globules of carbon disulfide containing dissolved sulfur; the aqueous solution contained ammonium chloride. The residue on the filter paper was crystallized from water, and gave silver chloride with silver nitrate, but no ammonia when boiled with alkali. The substance melted at 198° (m. p. of hydrazine dihydrochloride) and reduced Fehling's solution.

The author takes this opportunity of expressing his sincere thanks to Sir P. C. Rây and to Dr. P. C. Mitter for the kind interest they have shown during the progress of the work.

CALCUTTA, INDIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY COLLEGE OF SCIENCE OF CALCUTTA]

CONSTITUTION OF THE SO-CALLED DITHIO-URAZOLE OF MARTIN FREUND. II. NEW METHODS OF SYNTHESIS, ISOMERISM AND POLY-DERIVATIVES

BY PRAPHULLA CHANDRA GUHA

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In Part I,[1] the author put forward the amino-thiodiazole-thiol formula for the so-called dithio-urazole based upon the action of mild oxidizing agents such as iodine, ferric chloride, hydrogen peroxide; action of alkali, alkyl iodides, mercuric nitrite and on the different behaviors of the mono acyl and mono alkyl derivatives and so on. In the present paper a number of new methods for the synthesis of the parent amino-thiodiazole-thiol (the so-called dithio-urazole) and its mono- and di-derivatives will be described. These, it is expected, will throw additional light upon the problem of the constitution of this substance.

Up to the present time, only one method for the preparation of the so-called dithio-urazoles has been known, and that is by the elimination of ammonia from hydrazo-dithio-dicarbonamides by the action of conc. hydrochloric acid, when, simultaneously, imino-thio-urazole hydrochloride is formed with the elimination of a molecule of hydrogen sulfide.[2] It may be mentioned here that no method is known by which 3,5-disubstituted compounds can be prepared, either directly by synthesis or by subsequent introduction of groups into the parent thiodiazole molecule.

When thiosemicarbazide is treated with alcoholic potassium hydroxide and carbon disulfide, there is formed at first potassium hydrazothiocarbonamide dithiocarboxylate ($NH_2CSNHNHCSSK$). On raising the temperature of the reaction this potassium salt yields the potassium salt of a new closed-ring compound which has been found to be amino-thiodiazole-thiol (the so-called dithio-urazole).

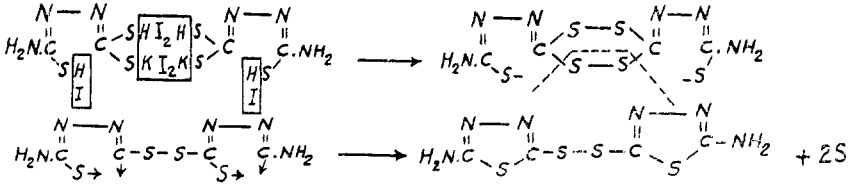
[1] Guha, THIS JOURNAL, **44**, 1502 (1922).

[2] Freund and Imgart, *Ber.*, **28**, 946 (1895).

$$NH_2CSNHNH_2 + CS_2 + KOH \longrightarrow NH_2CSNHNHCSSK + H_2O.$$

$$NH_2CSNHNHCSSK \xrightarrow[130\text{-}140^\circ]{\text{heat}} \underset{\text{5-Imino-2-thio-tetrahydro-thiodiazole}}{NH{=}C(NH)S{-}CS} \quad \text{or} \quad \underset{\text{5-Amino-2-thiol-thiodiazole}}{NHC(NH_2){=}N{-}CSH} \quad \text{I}$$

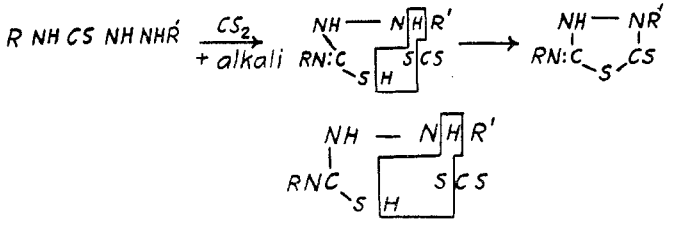
A modification of the above method consists in adding iodine to the original hot solution, when at once the disulfide of amino-thiodiazole-thiol is formed, together with free sulfur.



II

The SH- and SK- groups of each molecule, reacting with iodine, produce momentarily Compound II, which, being unstable, frees 2 atoms of sulfur, and the free bonds of the remaining pair of oxidized mercaptan sulfur atoms go to satisfy this pair of newly released bonds, giving the disulfide of the thiodiazole compound and free sulfur. From the disulfide the thiodiazole compound itself is obtained in a quantitative yield.

