ON THE CONSTITUTION OF CERTAIN THIAZOLIDONES

By

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MASTER OF SCIENCE

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Department of Chemistry.

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

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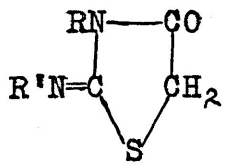
METHODS FOR THE PREPARATION OF THE THIAZOLIDONES.

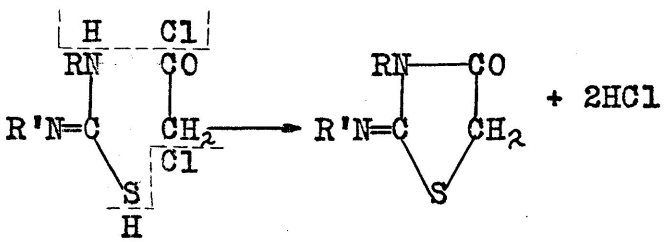
The thiazolidones, having the general formula,



may be made by several different methods.

The first method, and the one used entirely throughout this investigation, is by the reaction of various acid reagents on the substituted thio-ureas[1]. Four of these may be used, with varying success. They are chlor-acetyl chloride, chlor-acetic acid, ethyl chlor-acetate, and ammonium chlor-acetate.

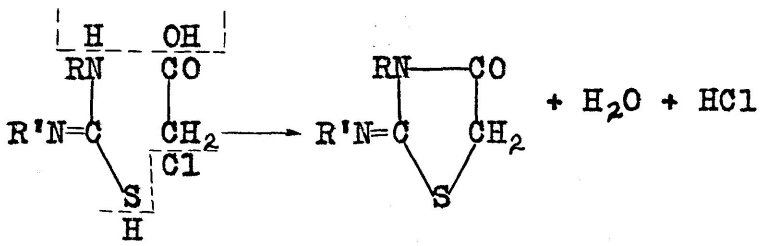
The reaction with chlor-acetyl chloride is best carried out in a cold acetone solution of the thio-ureas. The reaction takes place as follows:-



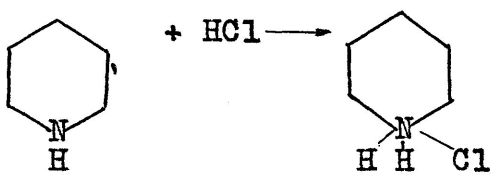
The presence of one or two moles of pyridine does not materially increase the yield.

The reaction with chlor-acetic acid may either be carried out by refluxing molecular quantities of the

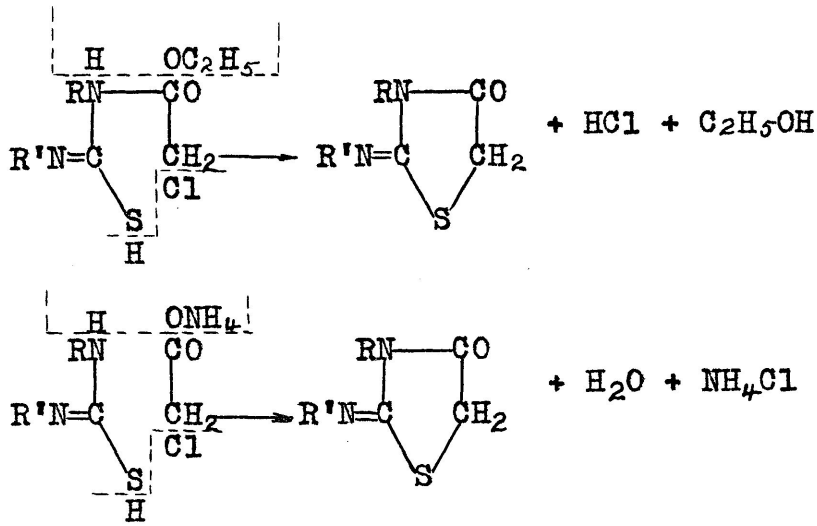
chlor-acetic acid, the substituted thio-urea, and pyridine, in alcohol, or by heating on a water bath for fifteen minutes, molecular quantities of the thio-urea and the acid. In either case, the following reaction takes place:-



The pyridine acts as an acid remover.

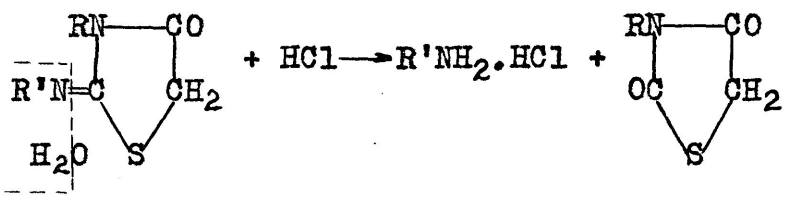


In the cases of the ethyl and ammonium chloracetate, the reagent is boiled with molecular quantities of the thio-urea and pyridine, which again removes HCl

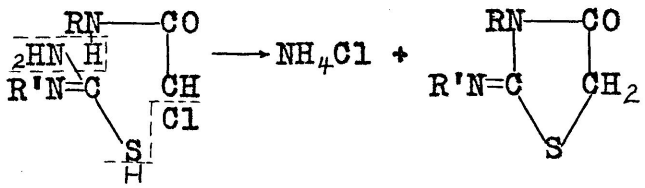


In the latter reaction, pyridine has to be present, because the HCl is split off much faster than the NH_4OH, altho equivalent portions are liberated in the end. In this case the thiazolidone must be washed with dilute acid to free it from pyridine.

