THE ACTION OF ETHYLENE BROMIDE ON CERTAIN SUBSTITUTED THIOUREAS.

By

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B. S. Ottawa University, 1918.

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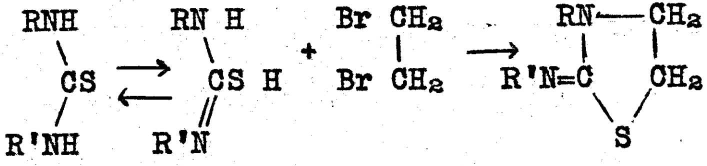
INTRODUCTION.

When ethylene dibromide reacts with certain substituted thioureas, the latter seems to react in a tautomeric form, which, with the loss of hydrogen bromide, gives a thiazolidine having a general formula of $SC(NR)NRCH_2CH_2$.



It is evident that if R and R' are different, two thiazolidines are possible. The problem of determining what influence the nature of the groups R and R' would have on the resulting thiazolidine has been the subject of a general investigation carried on at this University under the direction of Dr. F. B. Dains.

In the solution of this problem, it was first necessary to work out methods for the synthesis of both of these compounds in which the position of R and R' would be known. This much of the problem has already been completed and will be taken up later[1]. It is now possible by varying the groups R and R' to determine how their nature will affect the resulting thiazolidine. Some data has already been obtained where R and R' are aromatic. The specific problem of this investigation is the identification of the resulting compound when ethylene dibromide reacts with a substituted thiourea of the above type when R is phenyl and R' alkyl in nature.

[1] Jour. Amer. Chem. Soc. 44 3647

It was assumed to begin with that whatever groups were chosen for R and R' that a thiazolidine was always formed. Results were obtained, however, which showed that for certain substitutions this was not the case. When R' was methyl, ethyl or butyl, two mols of the thiourea reacted with one of ethylene bromide in the following manner:

$$RNHC(:NR')S\boxed{H + Br}CH_2CH_2\boxed{Br + H}S(R'N:)CNHR$$

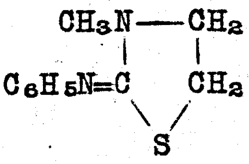
Thus, although little was accomplished on the original problem, several interesting results were obtained.

EXPERIMENTAL.

PREPARATION OF THE ETHYLENE ETHER OF PHENYL METHYL THIOUREA.

$$C_6H_5NHC(=NCH_3)SCH_2CH_2SC(:NCH_3)NHC_6H_5$$

Molar proportions of the symmetrical methyl phenyl thiourea and ethylene dibromide were heated to 110° on an oil bath. A vigorous reaction soon took place with the separation of a white solid, which was purified by washing with chloroform. Melting point 210°. This proved to the hydrobromide salt of a base and was precipitated as such from a water solution of the salt with ammonia. The base was recrystallized from alcohol and gave a melting point of 150°. This product was believed to be a thiazolidine similar to those obtained by Thompson[1]. If such was the case, it would have a formula:



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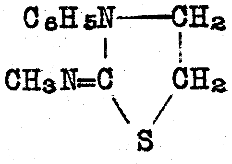
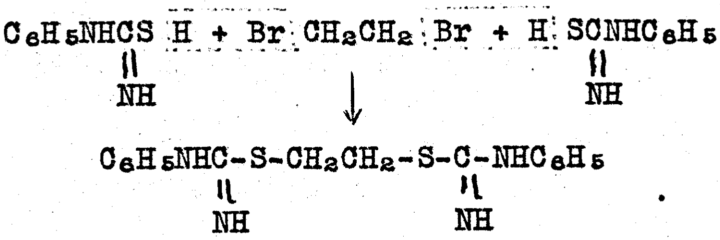


Both of these were synthesized by methods which will be described later but neither seemed to be identical to this compound.

Kucera[2] and Bertram[3] found that the unsubstituted thiourea and monophenyl thiourea reacted with ethylene dibromide to give a compound:



$$C_6H_5NH\underset{\underset{NH}{\|}}{C}S\,H + Br\,CH_2CH_2\,Br + H\,S\underset{\underset{NH}{\|}}{C}NHC_6H_5 \longrightarrow C_6H_5NH\underset{\underset{NH}{\|}}{C}-S-CH_2CH_2-S-\underset{\underset{NH}{\|}}{C}-NHC_6H_5$$

The dihydrobromide was first formed having a melting point of 213° from which the free base was precipitated, the latter having a melting point of 139°. It was thought that the compound obtained here with methyl phenyl thiourea was similar to the above compound prepared by Kucera. Accordingly, a second preparation was made using two mols of the thiourea to one of the bromide. An almost theoretical yield of the hydrobromide salt was obtained with no excess of the ethylene dibromide as was the case in the first preparation. This evidence for the ethylene ether formula was further supported by its nitrogen content and its molar weight.

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[2] Monatschefte für Chemie, 35, 137-157.
[3] Berichte, 25 , 59.

