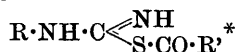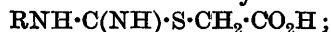## LXIV.—*Substituted* iso*Thiohydantoins.*

### By AUGUSTUS EDWARD DIXON and JOHN TAYLOR.

WHEN the chloride of a carboxylic acid is brought into contact with a hydrocarbon-monosubstituted thiourea, direct union occurs, the hydrochloride being formed of a basic substance,

$$R \cdot NH \cdot C {\displaystyle \mathop{<}^{NH}_{S \cdot CO \cdot R'}} {}^{*}$$

in which the acid radicle, $R \cdot CO \cdot$, is engaged with the sulphur of the thiourea (Dixon and Hawthorne, Trans., 1907, **91**, 122).

On the other hand, when chloroacetic acid reacts with such a thiourea, the chlorine atom, as before, withdraws the hydrogen of the SH-group, the sulphur of which, engaging with the residue of the acetic acid, forms a so-called "thiohydantoic" acid,

$$RNH \cdot C(NH) \cdot S \cdot CH_2 \cdot CO_2H;$$

by loss of the elements of water, this undergoes, more or less completely, condensation into the *iso*thiohydantoin,

$$RNH \cdot C {\displaystyle \mathop{<}^{N \cdot CO}_{S - CH_2}}.$$
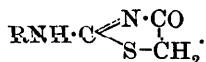
If, however, to a monosubstituted thiourea, chloroacetyl chloride is presented, both the hydrogen atoms are eliminated as hydrogen

* For the sake of simplicity, no reference is here made to the tautomeric variants, which may (and probably do) exist; for example,

$$RN {:} C {\displaystyle \mathop{<}^{NH_2}_{S \cdot COR}}, \text{ etc.}$$

chloride; in which case the product may obviously possess either of the following constitutions:

$$(a) \ \text{RNH·C} \begin{cases} \text{N·CO} \\ \text{S—CH}_2 \end{cases} \qquad (b) \ \text{RNH·C} \begin{cases} \text{N·CH}_2 \\ \text{S—CO} \end{cases}.$$

Experiment has shown (Dixon and Taylor, Trans., 1908, **93**, 21) that from these and similar materials, at temperatures down to $-8°$, form $(a)$ alone is produced; and hence, of the two groups, COCl and ·CH$_2$Cl, the latter seems preferentially to engage with the SH of a thiourea.

Further, it has been shown (Dixon and Hawthorne, *loc. cit.*, 141) that acid chlorides, R·COCl, fail to combine with thioureas containing already an acyl group. If, therefore, chloroacetyl chloride were presented to an acyl trisubstituted thiourea of the form

$$\text{R}_2\text{N·C(NAc)·SH},$$
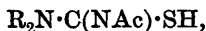
it might be anticipated that a somewhat complex acid chloride would result, as shown by the following equation:

$$\text{R}_2\text{N·C(NAc)·SH} + \text{ClCH}_2\text{·COCl} = \text{HCl} + \text{R}_2\text{N·C(NAc)·S·CH}_2\text{·COCl}.$$
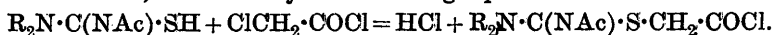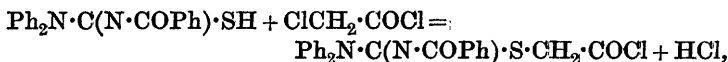
Experiment has curiously failed to justify this anticipation.

## EXPERIMENTAL.

### *ν-Diphenyl-n-benzoylthiourea and Chloroacetyl Chloride.*\*

These substances, mixed in the proportions required by the equation:

$$\text{Ph}_2\text{N·C(N·COPh)·SH} + \text{ClCH}_2\text{·COCl} =$$
$$\text{Ph}_2\text{N·C(N·COPh)·S·CH}_2\text{·COCl} + \text{HCl},$$

were gently warmed on the water-bath until the solid disappeared. A clear, brown, tenacious, gum-like mass resulted, having the sharp odour of an acid chloride, but possessing also the peculiar characteristic " benzoic " odour. The mass dissolved readily in hot acetone, from which it crystallised on cooling. By recrystallisation from alcohol, brilliant, white prisms were obtained, insoluble in water, sparingly soluble in cold, moderately so in hot, alcohol, and melting at 198° (corr.).

