

SYNTHESES OF THIAZANE DERIVATIVES.

By

Fleming G. Moore.

B.S. Texas Agricultural and Mechanical College, 1902.

Submitted to the Department of
Chemistry and the Faculty of the
Graduate School of the University
of Kansas in partial fulfillment of
the requirements for the degree of
DOCTOR OF PHILOSOPHY.

Approved by: J. B. Wains
Instructor in Charge.

H. P. Cady
Chairman of Department.

Diss
1925
Moore
c. 2

June, 1925.

R00055 38799

DEDICATED

to

FRANK BURNETT DAINS.

Versatile Chemist,
Cultured Gentleman,
and
Sympathetic Friend.

TABLE OF CONTENTS.

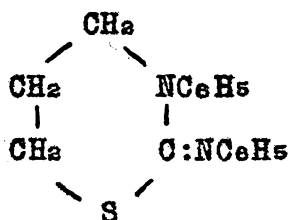
	<u>Page.</u>
INTRODUCTION-----	1
SYNTHESES OF 2-ARYLIMINO-3-ARYL-5-HYDROXY-1,3-THIAZANES FROM AMINES, EPICHLORHYDRIN, AND MUSTARD OILS--	5
2-PHENYLIMINO-3-PARA-BROMPHENYL-5-HYDROXY-1,3-THIAZANE-----	7
2-PARA-TOLYLIMINO-3-BETA-NAPHTHYL-5-HYDROXY-1,3-THIAZANE-----	10
2-PARA-TOLYLIMINO-3-PHENYL-5-HYDROXY-1,3-THIAZANE--	13
2-ORTHO-TOLYLIMINO-3-ORTHO-TOLYL-5-HYDROXY-1,3-THIAZANE-----	15
2-PHENYL-3-ORTHO-CHLORPHENYL-5-HYDROXY-1,3-THIAZANE-----	16
SYNTHESES OF 2-ARYLIMINO-3-ARYL-5-HYDROXY-1,3-THIAZANES FROM THIOUREAS AND EPICHLORHYDRIN-----	18
2-PHENYLIMINO-3-PHENYL-5-HYDROXY-1,3-THIAZANE-----	19
2-PARA-TOLYLIMINO-3-PARA-TOLYL-5-HYDROXY-1,3-THIAZANE-----	21
2-ORTHO-TOLYLIMINO-3-ORTHO-TOLYL-5-HYDROXY-1,3-THIAZANE-----	23
2-META-XYLYLIMINO-3-META-XYLYL-5-HYDROXY-1,3-THIAZANE-----	25
COMPARISON OF HYDROXY THIAZANES MADE BY TWO METHODS--	28
REACTIONS OF THIAZANES-----	29
THIAZANE AND OXALIC ACID-----	29
THIAZANE AND HYDROCHLORIC ACID-----	29
THIAZANE AND METHYL IODIDE-----	30
OXIDATION OF A THIAZANE-----	31
REACTION OF THIOCARBANILIDE AND ALPHA, GAMMA-DICHLORACETONE-----	33

	Page.
STUDY OF THE HYDROCHLORIDE-----	33
AMOUNT OF HCl IN THE HYDROCHLORIDE-----	34
CHLORINE IN THE HYDROCHLORIDE-----	36
NITROGEN IN HYDROCHLORIDE-----	39
HYDROCHLORIDE LOSES WEIGHT ON HEATING-----	38
STUDY OF THE BASE-----	40
NITROGEN IN THE BASE-----	42
A POSSIBLE FORMULA FOR THE BASE-----	42
REACTIVITY OF VARIOUS ALKYL BROMIDES WITH DIPHENYL THIOUREA-----	46
PREPARATION AND PURIFICATION OF REAGENTS-----	48
STANDARDIZATION OF SOLUTIONS USED IN TITRATION-----	50
A BLANK ON AgNO ₃ AND KCNS-----	50
A BLANK ON THIOCARBANILIDE AND ACETONE-----	51
ETHYL BROMIDE AND THIOCARBANILIDE-----	52 and 53
N-PROPYL BROMIDE AND THIOCARBANILIDE-----	52 and 54
ISO-PROPYL BROMIDE AND THIOCARBANILIDE-----	55 and 56
N-BUTYL BROMIDE AND THIOCARBANILIDE-----	55 and 57
ISO-BUTYL BROMIDE AND THIOCARBANILIDE-----	58 and 59
SEC-BUTYL BROMIDE AND THIOCARBANILIDE-----	58 and 60
TER-BUTYL BROMIDE AND THIOCARBANILIDE-----	61 and 62
COMPARISON OF REACTIVITIES OF VARIOUS ALKYL BRO- MIDES WITH THIOCARBANILIDE-----	61 and 63

INTRODUCTION.

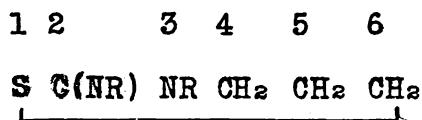
The thiazanes are compounds containing a six-membered heterocyclic ring consisting of four carbon atoms, one nitrogen atom, and one sulfur atom. If the sulfur and nitrogen atoms in the ring are in the meta position to one another, the compound is called a meta-thiazane.

The first record of the preparation of a meta-thiazane is by F. Foerster¹. By the reaction of trimethylene bromide with thiocarbanilide, he obtained what he called phenyl-imido-phenyl-thiocarbaminsäure trimethylene äther, to which he gave the formula



The current name for this compound is 2-phenylimino-3-phenyl-1, 3-thiazane.

The type formula for such a compound is



Compounds of this type have been made in a variety of ways:

1. By the reaction of trimethylene dibromide with thioureas.¹

2. By the reaction of trimethylene dibromide with

1. Ber. 21, 1872 (1888).

thioamides².

3. By the reaction of trimethylene chloro-bromide with thioamides³.

4. By the reaction of gamma-halogenated alkyl amines with carbon bisulfide, as well as alkali rhodanids, mustard, oils or thioamides⁴.

5. By splitting off water from the thioureas formed from gamma-oxy amines and mustard oils⁵.

6. By splitting off water from the product derived from the reaction of beta-iodopropionic acid and Xanthogenamid or di-thiocarbamic acid salts⁶.

7. By condensation of nitro-malonic-dialdehyde with thioureas⁷.

8. By the dehydration of the N-formyl-derivative of the gamma-amino-propyl mercaptans⁸.

In the Laboratory of Organic Chemistry at the University of Kansas, under the direction of Professor F. B. Dains, considerable work has been done on the synthesis

²Gabriel, Heymann, Ber., 23, 157 (1890); Ber., 24 783 (1891); Kahan, Ber., 30, 1320 (1897).

³Pinkus, Ber., 26, 1077 (1893); Rehländer Ber., 27, 2160 (1894); Saulmann, Ber., 33 2635 (1900).

⁴Gabriel, Lauer, Ber. 23, 87 (1890); Luchmann, Ber. 29 (1896) 1429-30; Kahan, Ber. 30, 1320-21 (1897).

⁵Kahan, Ber. 30, 1324 (1897)

⁶Langlet, Ber. 24, 3851 (1891).

⁷Hale, Brill, Am. Soc. 34, 295 (1912).

⁸Gabriel, Ber. 49, 1111, 1113 (1916)

of these meta-thiazane derivatives by the reaction of aryl gamma-hydroxy-propyl amines with the aryl isothiocyanates, the aryl-amino-propanols being prepared from trimethylene chlorohydrin and appropriate amines⁹. Another related line of work conducted in this laboratory has been the synthesis of 2-aryl-imino-3-aryl-5 hydroxy,-1,3-thiazanes¹⁰.

The research on which this thesis is based has been concerned mainly with the synthesis and properties of some of these hydroxy thiazane derivatives, and certain collateral problems which developed during this work. The first of these studies has had to do with the synthesis of the hydroxy thiazane derivatives from amines, epichlorhydrin, and mustard oils. The second set of studies has had to do with the synthesis of such derivatives from thioureas and epichlorhydrin. The results of these two parts of the work were very satisfactory. The constitution of the thiazanes made by the two methods is more firmly established by the close agreement of the properties and composition of the corresponding products.

Another portion of this research has involved a study of the reactivity of some of these thiazanes with various reagents. As a result of these reactions, it was hoped to make some new derivatives of a different type. This lead to the consideration of reactions of thioureas with

⁹Dains, et al, J. A. C. S., 44
2640 (1922).

¹⁰Dains, et al, J. A. C. S., 44
2641 (1922).

other halogen and oxygen derivatives of propane. Also, there arose the problem of determining the relative reactivity of certain alkyl groups, when their halides were allowed to react with various thioureas. In this lot of work, owing to difficulties of technique and lack of time, the results have not been so well rounded out as in the first parts of the work; but, as will appear in the body of this thesis, many very interesting results have been obtained; and there have developed numerous problems for further research.

SYNTHESES OF 2-ARYL-IMINO-3-ARYL-5-HYDROXY-1, 3-THIAZANES
FROM AMINES, EPICHLORHYDRIN, AND MUSTARD OILS.