Analysis (Kjeldahl Method).

	I	II
Weight of sample used (grams)	.2	.2
Volume of HCl	20.5	20.
Volume of NaOH	3.2	2.35
Correction for blank c.c. HCl	.5	.5
Percent nitrogen	15.25	15.28

HCl = .123 N NaOH = .088 N

Calculated for $C_{18}H_{22}N_4S_2$ -15.60

Molar Weight Determination.

	I	II
Freezing point pure solvent C_6H_6	4.74	4.74
" " solution	4.58	4.415
" " lowered	.16	.325
Weight of solvent	44.	44.
" " solute	.5	1.0
Molar Weight	355	350

Calculated for above 356.

ETHYLENE ETHER OF PHENYL ETHYL THIOUREA.

$C_6H_5NHC(=NC_2H_5)SCH_2CH_2SC(:NC_2H_5)NHC_6H_5$

Two mols of phenyl ethyl thiourea reacted with one of ethylene dibromide when heated to 110°. The dihydrobromide salt separated in the reaction flask and was purified by washing with chloroform. An almost theoretical yield of the salt was obtained. The free base was precipitated by making an aqueous solution alkaline with ammonia. A perchlorate salt was made by adding perchloric acid to a slightly acid solution of the base. The perchlorate salt crystallized out in almost transparent needles.

Melting point free base	130°
Melting point hydrobromide salt	196°
Melting point perchlorate salt	160°

On a second preparation, the components of the reaction were heated to 125 to 130°. The hydrobromide salt did not separate as before but instead hydrogen bromide was evolved as a gas. To obtain the base, the mixture was distilled with steam to remove excess of ethylene dibromide and the residue in flask made alkaline. The product of the reaction was precipitated, filtered and recrystallized from alcohol and benzene. This was identical with the previous preparation.

Analysis (Kjeldahl Method).

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	4.2	4.25
Correction for blank	.5	.5
Weight of sample	.2 grs.	.2 grs.
Percent of nitrogen	14.20	14.19

NaOH = .088 N HCl = .123 N

Calculated for $C_{20}H_{26}N_4S_2$ 14.50%

Molar Weight Determination.

Freezing point pure solvent C_6H_6	4.75
" " solution	4.595
" " lowered	.155
Weight of solvent	42.
" " solute	.5
Molar weight	370
Calculated for above	386

ETHYLENE ETHER OF NORMAL BUTYL PHENYL THIOUREA.

$C_6H_5NHC(:NC_4H_9)SCH_2CH_2SC(:NC_4H_9)NHC_6H_5$

Fifteen grams of normal butyl phenyl thiourea thiourea was heated at 110° for two hours with an equal weight of ethylene dibromide. Hydrogen bromide was evolved. No solid separated as it did in the two previous cases. The mixture was distilled with steam to remove any excess ethylene bromide. It was then made alkaline with ammonia and a base was precipitated. This was filtered off and recrystallized from alcohol. It was expected that this might be a thiazolidine since the butyl and phenyl groups are nearly equal in weight. Both the nitrogen content and molar weight, however, indicated that as before the ethylene ether type of compound was formed. Melting point 92°.

Analysis Nitrogen Kjeldahl Method.

	I	II
Volume of acid	20.0	20.0
" " alkalie	12.3	12.1
Correction for blank	.5	.5
Weight of sample	.15	.15
Percent Nitrogen	12.30	12.45

NaOH = .088 N HCl = .123 N

Calculated for $C_{24}H_{34}N_4S_2$ 12.67%

Molar Weight Determination.

Weight of solute	.5
Weight of solvent	44.0
Freezing point of solvent C_6H_6	4.735
" " " solution	4.610
" " lowered	.125
Molar weight	454
Calculated for above	444

PROPYLENE ETHER OF METHYL PHENYL THIOUREA.

$C_6H_5NHC(:NCH_3)SCH(CH_3)CH_2SC(:NCH_3)NHC_6H_5$

In order to see whether the propylene bromide would have a different effect on the resulting compound when heated with one of these thioureas, the former was heated at 110° with 10 grams of methyl phenyl thiourea. A solid separated as before which proved to be the hydrobromide salt of a base. An 80% yield of the salt was obtained with a melting point of 195°. The free base was precipitated with ammonia from a water solution. Melting point 120°. Analysis to obtain the percent of nitrogen indicated that the ethylene ether was formed here also and is represented by the above formula.

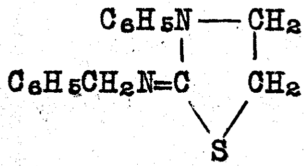
Analysis.

	I	II
Volume of acid used	20.0	20.0
Volume of alkalie used	8.8	8.65
Correction for blank	.5	.5
Weight of sample	.15	.15
Percent nitrogen	15.16	15.27

NaOH = .088 N   HCl = .123 N

Calculated for $C_{19}H_{25}N_4S_2$ = 15.01%

PREPARATION OF 2 BENZYLIMINO 3 PHENYL THIAZOLIDINE.



