II.—*The Chloroacetates of S-Alkylthiocarbamides.*

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IN a previous communication (T., 1917, **111**, 650), the theory was advanced that salts of *S*-alkylthiocarbamides have a sulphonium structure, $(\text{NH}_2)_2\text{C}:\text{SRX}$, where R is an alkyl group and X an acidic residue. The possibility of the existence of ammonium and of carbonium forms, $\text{XNH}_3\cdot\text{C}(:\text{NH})\cdot\text{SR}$ and $(\text{NH}_2)_2\text{CX}\cdot\text{SR}$, was considered.

The behaviour of the nitrites and thiocyanates of these compounds points to the improbability of an ammonium structure, whilst the ready ionisation of the salts points to the non-existence of carbonium structure. Occasionally, in the presence of strong acids, a second form of a salt is obtained differing considerably from that separating from a neutral solution. This second form is unstable, being readily converted into the first by recrystallisation from hot water. It was conjectured that this unstable form is of the ammonium type, its instability being paralleled by the instability of the salts of amides.

A study of the chloroacetates of *S*-alkylthiocarbamides, and in particular of the monochloroacetates, confirms the view that the salts have not an ammonium structure.

They are readily prepared by mixing a concentrated aqueous solution of thiocarbamide methyl nitrate or of thiocarbamide benzyl chloride with a solution of the sodium salt of the required acid, when the new compound separates from solution.

To the general rule that a thiocarbamide results from the interaction of a thiocarbimide and a primary or a secondary amine, there is one tolerably well-marked exception, namely, when the radicle of either contains a halogen constituent. In this case, although the primary union may run the normal course, there follows the production of a salt of a cyclic base in which the carbon atom, originally halogenated, is now attached to sulphur, thus:

(Gabriel, *Ber.*, 1889, **22**, 1148). Similarly,

(Dixon, T., 1897, **71**, 617). A similar behaviour is shown by halogen-substituted acylthiocarbimides:

(Dixon, *loc. cit.*). The same change results when an already formed non-halogenated thiocarbamide has halogen introduced into its molecule:

(Dixon, T., 1896, **69**, 25).

Only two exceptions to this rule appear to exist, namely, (1) where halogen is attached to an aromatic radicle, thus the compound $\text{C}_6\text{H}_4\text{Cl} \cdot \text{NH} \cdot \text{CS} \cdot \text{NH}_2$ is quite stable (Losanitsch, *Ber.*, 1872, **5**, 156), and (2) where halogen is part of an unsaturated radicle; thus the compound $\text{CH}_2 : \text{CCl} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CS} \cdot \text{NH}_2$ does not yield a cyclic compound (Henry, *Ber.*, 1872, **5**, 188; Dixon, T., 1901, **79**, 553).

It is clear, from these examples, that there is, in thiocarbamides, a very strong tendency towards the conversion of bivalent into quadrivalent sulphur when there is present a halogenated radicle not already linked to sulphur.

* These formulæ are written as the authors themselves gave them. The present author prefers to represent them as sulphonium compounds.

If thiocarbamide methyl monochloroacetate had an ammonium structure, that is, $\text{CH}_2\text{Cl}\cdot\text{CO}_2\cdot\text{NH}_3\cdot\text{C}(\text{:NH})\cdot\text{SMe}$, there would follow the formation of a cyclic compound,

Such a union occurs as the initial stage of the formation of thetines.

This compound would have its chlorine highly ionised, it would respond to Andreasch's test for thiolacetic acid (*Ber.*, 1879, **12**, 1385), and, further, the chloroacetate group, being now divided into two parts, could not be displaced wholly by another acid group.

Thiocarbamide methyl chloroacetate, prepared as described, agrees in no respect with these properties. Its aqueous solution does not yield silver chloride on the addition of silver nitrate, no purple colour is observed on applying Andreasch's test, hence the compound does not contain the grouping $\cdot\text{CO}\cdot\text{CH}_2\cdot\text{S}\cdot$, and, lastly, the picrate is identical with that obtained from thiocarbamide methyl nitrate, consequently the whole of the chloroacetate group has been displaced by the picrate residue.

It is thus highly probable that the chloroacetate group is not attached to nitrogen, and that, since ring closing does not occur, the chlorine forms part of a group already linked to sulphur which is already exerting its full valency, and therefore does not admit of further combination.

The structure of thiocarbamide methyl chloroacetate would appear to be represented by the formula

in agreement with that proposed for other salts of *S*-alkylthiocarbamides, and would correspond with its properties as described above.

That the chlorine of the chloroacetate residue would combine with sulphur if opportunity occurred is shown by the fact that, when this substance is heated in alcoholic solution with thiocarbamide, *isothiohydantoic* acid results. This is due to the initial formation of an additive compound of the original substances,

which readily loses hydrogen chloride. The acid, in turn, decomposes the methyl- ψ -thiourea ester of *isothiohydantoic* acid, leaving free *isothiohydantoic* acid,

When thiocarbamide benzyl chloroacetate instead of the methyl compound is combined with thiocarbamide, loss of hydrogen chloride alone follows, and the benzyl- ψ -thiourea ester of isothiohydantoic acid is obtained, showing that the reaction proceeds in the manner suggested.

