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ON THE ACTION OF CERTAIN ACID REAGENTS ON THE SUBSTITUTED UREAS.

[FIRST PAPER.]

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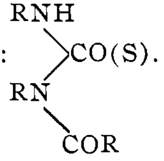
IN the course of an investigation on the isourea ethers,[1] the question arose regarding the anilido hydrogen as to its ease of replacement by, and its reactivity toward, acid reagents. Since the amount of experimental evidence concerning the action of acids and acid chlorides on the substituted ureas is relatively small, a study is being made of the behavior of these bodies toward such reagents.

With an easily replaceable hydrogen, a very interesting synthesis would be possible: namely, the direct formation of acyl thio and oxygen ureas of the general type:



$$\left.\begin{matrix}\text{RNH}\\ \text{RN}\diagdown\text{COR}\end{matrix}\right\rangle\text{CO(S)}.$$

When, however, acyl chlorides, acid anhydrides, and acids act upon these ureas, while it seems probable in many cases that the

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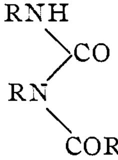
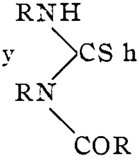
[1] This Journal, 21, 181.

anilido hydrogen is the first point of attack, with the intermediate formation of an acyl derivative, only under especial circumstances have these intermediate bodies been isolated when this method of preparation is used. For instance, the oxygen derivatives  $\genfrac{}{}{0pt}{}{\mathrm{RNH}}{\mathrm{RN{-}COR}}\!>\mathrm{CO}$ have never been prepared directly, but only by

(1) the addition of acetanilide to phenyl isocyanate,[1]

(2) the action of acid chlorides on the isourea ethers.[2]

The corresponding sulphur body  $\genfrac{}{}{0pt}{}{\mathrm{RNH}}{\mathrm{RN{-}COR}}\!>\mathrm{CS}$ has, however, been isolated in the following cases:

(1) Werner[3] heated dibenzyl thiourea and acetic anhydride to the boiling-point of the latter, and obtained acetyl dibenzyl thiourea, besides small quantities of benzyl mustard oil and benzyl acetamide, the usual products of the reaction. Werner thinks that with fatty thioureas such an acyl derivative is usually formed, but he only succeeded in isolating it in the above instance.

(2) Deninger has found that acetyl chloride and thiocarbanilide in pyridine solution give mono acetyl thiocarbanilide.[4]

(3) Recently Hugershoff,[5] by modifying the process used by Werner, and heating the mixture of thiocarbanilide and acetic anhydride only to the temperature of a boiling water bath, succeeded in isolating acetyl thiocarbanilide. A yield of 45 per cent. was obtained, the rest of the thiocarbanilide having formed mustard oil and acetanilide, the products obtained by Werner at the temperature of boiling acetic anhydride.

These acyl ureas are relatively unstable bodies, and readily dissociate above their melting-points into the corresponding cya-

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[1] McCreath : *Ber. d. chem. Ges.*, **8**, 1181.

[2] Dains : This Journal, **21**, 182.

[3] *J. Chem. Soc.*, 50, 406.

[4] *Ber. d. chem. Ges.*, **28**, 1322.

[5] *Ibid.* (1899), 3649.

nates and anilides, thus giving opportunity for secondary reactions.

While it seems extremely probable, and in a number of cases is definitely proved, that the acid chlorides and anhydrides react with the ureas with the formation of such intermediate acyl ureas, yet under the conditions of the experimental work in this paper, the temperature required to produce reaction was so high that such acyl ureas were never isolated, but only their decomposition products. This fact has given rise to some interesting results.

The work in this paper has been confined to a study of the action of acids and acid chlorides on such ureas as carbanilide and thiocarbanilide, the only exception being some experiments on the action of acetic anhydride and the above reagents on the oxygen and sulphur isourea ethers. The interaction between these reagents and the monosubstituted and acyl ureas will be discussed in a later paper.

EXPERIMENTAL.

Organic Acids and Carbanilide.—Werner[1] has shown that pure acetic acid decomposes diphenyl urea at 160°–170°, giving acetanilide, carbon dioxide, and water.

Organic Acids and Thioureas.—Cain and Cohen, while investigating the "action of acetic acid on phenyl thiocarbamide," heated absolute acetic acid and thiocarbanilide at 130°–140° for three to four hours. They simply state that diphenyl urea was one of the products.[2] This is wholly in accord with the general action of anhydrous acids at temperatures above 130°. At a lower temperature, somewhat different results are obtained. Thus 9 grams of thiocarbanilide and 20 cc. of pure acetic acid were heated in a water-bath for thirty hours. The residual solid, when filtered off and examined, proved to be thiocarbanilide, and not diphenyl urea. On distilling the acid filtrate with steam, phenyl mustard oil came over, while the distilling flask was found to contain acetanilide and a base that melted at 145°,—its picrate melted at 180°, and was, therefore, triphenyl guanidine. The picrate of pure triphenyl guanidine was found by

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[1] *J. Chem. Soc.*, 59, 550.