The product, already devoid of chlorine before the recrystallisation from spirit, was not affected by boiling with alkaline solution of lead, and gave but a slight darkening when boiled with ammoniacal silver nitrate; when fused with alkali and nitre, however, it yielded alkali sulphate. As the parent material (Dixon and Taylor, Trans., 1908, **93**, 693) is by no means readily desulphurised by lead salts, the failure of the product to yield its sulphur to alkaline solution of lead was not conclusive evidence that the

\* For nomenclature, see Trans., 1895, **67**, 564.

sulphur had become singly linked in the new molecule. Neverthe-
less, that this was the case was established by digesting the substance
with alcoholic potassium hydroxide; for the residue, when acidified
and treated with dilute ferric chloride followed by ammonia, gave
Andreasch's reaction for thiolacetic acid, $SH \cdot CH_2 \cdot CO_2H$ (*Ber.*,
1879, **12**, 1385), hence showing the presence of the group
$\cdot S \cdot CH_2 \cdot CO \cdot$.

The conjecture that the above compound was the hitherto
unknown *diphenyl*iso*thiohydantoin*, $Ph_2N \cdot C \begin{smallmatrix} N \cdot CO \\ | \\ S-CH_2 \end{smallmatrix}$, was verified
by the result of a sulphur determination:

$0 \cdot 3045$ gave $0 \cdot 2670$ $BaSO_4$.   $S = 12 \cdot 04$.
$C_{15}H_{12}ON_2S$ requires $S = 11 \cdot 94$ per cent.

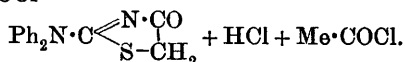### v-Diphenyl-n-acetylthiourea and Chloroacetyl Chloride.

As a check on the foregoing unexpected result, the experiment
was repeated, with the above-named materials, and in the same way
as before, save that the interaction vessel, surrounded by steam,
was provided with a delivery tube dipping into aniline, the object
of the latter being to catch the acetyl chloride, if this should be
evolved as such. The mixture behaved substantially as in the
preceding case, except that gas was evolved; the residue had the
pungent odour of acetyl chloride, and by treatment with alcohol
gave crystals melting at 198° (corr.).

In every way these resembled the product of the foregoing experi-
ment; and a mixture of the two substances in approximately equal
proportions showed no change of melting point.

The aniline had changed to a semi-solid; when treated with hot
dilute hydrochloric acid, this yielded a clear solution, from which,
on cooling, crystals were deposited. By recrystallisation from
water they were obtained in glistening plates, having the appearance
of acetanilide, and giving the reactions of this substance.

All these results may be summed up by the equation:
$$Ph_2N \cdot C(N \cdot COMe) \cdot SH + ClCH_2 \cdot COCl =$$
$$Ph_2N \cdot C \begin{smallmatrix} N \cdot CO \\ | \\ S-CH_2 \end{smallmatrix} + HCl + Me \cdot COCl.$$

### v-Diphenylthiourea and Chloroacetyl Chloride.

A mixture of the two substances in equimolecular proportions,
when fused on the water-bath, gave off hydrogen chloride, leaving
a clear resin, from which, by crystallisation from alcohol, a product
was obtained, indistinguishable in appearance and properties from
the compounds already described. Three tubes, charged respectively

with (i) the above substance obtained from ν-diphenylthiourea; (ii) its mixture with that obtained from n-benzoyl-ν-diphenylthiourea; (iii) its mixture with that obtained from n-acetyl-ν-diphenylthiourea, were attached to the same thermometer, and heat was applied; the contents of all three tubes melted simultaneously at 198° (corr.):

$$Ph_2N \cdot C(NH) \cdot SH + ClCH_2 \cdot COCl = 2HCl + Ph_2N \cdot C {\Large\lessgtr} {\overset{N \cdot CO}{\underset{S-CH_2}{|}}}.$$
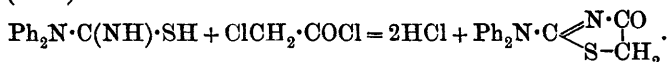
In all the preceding cases the acyl radicle—or the hydrogen atom —displaced from the thiourea was necessarily that attached to the doubly-linked nitrogen atom *; the question now arose whether the expulsion of this radicle depended on its being acidic in function, or whether the withdrawal was conditioned through its being held, initially, in an imino-group. This question, obviously, could be answered by the employment of a thiourea, containing an acyl radicle held in the amino-group, and having the imino-group paralysed by means of a hydrocarbon radicle.