In the work of Dains, Brewster, Blair, and Thompson¹¹, some 2-aryl-imino-3-aryl-5-hydroxy-1, 3-thiazanes were made. The first step was to make the alpha-amino-beta-hydroxy-gamma-chloropropane derivatives according to the method of Cohn and Friedlander¹² by adding epichlorhydrin to substituted amines in alcohol solution. To such solutions, Dains et al subsequently added mustard oils. After this, the material was extracted with dilute HCl and the free thiazane precipitated from the acid extract by the addition of NH₄OH in excess.

Some additional syntheses by these reactions have been made. In practically all cases, it has been found sufficient and easy to work according to the following method: The amine and epichlorhydrin, each in alcoholic solution, are put together in a beaker. The solution is allowed to stand over night or longer, evaporation being retarded by covering. Mustard oil in alcoholic solution is added. The solution is allowed to stand over night or longer, evaporation being retarded as before. The cover is removed and evaporation allowed to proceed spontaneously until a copious crop of crystals has formed and diminution of the liquid phase has apparently stopped. The mass is treated

¹¹J. A. C. S., 44, 2641 et seq (1922).

¹²Ber. 37, 3035 (1804).

with two or three times its volume of dilute HCl (1:5), warming on water-bath with frequent stirring for an hour or longer. Often it is advisable to repeat the extraction with HCl one or more times. After warming with the HCl, allow the mixture to cool and settle over night. Decant through filter. Dilute the filtrate with an equal volume of water, when more or less precipitate may form, rendering necessary a repetition of the separation process. The clear acid filtrate is poured, with constant stirring, into an excess of NH_4OH , when the basic thiazane precipitates. Sometimes a chunk of ice in the NH_4OH facilitates the hardening of the precipitate, which may be liquid at first while the mixture is warm from the heat of reaction. After settling, the precipitate is collected on a filter, suction usually being advisable, washed with dilute NH_4OH , and thoroughly drained. The thiazane is next dried on a plate. Further purification, as a rule, is readily effected by successive crystallization, once or more from alcohol and once or more from benzene.

The acid insoluble portion in the above process, when washed on the filter with cold denatured alcohol, usually leaves a residue, which in some cases has been proven, in other cases has been assumed to be a substituted thiourea, such as is formed by the direct action of the amine and mustard oil used.¹³

The alcoholic filtrate from the above residue, upon

¹³W. Weith, Ber. 6, 210 et seq (1873).

evaporation leaves a more or less viscous liquid. The exact nature of this portion of the separated products is not yet fully determined. The matter requires further study.

2-Phenyl-imino-3-para-brom-phenyl-5-hydroxy-

1, 3-thiazane.

34.4 grams para-Brom-aniline

18.5 grams Epichlorhydrin

27. grams Phenyl mustard oil

100 c.c. Denatured alcohol

The para-brom-aniline and the epichlorhydrin were dissolved in the alcohol, and the solution allowed to stand two days. The phenyl-mustard oil was added and the solution allowed to stand two days longer. About two hours after adding the mustard oil, white crystals had formed, and by the end of the two days crystals had formed throughout the mass and the excess solvent had largely evaporated.

The crystals were separated by filtration, digested with hot dilute HCl, again thrown on filter and washed with water. By successive crystallization from hot denatured alcohol, the crystals were purified, until a melting point of 157° was reached. These crystals were proved to be 4-brom-diphenyl-thiourea by making a sample of the latter from para-brom-aniline and phenyl mustard oil and comparing melting points: unknown sample, 157° ; known 4-brom-diphenyl-thiourea, 159° , mixture, 158° .

The mother liquor from these first crystals, upon standing another day, gave a second small crop of crystals.

These, when washed with denatured alcohol, were found similar to the main bulk of thiazane later separated; melting point 177° .

The acid washings from the first crop of crystals, when poured into excess NH_4OH gave a white precipitate. The precipitate was washed with dilute NH_4OH and recrystallized; from denatured alcohol, melting point $164-7^{\circ}$; from benzene, melting point 177° .

The mother liquor from the second crop of crystals was warmed with dilute HCl , resulting in a yellow oil underneath a milky aqueous layer. After settling the aqueous layer was repeatedly decanted through filter until clear.

The yellow oil was steam-distilled. There came over a small amount of almost white oil. This was proved to be phenyl mustard oil by treating with aniline and comparing the crystalline product, after washing with dilute HCl and alcohol, with a known sample of thiocarbanilide: unknown product, melting point 153° ; known thiocarbanilide, melting point 153° ; mixture, melting point 153 .

After the steam-distillation, there remained behind a very viscous yellow liquid. This was dissolved in alcohol, but the solution gave no crystals on standing. After the alcohol had evaporated, there still remained a thick syrupy liquid. It is insoluble in water. It is apparently neither an acid nor a base. It is soluble in

ether and in cold concentrated H_2SO_4 . The solution in H_2SO_4 , when poured on ice, yields a white precipitate becoming pasty on warming. So far, the identity of this thick liquid fraction is undetermined.

The clear acid aqueous layer from the digestion of the mother liquor with hot dilute HCl was poured into an excess of NH_4OH , producing a pinkish-white precipitate. This precipitate was purified by successive crystallization from alcohol: melting points observed being $143-9^\circ$, $147-9^\circ$, $150-5^\circ$.

It being quite evident that the crystals were impure, they were washed on filter with cold dilute HCl. The filtrate on standing gave crystals, evidently the hydrochloride, completely soluble in water; melting point 191° .

The residue from above treatment with cold dilute HCl, when treated with warm dilute HCl, practically all dissolved. This solution was filtered and poured into excess of NH_4OH . The white precipitate was successively crystallized: from alcohol, melting points 172° and 177° sharp; from benzene, melting point 177° sharp.

The total yield of base from the various fractions was about 20 grams.

The base was analyzed for nitrogen by the Gunning method: found, 7.52% and 7.36%; calculated for $C_{16}H_{16}ON_2SBr$, 7.71%.

	(1)	(2)	(B)
	.3155	.3459	
Correction	<u>.0025</u>	<u>.0025</u>	
Sample	.3130 gm.	.3434 gm.	0
H ₂ SO ₄	30 c.c.	30 c.c.	30 c.c.
NaOH	44.8	43.6	61.4

1 c.c. NaOH = .486 c.c. acid.

1 c.c. H₂SO₄ = .00292 grams N.

	44.8	43.6	61.4
x	<u>.486</u>	<u>.486</u>	<u>.486</u>
	21.77	21.19	29.84
	30	30	30
-	<u>21.77</u>	<u>21.19</u>	<u>29.84</u>
	8.23	8.81	.16
Deduct for blank	<u>.16</u>	<u>.16</u>	
	8.07	8.65	

$$(1) \frac{8.07 \times .00292 \times 100}{.3130} = 7.52\%$$

$$(2) \frac{8.65 \times .00292 \times 100}{.3434} = 7.36\%$$

Calculated for C₁₆H₁₅ON₂SBr = 7.71%

2-para-Tolyl-imino-3-beta-naphthyl-5-hydroxy-
1, 3-thiazane.

15 grams beta naphthyl amine.

10 grams Epichlorhydrin

q.s. 200 c.c. Denatured Alcohol

4 grams ~~Para-Tolyl-mustard oil.~~

8 grams ~~para-Tolyl-mustard oil.~~ *B-naph*

The beta-naphthyl amine was dissolved in 150 c.c. of alcohol. The epichlorhydrin, in its own volume of alcohol, was added. After standing over night, the solution was filtered, and enough alcohol was added to make 200 c.c. of solution.

To 50 c.c. of above solution, 4 grams of para-tolyl mustard oil was added. The violet-brown solution was warmed on the water bath until a thick brown syrup was formed. No crystals formed even after prolonged standing. When the syrup was treated with water containing a little HCl, the syrup partially dissolved. Upon filtering, there was obtained an orange-brown gummy residue and a nearly clear yellow filtrate. This filtrate was treated with dilute NaOH in slight excess, yielding a light orange precipitate. The precipitate was separated by filtering with suction and dried on paper. The yield was about 2 grams.

The process was repeated, except that double quantities were used, and NH_4OH was used to precipitate the thiazane. This time the yield was about 4 grams.

After drying on porous plate, the crystals had a melting point of $117-123^\circ$. The product was purified by successive crystallization from alcohol and washing with petro-

leum ether. The final product, though still slightly tinged with orange, seemed practically pure; melting point 152° .

The thiazane was analyzed for nitrogen by the Kjeldahl method: found 8.10% and 8.23%; calculated for $C_{21}H_{20}ON_2S$, 8.05%.

	(1)	(2)	(B)
Sample	.2000 gm.	.2000 gm.	0
H ₂ SO ₄	25 c.c.	25 c.c.	25 c.c.
NaOH	19.4	19.3	25.2
1 c.c. NaOH = .927 c.c. acid.			
1 c.c. H ₂ SO ₄ = .00301 gram N.			
	19.4	19.3	25.2
x	<u>.927</u>	<u>.927</u>	<u>.927</u>
	17.98	17.89	23.36
	25	25	25
-	<u>17.98</u>	<u>17.89</u>	<u>23.36</u>
	7.02	7.11	1.64
Deduct for blank	<u>1.64</u>	<u>1.64</u>	
	5.38	5.47	

$$(1) \frac{5.38 \times .00301 \times 100}{.2} = 8.10\%$$

$$(2) \frac{5.47 \times .00301 \times 100}{.2} = 8.23\%$$

Calculated for $C_{21}H_{20}ON_2S$ = 8.05%.