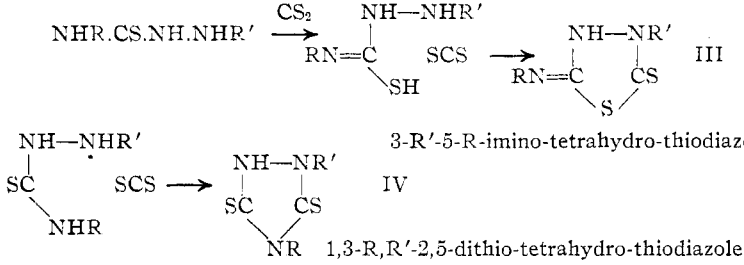
This method of synthesis has been found to apply in the cases of all substituted and unsubstituted thiosemicarbazides, when used in a slightly modified form. Except in the case of the thiosemicarbazide itself, the potassium salt of the dithio-carboxylic acid is rarely formed; and it is perhaps due to the pronounced basic character of thiosemicarbazide that it acts so singularly in this respect. On continued heating, all of the thiosemicarbazides, without exception, yield the corresponding thiodiazole derivatives. The reaction probably takes place, not as in the case of thiosemicarbazide as shown above in (I), but in a slightly modified form, as follows.



A list of the mono and disubstituted thiodiazole derivatives synthesized by the above method, is given below.

(1) 1-Phenyl-thiosemicarbazide ⟶ 2-thio-5-imino-4-phenyl-2,3,4,5-tetrahydro-1,3,4-thiodiazole.
(2) 4-Phenyl-thiosemicarbazide ⟶ 2-thio-5-phenylimino-2,3,4,5-tetrahydro-1,3,4-thiodiazole.[3]
(3) 1,4-Diphenyl-thiosemicarbazide ⟶ 3,5-diphenyl-2-thio-5-imino-tetrahydro-thiodiazole.
(4) 1,4-Ditolyl-thiosemicarbazide ⟶ 3,5-ditolyl-etc.
(5) 1,4-Dinaphthyl-thiosemicarbazide ⟶ 3,5-dinaphthyl-etc.
(6) 1,4-Phenyltolyl-thiosemicarbazide ⟶ 3-phenyl-5-tolylimino-2-thio-2,3,4,5-tetrahydro-1,3,4-thiodiazole.
(7) 1,4-Tolylphenyl-thiosemicarbazide ⟶ 3-tolyl-5-phenylimino-etc.
(8) 1,4-Phenylnaphthyl-thiosemicarbazide ⟶ 3-phenyl-5-naphthylimino-etc.
(9) 1,4-Phenylnaphthyl-thiosemicarbazide ⟶ 3-phenyl-5-naphthylimino-etc.
(10) 1,4-Naphthylphenyl-thiosemicarbazide ⟶ 3-naphthyl-5-phenylimino-etc.
(11) 1,4-Tolylnaphthyl-thiosemicarbazide ⟶ 3-tolyl-5-naphthylimino-etc.
(12) 1,4-Naphthyltolyl-thiosemicarbazide ⟶ 3-naphthyl-5-tolylimino-etc.
(13) 1,4-Phenylallyl-thiosemicarbazide ⟶ 3-phenyl-5-allylimino-etc.
(14) 1,4-Tolylallyl-thiosemicarbazide ⟶ 3-tolyl-5-allylimino-etc.
(15) 1,4-Phenylmethyl-thiosemicarbazide ⟶ 4-phenyl-5-methylimino-etc.
(16) 1,4-Tolylmethyl-thiosemicarbazide ⟶ 4-tolyl-5-methylimino-etc.
(17) 1,4-Naphthylmethyl-thiosemicarbazide ⟶ 3-naphthyl-5-methylimino-etc.
(18) 1,4-Naphthylmethyl-thiosemicarbazide ⟶ 4-naphthyl-5-methylimino-etc.

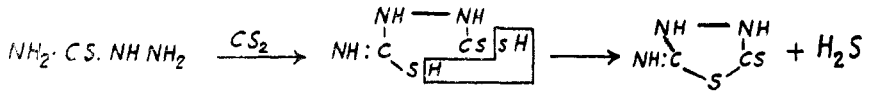
All of the above mentioned di-substituted thiodiazole derivatives, except Compounds 15, 16 and 18, are insoluble in alkali and they do not take up iodine to form disulfides, showing conclusively that there is no mercaptan group (either real or potential) present in the molecule.