Fifteen grams of benzyl phenyl thiourea was heated with an equivalent amount of ethylene dibromide at 125° for two hours. No solid separated as with the methyl and ethyl derivatives. The excess ethylene bromide was removed by steam distillation and the solution made alkaline. An oil was precipitated which could not be made to crystallize from any solvent. It was redissolved in dilute HCl and picric acid added to a part. This gave the picrate salt which melted at 140°. The rest was converted to the perchlorate in the same manner. This had a melting point of 85°.

Analysis showed that in this case the product was a thiazolidine and not the ethylene ether type of compound. The nitrogen content corresponds to the thiazolidine. It is also identical with the 2 benzylimino 3 phenyl thiazolidine as was synthesized from phenyl amino ethanol and benzyl mustard oil. This will be described later.

<u>Analysis of Nitrogen in $HClO_4$ Salt.</u>

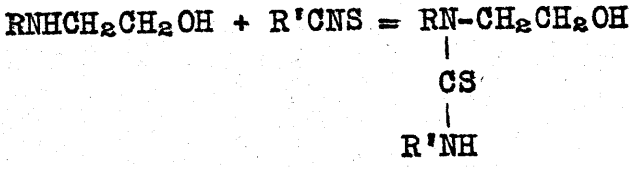
Volume of acid used	20.0
Volume of alkalie used	11.5
Correction for blank	.5
Weight of sample	.2513
Percent nitrogen	7.70

HCl = .123 N   NaOH = .088 N

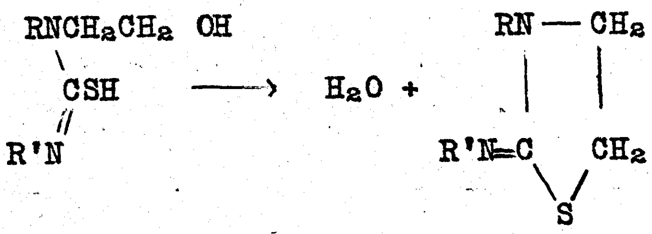
Calculated for $C_{16}H_{16}N_2SHClO_4$ = 7.65%

It has been stated that ethylene dibromide may react with these disubstituted thioureas in three ways. Two of these gives isomeric thiazolidines and the third an ethylene ether where two mols of the thiourea are joined by an ethylene grouping. In identifying the first two, it was necessary to synthesize both by the methods worked out by Thompson as mentioned before. These may be summarized here:

Aryl or alkyl amino ethanols react with the mustard oils to give ethanol thioureas, which by loss of water and ring closure, yield thiazolidines of known structure.



$$RNHCH_2CH_2OH + R'CNS = \begin{array}{c} RN{-}CH_2CH_2OH \\ | \\ CS \\ | \\ R'NH \end{array}$$



R and R' may be chosen as desired and the resulting thiazolidine be used for the identification of those where the position of R and R' is not known.

Thiazolidines were synthesized in this manner using groups for R and R' corresponding to those used in the thioureas which were treated with ethylene dibromide. In doing this, it was first necessary to prepare a quantity of the ethanols and of the mustard oils.

PREPARATION OF METHYL MUSTARD OIL.

Twenty-seven grams of carbon bisulfide together with 15 grams of NaOH in water solution were stirred with a turbine in an ice bath while 31 grams of 33% methyl amine solution was slowly added. One-half hour was used for the addition. The stirring was continued until almost completely solidified due to the separation of the sodium methyl di thio carb~~on~~amate. After standing for an hour, it was added to a solution of lead nitrate (110 grams) and the methyl mustard oil obtained by steam distillation. Yield 8 grams 31%. Melting point 31°. Boiling point 120°.

ETHYL MUSTARD OIL.

Forty-five grams of 33% solution ethyl amine were added slowly to a mixture of 27 grams carbon bisulfide and 15 grams sodium hydroxide in water solution. The mixture was kept in an ice bath and well stirred during the addition of the amine. The whole mixture solidified in a few minutes due to the separation of the sodium ethyl dithio carbamate. This was then added to a solution of 110 grs. lead nitrate. The ethyl mustard oil was then obtained by steam distillation. Yield 15 grams or 50%. B.P. - 131°

BENZYL MUSTARD OIL.

Fifteen grams of benzyl amine were added slowly to a mixture of 11 grams sodium hydroxide and 12 grams carbon bisulfide. The mixture was kept cool and stirred vigorously for two hours. No solid separated as before. Fifty grams of lead nitrate in solution was then added and steam distilled. The benzyl mustard oil separated in the receiver as an oil. This was separated and distilled. Yield 50%. Boiling point 240°.