2-para-Tolyl-imino-3-phenyl-5-hydroxy-1,3-thiazane.

50 grams Aniline

50 grams Epichlorhydrin

80 grams para-Tolyl mustard oil.

100 c.c. Denatured alcohol.

The aniline, freshly redistilled, and the epichlorhydrin, each in 50 c.c. of alcohol, were mixed and allowed to stand over night. The para-tolyl mustard oil was added in two lots about three days apart (no particular reason for the time of adding the mustard oil is now recalled except failure to add it all the first time.) The entire mixture was heated on the water bath for about three hours when it formed a thick reddish-brown syrup. Upon treatment with water acidulated with HCl, a considerable portion of yellowish-brown gummy substance would not dissolve. All the material was subjected to steam-distillation. Some 4 or 5 c.c. of light yellow oil, doubtless para-tolyl mustard oil came over. After this oil had practically ceased to distill, all of the gummy residue not being dissolved, the stuff remaining in the distilling flask was cooled and decanted through filter. Dilute NaOH was added in slight excess to the filtrate, resulting in the formation of a nearly white precipitate, gummy at first, but finally hardening to a chalk-like mass. The yield was about 70 grams.

Part of above base, 20 grams, was dissolved in dilute HCl, reprecipitated with NH_4OH , collected on filter, washed,

dried on paper, and finally dried on porous plate. The yield was 18 grams. Melting point was 116-117°. After successive crystallization from alcohol and washing with petroleum ether, the apparently pure thiazane gave a melting point at 139°.

The thiazane was analyzed for nitrogen by the Kjeldahl method: found 9.43% and 9.21%; calculated for $C_{17}H_{18}ON_2S$, 9.40%.

	(1)	(2)	(B)
Sample	.2000 gms.	.2000 gms.	0
H ₂ SO ₄	25 c.c.	25 c.c.	25 c.c.
NaOH	18.4	18.6	25.2

1 c.c. NaOH = .927 c.c. H₂SO₄.

1 c.c. H₂SO₄ = .00301 gram N.

	18.4	18.6	25.2
x	<u>.927</u>	<u>.927</u>	<u>.927</u>
	17.06	17.24	23.36
	25	25	25
-	<u>17.06</u>	<u>17.24</u>	<u>23.36</u>
	7.94	7.76	1.64
Deduct for blank	<u>1.64</u>	<u>1.64</u>	
	6.30	6.12	

$$(1) \frac{6.30 \times .00301 \times 100}{.2} = 9.43\%$$

$$(2) \frac{6.12 \times .00301 \times 100}{.2} = 9.21\%$$

Calculated for $C_{17}H_{18}ON_2S$ = 9.40%.

2-ortho-Tolyl-imino-3-ortho-tolyl-5-hydroxy-
1, 3-thiazane.

107 grams ortho-Toluidine.

92.5 grams Epichlorhydrin.

250 c.c. Denatured alcohol.

149 grams ortho-Tolyl Mustard Oil.

The ortho-toluidine and epichlorhydrin were dissolved in the alcohol and allowed to stand over night. The ortho-tolyl mustard oil was added. The mixture was allowed to stand a week, the solvent being allowed to evaporate spontaneously. The thick syrup was mixed with an equal amount of water containing a few c.c. of HCl, and digested at about 100° for about an hour. The acid solution was filtered off and poured into an excess of NH₄OH, cooled with ice. The precipitated base was collected on filter, washed, dried, and crystallized several times from alcohol. The yield was about 22 grams. The melting point was 139-140°.

The thiazane was analyzed for nitrogen by the Kjeldahl method: found 9.21% and 8.87%; calculated for C₁₈H₂₀ON₂S, 8.98%.

	(1)	(2)	(B)
	4.7636 gms.	4.7391 gms.	
	<u>4.5184</u>	<u>4.5184</u>	
Sample	.2452	.2207	0
H ₂ SO ₄	20 c.c.	20 c.c.	20 c.c.
NaOH	24.4	26.6	40.9
1 c.c. NaOH = .4762 c.c. H ₂ SO ₄ .			
1 c.c. H ₂ SO ₄ = .002873 gram N.			
	24.4	25.6	40.9
x	<u>.4762</u>	<u>.4762</u>	<u>.4762</u>
	11.62	12.67	19.48
	20	20	20
-	<u>11.62</u>	<u>12.67</u>	<u>19.48</u>
	8.38	7.33	.52
Deduct for blank	<u>.52</u>	<u>.52</u>	
	7.86	6.81	

$$(1) \frac{7.86 \times .002873 \times 100}{.2452} = 9.21\%$$

$$(2) \frac{6.81 \times .002873 \times 100}{.2207} = 8.87\%$$

Calculated for C₁₈H₂₀ON₂S = 8.98%.

2-Phenyl-3-ortho-chlorophenyl-5-hydroxy-

1, 3-thiazane, attempted.

25.5 grams ortho-Chloraniline.

18.5 grams Epichlorhydrin.

27 grams Phenyl mustard oil.

100 c.c. Denatured Alcohol.

The ortho-chlor aniline and epichlorhydrin were mixed in alcoholic solution and let stand over night. The phenyl mustard oil was added and the mixture allowed to stand several days. Got a viscous brown syrup. When treated with dilute HCl, part of the syrup dissolved. From this solution, alkali precipitated a light brown oil. This oil had basic properties. Efforts to get a solid by crystallization from alcohol, or by solution in acid and reprecipitation with NaOH or NH_4OH have thus far failed to give a crystalline product. Further work will be necessary before one can say whether the basic oil is a mixture or a chemical individual, and in the latter case, what.

SYNTHESES OF 2-ARYL-IMINO-3-ARYL-
5-HYDROXY-1, 3-THIAZANES FROM
THIOUREAS AND EPICHLORHYDRIN.

In the work of Dains, Brewster, Blair, and Thompson¹⁴ the 2-phenylimino-3-phenyl-5-hydroxy-1, 3 thiazane was made by heating thio-carbanilide and epichlorhydrin in acetone solution for some hours. From the products of this reaction, a base was obtained which was identical with the base obtained by the former method from aniline, epichlorhydrin, and phenyl mustard oil. Both products melted at 175°.

This reaction has been repeated and extended. In all, the diphenyl, di-ortho-tolyl, di-para-tolyl, and di-metaxylyl derivatives have been made. As a rule, the obtaining and purification of the crystalline bases was more tedious, and the yields seemed very much smaller than by the former method. There was obtained considerable oil, as yet unidentified, which had some of the properties of a mercaptan. The greater part of the crystalline material obtained had the high melting points and other properties of substituted ureas. It seemed that the various thio-ureas, under the influence of the epichlorhydrin, were converted into the corresponding ureas.

¹⁴J. A. C. S., 44, 2642
(1922).

2-Phenylimino-3-phenyl-5-hydroxy-1,3-thiazane.

50 grams Thiocarbanilide.

25 grams Epichlorhydrin.

100 c.c. Denatured alcohol.

The epichlorhydrin was dissolved in the alcohol and the thiocarbanilide was added. All of the thiocarbanilide did not dissolve at first, though all of it had dissolved by the time the mixture had been heated on a water bath under a reflux for about an hour. This heating was continued for about 8 hours. After standing over the weekend, the alcohol was distilled off on water bath. The residue was distilled with steam for about an hour. This distillate, after settling and filtering, was extracted with ether. The ether was allowed to evaporate, yielding yellow oil. This was soluble in HCl. The acid solution, when treated with excess NaOH, gave a precipitate like the original oil. The oil was soluble in water. When the aqueous solution was treated with a solution of $HgCl_2$, a heavy white curdy precipitate was formed. The identity or constitution of this oil has not yet been fully established.

The residue, after the steam distillation, was yellow and pasty. It was warmed on the water bath with dilute HCl. The mixture was allowed to settle and filtered. The residue, insoluble in HCl, was repeatedly crystallized from alcohol, digested with acetone, and boiled with pe-

petroleum ether. The white crystals obtained, melting point 234-235°, proved to be diphenyl urea.

The filtrate, from the digestion with HCl, was cooled with ice, and treated with an excess of NaOH, yielding a white precipitate, which was collected and washed on the filter. This precipitate was dissolved in hot acetone, and the solvent allowed to evaporate spontaneously, producing white crystals, tinged with red, melting point 167-168°. Further crystallization from acetone gave crystals melting at 170-172°. These crystals were finally boiled with petroleum ether and recrystallized from acetone. The yield was about 19 grams.

The product was identical with the thiazane obtained from aniline, epichlorhydrin, and phenyl mustard oil, both samples and their mixture melting sharp at 175°. This thiazane was analyzed for nitrogen by the Kjeldahl method: found 9.82% and 9.95%; calculated for $C_{16}H_{18}ON_2S$, 9.86%.

	(1)	(2)	(B)
	15.5820 gms.	15.1843 gms.	
	15.1843	14.8082	
Sample	.3937	.3761	
H ₂ SO ₄	25.05 c.c.	25.	25.1 c.c.
NaOH	21.6	22.4	49.6

1 c.c. NaOH = .48 c.c. H₂SO₄.