### n-*Phenyl-ν-carbethoxyphenylthiourea and Chloroacetyl Chloride.*

The above-named thiourea, $Ph(CO_2Et)N \cdot C(NPh) \cdot SH$, obtained first by Seidel from thiocarbanilide and ethyl chlorocarbonate (*J. pr. Chem.*, 1885, [ii], **32**, 263), was melted on the water-bath with 1 molecular proportion of chloroacetyl chloride, and the fusion dissolved in hot acetone; on keeping, a white solid was deposited, which crystallised from alcohol in flattened, vitreous prisms, melting sharply at 176°, insoluble in water, not desulphurised by alkaline salts of lead or of silver, and giving Andreasch's reaction for thiolacetic acid (the parent substance melts at 139°, is readily desulphurised, and does not afford the thiolacetic acid reaction). Analysis was considered unnecessary, the product being, obviously, the diphenyl*iso*thiohydantoin of Lange (*Ber.*, 1879, **12**, 595), melting at 176°.

From the facts now secured, it appears that when chloroacetyl chloride attacks a trisubstituted thiourea having an acyl radicle joined to one of its nitrogen atoms, that radicle is eliminated (as the corresponding chloride), independently of whether it forms part of an amino- or of an imino-group.

As stated earlier, the expulsion by chloroacetyl chloride of the acyl radicle contained in a trisubstituted thiourea is a phenomenon which we did not anticipate. In view, however, of the fact that

* The "thiourea," of course, might possess originally the thiocarbamidic structure; but, if so, the molecule, to produce an *iso*thiohydantoin, must sooner or later undergo transposition into the thiourea form.

ring-closing thus occurs, the question naturally presented itself whether, if a thiourea were employed having a hydrogen atom and an acyl radicle both available, the former or the latter would be withdrawn.    To test this point, *ab*-acetylphenylthiocarbamide was selected; whatever its static configuration may be, to produce an *iso*thiohydantoin it must interact in the thiourea form; and its substituents, namely, acetyl and phenyl, are respectively attached to the two different nitrogen atoms of the thiourea.    Here, therefore, the main issue is simple enough; for an *iso*thiohydantoin, if formed at all, must be either some form of acetylphenyl derivative (if hydrogen only is eliminated) or of a phenyl derivative (if the acetyl radicle is expelled).
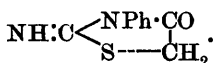
### ab-*Acetylphenylthiocarbamide and Chloroacetyl Chloride.*

A mixture of these substances, when heated on the water-bath, first liquefied, acetyl chloride and some hydrogen chloride being evolved, and then quickly re-solidified.    The nearly white residue, consisting partly of a base and partly of its hydrochloride, was resolved by two recrystallisations from alcohol (which readily withdraws the combined halogen acid) into the base alone.    This, when compared with a specimen of phenyl*iso*thiohydantoin made from phenylthiourea and chloroacetyl chloride, was indistinguishable from it in appearance, melting point, and chemical properties. These observations, together with the fact that acetyl chloride is expelled during the interaction, suffice to show the course of the latter, namely:

$$PhN{:}C{<}^{NHAc}_{SH} + ClCH_2{\cdot}COCl \; = \; PhN{:}C{<}^{NH{\cdot}CO}_{S{-}CH_2} + HCl + AcCl.$$
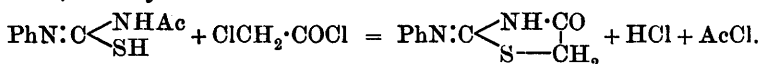
Since, in the above interaction, the phenyl and the acetyl radicles are attached originally to different nitrogen atoms, whilst ring-closing is effected through the elimination of the acetyl radicle, it follows that the phenyl radicle lies, so to speak, outside the thiazole ring, $^{C{\cdot}N}_{C{-}S}{>}C{\cdot}$, a conclusion already reached by one of us on quite different experimental grounds (Dixon, Trans., 1897, **71**, 628).