[2] Cain and Cohen: *J. Chem. Soc.*, 59, 328.

experiment to melt at 180°, and not at 178°, as given in the literature.

Under these conditions, then, the reaction follows out the lines of the decomposition of the thiocarbanilides with aqueous hydrochloric acid, the difference centering in the fact that the products of the reaction tend to form anilides with the organic acid present,—a tendency more apparent when higher temperatures are used. In this case there is first dissociation into phenyl mustard oil and aniline; and as secondary reactions, the formation of acetanilide from the aniline and the glacial acetic acid, and also, though more slowly, from the acid and the mustard oil. This interpretation is confirmed by the fact that, while at the above temperature no carbanilide is formed when absolute acid is used, with aqueous acid diphenyl urea is produced (as shown by experiment). This, as the investigation of Werner shows, is due to the action of the aqueous acid upon the phenyl thiocarbamide. It was found by direct experiment that the final products of 75 per cent. acetic acid, and thiocarbanilide at water-bath temperature are acetanilide and diphenyl urea, although the odor shows that mustard oil is an intermediate product.

Butyric Acid and Thiocarbanilide.—2.3 grams of thiocarbanilide and 2 grams of butyric acid were heated at 140°–160° for two hours. Reaction set in with the evolution of carbon dioxide and hydrogen sulphide. From the residue, by crystallization from alcohol, there was isolated butyric anilide and diphenyl urea. Carbon oxysulphide was probably evolved, but no effort was made to detect it in the presence of hydrogen sulphide and carbon dioxide. In all of these experiments, it may be said, traces of the free amine could be detected.

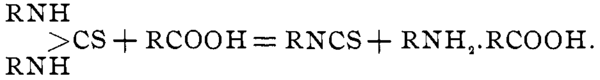
Benzoic Acid and Thiourea.—Molecular quantities of benzoic acid and diphenyl thiourea, at 160°–180°, evolve hydrogen sulphide, carbon dioxide, and water. As the formation of gas ceases, the melt becomes semisolid, and on examination is found to consist of a little benzoic acid which was extracted with dilute alkali, benzanilide, and a small amount of diphenyl urea.

Diparatolyl thiourea and benzoic acid, under like conditions, gave as gaseous products carbon dioxide and hydrogen sulphide, and a residue of *p*-benztoluid *p*-carbtoluid, and a little benzoic acid.

Salicylic Acid and Diphenyl Thiourea.—A mixture of these bodies in molecular proportions, when heated, liquefied at 140°, and at 150° slowly gave carbon dioxide and hydrogen sulphide. Caustic alkali separated the melt into two portions: one soluble in alkali, the other insoluble. This latter proved to be diphenyl urea. The portion soluble in the caustic soda consisted of salicylic anilide (m. p. 133.5°) and a little salicylic acid. Besides these products traces of aniline and phenol were formed,—the latter doubtless due to a slight decomposition of the salicylic acid.

The experiments presented show that the reaction between the thioureas and organic acids of the type RCOOH, proceeds along fairly definite lines. The products to be accounted for are carbon dioxide, hydrogen sulphide, water, the anilide, mustard oil and carbanilide.

The main reaction is the one already indicated:

I. 

$$\begin{matrix}\mathrm{RNH}\\ \mathrm{RNH}\end{matrix}{>}\mathrm{CS} + \mathrm{RCOOH} = \mathrm{RNCS} + \mathrm{RNH_2.RCOOH}.$$

At the temperature of the reaction the amine and the acid unite.

$$\text{II. } \mathrm{RCOOH} + \mathrm{RNH_2} = \mathrm{RNHCOR} + \mathrm{H_2O}.$$

At the same time the mustard oil is attacked.

$$\text{III. } \mathrm{RNCS} + \mathrm{RCOOH} = \mathrm{RNHCOR} + \mathrm{COS}. \ (\mathrm{HOH} + \mathrm{COS} = \mathrm{CO_2} + \mathrm{H_2S}.)$$

Only the carbanilide remains to be accounted for. This body, it will be remembered, is produced only when high temperatures are used in the reaction between thiocarbanilide and anhydrous acids. At the water-bath temperature none was formed. Werner, who has studied the reaction between acetic acid and phenyl mustard oil, says that the decomposition occurs according to the following equation:[1]

$$2\mathrm{RNCS} + 3\mathrm{H_2O} = (\mathrm{RNH})_2\mathrm{CO} + 2\mathrm{H_2S} + \mathrm{CO_2}.$$

In view of this it might be said that the carbanilide is due to the water formed in the reaction and the mustard oil set free at the same time. But such a conclusion must be erroneous for the following reasons:

a. At water-bath temperature none is formed;

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[1] *J. Chem. Soc.*, 59, 545.

b. Much, if not all, of the water escapes at the temperature of the reaction;

c. More carbanilide is often produced than the above equation accounts for.

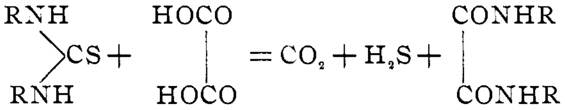
A very probable hypothesis is the following: at the high temperature employed, there is more or less dissociation of the thiocarbanilide into carbodiimide and hydrogen sulphide.