1 c.c. H₂SO₄ = .002888 gram N.

	21.6	22.4	49.6
x	<u>.48</u>	<u>.48</u>	<u>.48</u>
	10.57	10.75	23.81
	25.05	25.	25.1
-	<u>10.37</u>	<u>10.75</u>	<u>23.81</u>
	14.68	14.25	1.29
Deduct for blank	<u>1.29</u>	<u>1.29</u>	
	13.39	12.96	

$$(1) \frac{13.39 \times .002888 \times 100}{.3937} = 9.82\%$$

$$(2) \frac{12.96 \times .002888 \times 100}{.3761} = 9.95\%$$

Calculated for $C_{12}H_{12}ON_2S = 9.86\%$.

2-para-Tolylimino-3-para-tolyl-5-hydroxy-
1,3-thiazane.

30 grams Di-para-tolyl Thiourea.

21 grams Epichlorhydrin.

50 c.c. Denatured alcohol.

The dipara-tolyl thiourea was added to the solution of the epichlorhydrin in the alcohol. The mixture was heated on a water bath under a reflux until all the thiourea dissolved, taking about two hours. The mass was treated with 20 c.c. HCl in 200 c.c. alcohol, allowed to stand, and decanted through filter. The filtrate was cooled with ice and NH_4OH added in slight excess, yielding a white

precipitate, which was separated by suction-filtration. When the precipitate was treated with alcohol and HCl, it partly dissolved. From the residue, the corresponding oxygen urea was isolated.

The acid filtrate was cooled with ice and treated with an excess of NH_4OH . The white precipitate was successively crystallized from hot alcohol, dissolved in dilute HCl, poured into ice cold NH_4OH , collected, dried on plate, boiled with petroleum ether, and recrystallized from alcohol. The yield was about 12 grams.

The product, melting point $142-142.5^\circ$, was compared with the thiazane, melting point $141.5-142.5^\circ$, from para-toluidine, epichlorhydrin, and para-tolyl mustard oil, the mixture of the two bases melting at $142-143^\circ$. This thiazane was analyzed for nitrogen by the Kjeldahl method: found 8.77% and 8.76%; calculated for $\text{C}_{18}\text{H}_{20}\text{ON}_2\text{S}$, 8.98%.

	(1)	(2)	(B)
	4.6931 gms.	4.7324 gms.	
	4.5182	4.5182	
Sample	.1749	.2142	0
H_2SO_4	20 c.c.	20 c.c.	20.
NaOH	28.4 c.c.	25.9	39.6

1 c.c. NaOH = .4762 c.c. H_2SO_4 .

1 c.c. H_2SO_4 = .002873 gram N.

	28.4	25.9	39.6
x	<u>.4762</u>	<u>.4762</u>	<u>.4762</u>
	13.52	12.33	18.86
	20	20	20
-	<u>13.52</u>	<u>12.33</u>	<u>18.86</u>
	6.48	7.67	1.14
Deduct for blank	<u>1.14</u>	<u>1.14</u>	
	5.34	6.53	

$$(1) \frac{5.34 \times .002873 \times 100}{.1749} = 8.77\%$$

$$(2) \frac{6.53 \times .002873 \times 100}{.2142} = 8.76\%$$

Calculated for $C_{18}H_{20}ON_2S = 8.98\%$.

2-ortho-Tolylimino-3-ortho-tolyl-5-hydroxy-
1,3-thiazane.

60 grams Di-ortho-tolyl thiourea.

42 grams Epichlorhydrin.

100 c.c. Denatured alcohol.

The di-ortho-tolyl thiourea was added to the solution of epichlorhydrin in alcohol. The mixture was heated on a water bath, under a reflux, until the thiourea was all dissolved. The alcoholic solution was poured into water containing HCl and the mixture warmed. After settling, the residue was separated from the supernatant acid solution by decanting through filter. The corresponding oxygen urea

was recovered from this residue.

The acid filtrate was poured into excess of NH_4OH , cooled with ice. The precipitated base was purified by alternate crystallization from alcohol and boiling with petroleum ether. The yield was about 17 grams.

The product was compared with the thiazane obtained from ortho-toluidine, epichlorhydrin, and ortho-tolyl mustard oil; both samples and the mixture melted at $139-140^\circ$. This thiazane was analyzed for nitrogen by the Kjeldahl method: found 9.21% and 9.16%; calculated for $\text{C}_{18}\text{H}_{20}\text{ON}_2\text{S}$, 8.98%.

	(1)	(2)	(B)
	4.7534 gms.	4.7769 gms.	
	<u>4.5184</u>	<u>4.5184</u>	
Sample	.2350	.2585	0
H_2SO_4	20 c.c.	20 c.c.	20 c.c.
NaOH	25.1	23.6	40.9
1 c.c. NaOH = .4762 c.c. H_2SO_4 .			
1 c.c. H_2SO_4 = .002873 gram N.			
	25.1	23.6	40.9
x	<u>.4762</u>	<u>.4762</u>	<u>.4762</u>
	11.95	11.24	19.48
	20	20	20
-	<u>11.95</u>	<u>11.24</u>	<u>19.48</u>
	8.05	8.76	.52
Deduct for blank	<u>.52</u>	<u>.52</u>	
	7.53	8.24	

$$(1) \frac{7.53 \times .002873 \times 100}{.2350} = 9.21\%$$

$$(2) \frac{8.24 \times .002873 \times 100}{.2586} = 9.16\%$$

Calculated for $C_{18}H_{20}ON_2S = 9.98\%$

2-meta-Xylylimino-3-meta-xylyl-5-hydroxy-
1,3-thiazane.

The di meta-xylyl thioure was first prepared from

67 grams 1:3:4 Xylidine.

50 grams Carbon bisulfide.

1 gram Sulfur.

100 c.c. Denatured alcohol.

These ingredients were mixed and allowed to stand over night. The brown solution was then heated about four hours, on a water bath under a reflux. A white precipitate formed. The mother liquor was evaporated on a water bath, leaving a pinkish to brownish solid. This was purified by digesting with warm alcohol, and subsequent washing on filter with warm alcohol.

The di meta-xylyl thiourea from above.

20 c.c. Epichlorhydrin.

100 c.c. Denatured Alcohol.

These ingredients were mixed and heated on a water bath under a reflux for about eight hours. Not all of the solid material was in solution at the end of this time. Upon standing, more solid material crystallized out of the

solution. The liquid was filtered off. The solid was washed with alcohol. It was apparently the corresponding oxygen urea, more or less pure.

The filtrate and washings from above were diluted with water. A light brown oil was precipitated. The composition of this oil is as yet undetermined.

The aqueous layer from above was poured into ice cold NH_4OH . A dirty white pasty precipitate was formed. It was very difficult to get any of this basic material into crystalline form. But after several times redissolving in HCl and reprecipitating with NH_4OH , and after repeated crystallization from alcohol, a good sample of crystalline solid was secured. The yield was between 2 and 3 grams.

This thiazane was finally purified to the point where it melted sharply at 146° . It was analyzed for nitrogen by the Kjeldahl method: found 8.24-% and 8.24+%; calculated for $\text{C}_{10}\text{H}_{14}\text{ON}_2\text{S}$, 8.24-%.

	(1)	(2)	(B)
	4.7846 gms.	4.7964 gms.	
	<u>4.5179</u>	<u>4.5179</u>	
Sample	.2667	.2667	0
H_2SO_4	20 c.c.	20 c.c.	20 c.c.
NaOH	25.12	24.5	41

1 c.c. NaOH = .483 c.c. H_2SO_4 .

1 c.c. H_2SO_4 = .00288 gram N.

	25.2	24.5	41
x	<u>.483</u>	<u>.483</u>	<u>.483</u>
	12.17	11.83	19.80
	20	20	20
-	<u>12.17</u>	<u>11.83</u>	<u>19.80</u>
	7.83	8.17	.20
Deduct for blank	<u>.20</u>	<u>.20</u>	
	7.63	7.97	

$$(1) \frac{7.63 \times .00288 \times 100}{.2667} = 8.24\%$$

$$(2) \frac{7.97 \times .00288 \times 100}{.2785} = 8.24\%$$

Calculated for $\text{Ca}_0\text{H}_{40}\text{N}_2\text{S} = 8.24\%$.

COMPARISON OF HYDROXY THIAZANESMADE BY TWO METHODS.

Three of these thiazanes have been made by both methods. The corresponding derivatives are shown to be identical by agreement of melting points and checking of analyses. The data is summarized in the following table:

Derivative	Average % of N		Calculated % of N	First Method	Second Method	Mixture
	First Method	Second Method				
diphenyl	10.07	9.89	9.86	175	175	175
di-o-tolyl	9.19	9.04	8.98	139- 140	139- 140	139- 140
di p-tolyl	8.97	8.77	8.98	141.5- 142.5	142- 142.5	142- 143

REACTIONS OF THIAZANES.Thiazanes and Oxalic Acid.