Isomeric with the *ab*-acetylphenylthiocarbamide referred to above, is the *aa*-form, obtained first by Hugershoff (*Ber.*, 1899, **32**, 3649), and having both the acetyl radicle and the phenyl radicle attached to the same nitrogen atom.    Here, then, as it seemed, lay to hand the means of producing the hitherto unknown phenyl*iso*thio-hydantoin,

$$NH{:}C{<}^{NPh{\cdot}CO}_{S{-}CH_2}.$$

*aa-Acetylphenylthiocarbamide and Chloroacetyl Chloride.*

A mixture of these substances—the latter in excess—was fused on the water-bath, the resultant phenomena being in every way similar to those observed in the preceding experiment with the *ab*-compound. Instead, however, of an isomeride, the product was found to consist of ordinary phenyl*iso*thiohydantoin.

An explanation of this seeming discrepancy was not far to seek. for the material actually obtained could not originate directly from the parent substance; at all events, if it contains the group AcPhN·, which there is every reason to believe is the case. Consequently, the genesis from it of an *iso*thiohydantoin, in which the nitrogen atom concerned in the formation of the thiazole ring is not apparently contained in that ring, must be accounted for, either by a preliminary transformation of the *aa*- into the *ab*-thiocarbamide, or else by the assumption that the phenylic radicle at first contained in the ring wanders away from its original attachment and replaces the hydrogen of the external NH-group. For the latter assumption there is no substantial warrant; whereas, for the former, there is the fact that, in various ways, Hugershoff's thiocarbamide may be transformed into the *ab*-isomeride. Now, in the interaction mentioned above, hydrogen chloride is generated, a substance not unlikely to be capable of effecting this change. A direct experiment, made by heating an alcoholic solution of Hugershoff's thiocarbamide with hydrochloric acid on the water-bath, showed the transformation to be practically complete at the end of some four minutes—the time allowed in making the test. Considering the readiness with which the acetyl radicle can move about within the molecule of a thiocarbamide (or thiourea) until it reaches stability in the *ab*-position (Dixon and Hawthorne, *loc. cit.*; Dixon and Taylor, Trans., 1908, **93**, 18), we judge that the production of ordinary phenyl*iso*thiohydantoin from the materials named is due to a wandering of the acetyl radicle of the thiocarbamide, rather than to a migration of the phenyl in a thiohydantoin already formed.

In these circumstances, the prospect of obtaining the isomeric phenyl*iso*thiohydantoin appeared somewhat remote; nevertheless, as the production of this substance would probably serve towards the clearing up of some difficulties in respect of the constitution of the known form, we tried other methods of attacking the unstable acetylphenylthiocarbamide.

The presence of halogen acid being apparently detrimental, we sought first to establish conditions in which, as fast as formed, it would be neutralised. With this object, Hugershoff's thiocarb-

amide in alcohol was boiled for half-an-hour with a little more than the calculated amount of ethyl monochloroacetate, together with excess of finely-divided calcium carbonate. From the filtrate, on cooling, white crystals were deposited, which proved to be the original thiocarbamide, unchanged; the mother liquor, when tested by Andreasch's method, showed no sign of the presence of thiolacetic acid, and hence presumably contained no *iso*thiohydantoin.

Lest the presence of calcium carbonate might somehow have hindered the desired interaction, the experiment was repeated, but without the addition of the calcium carbonate; the result, however, was precisely the same as before.

Hugershoff's thiocarbamide having failed to yield a thiohydantoin under the above treatment, our next experiment was to boil for an hour a mixture of ethyl chloroacetate with *ab*-acetylphenylthiocarbamide in alcoholic solution; here, also, not a trace of phenyl*iso*thiohydantoin was produced, the acetylphenylthiocarbamide being recovered unchanged from the solution. To make certain that these negative results were not due to any accident, phenylthiourea itself was treated for half-an-hour as before with ethyl chloroacetate; this time the conversion into phenyl*iso*thiohydantoin was practically complete. In this experiment calcium carbonate was present; notwithstanding which, the thiohydantoin separated as usual, that is, partly as free base and partly as hydrochloride. It seems curious that the presence of calcium carbonate should not ensure the removal of the combined hydrogen chloride, whilst the latter is readily eliminated by mere recrystallisation from alcohol.