The reactions involved in the preparation of these mustard oils are given below:

$$RNH + CS_2 + KOH \longrightarrow RNHCSSK$$

$$RNHCSSK + Pb(NO_3)_2 \longrightarrow RNCS + KNO_3 + HNO_3$$

PREPARATION OF THE ETHANOLS.

PHENYL AMINO ETHANOL. (1ST METHOD).

Two mols of aniline and one of ethylene chlor hydrine were heated together for several hours at 120° to 130°.

$$C_6H_5NH\,H + Cl\,CH_2CH_2OH \longrightarrow C_6H_5NHCH_2CH_2OH + HCl$$

The extra mol of aniline takes up the hydrogen chloride liberated in the reaction. The mixture was then made alkaline and the excess aniline removed by steam distillation. The tarry residue is separated, dried, and distilled under reduced pressure. The distillate is the pure ethanol. Boiling point at 18 m.m. 167°. Yield 60%.

(SECOND METHOD).

Twenty-five ethylene chlor hydrine were allowed to react with solid NaOH. The ethylene oxide gas thus formed was passed into 31 grams of aniline. The gas dissolved with evolution of heat. The solution was warmed to 50° - 70° under sufficient pressure to keep the ethylene oxide from escaping. At first the pressure rose to 50 cm. above atmospheric but gradually decreased as the reaction proceeded. After three hours, the mixture was distilled under reduced pressure.

Yield: 20 grams $C_6H_5NHCH_2CH_2OH$
4 grams $C_6H_5N(CH_2CH_2OH)_2$
14 grams unchanged amine.

BENZYL AMINO ETHANOL.

$C_6H_5CH_2NHCH_2CH_2OH$

The calculated amount of ethylene chlor hydrin was treated with solid sodium hydroxide and the ethylene oxide gas formed passed into 12 grams of benzyl amine. The reaction was somewhat more rapid than with the phenyl derivative. It was necessary to cool the amine occasionally to prevent evaporation. The mixture was then heated under pressure as before and then distilled under reduced pressure. Boiling point at 65 m.m. 192°.

Yield: 5 1/2 grams unchanged amine
5 grams $C_6H_5CH_2NHCH_2CH_2OH$

ETHYL AMINO ETHANOL.

$C_2H_5NHCH_2CH_2OH$. Boiling Point 168°.

In the preparation of ethyl amino ethanol, the same method was used except that no heating under pressure was required. Here the ethylene oxide reacted vigorously with the amine. It was necessary to keep the reaction flask in cold water to prevent the excape of the ethyl amine. Under atmospheric pressure, the unchanged amine was completely removed by distillation up to 125°. The ethanol, together with some water in which it is soluble, was collected from 125° to 170°.

Eighteen grams of ethylene chlor hydrin and 24 grams of 33% ethyl amine solution gave a yield of:

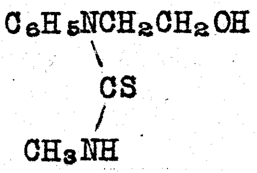
$C_2H_5NHCH_2CH_2OH$	50% solution	15 grs.
$C_2H_5(CH_2CH_2OH)_2$		6 grs.
$C_2H_5NH_2$	unchanged about 30% sol	8 grs.

METHYL AMINO ETHANOL.

$CH_3NHCH_2CH_2OH$. Boiling Point 157°.

The same method was used in the preparation of methyl amino ethanol as for the ethyl derivative and approximately the same yield obtained. The unchanged amine was treated with more ethylene oxide and a still greater yield obtained.

$\alpha\alpha$ PHENYL ETHANOL β METHYL THIOUREA.



$$\begin{array}{l} C_6H_5NCH_2CH_2OH \\ \qquad \backslash \\ \qquad CS \\ \qquad / \\ \quad CH_3NH \end{array}$$

Molar proportions of phenyl amino ethanol and methyl mustard oil ? were dissolved in alcohol and heated on a water bath for an hour. Upon standing and allowing the alcohol to evaporate, the thiourea separated in large cubical crystals. Yield 85%. Melting point 69°.

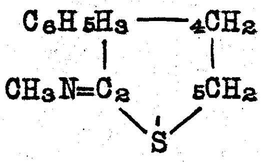
Analysis Nitrogen.

	I	II
Volume of acid	20.45	20.0
Volume of alkalie	6.85	5.5
Correction for blank	.5	.5
Weight of sample	.2	.2
Percent nitrogen	13.00	13.39

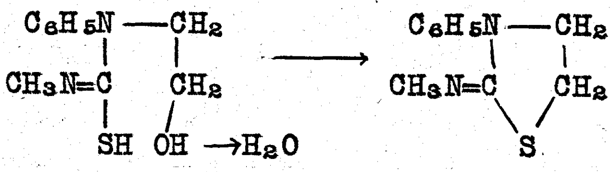
NaOH = .088 N HCl = .123 N

Calculated for $C_{10}H_{14}N_2SO$ 13.33%

2 METHYL-IMINO 3 PHENYL THIAZOLIDINE.



The phenyl ethanol methyl thiourea was heated with concentrated hydrochloric acid until completely dissolved. Water is lost and the ring closes giving a thiazolidine as the hydrochloride salt. The free base was precipitated by making alkaline with ammonia. The product was recrystallized from alcohol. Melting point 45°.