Attempts to remove hydrogen chloride alone from thiocarbamide methyl chloroacetate by the use of dilute alkali or of pyridine were quite unsuccessful. No indication of the formation of a glycine derivative was observed; the whole of the chloroacetate group was removed and the resulting ψ -thiourea decomposed.

Thiocarbamide and methyl chloroacetate unite additively on long contact in acetone solution. The product is isomeric with the thiocarbamide methyl chloroacetate previously described. There are many points of difference between the two substances; thus the additive compound is readily soluble in water, and the solution is acid, due to the formation of hydrochloric acid. When boiled in alcoholic solution, it loses methyl alcohol, and the hydrochloride of isothiohydantoic acid separates on cooling. With less than one equivalent of sodium hydroxide, both methyl alcohol and hydrochloric acid are lost and isothiohydantoin is obtained. The substance also readily responds to tests for thiolacetic acid.

These reactions are in sharp contrast with those previously described for thiocarbamide methyl chloroacetate, and point to the additive compound being the *hydrochloride of methyl isothiohydantoate*, $(\text{NH}_2)_2\text{C}:\text{S}:\text{Cl}\cdot\text{CH}_2\cdot\text{CO}_2\text{Me}$. Ethyl chloroacetate combines similarly with thiocarbamide.

Dichloroacetates and trichloroacetates of *S*-alkylthiocarbamides were also prepared. In general properties they closely resemble the monochloroacetates, with the exception that they are inert towards thiocarbamide.

EXPERIMENTAL.

Thiocarbamide methyl monochloroacetate is precipitated when to a concentrated aqueous solution of thiocarbamide methyl nitrate is added an excess of a concentrated aqueous solution of sodium monochloroacetate. On crystallisation from alcohol, it forms prisms, which decompose at about 157° . Its aqueous solution is neutral and furnishes a picrate, melting at 220° , identical with the picrates from other salts of *S*-methylthiocarbamides; an alkaline solution of lead acetate gives lead mercaptide, and an ammoniacal solution of silver nitrate gives silver mercaptide and silver cyanamide, no silver chloride being formed.

Found: N=15.01, and 100 parts gave 168 parts of silver as AgSMe and Ag₂CN₂.
 C₄H₉O₂N₂ClS requires N=15.17 per cent., and 100 parts require 175 parts of silver.

When the solid was heated with one equivalent of pyridine, methyl mercaptan escaped. Addition of one equivalent of *N*-sodium hydroxide to a dilute solution of the substance did not cause a precipitation of methyl- ψ -thiourea. When the alkaline solution was acidified with chloroacetic acid and then evaporated, the original substance was recovered. Attempts were made at various stages to obtain a copper derivative of glycine, but quite unsuccessfully.

Thiocarbamide benzyl monochloroacetate was prepared similarly from thiocarbamide benzyl chloride and sodium monochloroacetate. Water and alcohol each dissolve the substance readily, but it is sparingly soluble in a solution of sodium monochloroacetate. The usual reactions of a ψ -thiourea are given, and it yields a *picrate* which melts at 183°.

Decomposition occurs on heating to 156°.

Found: Cl=13.4; N=10.65.

C₉H₁₁O₂N₂ClS requires Cl=13.63; N=10.74 per cent.

Attempts to prepare sulphonium and ammonium forms of this compound were unsuccessful. Benzyl- ψ -thiourea dissolved in chloroacetic acid gave an uncrystallisable syrup. The ammonium form of thiocarbamide benzyl sulphate, on treatment with an acid solution of sodium monochloroacetate, yielded the same product as the sulphonium form gave when treated with a slightly alkaline solution of the same salt. Both were identical with the compound already described, and decomposed at the same temperature, namely, 157°.

Thiocarbamide methyl monochloroacetate and Thiocarbamide.
 —Alcoholic solutions of these substances in nearly equivalent proportions (the thiocarbamide in slight excess) were heated together on a steam-bath. After a short time, the liquid, originally clear, became turbid, and a white, amorphous solid separated which contained chlorine, and when heated with an alkaline solution of lead acetate gave, first, lead mercaptide, and, on prolonged heating, lead sulphide. It responded also to Andreasch's test for thiolacetic acid, thus showing the formation of a derivative of *isothiohydantoic* acid. The mother liquors gave a strong reaction for ψ -thiourea. Analysis of the first product gave no decisive figures and indicated a mixture. After the solid had been further heated with a further quantity of alcohol, the ψ -thiourea reactions became very faint.