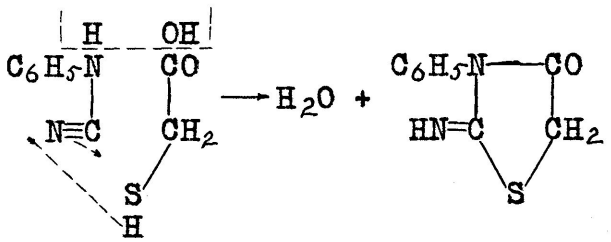
The presence of HCl is to be avoided, because it would hydrolyze the compound at the double bonded nitrogen, giving a thiazol-dione and a primary amine hydrochloride.



A second method for the preparation of the thiazolidones is by the action of a substituted chlor-acetamide upon a substituted thio-urea[2]. The reaction takes place as follows:



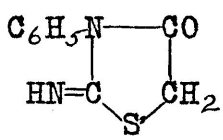
Another method which has been used for the preparation of these compounds is by treating a substituted cyanamide, say phenyl, with thio-glycolic acid.[2]



The fourth general method is one which was used a great deal by Wheeler and Johnson, at Yale[3]. They first treated a primary amine, such as aniline, with chlor-acetyl chloride, getting the chlor-acet aryl-amide.

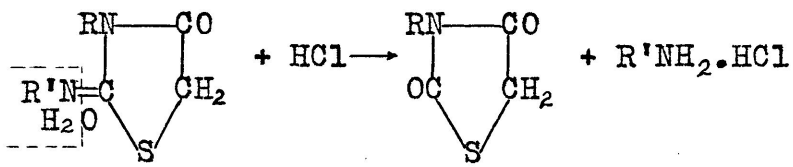
$$CH_2ClCOCl + HNHC_6H_5 \rightarrow CH_2ClCONHC_6H_5 + HCl$$

They then allow this to react with KCNS, getting KCl and $SCNCH_2CONHC_6H_5$, the iso-cyan-acet phenyl-amide. This very quickly changes over into the normal form, $NCSCH_2CONHC_6H_5$, the iso form being very hard to isolate. Now if this normal form be heated with water or alcohol it rearranges to the thiazolidone.



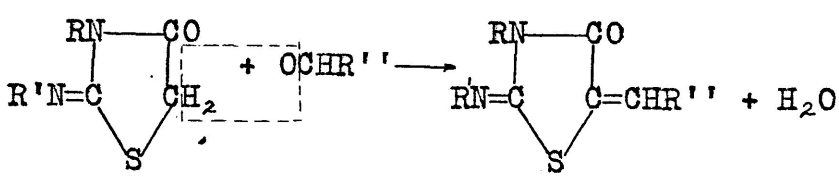
REACTIONS OF THE THIAZOLIDONES

The thiazolidones have only a limited number of reactions. Perhaps the most important of these, and the one used in determining the group attached to the double bonded nitrogen, is the hydrolysis with acids. Some of the thiazolidones hydrolyze very easily, being completely changed by merely boiling for two hours with alcohol and one mole of HCl. Others will remain unchanged after boiling all day with concentrated HCl. The hydrolysis goes in this manner:-

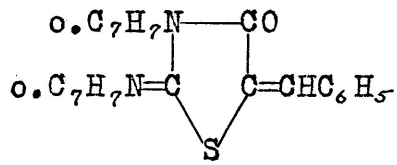


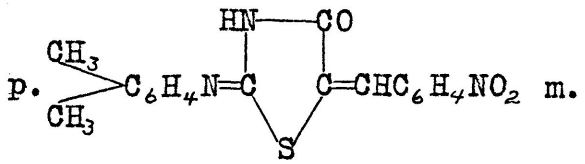
This reaction is very valuable for determining which nitrogen the group R or R' is attached to, as the primary amine which is set free may be isolated and identified, and the resulting diketo compound may be analyzed.

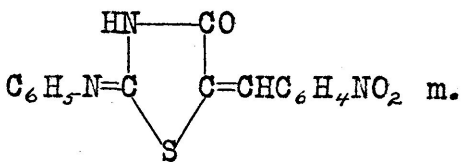
Another reaction which is useful as a means of identifying a thiazolidone, is it's condensation with aldehydes[4], the reaction taking place at the CH_2 group.



