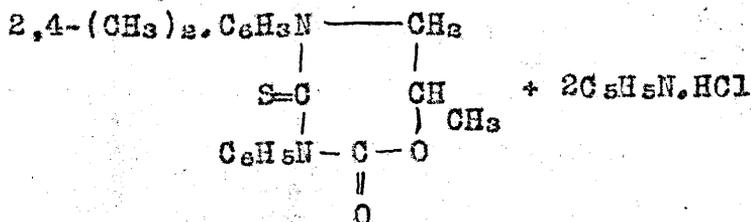
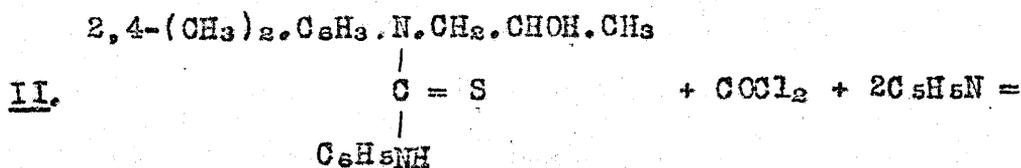
Five grams of the urea was dissolved in pyridine and five and a half grams of benzoyl chloride was added drop by

by drop with constant shaking. The color changed from light yellow to a purplish red, and much heat was evolved. A small quantity of alcohol was added to decompose any unchanged benzoyl chloride. The reaction mixture was poured into water. The gum that precipitated out was filtered off. The filtrate was made alkaline with sodium hydroxide and only a faint cloudiness appeared. All attempts to crystallize the gum from ordinary solvents failed.

ACTION OF CARBONYL CHLORIDE ON α -2 PROPANOL, α -2,4 XYLYL, β PHENYL THIOUREA IN THE PRESENCE OF PYRIDINE.

When carbonyl chloride or phosgene reacts with alpha-2 propanol, alpha-2,4 xylyl, beta phenyl thiourea, two possibilities present themselves. They are illustrated by the following equations:





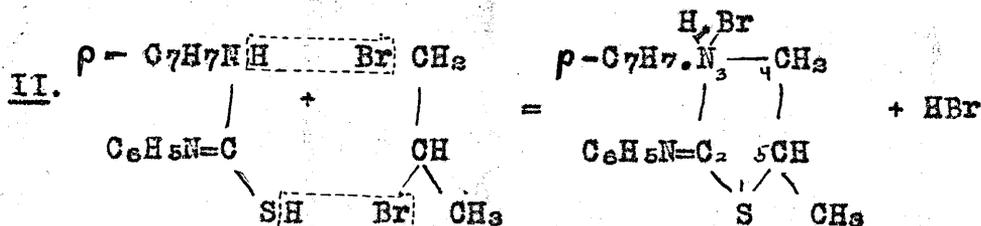
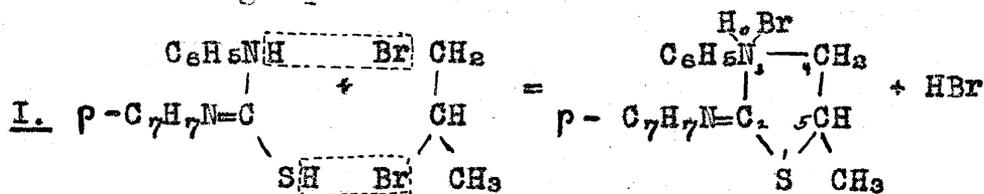
Ten grams of the urea was dissolved in fifty cubic centimeters of benzene, and to this solution three and a half grams of pyridine was added. A twenty per cent solution of phosgene in toluene was added until heat evolution ceased. During the addition of the phosgene, a red oil was thrown out of solution. The mixture was allowed to stand over night to rid itself of phosgene. The benzene was poured off and on evaporation was found to contain a considerable quantity of unchanged thiourea. The oily gum was heated with dilute hydrochloric acid and a part dissolved. The solution was filtered, made alkaline with sodium hydroxide, and the base that separated crystallized from alcohol. White prisms melting at 102° were formed. A qualitative test for sulfur proved its absence.

ACTION OF PROPYLENE DI BROMIDE ON α PHENYL.

β PARA TOLYL THIOUREA.