In the above cases where ethyl chloroacetate failed to interact, the thiourea employed contained an acyl radicle, together with a hydrocarbon radicle; on the other hand, in the case where it interacted, a single hydrocarbon substituent alone was present. Therefore, the failure might be due, either to the presence of an acyl radicle, or, independently of the nature of the radicle, to the fact of two hydrogen atoms in the thiourea being substituted.

To clear up this point the following experiments were made: (1) thiocarbanilide was boiled for half-an-hour with alcohol and ethyl chloroacetate; (2) acetylthiourea was similarly treated. In case (1) the product was Lange's diphenyl*iso*thiohydantoin (see above); it melted at 176°, was not desulphurised by boiling with alkaline lead hydroxide, and gave Andreasch's reaction for thiolacetic acid; thiocarbanilide melts at 151°, is readily desulphurised by hot alkaline lead solution, and does not respond to Andreasch's test. Consequently, the presence of two hydrocarbon radicles in a

thiourea is no more a bar against attack by ethyl chloroacetate than is the presence of one such radicle.

Case (2) proved different; some little hydrogen sulphide was evolved during the boiling, but the crystals which separated on cooling were nearly pure acetylthiourea, and the mother liquor from these, when tested by Andreasch's method, gave no reaction whatever for a thiohydantoin.

How the mere presence of an acyl radicle in a substituted thiourea precludes this from reacting with ethyl chloroacetate is not easy to understand.

Acyl substitution derivatives of the *iso*thiohydantoins appear to be unknown; and that no strong tendency exists towards their formation may be inferred from the results with chloroacetyl chloride described at the beginning of this paper; for in those cases where a hydrogen atom and an acyl radicle are equally available in the substituted thiourea, the *iso*thiohydantoin formed is that originating through the elimination, not of hydrogen chloride, but of acetyl chloride, or of some other acyl chloride. That an *iso*thiohydantoin should be acylated with difficulty, or perhaps not at all, or that such an acyl derivative should tend to resist formation, even in circumstances apparently favourable, is probably to be explained by the fact that the *iso*thiohydantoins are by no means strongly basic substances; this might be expected, seeing that they include already the glycolyl complex, $\cdot CH_2 \cdot CO \cdot$; and it may well be that the general electronegativeness (if such an expression may be allowed) of these bases has almost reached its limit with their formation, and that further to charge them with negative radicles is difficult, if not impossible. There seems, in fact, to be a fairly distinct limit to the power of thiourea and of its ordinary derivatives to take up acyl radicles; for acyl halides, which unite more or less readily with thiourea, and with its mono-, di-, and tri-substitution derivatives, fail to combine if the thiourea contains an acyl radicle.

In like manner, thiourea or its ordinary substitution derivatives may contain one acyl radicle, but rarely two of these.*

Whilst, however, the above considerations may furnish some reason, at least, for the non-production of acylated thiohydantoins of the class named, on the other hand, there does not appear to be any reason why the ethyl chloroacetate should fail to withdraw the acetyl radicle, seeing that it can so readily eliminate a hydrogen

* Deninger has described (*Ber.*, 1895, **28**, 1322) a 'dibenzoylthiocarbanilide obtained from thiocarbanilide in pyridine solution and benzoyl chloride. This is the only known compound of its class.

atom.    One might even, in fact, anticipate that ethyl acetate would
be formed more easily than ethyl alcohol; it is to be remembered,
however, that the acetyl radicle has to be dislodged before ethyl
acetate can result; and we do not yet know either the relative
affinities of acetyl and of hydrogen in the thiourea molecule, or in
what precise configurations these radicles are held.