A large number of these condensations have been carried out; using different thiazolidones and various aldehydes. Some of them are

(1) 

(2) 

(3) 

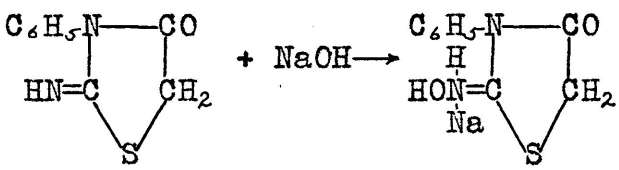
These aldehyde condensation products serve to identify a thiazolidone, which comes in very handy in a case where the thiazolidone has a low melting point. One such case is that of the 2-phenyl-imino-3methyl thiazolidone, which has a melting point of 60° C, and is exceedingly hard to crystalize. The benzaldehyde condensation product is a yellow, easily crystalized compound, having a melting point of 135° C.

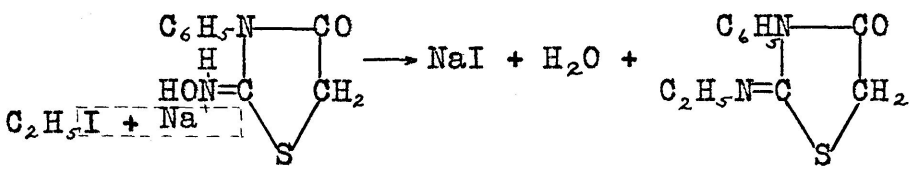
A third reaction which also helps to identify the compounds is that which takes place with acetic anhydride.

In case either the R or R' group, or both, happens to be a hydrogen, a di-acetyl derivative is formed. There is still considerable doubt as to the structure of these compounds.

A fourth reaction, which helps to indicate the structure of the thiazolidones, takes place with the mono-substituted compounds only. They will dissolve in NaOH or AgOH with the formation of a crystaline salt, which may even contain water of crystalization. When this sodium or silver salt is refluxed with an alkyl halide, the metallic halide is precipitated and the alkyl group enters into the thiazolidone.

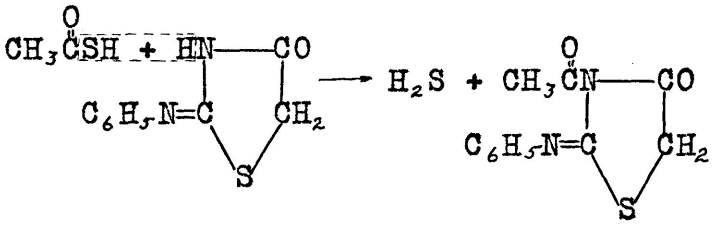
The probable course of the reaction may be represented by the following equations:[5]



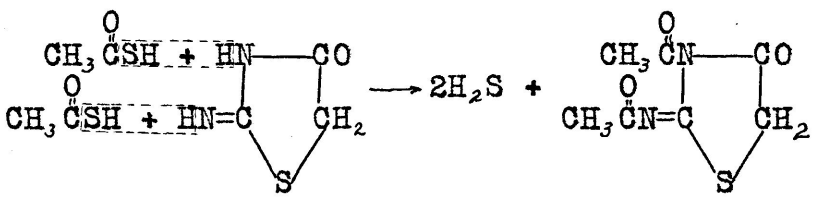


There is some doubt, however, as to the true course of the reaction, the above view having been given by Beckurts and Frerichs.

A thiazolidone which has a hydrogen attached to a nitrogen will also react with thio-acetic acid, producing hydrogen sulphide and an acetyl derivative.



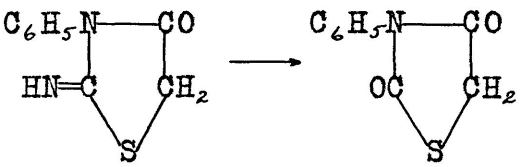
or



giving a di-acetyl derivative.

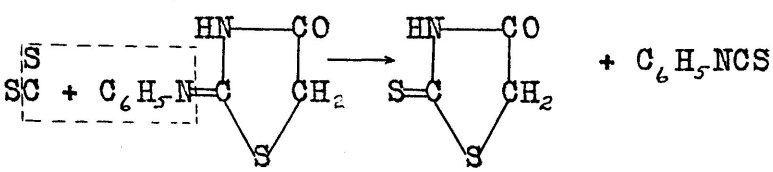
CONSTRUCTION OF THE THIAZOLIDONES.

This is a matter which has caused quite a little discussion since 1880. Along about this time, Meyer[6] prepared the mono-phenyl thiazolidone, both from chlor-acetanilide and thio-urea, and from mono-phenyl thio-urea and ethyl chlor-acetate. When he boiled this compound, he obtained the 2 - 4 diketo, 3 phenyl thiazoldione. He therefore gave the substance the following formula:



Liebermann and Lange[7], and Andreasch[2], also assigned the same formula to the substance.