The carbodiimide thereupon reacts with the organic acid as follows :[1]

$$(RN)_2C + 2RCOOH = (RNH)_2CO + (RCO)_2O.$$

Dibasic Acids and the Thioureas.—Diphenyl thiourea and oxalic acid were heated at 160°–170°. The mixture melted readily, decomposed with the evolution of gas, and then partially solidified.

The gaseous products consisted mainly of carbon dioxide and hydrogen sulphide. From the solid residue, hot alcohol extracted traces of phenyl mustard oil and a little unchanged thiourea. The insoluble portion proved to be oxanilide (m. p. 240). The main reaction, then, is as follows:



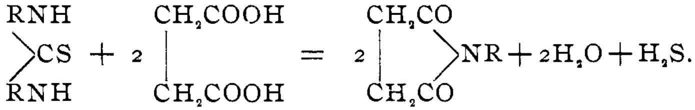
$$\begin{array}{l}RNH\\ \quad\rangle CS\\ RNH\end{array} + \begin{array}{c}HOCO\\ |\\ HOCO\end{array} = CO_2 + H_2S + \begin{array}{c}CONHR\\ |\\ CONHR\end{array}$$

Traces of aniline could also be detected, probably in the form of aniline oxalate. No oxanilide was discovered.

Thiocarbanilide (11 grams) and succinic acid (5 grams) require a temperature of 170° before reaction sets in. At this point, however, much carbon dioxide, hydrogen sulphide, and water are evolved. The other products consisted of small amounts of aniline and mustard oil, while the residual solid could be separated by fractional crystallization into succinanil and succinanilide.

The main results can be expressed as follows :—

I.



$$\begin{array}{l}RNH\\ \quad\rangle CS\\ RNH\end{array} + 2\begin{array}{c}CH_2COOH\\ |\\ CH_2COOH\end{array} = 2\begin{array}{c}CH_2CO\\ |\\ CH_2CO\end{array}\rangle NR + 2H_2O + H_2S.$$

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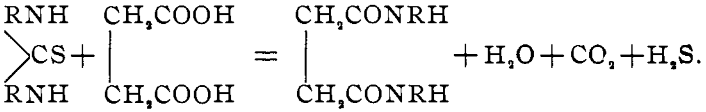
[1] Dains: This Journal, 21, 157.

II. 

$$\begin{array}{l}\mathrm{RNH}\\ \quad\rangle\mathrm{CS}\\ \mathrm{RNH}\end{array} + \begin{array}{l}\mathrm{CH_2COOH}\\ |\\ \mathrm{CH_2COOH}\end{array} = \begin{array}{l}\mathrm{CH_2CONRH}\\ |\\ \mathrm{CH_2CONRH}\end{array} + \mathrm{H_2O} + \mathrm{CO_2} + \mathrm{H_2S}.$$

These reactions are almost identical with those that occur when the anhydride is used instead of the acid. For instance, Dunlap[1] has found that succinic anhydride and thiocarbanilide give succinanil, succinanilide, carbonyl sulphide, and aniline. My own experiments confirm these results and show that with the elevation of temperature, there is increase in the amount of succinanilide formed. Thus, equal molecules of di-*p*-tolyl thiourea and succinic anhydride, when heated at 160°–180°, give as gaseous products carbon dioxide, hydrogen sulphide, water, and COS. The residue consisted of *p*-tolylsuccinimid and *p*-succintoluid.

It is possible that formation of succinic anhydride precedes the interaction with the thiocarbanilide, as seems to be the case with phthalic acid.

Thiocarbanilide and phthalic acid (equal molecules) reacted at 170°, with the evolution of hydrogen sulphide and carbon dioxide.

The residue was washed with cold alcohol: this removed, as was found, phenyl mustard oil, a little aniline, and a solid melting at 125°–130° which proved to be phthalic anhydride. The main product, which was insoluble in the cold alcohol, proved to be phthalanil (m. p. 205°). The reaction proceeds as if the anhydride had been used instead of the acid. The results again are in accordance with the experiments of Dunlap[1] who found that thiocarbanilide and phthalic anhydride react at 170° with the formation of phthalanil and mustard oil.

Before this paper of Dunlap's was seen, experiment showed that *p*-tolyl thiourea and phthalic anhydride react easily and smoothly at 160° yielding COS, traces of water and hydrogen sulphide, and practically quantitative amounts of p-tolyl mustard oil and *p*-tolyl phthalanil. An excess of the acid or acid anhydride increases the yield of phthalanil and decreases that of the mustard oil, since it was found by experiment that equal mole-

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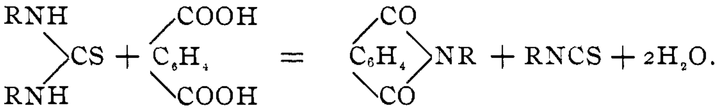
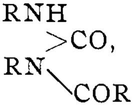
[1] *Am Chem. J.*, 18, 332.

cules of phthalic anhydride and mustard oil at 160° slowly give COS and phthalanil. On the contrary phenyl mustard oil and succinic anhydride do not react at 180°, but when boiled together tar is produced and an odor of phenyl isocyanate developed.