From the fact that in the combination of a thiocarbimide, $X \cdot NCS$,
with an amine, $Y \cdot NH_2$, the (hydrocarbon) radicles $X$ and $Y$ may
be exchanged without influencing the nature of the product, it has
been argued by various chemists that the latter must be a sym-
metrical thiocarbamide, $CS {<}{NHX \atop NHY}$. If this argument is a sound
one (which is not quite certain), there is at least some ground for
supposing that disubstituted " thiocarbamides " containing an acyl
radicle are not similarly constituted; for, whilst acetylthiocarbimide,
$Ac \cdot NCS$, unites with aniline to afford the so-called $ab$-acetylphenyl-
thiocarbamide, yet phenylthiocarbimide shows no tendency whatever
to combine with acetamide (or with amides in general).    Whatever
the real reason for this may be, a possible one is, that the compound
under consideration has the formula $AcN{:}C(NHPh) \cdot SH$.    If now,
in the union of a thiocarbimide with an amine or an amide, the
latter break into the fractions $H \cdot$ and $R \cdot NH \cdot$ (otherwise
$R \cdot CO \cdot NH \cdot$), which thereupon add themselves to the thiocarbimide,
$X \cdot NCS$—the alkyl symmetrically, and the acyl so as to form a
thiourea—the first process will run as follows:

$$X \cdot NCS + R \cdot NH_2 = X \cdot NH \cdot CS \cdot NH \cdot R\,;$$
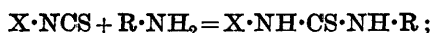
whereas to produce the thiourea, $R \cdot CO \cdot N{:}C(NHX) \cdot SH$, the amide
must lose 2H, instead of H, a change which it may not be disposed
to undergo.    On the other hand, the thiocarbimide, $R \cdot CO \cdot NCS$,
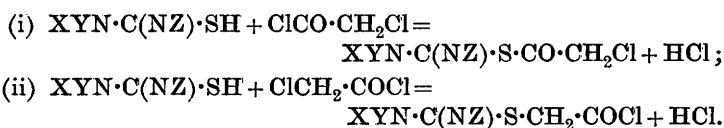taking up $H + XNH$, can afford directly $R \cdot CO \cdot N{:}C(NHX) \cdot SH$.

It is right to add that this is advanced as a mere conjecture;
for, in the first place, the constitution of the acylthioureas (or
thiocarbamides) is not yet definitely known, and in the second,
the non-interaction of the amides may be due to their general
chemical indifference.

The question whether chloroacetyl chloride is able to act directly
on $aa$-acetylphenylthiocarbimide remaining still unanswered, we
tried the experiment of mixing the two substances dissolved in
acetone in presence of a large excess of calcium carbonate.    In view
of the result already obtained with chloroacetyl chloride and the
$ab$-compound (where calcium carbonate failed to deprive the
product of its combined halogen acid), the method offered but little
hope of success; and in effect, although some effervescence took

place, the solid reaction product consisted of a mixture of ordinary phenyl*iso*thiohydantoin with its hydrochloride.

Since the hydrocarbon substituents of a thiourea do not appear to undergo the displacement which occurs so readily when an acyl radicle is present, we next sought to inquire how chloroacetyl chloride would behave towards a thiourea having all its hydrogen, save that of the SH-group, replaced by purely hydrocarbon radicles, X, Y, and Z.

Ring-closing being thus excluded, any interaction that may now take place must occur solely through the withdrawal of the SH-hydrogen, the primary change running on either (or both) of the lines:

(i) $XYN \cdot C(NZ) \cdot SH + ClCO \cdot CH_2Cl =$
$$XYN \cdot C(NZ) \cdot S \cdot CO \cdot CH_2Cl + HCl;$$

(ii) $XYN \cdot C(NZ) \cdot SH + ClCH_2 \cdot COCl =$
$$XYN \cdot C(NZ) \cdot S \cdot CH_2 \cdot COCl + HCl.$$