In 1897, however, Dixon[1], heated the mono-phenyl thiazolidone with carbon disulphide, at a high temperature. He obtained phenyl mustard oil and rhodanic acid. He thinks the reaction took place as follows:

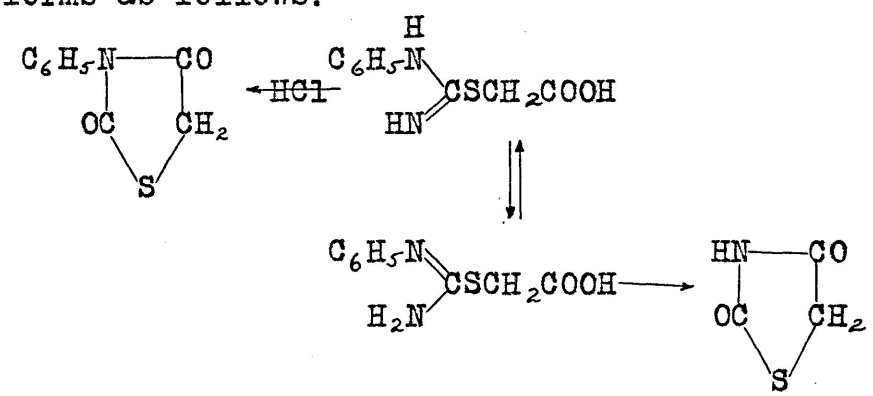


This would seem to show that the phenyl group was attached to the double bonded nitrogen, but would leave unexplained the formation of the 2 - 4 diketo - 3 phenyl

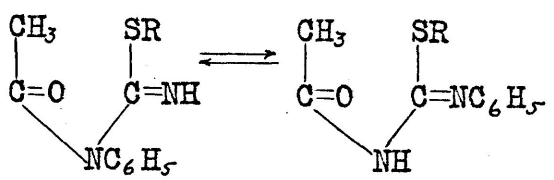
thiazolidone upon boiling with hydrochloric acid. Neither would it explain the formation of the thiazolidone from thio-urea and phenyl-chlor-acetamide, and from thiocyanacetanilide upon boiling with alcohol.

Wheeler and Johnson[3], in previous researches, had found out that phenyl pseudo-thiohydantoin

behaves in a tautomeric manner, the double bond shifting from one nitrogen to another. Thus when they boiled it with hydrochloric acid, they found that they got products resulting from both of the tautomeric forms as follows:

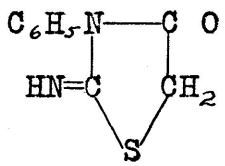


They also have shown[8] that the unsymmetrical acetyl-phenyl-pseudo-thioureas will undergo a tautomeric rearrangement as follows:



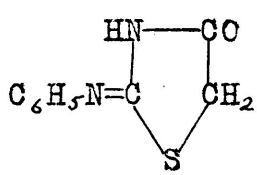
This suggested to them that perhaps this was the case with the thiazolidones. They accordingly set to work to determine if this was the case.

They first prepared normal thio-cyan-acetanilide by the action of KCNS upon chlor-acetanilide. They then melted this on a steam bath for fifteen minutes and got what they thought was the 2 imino - 3 phenyl thiazolidone, melting at 148°.



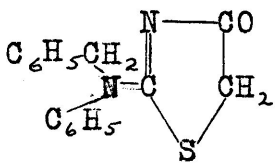
Their reasons for the above statement were that upon treatment with thio acetic acid, they got H_2S and an acetyl derivative, and the substance seemed to be the first condensation product of the normal thiocyan-acetanilide.

When this so-called "labile" thiazolidone is heated on an oil bath for a few minutes, it is converted into the "stable" form, or 2 phenyl-imino thiazolidone, melting at 178° C.

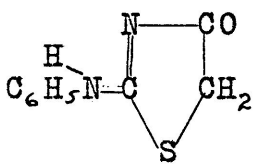


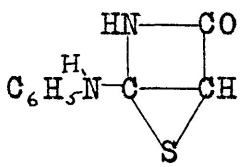
This was the compound obtained by Dixon, Meyer, and others.

Then reasons for assigning the above formula to the compound are: They obtained the same compound by boiling unsymmetrical phenyl-benzyl thiourea with ethyl chlor-acetate as they did by treating the stable thiazolidone with NaOH and benzyl chloride.



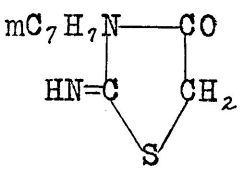
They also found that the stable form was soluble in alkali, therefore such formulas as:



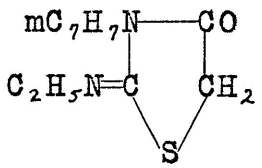


being merely substituted anilines, would not dissolve.

Beckurts and Frerichs[5], however, do not believe that Wheeler and Johnson's stable form exists. By the action of KCNS on $CH_2ClCONHC_7H_7(m)$, they got what they called



They then dissolved this in NaOH, the resulting crystaline salt having four moles of water of crystalization. This they boiled with ethyl iodide, getting NaI and a compound to which they gave the formula



melting at 106° C.

They made a number of similar compounds, varying the aryl and alkyl groups, but giving all of them the same general formula.