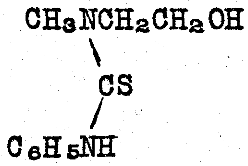
Analysis Nitrogen.

	I	II
Volume alkalie	4.0	3.9
Volume acid	20.05	20.1
Correction for blank	.5	.5
Weight of sample	.2	.2
Percent nitrogen	14.36	14.38

NaOH = .088 N HCl = .123 N

Calculated for $C_{10}H_{12}N_2S$ -14.58%

αα METHYL ETHANOL β PHENYL THIOUREA.



Molar proportions of methyl amino ethanol and phenyl mustard oil reacted vigorously when mixed. The thiourea separated as a solid. It was filtered off and recrystallized from alcohol. Melting point 95°.

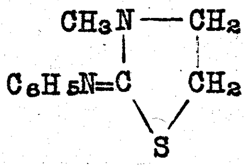
Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	10.5	10.3
Correction for blank	.75	.75
Weight of sample	.15	.15
Percent nitrogen	13.47	~~15.64~~ 13.60

NaOH = .088 N HCl = .123 N

Calculated for $C_{10}H_{1\underset{4}{\cancel{6}}}N_2OS$ 13~~.21%~~ 34

2 PHENYL-IMINO 3 METHYL THIAZOLIDINE.



When the methyl ethanol phenyl thiourea was warmed with concentrated hydrochloric acid until completely dissolved, water is formed and the ring closes giving a thiazolidine. This is identical with the one made from methyl mustard oil except here the methyl and phenyl groups are reversed. Melting point 89°.

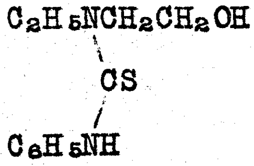
Analysis Nitrogen.

	I	II
Volume of acid	20.05	20.0
Volume of alkalie	4.0	3.9
Correction for blank	.5	.5
Weight of sample	.2	.2
Percent of nitrogen	14.36	14.40

NaOH = .088 N HCl = .123 N

Calculated for $C_{10}H_{12}N_2S$ = 14.58%

α α ETHYL ETHANOL β PHENYL THIOUREA.



$$\begin{array}{l} C_2H_5NCH_2CH_2OH \\ \quad \diagdown \\ \qquad CS \\ \quad \diagup \\ C_6H_5NH \end{array}$$

The reaction here is the same as with the methyl derivative. Seven grams of the ethanol with an equivalent quantity of phenyl mustard oil gave a yield of seven grams of the thiourea. This was recrystallized from alcohol or can be purified by washing with a little benzene. Melting point 152°.

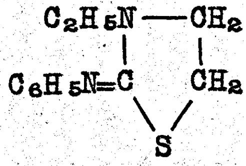
Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	8.5	13.0
Correction for blank	.5	.5
Weight of sample	.184	.138
Percent of nitrogen	12.62	12.74

NaOH = .088 N HCl = .123 N

Calculated for $C_{11}H_{16}ON_2S$ -12.50%

2 PHENYL-IMINO 3 ETHYL THIAZOLIDINE.



The same method for preparation of the thiazolidines from ethanol thioureas was tried in this case but without success. When ethyl ethanol phenyl thiourea was warmed with concentrated hydrochloric acid, it partially dissolved. When this was filtered and made alkaline, an oil was precipitated. The same result was obtained with hydrobromic acid and acetyl chloride. The oil was redissolved in dilute acid and perchloric acid added. A salt slowly crystallized out which an analysis of the nitrogen content corresponded to the calculated value for the perchlorate salt of the above thiazolidine. Melting point 90°.

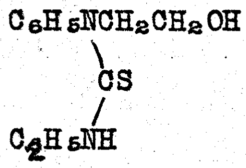
Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	16.5	16.65
Correction for blank	.5	.5
Weight of sample	.15	.15
Percent of nitrogen	8.80	8.75

NaOH = .088 N HCl = .123 N

Calculated for $C_{11}H_{14}N_2S.HClO_4$ 9.10%

αα PHENYL ETHANOL β ETHYL THIOUREA.



$$\begin{array}{l} C_6H_5NCH_2CH_2OH \\ \quad \diagdown \\ \quad\ CS \\ \quad / \\ C_2H_5NH \end{array}$$

Phenyl amino ethanol and ethyl mustard reacted in molar proportions either alone or in alcohol solution. An almost theoretical yield was obtained in each case. On standing and allowing the alcohol to evaporate, large crystals of the thiourea separated which had a melting point of 97°.

Analysis Nitrogen.