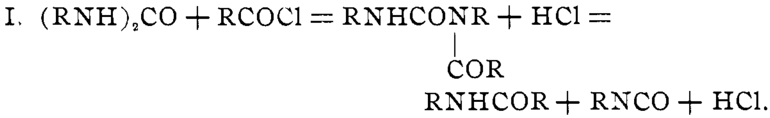


$$\begin{matrix}RNH\\ \\ RNH\end{matrix}\!\!>\!CS + C_6H_4\begin{matrix}\diagup COOH\\ \\ \diagdown COOH\end{matrix} = C_6H_4\begin{matrix}\diagup CO\\ \\ \diagdown CO\end{matrix}\!\!>\!NR + RNCS + 2H_2O.$$

Acid Chlorides and Ureas.—When acid reagents like the acid anhydrides and the acid chlorides act upon the disubstituted ureas, the anilido hydrogen seems to be the main point of attack, although the actual mechanism of the reaction, whether it be one of addition or direct replacement of the hydrogen, cannot as yet be settled experimentally. The evidence points, however, to the intermediate formation in some way of an acyl derivative.

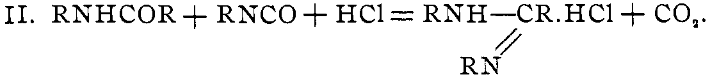
With the oxygen ureas such a compound,  $\begin{matrix}RNH\\ RN\diagdown COR\end{matrix}\!\!>\!CO,$ can never be obtained by the direct action of the acid chloride since the acyl body decomposes at a temperature below that at which the reaction is carried out.

The equations evolved in the interaction of an acid chloride and carbanilide can be represented as follows :



$$\text{I. } (RNH)_2CO + RCOCl = RNHCO\underset{\overset{|}{COR}}{N}R + HCl = RNHCOR + RNCO + HCl.$$

Under the conditions of the experiment, the acyldialphyl urea breaks down into an anilide and isocyanate, which in turn react, giving carbon dioxide and an amidine derivative.



$$\text{II. } RNHCOR + RNCO + HCl = RNH\!-\!\underset{\overset{\diagup\!\!\diagup}{RN}}{C}R.HCl + CO_2.$$

Diphenyl urea was heated with a slight excess over 1 molecule of acetyl chloride in a sealed tube for three hours at 150°. The tube opened with pressure due to carbon dioxide and a little hydrochloric acid. After the addition of water the reaction-product was shaken out with ether. This removed acetanilide.

On treating the water solution with an alkali, a base was precipitated which, on examination, was found to be acetdiphenylamidine, m. p. 131°–132° (α-phenylimido-α-phenylamidoethane). This base can be purified by recrystallization from alcohol or by dissolving in benzene, passing in hydrogen chloride, and then extracting the pure hydrochloride with water. This removes gummy impurities that are apt to remain persistently with the base. It was further identified by its platinum salt, which melted at 210°.

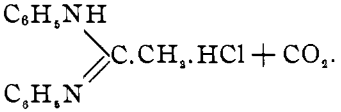
Analysis of two separate preparations :

1. 0.1810 gram substance gave 0.0430 gram platinum.
2. 0.1400 gram substance gave 0.0326 gram platinum.

	Calculated for $(C_{14}H_{14}N_2)_2H_2PtCl_6$.	Found. 1.	Found. 2.
Platinum	23.47	23.75	23.30

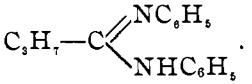
The picrate of this base melts at 165°.

I. $(C_6H_5NH)_2CO + CH_3COCl = C_6H_5NHCOCH_3 + C_6H_5NCO + HCl.$

II.


$$\begin{matrix} C_6H_5NH \diagdown \\ C_6H_5N \diagup\!\!\diagup \end{matrix} C.CH_3.HCl + CO_2.$$

Nine grams carbanilide and 5 cc. butyryl chloride were heated at 150°–170° for four hours. The tube opened with much pressure due to carbon dioxide and hydrogen chloride. The contents, which formed an oily mass filled with bubbles of gas, were dissolved in alcohol and the alcohol evaporated to remove excess of the acid chloride. The ether extract gave 0.5 gram of butyric anilide, which crystallized from ligroin in square plates.

The water solution was found to contain a base, α-diphenyl butane amidine,  $C_3H_7{-}C\begin{matrix} \diagup\!\!\diagup NC_6H_5 \\ \diagdown NHC_6H_5 \end{matrix}$. [Diphenyl butyryl amidine.] This crystallizes from alcohol, in which it is very soluble, in fine star clumps of needles, which melt at 105°.

Analysis resulted as follows :

0.600 gram substance (Kjeldahl) required 4.9 cc. normal acid.