These compounds were hydrolyzed with eight times their weight of 25% HCl, and in each case they got a diketo derivative and the alkylamine, the aryl group remaining on the ring. This would seem to support the constitution which they give.

PURPOSE OF THIS INVESTIGATION.

We now come to the purpose of the present investigation, which was two-fold.

First: It is without doubt that there is a selective action on the part of the acid reagents when they react with a di-substituted thio-urea. For instance, we may take thio-ureas which have the phenyl group in common and vary the other group. Allow these thio-ureas to react with an acid reagent and get the thiazolidone. By a hydrolysis, we can get a primary amine and a diketo derivative, which may both be identified, telling which of the groups was attached to the double bonded nitrogen. Our intention was to find the effect of tolyl, halogen substituted rings, and alkyl groups.

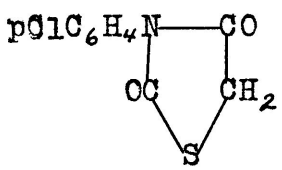
The second purpose of the investigation was to further satisfy ourselves as to the constitution of the product resulting from the treatment of a mono-substituted thiazolidone with NaOH and an alkyl halide. The work of Beckurts and Frerichs seemed to be a direct contradiction to the rather careful work of Wheeler and Johnson.

EXPERIMENTAL WORK.

The first work entered upon was to try to find the best conditions for a good yield of substituted thiazolidones from the thio-ureas and some acid reagent. The first reagent tried was chlor-acetic acid.

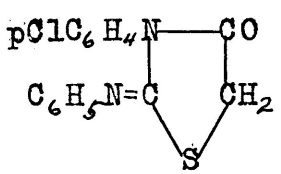
6.55 grams of monopara-chlor di-phenyl thio-urea were ground in a mortar with .35 grams chlor-acetic acid, and heated on a water bath for an hour. No reaction was apparent, so the same material was heated on an oil bath for fifteen minutes at 150° C. Fumes of HCl were given off and the mix melted.

This was divided into two portions, the hot water soluble and the alcohol soluble. The first portion, upon being recrystalized, melted at 137° C. This was the diketo product.



M.P. = 137°

obtained from the hydrolysis of the mono para-chlor di-phenyl thiazolidone



M.P. = 185°

which crystalized from the alcohol soluble portion and melted at 185° C. These melting points correspond with those given by Dains, Irvin, and Harrell[9]. The yields were exceedingly small.

The next method tried was to reflux for a half an hour, 13.15 grams mono para-chlor diphenyl thio-urea, 4.7 grams chlor-acetic acid and 9.1 grams pyridine. This gave a 25% yield of the thiazolidone, M. P. 185° C.

We next refluxed for a half an hour, 22.8 grams of thio-carbanilide with molecular proportions of pyridine and ethyl chlor-acetate, using acetone as a solvent. An 85-90% yield of the diphenyl thiazolidone, M. P. 176° C, was obtained. This melting point is the same as that given by Richter.

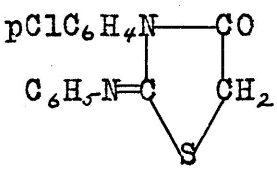
Finally we tried dissolving the thio-urea in acetone, placing it in an ice bath, and slowly adding one mole of chlor-acetyl chloride. Practically 100% yields were obtained by this method. The thiazolidones frequently crystalize out before all of the chlor-acetyl chloride has been added, and are in a nearly pure condition. However, this method fails to work when one of the substituted groups in the thio-urea is an alkyl or even a benzyl group. In this case we seem to get a

urea hydrochloride which decomposes in water to give HCl and the thio-urea back again.

In the case of this latter type of thio-urea, we had to rely on another method, i. e. refluxing the thio-urea with molecular quantities of pyridine and ethyl chlor-acetate, this time using alcohol as a solvent, and heating for two hours instead of one half an hour. In this manner we got from 90 - 95% yields. On the whole, the two latter methods were found to be most satisfactory, and were used almost entirely.

The following compounds were prepared:

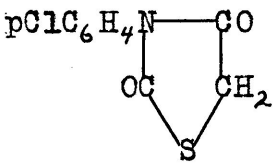
2phenyl-imino-3para-chlor-phenyl thiazolidone



M. P. = 185° C.

This was obtained from phenyl para-chlor-phenyl thio-urea by boiling with molecular quantities of ethyl chlor-acetate and pyridine in alcoholic solution, for four hours. It crystalizes readily from alcohol or acetone in small colorless prisms. The melting point is 185° C, corresponding to that given by Dains, Irvin and Harrell.[9]

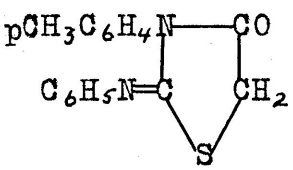
2keto-3para-chlor-phenyl thiazolidone



M. P. = 137° C.

Upon boiling the above compound with equal parts of alcohol and concentrated HCl for four hours, aniline was split off and the diketo compound formed. It crystalizes from hot water or alcohol in flat plates, having the melting point observed by Dains, Irvin , and Harrell[9]. The aniline was tested for by adding NaOH and bleaching powder to the acid filtrate from the diketo product. A purple color indicates the aniline.