In case (ii) the product, being an acid chloride, would probably tend to react with another molecule of the thiourea, so as to afford a compound:

$$XYN \cdot C(NZ) \cdot S \cdot CH_2 \cdot CO \cdot S \cdot C(NZ) \cdot NXY.$$
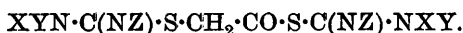
Which of these two reactions would be the more likely to occur, it is not possible to foresee. When the two chlorine atoms of chloroacetyl chloride are presented to the SH-hydrogen of thiourea, or of a monosubstituted, or of a disubstituted thiourea (or even, as now shown, of a trisubstituted thiourea containing an acyl group), that hydrogen picks out, definitely enough, the chlorine of the fraction $CH_2Cl$; or, rather, it seems to do so; but since in all cases hitherto tested the second chlorine atom is also eliminated with formation of a ring, it is evident that the sulphur atom is not quite free to select between the $CH_2$ and the CO; in fact, the end result must depend on which of the two configurations:

$$\cdot C{<}^{N \cdot CH_2}_{\phantom{N}S-CO} \quad \text{and} \quad \cdot C{<}^{N \cdot CO}_{\phantom{N}S-CH_2}$$
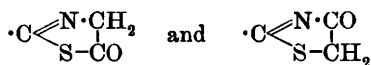
can more easily be formed; and this will depend, not alone on the tendency of S to unite with $\cdot CO \cdot CH_2 \cdot$ or $\cdot CH_2 \cdot CO \cdot$, as the case may be, but also, conjointly, on the readiness of the nitrogen atom to form the combination $:N \cdot CH_2 \cdot$ or $:N \cdot CO \cdot$. In general, the alkyl halides are much less disposed to yield amines than the acyl halides to yield amides; and hence it may reasonably be conjectured that the reason why the sulphur of the thiourea engages with the $CH_2$ of the chloroacetyl chloride is not so much because the combination $\cdot S \cdot CH_2 \cdot$ is more stable than $\cdot S \cdot CO \cdot$, but rather

because the nitrogen atom of the thiourea is simultaneously competing for possession of the CO-group.

Neither, in the case of the equations formulated above, is the issue quite a clear one; for in (ii) the product, being an acid chloride, would not be likely to retain the hydrogen chloride formed, whereas in (i) the product, being a kind of base, would probably combine with the eliminated acid, thereby tending to produce, on the whole, a more stable system.

Experiment yielded the results described below.

### n-*Phenyl-v-methylphenylthiourea and Chloroacetyl Chloride.*

The thiourea, $PhMeN \cdot C(NPh) \cdot SH$ (Gebhardt, *Ber.*, 1884, **17**, 2089), dissolved in dry acetone was mixed with 1 molecular proportion of chloroacetyl chloride diluted with the same solvent. No perceptible rise of temperature occurred, but the solution, when concentrated at the ordinary temperature under diminished pressure, yielded a mass of pure, white, glistening needles; these were collected, washed quickly with dry acetone, and dried over sulphuric acid in a vacuum.

The product, rather deliquescent (m. p. about 147°, with evolution of hydrogen chloride), was easily and completely soluble in water, the solution, which was strongly acid, yielding with nitric acid and silver nitrate a white precipitate of silver chloride; further, the original solid, when treated with cold sulphuric acid, evolved fumes of hydrogen chloride.

Moreover, the aqueous solution, on the addition of alkali hydroxide, gave a white precipitate, easily soluble in dilute acid; and when treated with aqueous picric acid yielded a bright, orange-yellow picrate. From these properties it was evident that the white solid was the hydrochloride of a base, presumably (from the method of its formation) $PhMeN \cdot C(NPh) \cdot S \cdot CO \cdot CH_2Cl$; and that the carbon group engaged with the sulphur atom was not $\cdot CH_2 \cdot$ was shown by the failure of the substance, when evaporated with alcoholic potassium hydroxide, to afford Andreasch's purple thiolacetic acid reaction:

0·505 required 26·8 c.c. $N/10\text{-}AgNO_3$.   Cl$=18\cdot9$.

0·367 gave 0·234 BaSO$_4$.   S$=8\cdot76$.

$C_{16}H_{16}ON_2ClS, HCl$ requires Cl$=20\cdot00$; S$=9\cdot01$ per cent.

The lowness of these numbers (which give the ratio $N_2$ : S) is probably due to the retention by the deliquescent salt of a little moisture.