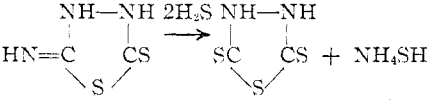
According to the older belief in dithio-urazole, the di-R-substituted compound as represented by Formula IV contains a mercaptan group (real or potential); if this were actually the case there is no reason why it should not behave as a mercaptan with alkali hydroxides or to form disulfides with oxidizing agents such as iodine.

Of special significance is the synthesis of amino-thiodiazole-thiol from thiosemicarbazide, by the direct action of carbon disulfide, when thiodiazole-disulfhydrate is also formed in a small quantity.

[3] This compound was prepared by Freund and Imgart (Ref. 2) by the action of hydrochloric acid upon hydrazo-diphenyl-dithio-dicarbonamide, and they called it phenyldithio-urazole.



The hydrogen sulfide thus formed acts at the high temperature of the reaction (at 150° in a sealed tube) upon the thiodiazole compound and thus forms a small quantity of thiodiazole-disulfhydrate.



The above synthesis of the thiodiazole derivative by the direct action of carbon disulfide is not, however, of general application. In the opinion of the present author[4] the 1-position of the thiosemicarbazide should always be unsubstituted, or substituted by positive groups such as methyl or ethyl; or, in other words, the basic character of the thiosemicarbazide should be kept unimpaired, so that carbon disulfide can combine with it directly. In fact, 1-phenyl-thiosemicarbazide was found not to react with carbon disulfide even at 190°, while 4-phenyl-thiosemicarbazide, in which the hydrazine residue is unsubstituted, gave as usual the phenyl-substituted thiodiazole compound.

The parent thiodiazole compound as obtained by Freund melts at 245°, although it has been found that after about 3 months it melts at 232°. When it is heated in a sealed tube at 150° with conc. hydrochloric acid, a compound is obtained which melts at 224°. All of these by analysis yield identical compositions and show the same chemical behavior; with iodine all of them give the same disulfide, with alkyl iodide the same monoalkyl derivative, and so on. Their color and crystalline structures are, however, different, the first being yellowish white prismatic needles, the second, transparent white cubes, and the third brownish yellow rectangular plates.

Some further systematic study of their physical properties still remains to be undertaken, to settle the question of their isomerism.

To the so-called phenyl-dithio-urazole, Freund and Imgart ascribed the melting point 219°; and they described its crystals as colorless leaflets. It has been found, however, that on de-acetylating the mono-acetyl compound, a tautomeric variety of the so-called phenyl-dithio-urazole is obtained which melts at 208° and consists of dull yellow, crystalline needles.

Another case of this sort of isomerism has been found in the mono-acetyl derivative of the so-called phenyl-dithio-urazole. When freshly prepared, this substance melts at 244° (not 252° as described by Freund and Imgart); but after several weeks it melts at 236°. The diacetyl

[4] Exhaustive work yet remains to be completed in this direction to settle the question, which could not be undertaken at present for want of necessary chemicals.