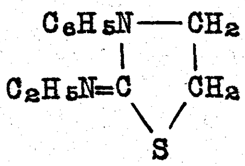
	I	II
Volume of acid	20.0	20.0
Volume of alkalie	6.8	8.95
Correction for blank	.5	.5
Weight of sample	.2	.1837
Percent of nitrogen	12.55	12 .30

HCl = .123 N NaOH = .088 N

Calculated for $C_{11}H_{16}ON_2S$ 12.50%

0

2 ETHYL-IMINO 3 PHENYL THIAZOLIDINE.



The phenyl ethanol ethyl thiourea on warming with concentrated hydrochloric acid suffered ring closure and loss of water giving the above thiazolidine. It was precipitated from the acid solution with ammonia and recrystallized from alcohol. Melting point 42°. Part of it was converted to the perchlorate salt which was precipitated from a very dilute acid solution on the addition of perchloric acid. Melting point 68°.

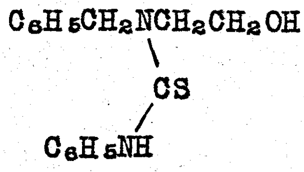
Analysis nitrogen.

	I	II
Volume of acid	20.0	20.6
Volume of alkalie	10.7	5.8
Correction for blank	.5	.5
Weight of sample	.15	.2
Percent of nitrogen	13.5	13.7

HCl = .123 N NaOH = .088

Calculated for $C_{11}H_{14}N_2S$ 13.6%

αα BENZYL ETHANOL β PHENYL THIOUREA.



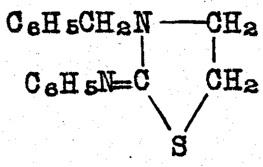
Benzyl amino ethanol reacted vigorously with phenyl mustard oil. A thick syrupy liquid was formed which crystallized out from benzene solution. Melting point 110°.

Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.15
Volume of alkalie	16.0	15.9
Correction for blank	.5	.5
Weight of sample	.15	.15
Percent of nitrogen	9.26	9.52

Calculated for $C_{16}H_{18}ON_2S$ 9.79%

2 PHENYL-IMINO 3 BENZYL THIAZOLIDINE.



Benzyl ethanol phenyl thiourea gave the corresponding thiazolidine when warmed with concentrated hydrochloric acid. When it was completely dissolved in the acid, the solution was made alkaline and the thiazolidine thus precipitated. This was recrystallized from benzene. Melting point 100°. Due to lack of reagents and only a fair yield, only enough for one analysis was obtained.

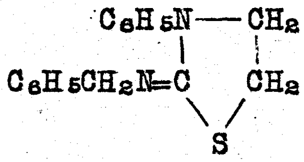
Analysis Nitrogen.

Volume of acid	20.0
Volume of alkalie	14.2
Correction for blank	.5
Weight of sample	.15
Percent of nitrogen	10.60

NaOH = .088 HCl = .123 N

Calculated for $C_{16}H_{14}N_2S$ = 10.45%

2 BENZYL-IMINO 3 PHENYL THIAZOLIDINE.



Benzyl mustard oil was allowed to react with phenyl amino ethanol. Heat was evolved but the thiourea thus formed could not be separated as a solid. It remained as a heavy oil. This was heated with concentrated hydrochloric acid until almost completely dissolved. Ammonia was then added to alkaline reaction. An oil was precipitated, which could not be made to crystallize from any solvent. It was redissolved in dilute acid and enough perchloric acid added to completely reprecipitate it as the perchlorate salt. This was first formed as a gummy substance but on standing gradually changed to a crystalline mass. Melting point 85°.

Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	11.5	13.0
Correction for blank	.5	.7
Weight of sample	.2513	.237
Percent of nitrogen	7.73	7.42

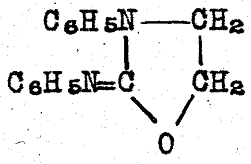
NaOH = .088 N HCl = .123 N

Calculated for $C_{16}H_{16}N_2S.HClO_4$ 7.61%

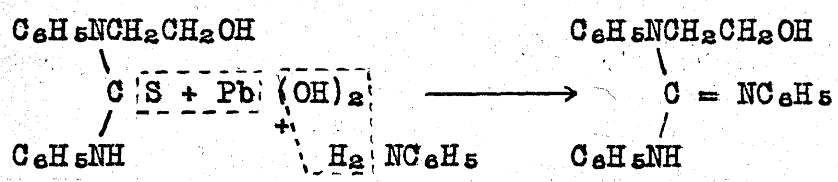
This compound is identical with that obtained from benzyl phenyl thiourea and ethylene dibromide. Both are oils and give perchlorate salts which are solids of the same melting point and whose mixed melting point does not change.

Insufficient data has been obtained to make any generalizations as to what effect the nature of the substituted groups has on these three ways in which the thioureas react with ethylene dibromide. In all cases which have been tried, the ethylene ether is formed when one substituted group is hydrogen or an alkyl group. If both are aryl, a thiazolidine is formed. However, since the benzyl group usually reacts as an alkyl group, the difference may be due more to the difference in weight of the substituted groups than to their aromatic or aliphatic nature.