In the circumstances described above, interaction is determined by the union of the SH-hydrogen with the chlorine of the group COCl, the group $CH_2Cl$ apparently remaining unaffected. Never-

theless, there is some reason to believe that the chlorine of the latter group is not quite devoid of power to interact; for when *n*-phenyl-*v*-phenylmethylthiourea was heated directly with chloroacetyl chloride in the absence of any solvent, hydrogen chloride escaped, a deep crimson liquid being formed, which soon solidified. The solid consisted largely of the foregoing hydrochloride, but not entirely so, for it responded very distinctly to Andreasch's test for thiolacetic acid, and hence contained some material having the linking $\cdot S\cdot CH_2\cdot CO\cdot$.

The picrate obtained from the aqueous solution of the hydrochloride, $PhN\colon C(NMePh)\cdot S\cdot CO\cdot CH_2Cl, HCl$, was obtained as an amorphous, rather clotted precipitate; when heated with water it dissolved partly, but with change of colour, suggesting decomposition, and the filtered liquid on cooling gave but a trifling deposit of a solid, which did not seem to be a pure compound. The corresponding hydrochloride, too, is very readily decomposed, an attempt to recrystallise it from 93 per cent. alcohol resulting in the withdrawal of the elements of chloroacetyl chloride and regeneration of the methyldiphenylthiourea. In another experiment, made in the hope of isolating the base, $PhN\colon C(NPhMe)\cdot S\cdot CO\cdot CH_2Cl$, the solution of the hydrochloride in acetone was treated, little by little, with dry calcium carbonate. Until one equivalent had been added the mixture remained clear; but on the addition of a further quantity it became turbid, and continued to effervesce. The brown acid filtrate, when concentrated by slow evaporation, gave a viscid, deep red oil, from which nothing definite could be isolated.

In fact, all the hydrochlorides so far obtained from trisubstituted thioureas appear to possess little stability. Acetyl chloride combined spontaneously in the cold with Gebhardt's methyldiphenylthiourea; but the product formed exceedingly deliquescent crystals, too impure for analysis, and when it was attempted to recrystallise them from alcohol, they decomposed, with regeneration of the original thiourea. Similar results were obtained with ethyl chlorocarbonate.

The general outcome of the present inquiry, and of certain other similar investigations, may now be summarised approximately as follows:

(1) The chlorides, $R\cdot COCl$, of monocarboxylic acids unite directly with thiourea, or with its mono-, di-, or tri-substitution derivatives, to yield substances of the form $XYN\cdot C(NZ)\cdot S\cdot COR, HCl$, X, Y, and Z being hydrogen or hydrocarbon radicles. Whether these are hydrochlorides, containing a quinquevalent nitrogen atom, or sulphonium chlorides is still uncertain.

If the thiourea contains an acyl substituent, such union does not occur.

In the case of thiourea and of its monosubstitution derivatives, withdrawal of the combined halogen acid may be followed by a migration of the acyl radicle to one of the nitrogen atoms of the thiourea. If the thiourea is monosubstituted, the acyl radicle leaving the sulphur tends to migrate first to the nitrogen atom which already holds a hydrocarbon radicle; from this position it may usually be caused to move (and sometimes moves spontaneously) to the other non-substituted nitrogen atom.

(2) Chloroacetyl chloride acts on thiourea and on its hydrocarbon mono- or di-substitution derivatives solely by ring-closing, with production of *iso*thiohydantoins (from the work of various observers, it appears that this is true also of chloroacetic acid).

Thioureas containing an acyl radicle are attacked by chloroacetyl chloride, with expulsion of that radicle (as an acyl chloride), and formation of the corresponding non-acylated *iso*thiohydantoin; but *aa*-acetylphenylthiocarbamide yields the same compound as that obtained from the *ab*-derivative.

Trisubstituted thioureas, including purely hydrocarbon radicles, unite directly with chloroacetyl chloride to form hydrochlorides, $XYN \cdot C(NZ) \cdot S \cdot CO \cdot CH_2Cl, HCl$ (or, possibly, sulphonium chlorides).

(3) Ethyl chloroacetate behaves towards thiourea and towards its hydrocarbon mono- or di-substitution derivatives in the same way as does chloroacetyl chloride. If, however, the thiourea contains an acyl substituent, no interaction takes place.

CHEMICAL DEPARTMENT,
UNIVERSITY COLLEGE, CORK.