2phenyl-imino-3paratolyl thiazolidone



M. P. = 167° C.

This compound was made from symmetrical phenyl para-tolyl thio-urea, pyridine, and ethyl chlor-acetate. It crystalizes from alcohol and acetone in colorless prisms, having a melting point of 167° C.

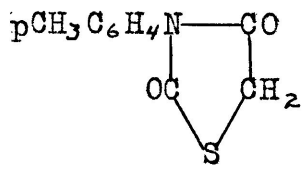
ANALYSIS.

Weight of Sample	0.3682	0.1961
Volume of Acid	25.55	24.55
Volume of Alkali	31.21	35.14
% Nitrogen Found	9.65	10.05

$NaOH = .1874N$ $H_2SO_4 = .3287N$

Calculated for $C_{16}H_{14}ON_2S$ $N_2 = 9.93\%$

2keto-3para-tolyl thiazolidone



M. P. = 138° C.

The above di-substituted thiazolidone was boiled with equal parts of alcohol and concentrated HCl for four hours. Upon cooling, the diketo compound crystalized out and the filtrate gave a good test for aniline with bleaching powder.

The melting point, however, is low, Irvin, Dains and Harrell[9] giving it as 162° C. The analysis, however, is very good, and a mixed melting point with the 3-phenyl 2-4 diketo thiazolidone melts at about 122° C, while the two pure components melt at 138° C and 148° C respectively. The phenyl diketo product was prepared

from the diphenyl thiazolidone.

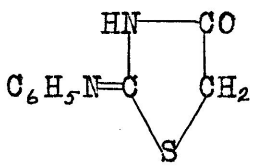
ANALYSIS.

Weight of Sample	0.2472	0.1947
Volume of Acid	10.09	9.94
Volume of Alkali	4.05	5.20
% Nitrogen Found	6.86	6.73

NaOH = .2032N H_2SO_4 = .2202N Blank = .85 C.C. acid.

Calculated for $C_{10}H_9O_2NS$ N_2 = 6.76%.

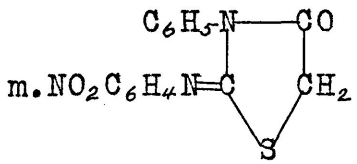
2phenyl-imino thiazolidone



M. P. = 176° C.

An attempt was made to prepare the labile form of the mono-phenyl thiazolidone obtained by Wheeler and Johnson[3]. Some mono-phenyl thio urea was dissolved in acetone, placed in an ice bath, and treated with CH ClCOCl. Two moles of pyridine were present. It was hoped that by keeping both the temperature and the acid down that the labile form might be obtained. Instead, however, a theoretical yield of the stable form resulted, M. P. = 176° C.

2meta-nitro-phenyl-imino-3phenyl thiazolidone



M. P. = 159° C

This was prepared by treating molecular quantities mono meta-nitro diphenyl thio-urea with CH ClCOCl in cold acetone. The thio-urea melted at 159° C, the same as that given by Dains, Irvin, and Harrell[9], but Richter gives 155° C. Only a small yield was obtained by this method, so we tried boiling the thio-urea with pyridine and ethyl chlor-acetate. Somewhat better yields were obtained, but the product was impure and very hard to crystalize from any of the common solvents. Some was finally obtained in a fairly pure state. The crystals were clear yellow prisms, a great many of them twinned, giving the effect of a cross. They melted at 159° C, the same as the thio-urea, but a mixed melting point came out 152° C.

ANALYSIS

Weight of Sample	0.4680	0.3821
Volume of acid	24.80	24.91
Volume of Alkali	17.65	21.77
% Nitrogen	14.15%	14.66%

NaOH = .1874N H_2SO_4 = .3287N Blank = .36 c.c. acid

Calculated for $C_{15}H_{11}O_3N_2S$ $N_2 = 14.55\%$.

When some of the material was boiled with alcohol and HCl, 3 grams of meta-nitro aniline was obtained and a diketo product melting at 137° C. This was evidently the 3phenyl- 2-4-diketo thiazoldione, which should have melted at 148° C.

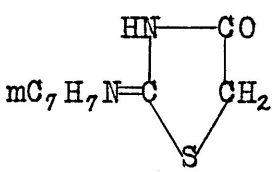
ANALYSIS.

Weight of Sample	0.1644	0.1206
Volume of Acid	10.58	10.07
Volume of Alkali	14.07	14.27
% Nitrogen Found	7.14	7.36

$NaOH = .1874N$ $H_2SO_4 = .3287N$

Calculated for $C_9H_7O_2NS$ $N_2 = 7.25\%$.

2meta-tolyl-imino thiazolidone



M. P. = 165° C.

This compound was made by boiling mono meta-tolyl thio-urea with molecular proportions of ethyl chloracetate and pyridine. It crystalizes out in clear colorless prisms, having a melting point of 165° C.