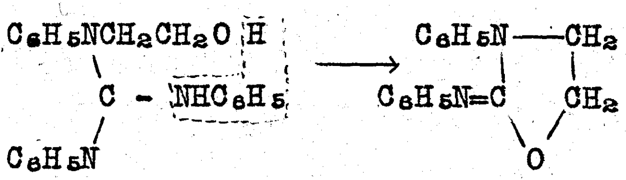
2 PHENYL-IMINO 3 PHENYL OXAZOLIDINE.



Among some of the attempted reactions was that of desulphurizing agents in the presence of aniline on the ethanol thioureas. Thirty grams of diphenyl ethanol thiourea was heated on a water bath for five hours in alcohol solution with lead hydroxide and an equivalent amount of aniline. The lead sulfide formed was filtered off while hot and the product of the reaction crystallized out on cooling. Melting point 113°. The reaction was tried in the hope of finding another method for the synthesis of certain oxazolidines.



This ethanol substituted triphenyl quanidine could then, by loss of aniline and ring closure, give an oxazolidine.



The product that was obtained was the 2 phenyl-imino 3 phenyl oxazolidine, identical with that obtained by Malm[1] in the desulphurization of diphenyl ethanol thiourea with

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[1] Jour. Amer. Chem. Soc., 44, 3647.

mercuric oxide. If the reaction did go as the equations given indicate, the intermediate product of triphenyl quanidine could not be isolated. The same reaction was tried using ammonia in place of aniline and the same result obtained.

Analysis Nitrogen.

	I	II
Volume of acid	20.0	20.0
Volume of alkalie	8.35	8.2
Correction for blank	.5	.5
Weight of sample	.2	.2
Percent of nitrogen	11.65	11.73

NaOH = .088 N HCl = .123 N

Calculated for $C_{15}H_{14}ON_2$ 11.70%

ETHYLENE ETHER OF MONOPHENYL THIOUREA.

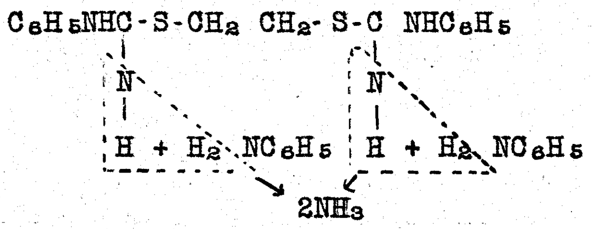
$C_6H_5NHC(:NH)SCH_2CH_2SC(:NH)NHC_6H_5$

Two gram mols of aniline were added to an equivalent amount of hydrochloric acid and the whole mixed with two gram mols of ammonium thiocyanate in water solution. The mixture was then evaporated nearly to dryness on a water bath. Water was then added, filtered, and washed again with water. Yield 170 grams. Monophenyl thiourea. Melting point 152°. This was then heated with 75 grams of ethylene dibromide on a water bath. A vigorous reaction soon took place with the separation of the hydrobromide salt of the ethylene ether of monophenyl thiourea. Yield

150 grams. The free base was precipitated from a water solution of the salt with ammonia. Melting point 139°. This compound was previously prepared by Bertram.[1]

2 PHENYL-IMINO 3 PHENYL THIAZOLIDINE.

It was thought that this ethylene ether might, by heating with aniline, substitute $C_6H_5N=$ for the $=NH$ group with loss of ammonia in the following manner:



This would give a tetra phenyl derivative such as could not be obtained from the thiourea and ethylene dibromide because the latter gives a thiazolidine instead. With this in mind, 70 grams of the ethylene ether was heated on an oil bath at 125° for four hours with 40 grams of aniline. Ammonia was liberated during the reaction. The excess aniline was then removed by distilling with steam. The residue in the flask solidified on cooling, was separated from the water, and recrystallized from alcohol. It was necessary to recrystallize several times to obtain the product in pure enough form for analysis. The alcohol filtrate on allowing to evaporate, left a sticky mass which could not be made to crystallize from any other solvent. The attempt to identify this by-product was abandoned.

[1] Berichte, 25, p. 59.

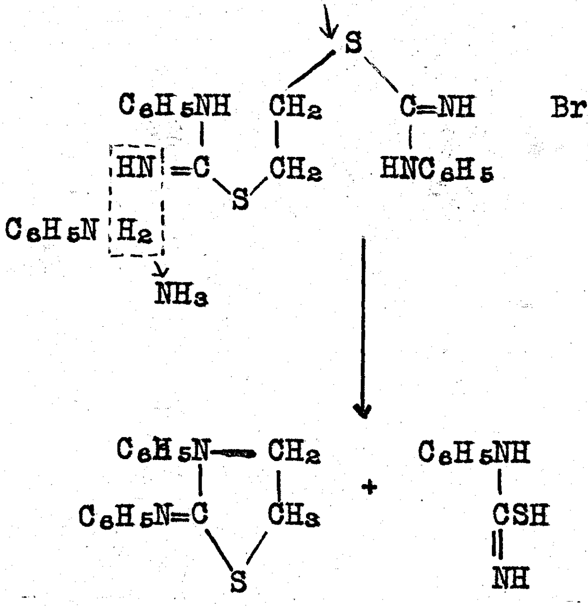
Melting point of the first product was 136°. A mixed melting point with the original compound was 125°, showing the two to be different.