Oxalic acid was dehydrated by heating to about 110° for nearly a day with frequent stirring. Five grams of this dehydrated acid was mixed with five grams of 2-para-tolylimino-3-para-tolyl-5-hydroxy-1,3-thiazane. The mixture was heated on an oil bath for about one hour, at approximately the melting point of the thiazane, $141-142^{\circ}$. The material melted with frothing. It cooled to a vitreous mass. Nearly all of the product dissolved in alcohol. The alcoholic solution was concentrated by spontaneous evaporation. Upon addition of water, a white precipitate formed. Nearly all dissolved in dilute HCl. The residue was yellowish and pasty. From the acid solution, NH_4OH gave a pinkish precipitate. This was crystallized from alcohol, yielding fine white grains which were dried on a porous plate. The original thiazane, the product, and a mixture of the two had the same melting points $141-143^{\circ}$. Apparently the fusion with oxalic acid had no effect on the thiazane.

Thiazane and Hydrochloric Acid.

One gram of crude 2-phenylimino-3-phenyl-5-hydroxy-1,3-thiazane was boiled for three hours with 50 c.c. HCl (1:1). The thiazane completely dissolved. The solution was treated with 20% NaOH solution in excess, yielding a white precipitate. This precipitated was collected on filter, washed, and dried. The yield was .95 grams. The

original thiazane, the product, and a mixture of the two had melting points between 158-160°.

Some of the above thiazane was recrystallized from alcohol. About five grams (rough balance) of same was boiled gently for eight hours with 100 c.c. HCl (1:1). After cooling, the solution was neutralized with 20% NaOH solution. The precipitate was collected, washed, dried, and recrystallized from alcohol. The yield was about 4.85 grams. The original thiazane, the product, and a mixture of the two had melting points between 173-174°.

Apparently, boiling the thiazane with HCl (1:1) was without appreciable effect.

Thiazane and Methyl Iodide.

Eleven grams of 2-phenylimino-3-phenyl-5-hydroxy-1,3-thiazane and 18 c.c. of methyl iodide were mixed in a small flask and allowed to stand. The mixture formed a red paste after about a week, the crystals of thiazane seeming to disintegrate, more or less. The material was heated on the water bath under a reflux for about eight hours. After this, it was allowed to stand another week. The red paste seemed thicker. Various solvents, including petroleum ether, ether, alcohol, chloroform, carbon tetrachloride, and benzene, were used in the effort to isolate something which would look like a chemical individual. But nothing was recovered from these solvents but red gummy residues. So far, the product of the above reaction has not been determined.

Oxidation of a Thiazane.

26 grams di-phenyl-hydroxy thiazane
(crude, melting point 142-3°)

7.5 grams Potassium permanganate.

100 c.c. Glacial acetic acid.

The thiazane was dissolved in a mixture of 100 c.c. H₂O and the 100 c.c. of acetic acid. The permanganate was dissolved in 100 c.c. of H₂O. The permanganate solution was run slowly from a separatory funnel into the thiazane solution. The color of the liquid became brownish green. There was a moderate evolution of heat. Brown precipitate formed. After standing, the stuff was filtered to separate the brown filtrate from the dark brown residue. The filtrate was left standing in a beaker exposed to the air.

The residue was treated with dilute H₂SO₄ dissolving partly. The material was filtered. The residue was covered with water and left standing in a beaker exposed to the air. The filtrate was cooled with ice and poured into an excess of NH₄OH, yielding a brownish precipitate.

This precipitate was collected on filter and washed. It was redissolved in H₂SO₄ and reprecipitated with NH₄OH twice. The base, now white with pale brownish tinge, was dried on plate. Melting point 149°; melting point of original sample of thiazane 142-3°; melting point of mixture 130-140°.

One gram of above base was covered with 20 c.c. alcohol and boiled. After filtering, the filtrate was allowed

to evaporate spontaneously, yielding white crystals, melting point 82-87°.

Another gram of the above base was digested with 20 c.c. dilute HCl. After filtering, the filtrate was treated with slight excess of NH_4OH . The precipitate was dried on a plate; melting point 142-145°; original base 142-3°; mixture 142-144°.

Evidently, there has been secured at least two new products not the same as the original thiazane. This reaction should be studied further.

REACTION OF THIOCARBANILIDE AND ALPHA, GAMMA-
DI CHLORACETONE.

4.5 grams Thiocarbanilide.

25.4 grams alpha, gamma-Di-chloracetone.

550 c.c. Acetone.

The thiocarbanilide was dissolved in 450 c.c. of acetone. To this was added the dichloracetone dissolved in the balance of the acetone. The light brown solution was allowed to stand in a corked flask. After four days, wart-like, light brown, crystal growths appeared. After twelve days, some small red crystals were observed growing on the brown warts. The yield was about 50 grams.

Study of the Hydrochloride.

Some of the crystalline material was pulverized. Toward the last, the powder had a tendency to stick together, which was not apparent at first. The powder was placed in a desiccator, containing H_2SO_4 connected with water suction, and let stand over the week end before weighing out samples for analyses.

The solubility of this sample was tested in a variety of ways. With water, it gave an acid solution and a curdy white residue. Alcohol readily dissolved it. At first, it dissolved in chloroform, but very quickly a chalk white precipitate was formed. In benzene, toluene, petroleum ether and ether, it was sparingly soluble. Acetone dissolved it more readily.

The melting point of the material dried in the desiccator was determined: darkened from 155° on; blackened at 185°; completely fused to a black liquid at 187°. Some of the precipitate settling out of the chloroform solution was washed with chloroform and dried on a plate. Its melting point was determined: darkened about 150°; blackened about 180°; completely fused to a black liquid at 186-187°. A sample of the original wart like formation was soaked in acetone for several days, washed with acetone, crystallized from alcohol, again washed with acetone. This sample darkened about 160-170°; fused at 188-190.5°. Some of the material dried in the desiccator was crystallized from benzene and washed with acetone. It darkened around 185-190° and melted at 195-196°, the highest melting point that was obtained for this product.

This data on melting points, the results of solubility tests, and the method of formation all point to these wart-like deposits being a hydrochloride of a base.

Amount of HCl in the Hydrochloride.

Some of this hydrochloride was suspended in water and its acidity determined by running in a measured amount of NaOH solution and titrating back with H₂SO₄ solution. Two sets of determinations were made, one with methyl red as an indicator, the other with phenol phthalein. With methyl red, the percentage of HCl was found to be 12.22% and 11.62%, average 11.92%. With phenolphthalein, the

percentage of HCl was found to be 12.16% and 12.35%, average 12.26%. The average of the two sets of results is 12.21%.

With Phenolphthalein as Indicator:

	(1)	(2)
	14.6709	13.8216
	<u>13.8216</u>	<u>13.4987</u>
Sample	.8493	.3229
NaOH	30. c.c. 30.3 c.c. 30.3 c.c.	12.65 c.c. 13.1 c.c.
H ₂ SO ₄	.8 cc. .9 c.c. 1. c.c.	.85 c.c. 1. c.c.

1 c.c. H₂SO₄ = 2.09 c.c. NaOH.

NaOH = .1 N.

	.8	.9	1	.85	1
x	<u>2.09</u>	<u>2.09</u>	<u>2.09</u>	<u>2.09</u>	<u>2.09</u>
	1.67	1.88	2.09	1.78	2.09
	30.	30.3	30.3	12.65	13.1
-	<u>1.67</u>	<u>1.88</u>	<u>2.09</u>	<u>1.78</u>	<u>2.09</u>
	28.33	28.42	28.21	10.87	11.01
	28.42			<u>11.01</u>	
	<u>28.21</u>			2 <u>21.88</u>	
3	<u>84.96</u>			10.94 average.	
	28.32				

$$(1) \frac{28.32 \times .1 \times 36.46 \times 100}{.8493 \times 1000} = 12.16\% \text{ HCl}$$

$$(2) \frac{10.94 \times .1 \times 36.46 \times 100}{.3229} = 12.35\% \text{ HCl}$$

$$2 \mid \frac{24.51}{12.26 \text{ average.}}$$

With Methyl Red as Indicator:

	(1)	(2)
	16.1280	15.4570
	<u>15.4570</u>	<u>14.8174</u>
Sample	.6710	.6396
NaOH used	50. c.c.	50. c.c.
H ₂ SO ₄ used	13.6 c.c.	14.6 c.c.

1 c.c. H₂SO₄ = 2.06 c.c. NaOH

NaOH = .1023 N.

	13.6	14.6
x	<u>2.06</u>	<u>2.06</u>
	28.02	30.08
	50	50
-	<u>28.02</u>	<u>30.08</u>
	21.98	19.92

$$(1) \frac{21.98 \times .1023 \times 36.46 \times 100}{.6710 \times 1000} = 12.22\%$$

$$(2) \frac{19.92 \times .1023 \times 36.46 \times 100}{.6396 \times 1000} = 11.62\%$$

$$2 \sqrt{23.84}$$

11.92% average.

Chlorine in the Hydrochloride.

The amount of chlorine in the hydrochloride was determined by the liquid ammonia method¹⁵. Two sets of analyses are given. The first set gave chlorine 23.56% and 23.29%.

¹⁵Dains and Brewster, J. A. C. S. 42, 1573 (1920).

average 23.48%. The second set gave chlorine 20.26% and 20.40%, average 20.33%. The average of the two sets is chlorine 21.91%.