ANALYSIS

Weight of Sample	0.2038	o.2522
Volume of Acid	20.24	20.22
Volume of Alkali	11.72	9.38
%Nitrogen Found	13.09	13.10

NaOH = .2032N H_2SO_4 = .2202N Blank = .85 c.c.acid

Calculated for $C_{10}H_{10}ON_2S$ N_2 = 13.59%.

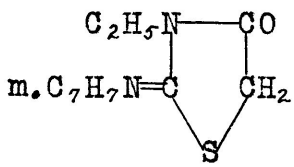
This compound was very hard to hydrolyze. Alcoholic potash gave no results, and acid was tried repeatedly. The only results obtained at all were small yields of meta-toluidine on two occasions. This was identified as the benzoyl derivative, M. P. 122° C. This would indicate the structure given above, and would comply with Wheeler and Johnson's theory as to the structure of the stable form. No diketo product was ever isolated.

When the meta-tolyl thiazolidone was warmed with the theoretical quantity of dilute NaOH, it dissolved and upon cooling, a great mass of flat plates were crystalized out. These were dried, weighed, and boiled with an excess of C_2H_5I. The resulting compound was very hard to crystalize, the best crystals melting

in the neighborhood of 90°. These were very impure, the melting point having a range of about fifteen degrees.

No results were obtained by boiling sodium, ethyl iodide, and the thiazolidone in absolute alcohol. The resulting tar could not be purified.

2-meta-tolyl-imino-3ethyl thiazolidone.



M. P. = 57° C.

The constitution of the above substance is not conclusively proven, the ethyl and meta-tolyl groups possibly being interchanged. It was obtained by boiling symmetrical ethyl meta-tolyl thio-urea with ethyl chlor-acetate and pyridine. The substance is very hard to obtain in a crystaline form. It must first be washed free of pyridine with dilute HCl and then allowed to stand in a dessicator. Upon recrystalizing from ether, large clear crystals are formed, having a melting point of 57° C.

ANALYSIS

Weight of Sample	0.3250	Blank
Volume of Acid	20.19	.60 c.c.acid
Volume of Alkali	8.10	
% Nitrogen Found	11.51	

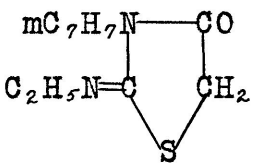
NaOH = .2032 H_2SO_4 = .2202

Calculated for $C_{12}H_{14}ON_2S$ N_2 = 11.54%.

It was apparently impossible to hydrolyze this compound, the results of all the trials being decomposition rather than hydrolysis. Varying strengths of acid were used, from pure HCl down to a very dilute solution of acid in alcohol. In this case, a compound was formed having a melting point of 101° C. It consisted of white needles radiating from a common center. They contained no sulphur. When the kjeldahl was run, the nitrogen came out so much higher than what was expected, that it more than neutralized the acid. The compound, yet unidentified, contains more than 15.5% nitrogen.

As the hydrolysis was unsuccessful, it left the structure of the compound undetermined. The reasons for giving it the above structure are:

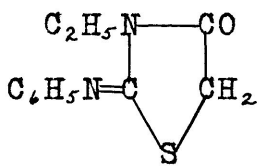
Beckurts and Frerichs[5] took what they called the meta-tolyl thiazolidone and treated it with NaOH and C_2H_5I. They got a compound to which they gave the formula



M. P. = 106° C

This substance, when hydrolyzed, gave the meta-tolyl diketo product, with a melting point of 90° C, which agrees with that cited by Dains, Irvin, and Harrell[9]. As Beckurts' compound melted at 106°C, and ours at 57° C, we give ours the other formula.

2phenyl-imino 3ethyl thiazolidone



M. P. = 70° C.

This substance was obtained from symmetrical ethyl phenyl thio-urea and ethyl chlor-acetate, by boiling with alcohol and pyridine. The above structure was given it, as it is an analagous compound to the preceeding one. It crystalizes from ether in quite large colorless prisms having a melting point of 70° C.

ANALYSIS

Weight of Sample	0.4449	0.4640
Volume of acid	49.73	49.72
Volume of Alkali	14.61	12.15
% Nitrogen Found	11.95	12.32

NaOH = .1139N H_2SO_4 = .1125 N Blank = .3 c.c.acid.

Calculated for $C_{11}H_{12}ON_2S$ N_2 = 12.72%.

When this product was boiled with dilute acid, a small number of white needles were obtained, which melted at 158° C and contained the same per cent of nitrogen as the original substance. Only enough for one kjeldahl was obtained. This substance is still unidentified.

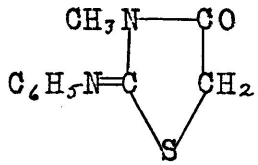
ANALYSIS.

Weight of Sample	0.2155	Blank
Volume of Acid	10.44	.60 c.c. Acid
Volume of Alkali	0.90	
% Nitrogen Found	12.91	

NaOH = .2032N H_2SO_4 = .2202N

Calculated for $C_{11}H_{12}ON_2S$ N_2 = 12.72%.