PREPARATION AND ANALYSES OF COMPOUNDS

Compound	Preparation	Properties	M. p.	Formula	Analyses Calc.				Found			
Derivative of 2,3,4,5-tetrahydro-1,3,4-thiodiazole			°C.		C	H	N	S	C	H	N	S
2-Thio-5-imino-4-phenyl	1 g. of 1-phenyl-t.s.;[3] 0.6 g. KOH, 1 cc. CS_2, 10 cc. MeOH (abs.) heated in sealed tube for 4 hrs. Diluted with water and HCl added	Dull-yellow needles after redissolving in alkali and adding HCl to slight turbidity	183	$C_8H_7N_3S_2$	45.93	3.35	...	30.63	45.29	3.84	...	30.65
2-Thio-5-phenylimino	1 g. of 4-phenyl-t.s.;[6] 0.6 g. of KOH 1 cc. of CS_2, 15 cc. of EtOH		208	$C_8H_7N_3S_2$	45.93	3.35	20.09	...	45.54	3.71	20.41	...
3-Phenyl-5-phenylimino	0.5 g. of 1,4-diphenyl-t.s.; 0.3 g. of KOH, 0.2 cc. of CS_2, 15 cc. of EtOH heated for 3 hrs.; mixed with water; recryst. from EtOH	Insol. in alkali	202	$C_{14}H_{11}N_3S_2$	59.09	..	...	22.46	59.62	..	...	22.38
3-Tolyl-5-tolylimino-2-thio	0.8 g. of 1,4-ditolyl-t.s.; 0.4 g. of KOH; 0.4 cc. of CS_2 in EtOH	Insol. in alkali	205	$C_{16}H_{15}N_3S_2$	...	..	13.41	20.44	...	..	13.15	20.56
3-Naphthyl-5-naphthylimino-2-thio	0.6 g. of 1,4-dinaphthyl-t.s.; 0.25 g. of KOH; 0.2 cc. of CS_2; 15 cc. of EtOH	Insol. in alkali	218	$C_{22}H_{15}N_3S_2$	...	..	10.91	16.62	...	..	10.6	16.71
3-Phenyl-5-tolylimino-2-thio	1 g. of 1,4-phenyl-tolyl-t.s.; 0.5 g. KOH; 0.5 cc. of CS_2; 17 cc. of EtOH	Insol. in alkali	188–189	$C_{15}H_{13}N_3S_2$	...	..	...	21.40	...	..	...	20.64
3-Tolyl-5-phenylimino		Insol. in alkali	222	$C_{15}H_{13}N_3S_2$	...	..	14.00	21.40	...	..	14.35	21.63
3-Phenyl-5-naphthylimino-2-thio	0.7 g. of 1,4-phenyl-naphthyl-t.s.; 0.3 g. of KOH; 0.2 cc. of CS_2; 18 cc. of EtOH	Insol. in alkali	219	$C_{18}H_{13}N_3S_2$	...	..	...	19.10	...	..	...	19.19

3-Naphthyl-5-phenylimino-2-thio	1,4-naphthylphenyl-t.s. used	Sparingly sol. in EtOH; cryst. from acetone	261	$C_{18}H_{13}N_3S_2$	...	..	12.54	19.10	...	..	12.29	19.39
3-Tolyl-5-naphthylimino-2-thio	0.8 g. of 1,4-tolyl-naphthyl-t.s.; 0.4 g. of KOH; 0.3 cc. of CS_2; 20 cc. of EtOH	Insol. in alkali	217	$C_{19}H_{15}N_3S_2$	...	..	12.03	18.34	...	..	11.71	18.86
3-Naphthyl-5-tolylimino-2-thio	Cryst. from much acetone		268	$C_{19}H_{15}N_3S_2$	...	..	12.03	18.11	...	..	12.31	19.11
3-Phenyl-5-allylimino-2-thio	0.9 g. of 1,4-phenyl-allyl-t.s.; 0.5 g. of KOH; 0.3 cc. of CS_2; 17 cc. of EtOH	Insol. in alkali	145	$C_{11}H_{11}N_3S_2$	53.03	4.42	...	25.70	53.53	4.80	...	25.49
3-Tolyl-5-allylimino-2-thio		Dull-yellow needles from EtOH	125–126	$C_{12}H_{13}N_3S_2$	54.70	..	...	24.33	54.91	..	...	24.71
4-Phenyl-5-methylimino-2-thio	0.5 g. of phenyl-methyl-t.s.; 0.4 g. of KOH; 0.25 cc. of CS_2; 24 cc. of EtOH heated at 100° for 4 hrs. added to water; boiled; HCl added; precipitate dissolved in EtOH; water added; filtered; HCl added	Dull-yellow crystals, soluble in alkali	142–143	$C_9H_9N_3S_2$	48.43	..	...	28.70	48.10	..	...	28.52
4-Tolyl-5-methylimino-2-thio		Dull-yellow needle shaped crystals	174–175	$C_{10}H_{11}N_3S_2$	...	..	...	27.00	...	..	...	27.42
3-And 4-naphthyl-5-methyl-imino-2-thio	1.5 g. of 1,4-naphthyl-methyl-t.s.; 0.4 cc. of CS_2; 0.8 g. of KOH; 20 cc. of EtOH; heated in sealed tube for 4 hrs. Cryst. from dil. EtOH	Insol. in alkali	183	$C_{13}H_{11}N_3S_2$	...	..	...	23.44	...	..	...	23.14
	Alkaline filtrate + HCl	White precipitate shrinks at 165°	175	$C_{13}H_{11}N_3S_2$	...	..	...	23.44	...	..	...	23.71

[a] t. s. = thiosemicarbazide.

[6] Cf. *Ber.*, **33**, 1061 (1900).

derivative gives the same new variety of mono-acetyl derivative (m. p. 236°) when it is heated slightly above its melting point. Loss of one of the acetyl groups, and conversion into a different isomeric mono-acetyl derivative take place simultaneously.