The results of analysis for the nitrogen content did not check with that of the tetra phenyl substituted ethylene ether; also, the molar weight as determined from the freezing point in benzene solution was approximately half the calculated value.

An attempt was made to prepare a chlorine derivative by using para chlor aniline in the first reaction. Ammonia was liberated in this case, but the only product that could be isolated could not be obtained in pure enough form to give consistent results on analysis. It was boiled for six hours in alcohol solution with animal charcoal. On filtering and allowing the filtrate to cool, a product crystallized out which gave a melting point of 115° to 123°.

The product obtained with aniline was boiled for four hours with alcoholic sodium hydroxide. No reaction occurred. This would indicate that it must be much more stable than the ethylene ether from which it was made, since that latter undergoes decomposition.

In trying to arrive at some other possibility for the constitution of this compound, three facts were considered: (1) its stability which might indicate a ring structure, (2) relatively low molar weight and (3) at least one other by product besides ammonia. Decomposition must then take place. The following equation represents the only possibility which will fulfill all of these conditions:



Breaks at arrow.

The compound obtained was identical with 2 phenyl-imino 3 phenyl thiazolidine. The same was synthesized from ethylene dibromide and diphenyl thiourea. Both had melting points of 136°. A mixed melting point was unchanged.

<u>Analysis Nitrogen.</u>

	I	II	III
Volume of acid	20.4	20.	20.
Volume of alkalie	10.4	9.5	14.
Correction for blank	.5	.5	.5
Weight of sample	.2	.2	.15
Percent nitrogen	10.75	10.93	10.90

NaOH = .088 N HCl = .123 N

Calculated for $C_{15}H_{14}N_2S$ = 11.02%

Molar Weight Determination.

	I	II
Freezing point pure solvent C_6H_6	3.915	3.915
" " solution	3.680	3.455
" " lowered	.235	.460
Weight of solvent	44.	44.
" " solute	.5	1.0
Molar weight	242.	247.

Calculated for above 254.

SUMMARY

Insufficient data has been obtained to make any very general conclusions regarding the action of ethylene dibromide on the disubstituted thioureas. This investigation has been limited to those substitutions where the group attached to nitrogen is alkyl and to the other phenyl. If the benzyl group may be considered as aromatic, then all data thus far obtained seems to indicate that when at least one substituted group is hydrogen or aliphatic in nature an ethylene ether type of compound is formed. If both groups are aromatic in nature, a thiazolidine is formed. As was mentioned previously, two thiazolidines are possible. With benzyl phenyl thiourea 2 benzyl-imino 3 phenyl is the one formed.

The following gives the product formed with ethylene bromide on the various thioureas together with their melting points and results of analysis.

Thiourea	M.P.	% Nitrogen		Molar Wt.		Type of Compound Formed
		Found	Calc.	Found	Calc.	
Methyl Phenyl	152	15.26	15.60	353	356	Ethylene Ether
Ethyl Phenyl	130	14.20	14.50	370	386	Ethylene Ether
Butyl Phenyl	92	12.40	12.67	454	444	Ethylene Ether
Benzyl Phenyl ($HClO_4$ salt).	85	7.70	7.65	---	---	Thiazolidine

The following table gives the melting points and results of analysis of the ethanol thioureas and the thiazolidines formed therefrom when the amino ethanols react with the mustard oils.

$$RNHCH_2CH_2OH + R'NCS$$

R	R'	THIOUREAS			THIAZOLIDINES		
		M.P.	Found	Calc.	M.P.	Found	Calc.
Phenyl	Methyl	69	13.20	13.33	45	14.37	14.58
Phenyl	Ethyl	97	12.42	12.54	42	13.60	13.60
Phenyl	Benzyl	oil	------	------	$HClO_4$ salt 85°	7.56	7.61
Methyl	Phenyl	95	13.55	13.21	89	14.38	14.58
Ethyl	Phenyl	152	12.67	12.50	$HClO_4$ salt 90°	8.80	9.10
Benzyl	Phenyl	110°	9.52	9.79	100	10.60	10.45

In concluding this paper, the writer wishes to express his appreciation to Dr. F. B. Dains and Dr. R. Q. Brewster for the direction of this work and for their many helpful suggestions.

Chemical Laboratories,
University of Kansas,
June, 1923.

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