2phenyl-imino-3methyl thiazolidone



M. P. = 60° C

The constitution of the above compound was given as above because it is analagous to the two preceeding ones. It was obtained by boiling symmetrical methyl-phenyl thio-urea with ethyl chlor-acetate and pyridine. The resulting product is very hard to crystalize. Upon slow recrystalization from ether, it melts at 60° C. The crystals are large, clear prisms frequently weighing as much as a half a gram.

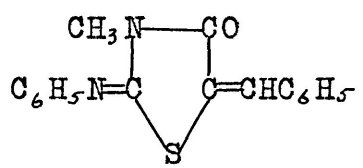
ANALYSIS. (By Olin E. Mace)

$N_2 = 13.50\%$

Calculated for $C_{10}H_{10}ON_2S = 13.59\%\ N_2$.

When this compound is boiled with dilute acid, it is decomposed into a substance which contains sulphur and melts at 120° C. This is, as yet, unidentified. Not enough obtained for analysis.

2phenyl-imino 3 methyl 5benzal thiazolidone



M. P. = 135° C

When the phenyl methyl thiazolidone is warmed in alcohol with a drop of piperdine and some benzaldehyde, the two hydrogens in the "5" position condense with the oxygen of the aldehyde, to give water and the benzal derivative. It crystalizes from alcohol in small yellow needles, having a melting point of 135°.

ANALYSIS

Weight of Sample	0.2286	Blank
Volume of Acid	20.70	.69 c.c. Acid
Volume of Alkali	6.75	
% Nitrogen Found	9.13	

NaOH = .1139N H_2SO_4 = .1125N

Calculated for $C_{17}H_{14}ON_2S$ N_2 = 9.53%

Ethyl-meta-tolyl-amine

$m.C_7H_7NHC_2H_5$

75 grams of meta-toluidine was boiled with an equal weight of formic acid for 10 hours. The excess of water and formic acid was then distilled off. Meta-formtoluid was left

$$m.C_7H_7NH_2 + HCOOH = m.C_7H_7NHCHO + H_2O$$

This was then dissolved in alcohol and the theoretical amount of NaOH, also dissolved in alcohol, was slowly added. The sodium salt crystalized out in small

needles, and was dried in an oven.

$$m.C_7H_7NHCHO + NaOH = m.C_7H_7NNaCHO + H_2O$$

The sodium salt was next refluxed for two hours with an excess of ethyl iodide. The character of the precipitate was changed to a more crystaline form. By this process, the ethyl group was hooked onto the nitrogen.

$$m.C_7H_7NNaCHO + C_2H_5I = NaI + m.C_7H_7NC_2H_5CHO$$

This was then refluxed with HCl for two hours, hydrolyzing off the CHO group.

$$mC_7H_7NC_2H_5CHO + H_2O + HCl = mC_7H_7NHC_2H_5.HCl + HCOOH$$

It was then made alkaline and steam distilled. A light yellow oil, which floated on top of the water, was separated off, dried over CaCl , and redistilled. It boiled at 226° - 230° C.

ANALYSIS.

Weight of Sample	0.7966	0.8677
Volume of Acid	22.35	25.30
Volume of Alkali	8.65	9.88
% Nitrogen Found	9.87%	10.25%

NaOH = .1874N H_2SO_4 = .3287N Blank = .34 c.c.Acid

Calculated for $C_9H_{13}N$ N_2 = 10.37%

An effort was now made to prepare unsymmetrical ethyl meta-tolyl thio-urea by treating this secondary amine with HCl and NH_4NCS.

Some of the secondary amine was dissolved in an excess of HCl, and a mole and a half of NH_4SCN, dissolved in water, was added. Very large quantities of water had to be present to prevent the NH SCN from salting out the amine. This solution, when evaporated, should give a fair yield of the unsymmetrical thio-urea, but instead, as soon as it got hot, a great mass of yellow to orange crystals separate out. These crystals are not soluble in any of the organic solvents, and only about one part in five hundred in water. They dissolve in NaOH, to be reprecipitated upon acidification. They do not dissolve in dilute or concentrated HCl, but do dissolve in hot 20% H_2SO_4 and recrystalize on cooling in long yellow needles. These crystals will not melt, but decompose at 194° C. They will not give a test for the SCN^- ion.

ANALYSIS

Weight of Sample	0.2263	0.3085
Volume of Acid	40.05	59.80
Volume of Alkali	12.70	23.12
% Nitrogen Found	18.54	18.35

NaOH = .1138N H_2SO_4 = .1125N Blank = .69 c.c. Acid

Calculated for $(HSCN)_x$ N_2= 23.72%

Calculated for ethyl meta-tolyl thio-urea $C_{10}H_{14}N_2S$ N_2 = 14.43%

It is not known what this substance might be.

An attempt was also made to prepare the thio-urea by means of thio-phosgene, but the reaction would not go in the manner desired.

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