	<u>First Set</u>		
	(1)	(2)	(B)
	11.5589	4.8106	
	<u>11.2523</u>	<u>4.5178</u>	
Sample	.3066	.2928	0
Ppt. + Gooch	15.4256	15.6324	16.8026
Gooch	<u>15.1328</u>	<u>15.3530</u>	<u>16.7988</u>
Precipitate	.2958	.2794	.0038
Deduct for blank	<u>.0038</u>	<u>.0038</u>	
AgCl	.2920	.2756	

Factor for Cl₂ in AgCl = .24738.

$$(1) \frac{.2920 \times .24738 \times 100}{.3066} = 23.56\%$$

$$(2) \frac{.2756 \times .24738 \times 100}{.2928} = 23.29\%$$

$$2 \mid 46.85$$

Average 23.48

	<u>Second Set.</u>		
	(1)	(2)	(B)
	15.7537	15.3589	
	<u>15.3589</u>	<u>14.6734</u>	
Sample	.3948	.6855	0

Ppt. + Gooch	15.4032	16.6765	15.5264
Gooch	<u>15.0648</u>	<u>16.0961</u>	<u>15.5113</u>
Precipitate	.3384	.5804	.0151
Deduct for blank	<u>.0151</u>	<u>.0151</u>	
AgCl	.3233	.5653	

Factor for Cl₂ in AgCl = .24738.

$$(1) \frac{.3233 \times .24738 \times 100}{.3948} = 20.26\%$$

$$(2) \frac{.5653 \times .24738 \times 100}{.6855} = 20.40\%$$

$$2 \mid 40.66\%$$

Average 20.33%

Hydrochloride Continues to Lose Weight
on Heating.

It was thought that the variation in the above analyses for chlorine in the hydrochloride might be due to samples not being dried to the same extent, so a weighing bottle, filled with the hydrochloride, was placed in a drying oven at 50-60°. Weight was continually lost throughout the time of observation, twenty-seven days as shown below in tabular form. Hence, it was concluded that the difference in the two analyses was probably due to differences in degree of purity or changes in composition on standing. The two samples were not the same to start with.

Changes in Weight of HydrochlorideWhen Dried at 50 - 60°.

Date	Weight of Bottle and Sample.
12/12/23	14.0402
12/14/23	13.0974
12/18/23	12.8451
12/20/23	12.8251
12/27/23	12.5149
12/31/23	12.3784
1/1/24	12.3594
1/2/24	12.3524
1/3/24	12.3436
1/4/24	12.3367
1/5/24	12.3339
1/7/24	12.3271
1/8/24	12.3240

Nitrogen in the Hydrochloride.

The nitrogen in the hydrochloride was determined by the Gunning method: found 8.17% and 8.16%, average 8.16%.

	(1)	(2)	(B)
	17.2212	16.6780	
	<u>16.6780</u>	<u>16.1280</u>	
Sample	.5432	.5432	0
H ₂ SO ₄ used	30.2 c.c.	30.6 c.c.	30.1 c.c.
NaOH used	30.5	31.	61.3

1 c.c. H₂SO₄ = 2.06 c.c. NaOH

1 c.c. H₂SO₄ = .2107 N.

$$\frac{30.5}{2.06} = 14.81 \quad \frac{31}{2.06} = 15.05 \quad \frac{61.3}{2.06} = 29.76$$

	30.2	30.6	30.1
-	<u>14.81</u>	<u>15.05</u>	<u>29.76</u>
	15.39	15.55	.34
Deduct for blank	<u>.34</u>	<u>.34</u>	
	15.05	15.21	

$$(1) \frac{15.05 \times .2107 \times 14 \times 100}{.5432 \times 1000} = 8.173\%$$

$$(2) \frac{15.21 \times .2107 \times 14 \times 100}{.5500 \times 1000} = 8.158\%$$

Study of the Base.

Took a small quantity of the hydrochloride and treated with water. A white curdy residue and a yellow dense liquid layer separated under the water. The yellow liquid layer disappeared on stirring. After standing, the residue was collected on a filter and washed. After drying, an ef-

fort was made to determine the melting point; darkened at 70° ; softened with apparent decomposition at $80-85^{\circ}$; commenced to fuse at 110° ; completely fused to a brown liquid at 116° .

The filtrate from above was treated with an excess of NH_4OH , the white precipitate being collected and washed. After drying, the efforts to get a melting point resulted about the same as the preceding: darkened, 60° ; softened, $70-75^{\circ}$; commenced to fuse, $90-95^{\circ}$; completely fused to amber liquid, 111° .

The rest of the hydrochloride was dissolved in dilute HCl , except a small residue which was separated by filtering. The filtrate was poured into ice cold NH_4OH in excess. The precipitate was collected, washed and dried; melting point $95-100^{\circ}$. This base was purified by crystallization from gasoline, melting point 147° ; from acetone, melting point 148° ; from gasoline, melting point 150° ; from benzene, followed by washing with acetone, melting point $150-151^{\circ}$. Another sample was purified by successive crystallization from acetone: melting points, 147 ; $149-150^{\circ}$; $150-151^{\circ}$; $151-152^{\circ}$; 152° .

Nitrogen in the Base.

The nitrogen in the base was determined by the Gunning method:

	(1)	(2)	(B)
	15.7215	15.2828	
	<u>15.2828</u>	<u>14.7579</u>	
Sample	.4387	.5249	0
H ₂ SO ₄ used	25 c.c.	25 c.c.	25 c.c.
NaOH used	(Sucked back)	16.5	49.9
	1 c.c. H ₂ SO ₄ =	2.04 c.c. NaOH	
	H ₂ SO ₄ =	.2107 N.	

$$\frac{16.5}{2.04} = 8.088 \quad \frac{49.9}{2.04} = 24.46$$

	25	25
-	<u>8.09</u>	<u>24.46</u>
	16.91	.54
Deduct for blank	<u>.54</u>	
	16.37	

(1) Lost.

$$(2) \frac{16.37 \times .2107 \times 14 \times 100}{.5249 \times 1000} = 9.20\%$$

A Possible Formula for the Base.

If we suppose that the dichloroacetone and thiocarbonyl chloride react with the loss of a mole of water and a mole of HCl according to the scheme:

21.07 - 10.53% = 10.54%, the theoretical amount of chlorine in the hydrochloride not due to the HCl. 21.91 - 11.87 = 10.04%, the amount of chlorine in the hydrochloride as calculated from the actual measurements. All this may be represented in tabular form as follows:

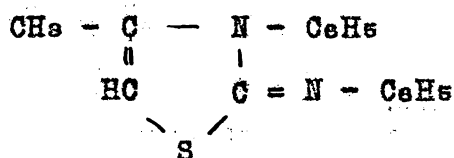
	Hydrochloride	Base
Nitrogen	Theory 8.31%	9.32%
	Found 8.16%	9.20%
Total Cl	Theory 21.07%	
	Found 21.91%	
HCl	Theory 10.83%	
	Found 12.21%	
Cl in HCl	Theory 10.53%	
	Found 11.87%	
Cl not in HCl	Theory 10.54%	
	Found 10.04%	

Thus, it will be seen that while the figures relating to nitrogen point fairly to the formula proposed, the calculations and results concerning chlorine are not so conclusive. Further work on composition, molecular weight, and reactions to show constitution will be necessary before accepting or rejecting the proposed formula.

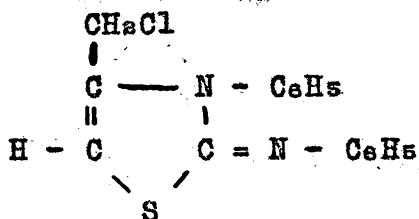
It might also be mentioned that the original reason for studying this reaction was the possibility of getting a thiazane derivative which would be identical with a pro-

duct theoretically possible as a result of oxidizing the di-phenyl-hydroxy thiazane. So far, the results of the two sets of work do not point toward such a theoretical coincidence.

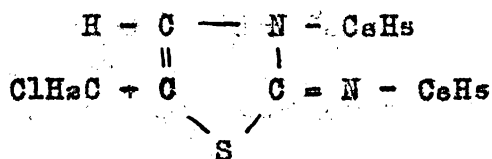
Theoretical support for the above proposed formula is found in the work of Traumann¹⁶. He made diphenyl-imido-methyl-thiazolin from di-phenyl-thiourea and mono-chlor-acetone. For the product of this reaction, he developed the formula:



It is not yet clear, however, whether we should or did get a compound corresponding to the formula proposed,



or its isomer



¹⁶A. 249, 51 (1888)

REACTIVITY OF VARIOUS ALKYL BROMIDESWITH DI PHENYL THIOUREA.

In the hope that light might be thrown on the probable isomer produced in the reaction between thiocarbanilide and dichloroacetone, a study was made of the reactivity of various alkyl bromides with thiocarbanilide. This was done to determine, if possible, which type of alkyl bromide reacted most readily with the -SH group in one of the tautomeric forms of diphenyl thiourea.

Earlier work¹⁷ as well as more recent work done in this laboratory¹⁸ has shown that a characteristic reaction of the substituted thioureas is their ability to add directly alkyl halides, according to the type reaction



From the halogen halide salts, thus formed, the action of alkalies sets free the thiourea ethers.