When alpha-phenyl, beta para tolyl thiourea reacts with propylene di bromide, two products are possible, as shown by

the following equations:

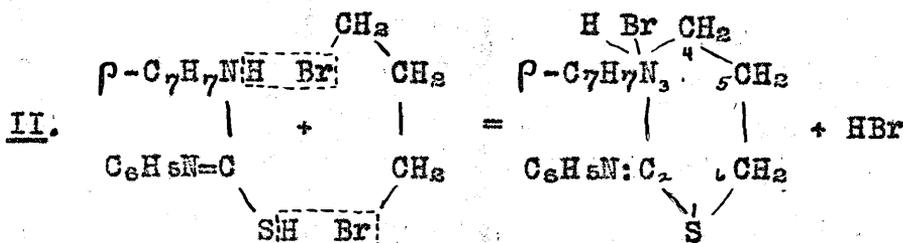
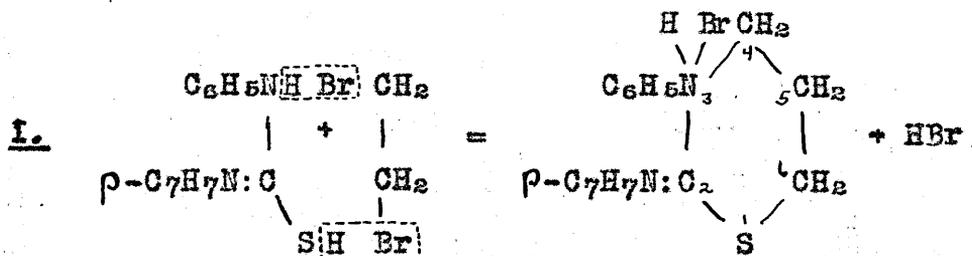


Ten grams of the thiourea was dissolved in alcohol and together with ten grams of propylene di bromide was placed in a round bottom flask and refluxed on a water bath for eight hours. The mixture was then steam distilled to remove the propylene dibromide. The oily residue was dissolved in dilute acid filtered and precipitated with sodium hydroxide. The base was crystallized from alcohol. Only a very small quantity of white crystals melting at 147° were obtained, while the residue remained a gum.

ACTION OF TRI METHYLENE BROMIDE ON α PHENYL.

β PARA TOLYL THIOUREA.

As with propylene dibromide, tri methylene bromide with alpha phenyl, beta para tolyl thiourea can react with the formation of two possible products.



Ten grams of the thiourea was dissolved in alcohol and was placed in a round bottom flask with ten grams of tri methylene bromide. The mixture was refluxed on a water bath for eight hours. The mixture was steam distilled to remove the unchanged trimethylene bromide. The oily residue was dissolved in dilute acid, filtered, and precipitated with sodium hydroxide. Attempts to crystallize the base failed. It formed what appeared to be a mixed picrate, for at room temperatures it became gummy. From this a few crystals melting at 198° were obtained.

ACTION OF PROPYLENE DIBROMIDE ON α PHENYL.

β -2,4 XYLYL THIOUREA.

When alpha phenyl, beta-2,4 xylyl thiourea is treated with propylene dibromide, there are two products possible.

BIBLIOGRAPHY.

1. S. Gabriel, Ber. 22, 2986 (1889).
2. B. Prager, Ber. 22, 2992, (1889).
3. F. B. Dains, J. A. C. S., 22, 192 (1900).
4. F. B. Dains, R. C. Roberts, and R. Q. Brewster, J. A. C. S. 38, 131-140 (1916).
5. Young and Crookes, J. A. C. S., 89, 59-76 (____).
6. Dersin, Ber. 26, 1281 (1903).
7. F. B. Dains, R. Q. Brewster, J. S. Blair, and W. C. Thompson, J. A. C. S., 44, 2637 (1922).
8. Will, Ber. 14, 1490 (1881).
9. F. G. Stubbs, Thesis, 1923, University of Kansas.
10. Deninger, Ber. 28, 1332 (1895).
11. Dixon, J. A. C. S., 101, 2522 (1912).
12. F. B. Dains, J. A. C. S., 22, 191 (1900).
13. Dixon and Taylor, J. A. C. S., 75, 405 (1899).
14. F. B. Dains, R. Q. Brewster and C. P. Olander, Kansas University Science Bulletin, Vol. 13, No. 10, July, 1922.

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Ber. = Berichte der Deutschen Chemischen Gesellschaft.
J.A.C.S. = Journal of the American Chemical Society.
J. Chem. Soc. = Journal of the Chemical Society.
Ann. = Justus Liebig's Annalen der Chemie.