	Calculated for $C_{16}H_{18}N_2$.	Found.
Nitrogen	11.78	11.46

When a solution of the amidine hydrochloride and chlorplatinic acid is allowed to evaporate slowly, a red platinum salt is produced.

Analysis gave the following :

0.3780 gram salt gave 0.0832 gram platinum.

	Calculated for $C_{32}H_{38}N_2Pt.Cl_6$.	Found.
Platinum	21,98	22.01

Molecular proportions of carbanilide and benzoyl chloride were heated at 160°–170° for four hours. As before, carbon dioxide was formed. From the solid contents of the tube, benzene extracted benzanilide, m. p. 161°. The residue insoluble in benzene dissolved readily in water and proved to be the hydrochloride of a base, diphenyl benzenyl amidine, formed by the action of the phenyl isocyanate on the benzanilide.

Thus Kuhn[1] has shown that phenyl isocyanate and benzanilide react at 180°–200° to form the above amidine and carbon dioxide. The base that melted at 145° was further identified by its platinum salt. This melted at 212° and gave the following figures on analysis :

0.1892 gram substance gave 0.0382 gram platinum.

	Calculated for $C_{38}H_{34}N_4PtCl_6$.	Found.
Platinum	20.39	20.19

When molecular proportions of benzoyl chloride and carbanilide are heated in an open flask at 160°–200°, carbon dioxide and hydrochloric acid are given off and the intermediate formation of phenyl isocyanate is very apparent from the odor. Diphenyl benzenyl amidine was isolated as before and was identified by its own melting-point and that of its picrate (m. p. 216°).

Acyl Chlorides and Dialphyl Thioureas.—Reagents of this class act more readily on the thioureas than on the corresponding oxygen derivatives. The products of the reaction are largely dependent upon the following conditions : the presence of a solvent such as pyridine, the temperature, and the fact that the mustard oils

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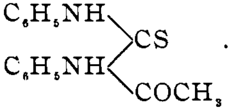
[1] *Ber. d. chem. Ges.*, **18**, 1476.

are less reactive than the corresponding isocyanates, and so do not tend to react with the anilide formed.

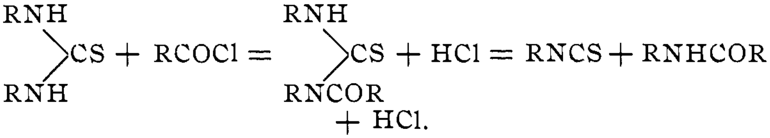
Deninger[1] has shown that by dissolving thiocarbanilide in pyridine, acyl chlorides attack the anilido hydrogen with great ease at ordinary temperatures, forming a stable substitution product. For instance, acetyl chloride and thiocarbanilide, under these conditions, give acetyl thiocarbanilide.



With benzoyl chloride and diphenyl thiourea, a dibenzoyl derivative was obtained. Like the oxygen bodies of similar constitution, these acyl thiocarbanilides are easily decomposed. Thus, acetyl thiocarbanilide, when heated above its melting-point or when boiled with water, gives phenyl mustard oil and acetanilide, which two components show no tendency to unite again even when heated. On the other hand, phenyl isocyanate and acetanilide heated in a sealed tube to 150° unite to form acetyl diphenyl urea.[2]

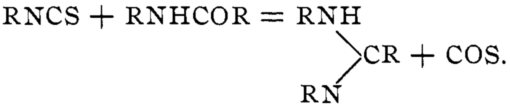
In the absence of pyridine, which combines with the hydrochloric acid set free, my experiments show that heat is required to effect complete reaction between the acyl chloride and the thioureas, and that under these conditions no intermediate product corresponding to the acyl thiocarbanilide can be isolated.

The general reaction between an acyl chloride and a dialphyl thiourea can be expressed as follows :



$$\begin{matrix} RNH \\ RNH \end{matrix}\!\!>\!CS + RCOCl = \begin{matrix} RNH \\ RNCOR \end{matrix}\!\!>\!CS + HCl = RNCS + RNHCOR + HCl.$$

Mustard oil and an acyl anilide are the main products, while occasionally small quantities of an amidine base are formed.



$$RNCS + RNHCOR = \begin{matrix} RNH \\ RN \end{matrix}\!\!>\!CR + COS.$$

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[1] *Ber. d. chem. Ges.*, 28, 1332.

[2] McCreath : *Ibid.*, 8, 1181.

Acetyl Chloride and Thiocarbanilide.—Diphenyl thiourea was treated with a slight excess over 1 molecule of acetyl chloride, and, as no reaction occurred at ordinary temperatures, the mixture was warmed to 50° on the water-bath, until the evolution of hydrochloric acid ceased. The oily product, which became semisolid on cooling, was distilled with steam. Phenyl mustard oil came over. This was identified by its properties, and the formation of monophenyl thiourea. On concentrating the water solution of the residue not volatile with steam, acetanilide (m. p. 114°) was obtained. The filtrate from this, when neutralized with alkali, gave small quantities of a base which proved to be acetdiphenyl amidine, a product formed in much larger quantities in the reaction between acetyl chloride and carbanilide, and identical with the body thus obtained.