It is obvious that the hydrogen halide, formed in this reaction, should form a salt with the alkali. If this salt

¹⁷Claus, Ber. 7, 235 (1874) and 8, 41 (1875); Bernthsen and Klinger, Ber. 11, 492 (1878) and 12, 574 (1879); Bernthsen and Friese, Ber. 15, 566 (1882); Will, Ber. 14, 1485 (1881) and 15, 338 (1882); Rathke, Ber. 14, 1774 (1881); Evers, Ber. 21, 962 (1888).

¹⁸Dains and Thompson, Kansas University Science Bulletin 13, 117 (1922)

is extracted from other things with water, the measure of the amount of halide in this aqueous solution should give a measure of the amount of thiourea and alkyl halide reacting.

In carrying out this work in the laboratory, the reactions were allowed to take place in a three necked flask. In the central one of these necks, there was inserted a water condenser, in the top of which there was inserted a small bore tube to serve as an air condenser, each condenser being about a yard long. In a second one of the necks was inserted a short-stemmed thermometer, the bulb of which could reach into any solution in the flask. In the third neck was inserted a 10 c.c. pipette, the inner end of which could dip into any solution in the flask, the outer end being closed with a short piece of rubber tubing and a clamp. All insertions were made through tight fitting corks.

All the reactions studied in this set of experiments have been carried out in acetone solution. The calculated weight of thiocarbanilide was introduced into the flask. About three fourths of the appropriate volume of acetone was added. The connections were properly adjusted and the flask immersed in a water bath. The temperature of this bath was kept between 65 and 70° sufficient to keep the solution inside the flask at its boiling point. When the solution of thiocarbanilide in acetone began to boil, five c. c. of the alkyl bromide dissolved in about half of the re-

mainder of the acetone was carefully poured in through the water condenser, and washed down with the balance of the acetone.

From time to time, 10 c.c. portions of the solution were drawn out and run into flasks containing 10 c.c. of saturated NaHCO_3 solution and 10 c.c. of water. After thorough shaking, the aqueous solution was poured through a filter and the precipitated material washed on the filter. Washings and filtrate amounted to practically 100 c.c. in each case. Ten c.c. of HNO_3 solution and 5 c.c. of ferric ammonium alum solution were added. A measured volume of AgNO_3 solution was run in, enough to be in slight excess. This mixture was then titrated with KCNS until the red end point was reached.

Preparation and Purification of Reagents.

Acetone, a good grade from general stock, was purified by allowing to stand several days over sticks of NaOH , decanting off the acetone layer, and distilling from the flask containing a stick of NaOH , using a fractionating column, collecting that portion boiling between 56 and 57° . This was redistilled, again collecting the fraction boiling between 56 and 57° .

Thiocarbamilide was prepared by mixing equal weights (500 grams) of denatured alcohol, carbon bisulfide, and freshly redistilled aniline. After two weeks standing in flask with air condenser at room temperature, the crystals

of thiocarbanilide had formed abundantly. The mother liquor was filtered at pump. After draining, the crystals were successively washed with alcohol, dilute HCl, more alcohol. The product was thoroughly drained and dried. It melted at 153° .

Alkyl bromides, except the tertiary butyl bromide, were made by students, according to the sodium bromide - sulfuric acid method described in "Organic Syntheses" by Roger Adams et al (Wiley, New York, 1921) Vol. I, page 6. The alcohols used were as follows:

Ethyl - 95% denatured from general stock.

n-Propyl - Eastman Kodak Co.

iso-Propyl - " " "

n - Butyl - " " "

iso-Butyl - " " "

sec-Butyl - Standard Oil Co.

ter-Butyl alcohol was not used, the ter-Butyl Bromide being obtained from the Eastman Kodak Company.

The various alkyl bromides were purified by successive washing with water, cold concentrated H_2SO_4 , and Na_2CO_3 solution. They were then separated as completely as possible from the aqueous layer, and dried by standing over night with anhydrous calcium chloride. The halides were then repeatedly distilled, using a fractionating column for the lower boiling samples but omitting it with the higher boiling samples. Fractions were finally reserved which boiled

within one degree above or below the following temperatures selected from Beilstein:

Ethyl bromide	- 38.37
n Propyl bromide	- 70.82
iso Propyl bromide	- 60.00
n Butyl bromide	- 99.88
iso Butyl bromide	- 92.33
sec Butyl bromide	- 91.30
ter Butyl bromide	- 72.00

Standardization of Solutions Used in Titration, was effected by first making a gravimetric determination of the amount of bromine in a potassium bromide solution, precipitating the bromine as silver bromide. This KBr solution was found to be .00929 N. The AgNO₃ solution was then titrated against the KBr solution by Mohr's method, using K₂CrO₄ as an indicator in neutral solution. This AgNO₃ solution was found to be .09775 N. The KCNS solution was then titrated against the AgNO₃ solution by Volhard's method using ferric ammonium alum as an indicator in HNO₃ solution. This KCNS solution was found to be .1084 N. The NaHCO₃ solution was tested for halogens according to the Volhard method using the above standardized solutions. This NaHCO₃ solution was found to be .0001955 N for halogens. The KCNS being .1084 N, 1 c.c. is equal to .00964 grams HBr.

A Blank on AgNO₃ and KCNS.

A mixture was made of 10 c.c. H₂O, 10 c.c. NaHCO₃ so-

lution, and 5 c.c. ferric ammonium alum. In this solution, the AgNO₃ was titrated against the KCNS.

AgNO ₃	KCNS
26 - 25 = 1 c.c.	25. - 24.6 = .9 c.c.
27 - 26 = 1 c.c.	26.4 - 25.5 = .9 c.c.
28 - 27 = 1 c.c.	27.3 - 26.4 = .9 c.c.

Average 1 c.c. AgNO₃ = .9 c.c. KCNS.

A Blank on Thiocarbanilide and Acetone.

Substance		Density	No. c.c.	No. Grams	Mole Fraction.
Thiocarbanilide	228			4.56	.02
Acetone	58	.792	50.5	40.	2000 gms. per mole of thiocarbanilide.

Time	Temp.	C.C. of Mixture Wd.	C. C. AgNO ₃ Used.	C.C. KCNS Used	AgNO ₃ = KCNS	Dif. in C.C. KCNS	Equal to gms. HBr
2:10 [#]	58°	10	1	.6	.9	.3	.0289
2:40	58°	10	1	.7	.9	.2	.0193
3:10	58°	10	1	.5	.9	.4	.0386
						3 .9 3	.0868
						.3	.0289

On the average, 10 c.c. acetone and thiocarbanilide contain the equivalent of .0289 gram HBr and show a difference of .3 c.c. KCNS for the KCNS used and the KCNS equivalent of the AgNO₃ used.

Ethyl Bromide and Thiocarbanilide¹

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mole Fraction.
Ethyl Bromide	109	1.45	5.	7.25	.06651
Thiocarbanilide	228			15.16	.06651
Acetone	58	.792	167.9	133.	2000 grams per mole of Ethyl Bromide or Thiocarbanilide.

Normal-Propyl Bromide and Thio-carbanilide²

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mole Fraction.
n-Propyl Bromide	123	1.353	5.	6.765	.055
Thiocarbanilide	228			12.54	.055
Acetone	58	.792	138.8	110.	2000 gms. per mole of Propyl bromide or Thiocarbanilide

¹See page 53.

²See page 54.

Ethyl Bromide and Thiocarbonyl Sulfide.¹

Time	Temp. Deg.	C.C. of Mixture Used.	C.C. HgNO ₃ Used.	C.C. KCNS Used	AgNO ₃ = KCNS.	Dif. in CC. KCNS.	After Deducting .3 CC. for Blank.	Equal to Gms. HBr	Max. Gms. HBr possible if Reaction Complete	% Actually Reacted.
1:50 [#]	58.5									
1:55	59.	10	5	4.2	4.5	.3	0.	0	.3206	0
2:01	60	10	5	3.85	4.5	.65	.35	.00337	.3206	1.05
2:10	59	10-	5	3.5	4.5	1.	.7	.00675	.3206	2.11
2:20	59.5	10	5	3.15	4.5	1.35	1.05	.01002	.3206	3.13
2:40	59	10	5	2.6	4.5	1.9	1.6	.01542	.3206	4.81
3:19	58.5	10-	5	1.8	4.5	2.7	2.4	.02314	.3206	7.22
3:50	58.	10 ?	5	1.0	4.5	3.5	3.2	.03085	.3206	9.62
4:25	57.5	10	5	.4	4.5	4.1	3.8	.03663	.3206	11.43
4:40	58.	10	5	.2	4.5	4.3	4.0	.03856	.3206	12.08
5:00	57.	10	5	.05	4.5	4.45	4.15	.04001	.3206	12.48

[#] started.

¹See "1" Page 52.