The analysis and general properties of the solid now showed it to be rather impure *isothiohydantoic acid*. The substance chars at about 205° (Found: $N=20.1$; $S=23.1$. $C_3H_6O_2N_2S$ requires $N=20.9$; $S=23.88$ per cent.).

Thiocarbamide benzyl monochloroacetate and Thiocarbamide.—Combination was effected as in the preceding case. The product, free from chlorine, gave a strong reaction for ψ -thiourea, and responded to the tests for thiolacetic acid. It decomposed on heating to 190° . Analysis showed that the components had united with loss of hydrogen chloride, and that little, if any, further decomposition had occurred. The substance may be regarded as the *benzyl- ψ -thiourea ester of isothiohydantoic acid*.

Found: $N=18.77$; $S=20.9$.

$C_{11}H_{16}O_2N_4S_2$ requires $N=18.6$; $S=21.3$ per cent.

An attempt to prepare the real additive compound by allowing the materials to remain together in cold acetone solution for several days resulted in the isolation of a solid containing $Cl=5.7$, instead of 10.6 per cent. required by the additive compound.

Thiocarbamide and Methyl monochloroacetate.—Direct addition of these substances was effected by allowing equivalent weights, mixed in acetone solution, to remain for two days. Colourless crystals, which decomposed at 200° , separated from the solution. The crystals readily dissolved in water and gave a strongly acid solution. The *picrate* decomposes at 175° . When the compound was heated with an alkaline solution of lead acetate, no trace of mercaptide was observed, but lead sulphide formed readily. Silver nitrate gave a white precipitate which was soluble in ammonium hydroxide. The ammoniacal solution did not yield mercaptide or sulphide when heated, thus indicating the formation of a silver compound of *isothiohydantoic acid*. A purple coloration in Andreasch's test proved the presence of the group $\cdot CO \cdot CH_2 \cdot S \cdot$. Hence the compound is the *hydrochloride of methyl isothiohydantoate*.

Found: $Cl=19.4$.

$C_4H_9O_2N_2ClS$ requires $Cl=19.2$ per cent.

On boiling with alcohol, it was hydrolysed to the hydrochloride of *isothiohydantoic acid* (Found: $Cl=23.28$. Calc.: $Cl=22.86$ per cent.). When rather less than one equivalent of sodium hydroxide was added to an aqueous solution of the original compound, prisms, recognised as *isothiohydantoin* (Found: $S=27.39$. Calc.: $S=27.58$ per cent.), separated from solution. The substance decomposed at 220° .

Thiocarbamide and Ethyl monochloroacetate.—These substances

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were combined by a similar method to the above. The products separated in glassy, six-sided pyramids which dissolved in water, giving an acid solution. It melts at 107° and decomposes at about 120° .

Found: Cl=17.54.

$C_5H_{11}O_2N_2ClS$ requires Cl=17.63 per cent.

Thiocarbamide methyl dichloroacetate was precipitated on mixing concentrated aqueous solutions of thiocarbamide methyl nitrate and sodium dichloroacetate. White crystals were obtained on crystallising the substance from alcohol. The substance showed all the usual reactions of methyl- ψ -thiourea and none of *isothiohydantoin*. It decomposes at 165° .

Found: Cl=32.01.

$C_4H_8O_2N_2Cl_2S$ requires Cl=32.4 per cent.

Heating with even deficit of alkali caused the evolution of mercaptan. No sign of further combination was observed after the substance had been heated for several hours in alcoholic solution with thiocarbamide.

Thiocarbamide benzyl dichloroacetate was prepared similarly. No striking peculiarity was observed in its behaviour. It decomposes at 153° .

Found: N=10.2.

$C_{10}H_{12}O_2N_2Cl_2S$ requires N=9.6 per cent.

Thiocarbamide methyl trichloroacetate crystallised in shining leaflets on mixing aqueous solutions of thiocarbamide methyl sulphate and sodium trichloroacetate. Its behaviour was that of an ordinary salt of methyl- ψ -thiourea. Heating with pyridine caused complete decomposition, and on being heated alone it decomposed at 187° . One hundred parts of the substance gave 124.2 parts of silver, whereas 100 parts of $C_4H_7O_2N_2Cl_3S$ require 127.4 parts of silver.

Thiocarbamide benzyl trichloroacetate was prepared similarly. It resembled the preceding compound in appearance and behaviour and decomposed at 150° . An identical product was obtained by heating together benzyl- ψ -thiourea and trichloroacetic acid.

Found: N=8.52; Cl=31.4.

$C_{10}H_{11}O_2N_2Cl_3S$ requires N=8.45; Cl=32.3 per cent.

Alcoholic solutions of this compound were heated for several hours with one, two, and three equivalents, respectively, of thiocarbamide, but no indication of the formation of *isothiohydantoin*

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derivatives was observed. The residue from the evaporation of the alcoholic solution also failed to indicate the presence of *isothiohydantoin*, but reacted freely for ψ -thiourea.

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