Butyryl chloride and diphenyl thiourea react with ease, giving much hydrochloric acid, and an oily product from which can be isolated phenyl mustard oil and butyric anilide. Small amounts of an impure base are also formed.

When molecular quantities of benzoyl chloride and thiocarbanilide are heated to 150°, reaction ensues with the evolution of hydrogen chloride, a little carbon dioxide, and a gas that blackens lead acetate paper. On distilling the product with steam, or by separating with cold alcohol, there can be isolated almost quantitatively phenyl mustard oil and benzanilide. Traces of the base diphenylbenzenyl amidine are also formed.

Di-*m*-xylyl thiourea and benzoyl chloride, under like conditions, react at 120°. The products were the benzoyl derivative of metaxylidine ($CH_3CH_3NH_2$1,3,4 (m. p. 192°), and xylyl mustard oil, which, with alcoholic ammonia, gave the monothiourea (m. p. 175°). Traces of an impure base were also formed.

Greater elevation of temperature does not favor this reaction between the acid chlorides and the thioureas. For instance, molecular quantities of benzoyl chloride and di-*o*-tolyl thiourea were heated in a sealed tube at 180°–200°. The tube opened with slight pressure, and the issuing gas burned with a pale blue flame. The contents of the tube consisted of *o*-tolyl mustard oil, *o*-benztoluide, much tar, and a small amount of an impure base.

Allylphenyl thiourea was warmed on the water-bath with a slight excess of acetyl chloride. The reaction-product formed a thick oil, with the evolution of a little hydrogen chloride. On distilling this oil with steam, a few drops only of phenyl mustard oil were obtained, and the residue in the distilling flask, with the exception of a little tar, was completely soluble in water. From this, alkali threw down a base which, without further purification, melted at 115° and gave a picrate (m. p. 153°). It was, therefore, *N*-phenyl propylene pseudo thiourea. (2-Phenyl amido-5-methyl-4,5-dihydrothiazol.) This was further established by the analysis of the platinum salt.

0.6003 gram substance gave 0.1477 gram platinum.

	Calculated for $(C_{10}H_{12}N_2S)_2H_2PtCl_6$.	Found.
Platinum	24.53	24.60

The acyl chloride evidently causes a practically quantitative rearrangement. Boiling with hydrochloric acid brings about the same change.[1]

The Action of Acid Reagents on Isourea Ethers.—A study begun in a former paper on the action of acids, acid chlorides, and acid anhydrides on the isourea ethers is here continued and extended to the corresponding sulphur ethers.

Organic acids act with great ease upon the isourea ethers. Thus ethylisodi-*o*-tolyl urea and glacial acetic acid give ethyl acetate and carbanilide, as has been shown in a former paper.[2]

Towards acids and acid reagents the thio ethers show remarkable stability. Ethyl isothiocarbanilide can be boiled with glacial acetic acid without effect, the original base being recovered unchanged. When heated at 180° with acetic acid the tube opens with pressure; the issuing gases burn and form a white precipitate with a silver nitrate solution. The solid residue consists of pure acetanilide. The odor of mercaptan is apparent.

Acid of Acetic Anhydride upon the Oxygen Urea Ethers.—Ten grams of amylisodi-*o*-tolylurea and 3.5 grams of acetic anhydride were mixed. Since no apparent reaction took place after standing at ordinary temperatures, the solution was heated in an oil-bath at 150°–160° for one and one-half hours. The product, which remained oily after twelve hours' standing, was distilled at 12 mm. pressure; there was isolated amyl acetate, a

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[1] Prager: *Ber. d. chem. Ges.*, **22**, 2991.

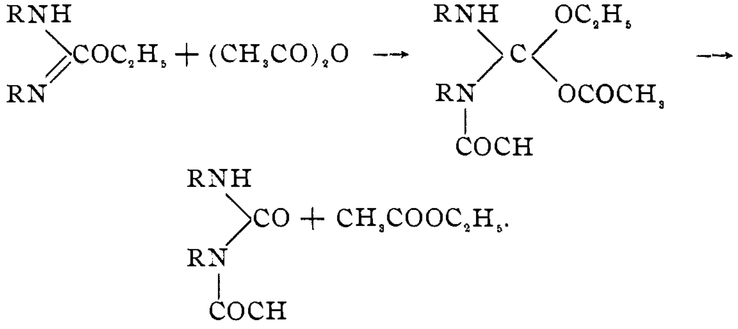
[2] This Journal, **21**, 170.

little unchanged acetic anhydride, *o*-acettoluide, and a trace of *o*-ditolylurea. The latter may be due to traces of moisture or of acetic acid in the anhydride.