Normal-Propyl Bromide and Thiocarbanilide.²

Time	Temp. Deg.	C.C. of Mixture Wd.	C.C. AgNO ₃ Used.	C.C. KCNS Used	AgNO ₃ = KCNS.	Dif. in CC. KCNS.	After Deducting .3 c.c. for Blank.	Equal to Gms. HBr	Max. Gms. HBr possible if Reaction Complete	% Actually Reacted
2:08 [#]										
2:13	58	10	5	2.6	4.5	1.9	1.6	.01542	.3207	4.81
2:19	58+	10+	5	1.6	4.5	2.9	2.6	.02506	.3207	7.82
2:28	58	10	5	1.4	4.5	3.1	2.8	.02709	.3207	8.45
2:38	58+	10	5	.95	4.5	3.55	3.25	.03133	.3207	9.77
3:08	58-	10	5	.35	4.5	4.15	3.85	.03711	.3207	11.57
3:38	57	10	5	.25	4.5	4.25	3.95	.03808	.3207	11.87
4:08	57	10	5	.15	4.5	4.35	4.05	.03904	.3207	12.15
4:38	57	10-	5	.05	4.5	4.45	4.15	.04001	.3207	12.48

²See "a" Page 52.
[#]Started.

Iso-Propyl Bromide and Thiocarbanilide.¹

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mole Fraction.
iso-Propyl Bromide.	123	1.31	5.	6.55	.05325
Thiocarbanilide.	228			12.14	.05325
Acetone	58	.792	134.5	106.5	2000 gms. per mole of Propyl bromide or Thiocarbanilide.

¹See Page 56.Normal Butyl Bromide and Thiocarbanilide.²

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	
n-Butyl Bromide	137	1.3	5.	6.5	.04745
Thiocarbanilide	228			10.82	.04745
Acetone	58	.792	119.8	94.89	2000 gms. per mole of Butyl Bromide or Thiocarbanilide

²See page 57.

Iso-Propyl Bromide and Thiocarbanilide.¹

Time	Temp. Deg.	C.C. of Mixture Wd.	C.G. AgNO ₃ Used.	C.C. KCNS Used	AgNO ₃ = KCNS.	Dif. in CC. KCNS.	After Deducting .3 c.c. for Blank	Equal to Gms. HBr	Max. Gms. HBr possible if Reaction Complete	% Actually Reacted.
9:35 [#]										
9:40	58	10	6.5	4.8	5.85	1.05	.75	.00723	.3203	2.26
9:45	58	10	5.	3.2	4.5	1.3	1.0	.00964	.3203	3.01
9:55	58	10	5	3.2	4.5	1.3	1.0	.00964	.3203	3.01
10:05	58	10	5	3.3	4.5	1.2	0.9	.00868	.3203	2.71
10:35	58	10-	5	3.2	4.5	1.3	1.0	.00964	.3203	3.01
11:35	58	10	5	3.2	4.5	1.3	1.0	.00964	.3203	3.01

¹See Page 55 "1".

[#]Started.

Normal Butyl Bromide and Thiocarbanilide.¹

Time	Temp. Deg.	C.C. of Mixture Wd	C.C. AgNO ₃ Used	C.C. KCNS Used	AgNO ₃ = KCNS	Dif. in CC. KCNS	After Deducting .3 c.c. for	Equal to Gms. HBr	Max. Gms. HBr possible if Reaction Complete	% Actually Reacted
1:55 [#]	60									
2:00	60	10	5	4.1	4.5	.4	.1	.00096	.3205	.30
2:05	60	10	5	4.	4.5	.5	.2	.00193	.3205	.60
2:15	60	10-	5	3.9	4.5	.6	.3	.00289	.3205	.90
2:25	60	10	5	3.65	4.5	.85	.55	.00530	.3205	1.65
2:55	58	10	5	3.25	4.5	1.25	.95	.00916	.3205	2.86
3:25	58	10	5	2.85	4.5	1.65	1.35	.01301	.3205	4.15
3:55	58	10-	5	2.3	4.5	2.2	1.9	.01832	.3205	5.72
4:25	58	10	5	1.9	4.5	2.6	2.3	.02217	.3205	6.92
4:55	57	10	5	1.6	4.5	2.9	2.6	.02506	.3205	7.82

[#] started.

¹See "2" page 55.

Iso-Butyl Bromide and Thiocarbanilide.¹

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mol. Fraction.
Iso-Butyl Bromide	137	1.26	5.	6.3	.046
Thiocarbanilide	228			10.49	.046
Acetone	58	.792	116.2	92.	2000 grams per mole of Butyl Bromide or Thiocarbanilide.

¹See Page 59.Secondary Butyl Bromide and Thiocarbanilide.²

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mol. Fraction.
Sec Butyl Bromide.	137	1.25	5.	6.25	.0456
Thiocarbanilide.	228			10.4	.0456
Acetone	58	.792	115.15	91.2	2000 grams per mole of Butyl Bromide or Thiocarbanilide.

²See Page 60.

Iso-Butyl Bromide and Thiocarbanilide.¹

Time	Temp. Deg.	C.C. of Mixture Wd.	C.C. AgNO ₃ Used	C.C. KCNS Used	AgNO ₃ = KCNS	Dif. in CC. KCNS.	After Deducting .3 c.c. for Blank.	Equal to Gms. HBr	Max. Gms. HBr Possible if Reaction Complete	% Actually Reacted
1:46 [#]	60									
1:51	60	10	5	2.7	4.5	1.8	1.5	.01446	.3204	4.51
1:56	60	10	5	2.35	4.5	2.15	1.85	.01834	.3204	5.73
2:06	59	10	5	2.6	4.5	1.9	1.6	.01542	.3204	4.81
2:16	59	10+	5	2.55	4.5	1.95	1.65	.01591	.3204	4.97
2:46	59	10	5	2.5	4.5	2.	1.7	.01639	.3204	5.12
3:16	58	10+	5	2.6	4.5	1.9	1.6	.01542	.3204	4.81

[#]Started.

¹See "1" Page 58.

Secondary Butyl Bromide and Thiocarbanilide.¹

Time	Temp. Deg.	C.C. of Mixture Wd.	C.C. AgNO ₃ Used	C.C. KCNS Used	AgNO ₃ = KCNS	Dif. in CC. KCNS	After Deducting .3 cc. for Blank	Equal to Gms. HBr	Max. Gms. HBr Possible if Reaction Complete	% Actually Reacted
1:58 [#]	58									
2:03	60	10	5	3.8	4.5	.7	.4	.00386	.3203	1.21
2:08	60	10	5	3.6	4.5	.9	.6	.00578	.3203	1.81
2:18	60	10	5	3.6	4.5	.9	.6	.00578	.3203	1.81
2:28	60	10	5	3.7	4.5	.8	.5	.00482	.3203	1.51
2:58	60	10	5	3.7	4.5	.8	.5	.00482	.3203	1.51

#Started.

¹See "c" Page 58.

Tertiary Butyl Bromide and Thiocarbanilide.¹

Substance	Mol. Wt.	Density	No. C.C.	No. Grams	Mol. Fraction.
Ter Butyl Bromide	137	1.19	5.	5.95	.04343
Thiocarbanilide	228		109.67	9.9	.04343
Acetone	58	.792	109.67	86.86	2000 grams per mole of Butyl Bromide or Thiocarbanilide.

¹See Page 62.Comparison of the Reactivities of the Various Alkyl Bromides with Thiocarbanilide.

It would be very unsafe to make any statements of a quantitative nature regarding these reactions without more extensive study. One may, however, note the following facts. (See Page 63).

Tertiary Butyl Bromide and Thiocarbanilide¹.

Time	Temp. Deg.	C.C. of Mixture Wd.	C.C. AgNO ₃ Used	C.C. KCNS Used	AgNO ₃ = KCNS	Dif. in CC. KCNS.	After Deducting .3 cc. for Blank	Equal to Gms. HBr	Max. Gms. HBr Possible if Reaction Complete	% Actually Reacted.
8:41 [#]	58									
8:46	59	10	25	1.25	22.5	21.25	20.95	.20196	.3204	63.04
8:51	60	10	30	4.45	27.	22.25	22.25	.21449	.3204	66.95
9:01	60	10	30	4.2	27.	22.8	22.5	.21690	.3204	67.70
9:11	59	10	30	4.	27.	23.	22.7	.21883	.3204	68.29
9:41	58	10	30	5.7	27.	21.3	21.0	.20244	.3204	63.17
10:11	58	10	25	3.05	22.5	19.45	19.15	.18461	.3204	57.62

[#]started.

¹See "1" Page 61.

Comparison of the Bromides.

Bromide.	Time from Beginning Reaction.	% Re-acted	Remarks (All time from beginning).
Ethyl	2 Hrs	9.62	At end of 3 hrs 10 min. 12.48% reacted; equilibrium not yet reached.
n-Propyl	2 Hrs	12.15	At end of 2 hrs. 30 min. 12.48% reacted; equilibrium not yet reached.
iso-Propyl	2 Hrs	3.01	This was equilibrium; reached at end of 10 min.
n-Butyl	2 Hrs	5.72	At end of 3 hrs., 7.82% reacted; equilibrium not yet reached.
iso-Butyl	1 1/2 Hrs	5.0	Equilibrium.
sec-Butyl	1 Hour	1.6-	Equilibrium.
ter-Butyl	1/2 Hr	68.29	Maximum; % reacted commenced to decline.

Within the limits of this work, one may arrange these bromides according to relative reactivity in the following order:

1. Ter-Butyl.
2. n-Propyl.
3. Ethyl.
4. n-Butyl.
5. Iso-Butyl.
6. Iso-Propyl.
7. Sec-Butyl.