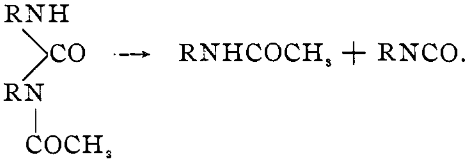
Equal molecules of ethyl isocarbanilide and of acetic anhydride were heated in a test-tube fitted with an air-condenser and a calcium chloride tube for eight hours at 160°–170°. Ethyl acetate was detected by its odor. The oily product was treated with alcohol to get rid of the excess of the acetic anhydride and then recrystallized from water. Acetanilide was isolated. This same reaction was found to take place with equal ease at 130°–140°. At this latter temperature methylisocarbtoluide and acetic anhydride give methyl acetate and *o*-acettoluide. The yield of acetanilide or of *o*-acettoluide seems to be quantitative.

As in all reactions with acidic reagents there is doubtless first addition to the double bond with the formation of an unstable addition-product.

I.



II. (*a*)



(*b*) $RNCO + O(COCH_3)_2 \longrightarrow RN(COCH_3)_2 + CO_2.$

At the temperature of the experiments, 130°–140°, not only is this intermediate addition-product broken down, but the acetyl diphenyl urea formed is dissociated into phenyl cyanate and acetanilide: and the phenyl cyanate in turn reacts with the excess of acetic anhydride to form diacetanilide. That the diacetanilide was not isolated is not surprising, since it is very easily saponified.[1]

The experimental evidence for equation II is as follows:

(*a*) Acetyl diphenyl urea, when heated a little above its melting-point, dissociates, giving phenyl isocyanate and acetanilide.

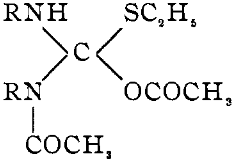
(*b*) Acetyl diphenyl urea, when heated with acetic anhydride at 130° for two hours, and the resulting product recrystallized from water, gives a quantitative yield of acetanilide.[2]

(*c*) Phenyl isocyanate and acetic anhydride give acetanilide.

In the oxygen ethers, the existence of an intermediate product due to the addition of the acid anhydride to the double bonding of the ether was assumed. With the thioethers the existence of such an addition-product was definitely proved.

Ethyl isodiphenyl thiourea and acetic anhydride can be heated to the boiling-point of the latter without seeming change, or the formation of ethyl acetate; and on careful treatment with alkali, the original base can be regenerated.

If, however, the excess of anhydride be decomposed with alcohol, the resulting oil is no longer soluble in dilute mineral acids. Alcoholic potash yields mercaptan and carbanilide, the decomposition taking place with great ease. An effort was made to purify this oil by dissolving in ether and washing with dilute sodium carbonate and water, and drying. The evaporation of the ether left a yellow oil insoluble in water and dilute alkalies. Experiment showed that alcoholic potash gave, on warming with this, mercaptan and diphenyl urea. Hence, if the body is the expected addition-product, it must decompose as follows:



$$\mathrm{(RNH)(RN(COCH_3))C(SC_2H_5)(OCOCH_3)} + 2\mathrm{NaOH} = \mathrm{(RNH)_2CO} + \mathrm{C_2H_5SH} + 2\mathrm{CH_3COONa} + \mathrm{H_2O}.$$

The oil was analyzed by dissolving it in alcohol, adding a definite quantity of standard sodium hydroxide, boiling with a reflux

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[1] Gumpert (*J. prakt. Chem.*, 31, 121), who tried the action of phenyl isocyanate and acetic anhydride, obtained only acetanilide, a result probably due to moisture.

[2] Experiments have shown that diphenyl urea and boiling acetic anhydride give acetanilide and carbon dioxide.

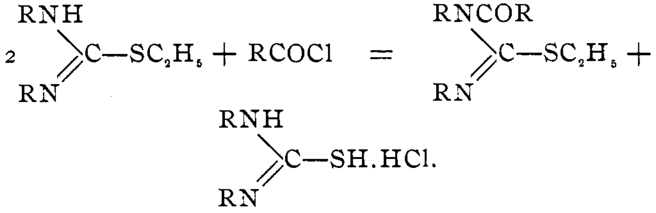
condenser until decomposition was effected, and then titrating the excess of alkali, using phenol phthalein as an indicator. The amount of acetic anhydride could thus be determined, since 1 cc. normal alkali is equal to 0.05103 gram acetic anhydride.

1. 1.7065 grams substance required 9.3 cc. alkali.
2. 1.7965 grams substance required 9.76 cc. alkali.

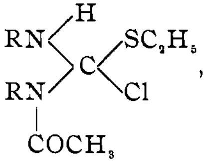
	Calculated for $C_{19}H_{22}N_2O_3S$.	Found. 1.	Found. 2.
$(CH_3CO)_2O$	28.48	27.81	27.72

The difficulty of purifying such a compound, and the ease with which it breaks down, account for the low results. At high temperatures complete reaction follows between the acetic anhydride and the ethyl isothiocarbanilide. Thus, after heating at 190°, the tube opened with pressure due to inflammable gases, while mercaptan and ethyl acetate were recognized by the odor. The solid residue in the tube was pure acetanilide.

Action of Acetyl Chloride upon Ethyl Isothiodiphenyl Urea.—Experiments in a previous paper[1] have shown that with the oxygen urea ethers, acid chlorides react, giving, by addition and subsequent decomposition, ethyl chloride and acyl diphenyl urea. With the sulphur derivatives the reaction proceeds in an entirely different manner, due doubtless to the greater stability of the thio ethers toward acid reagents, and to the more negative character of the molecule. The general reaction between the thioethers and acid chlorides is as follows:



Either the anilido hydrogen is replaced directly by the acyl group, or there is first, addition to the double bond,



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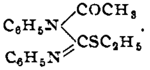
[1] This Journal, 21, 181.

and then loss of hydrogen chloride, which unites with a second molecule of the urea ether to form the hydrochloride.[1]

Two molecules of the thioether were dissolved in chloroform and treated with 1 molecule of acetyl chloride. After standing for twenty-four hours, the solution was washed with water, the excess of chloroform evaporated, and the residual oil taken up with ether; this was washed again with a solution of sodium bicarbonate to remove all traces of free acid. After drying, the evaporation of the solvent left a thick oil, which could not be crystallized, and was no longer soluble in dilute acid. This was analyzed, as in the previous case, by boiling in an alcoholic solution with a standard caustic alkali, the products being sodium acetate, mercaptan, and carbanilide.

1.3554 grams substance required 4.545 cc. normal NaOH. This is equivalent to 0.1954 gram CH_3CO.

	Calculated for  $C_6H_5N\left\langle{COCH_3 \atop CSC_2H_5}\right. \!=\! NC_6H_5$.	Found.
CH_3CO	14.42	14.41

This body, monoacetylethylisodiphenyl thiourea, is interesting as being the first acyl derivative of the isourea ethers that has been isolated. The action of this substance toward glacial acetic acid has also a direct bearing upon the mechanism of the acetic anhydride reaction described on page 195.

Thus, when acetyl ethyl isodiphenyl thiourea was heated to the boiling-point with an excess of glacial acetic acid and allowed to stand for twenty-four hours, the product then being poured into water and purified as in the preceding cases, the original oil was recovered, and not an acetic acid addition-product identical with the product from acetic anhydride.

0.7420 gram oil required 4.9 cc. half-normal NaOH.

	Calculated for $C_{17}H_{18}ON_2S$.	Found.
CH_3CO …………………	14.42	14.33

This points to the conclusion that the acetic anhydride acts by direct addition to the double bond, and not by first replacing the anilido hydrogen with an acetyl group and then adding acetic acid, as follows:

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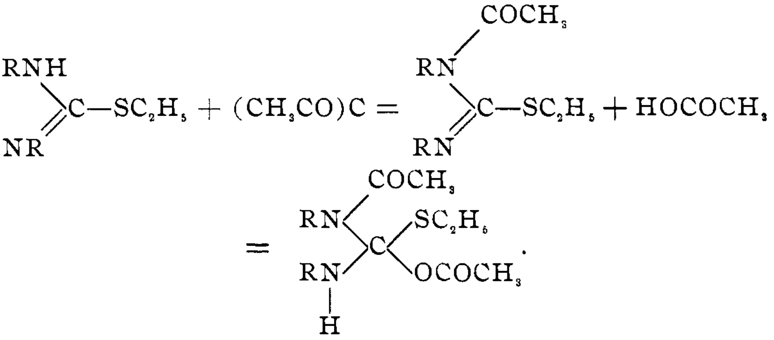
[1] *Am. Chem. J.*, 19, 136.



$$\begin{matrix}RNH\\NR\end{matrix}\!\!>C-SC_2H_5 + (CH_3CO)C = \begin{matrix}RN-COCH_3\\RN\end{matrix}\!\!>C-SC_2H_5 + HOCOCH_3$$

$$= \begin{matrix}RN-COCH_3\\RN-H\end{matrix}\!\!>C<\!\!\begin{matrix}SC_2H_5\\OCOCH_3\end{matrix}.$$

Action of Benzoyl Chloride.—Ten grams of ethyl isodiphenyl thiourea and 3 grams of benzoyl chloride were dissolved in benzene and allowed to stand for a week. The crystals that separated weighed 5.7 grams and consisted of the pure hydrochloride of the ethyl ether (m. p. 178°). After distilling off the benzene, an oil was left, insoluble in ammonia or dilute hydrochloric acid, the benzoyl ethyl thiodiphenyl urea. It was not obtained pure enough for analysis. An effort was made to distil the oil but decomposition ensued, with the formation of much tar, some phenyl isocyanate, and carbodiphenyl imide. Another portion heated in a sealed tube with hydrochloric acid, at 140°, gave ethyl chloride, carbon dioxide, mercaptan, aniline, and benzoic acid, so that while the body was not analyzed, its identity is fairly well established.

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March, 1900.

THE TECHNICAL ESTIMATION OF ZINC.

BY ALBERT H. LOW.

Received February 26, 1900.

IN a report read June 11, 1892, before the Colorado Scientific Society, the method devised by the writer for the technical estimation of zinc in ores, etc., was approved as the best that had come to the attention of the committee. Although it had its weak points, some of which were recognized at the time, it was nevertheless well adapted for rapid and accurate work on the majority of Colorado ores and, in fact, no better method has since been offered.