Experimental Part

Potassium Thiosemicarbazide-dithiocarboxylate, $NH_2CSNHNHCSSK$, was prepared by heating under a reflux condenser at 70–75° for about 10 minutes a mixture of an equilimolecular proportion of thiosemicarbazide, alcoholic potassium hydroxide and carbon disulfide, in an alcoholic solution. The compound was crystallized from dil. alcohol.

Analyses. Subs., 0.2015: K_2SO_4, 0.0842. Subs., 0.1034: $BaSO_4$, 0.3499. Calc. for $C_2H_4N_3S_3K$: K, 19.02; S, 46.83. Found: K, 18.75; S, 46.46.

On heating this potassium salt in a sealed tube at 130–140° for 3 to 4 hours in alcoholic solution, the potassium salt of the amino-thiodiazole-thiol was formed. This was dissolved in water and the free thiol compound was obtained by the addition of hydrochloric acid. The latter was crystallized twice from hot water, m. p. 232°. It gave the disulfide, $(C_2H_2N_3S)—S—S—(C_2H_2N_3S)$, with iodine and the mono-ethyl ether of m. p. 136° with ethyl iodide.

Analyses. Subs., 0.1032: CO_2, 0.0672; H_2O, 0.0240. Subs., 0.1352: $BaSO_4$, 0.4760. Calc. for $C_2H_3N_3S_2$: C, 18.04; H, 2.26; S, 48.10. Found: C, 17.75; H, 2.58; S, 48.35.

Potassium Thiosemicarbazide-dithiocarboxylate and Iodine. Formation of the Disulfide of Amino-thiodiazole-thiol.—To an aqueous solution of the potassium salt was added an excess of iodine dissolved in potassium iodide solution. A yellow precipitate was thus obtained which was carefully washed, and dried in a steam oven, it softened at 209° and melted with decomposition at 220–225°. After repeated washing with carbon disulfide the yellow substance showed a sharp melting point of 245° and the solution on evaporation gave sulfur. On boiling the disulfide (m. p. 245°), with sodium hydroxide, a yellow solution was formed from which the free 5-amino-2-thiol-1,3,4-thiodiazole melting at 244–245° was obtained by the addition of hydrochloric acid. This was identical with the so-called dithio-urazole.

Analysis. Subs., 0.1112: $BaSO_4$, 0.3861. Calc. for $C_2H_3N_3S_2$: S, 48.10. Found: 47.68.

Potassium thiosemicarbazide-dithiocarboxylate, after about a month, changed to a yellow amorphous powder. This was found to be the disulfide of amino-thiodiazole-thiol, and from it the thiol compound was obtained by boiling with alkali and adding hydrochloric acid to the alkaline solution. When crystallized from water it melted at 244° and was identified as the amino-thiodiazole-thiol (the so-called dithio-urazole). The yield is almost quantitative.

Direct Action of Carbon Disulfide upon Thiosemicarbazide. Formation of 2-Thio-5-imino-2,3,4,5-tetrahydro-1,3,4-thiodiazole.—Three g. of thiosemicarbazide, 4 cc. of carbon disulfide and 10 cc. of water were heated in a sealed tube at 150° for 4 hours. Later, long colorless needle-shaped crystals were found to have separated, and on opening the tube there was a rapid escape of hydrogen sulfide. The contents of the tube were carefully collected in a beaker, filtered and washed twice with small quantities of cold water. The residue was crystallized from hot water; yield, 3.2 g. It gave the same mono-ethyl derivative with ethyl iodide, the same disulfide with iodine and the same analytical results as the so-called dithio-urazole. The yield, according to the method of Freund and Imgart, starting from 50 g. of hydrazine sulfate, through the inter-

mediate compound hydrazo-dithio-dicarbonamide should be 7 g.; but in these experiments the yield was never higher than 5 g. According to this method, starting from 50 g. of hydrazine sulfate, through the intermediate compound, thiosemicarbazide, the yield is 28 g.

The aqueous filtrate after the separation of amino-thiodiazole-thiol was boiled for a few minutes to drive off the excess of carbon disulfide. On adding hydrochloric acid to the cold solution, a small quantity of a white crystalline compound (thiodiazole-disulfhydrate) was obtained which when recrystallized from dil. alcohol melted at 167°.

Analyses. Calc. for $C_2H_2N_2S_3$: C, 16.00; N, 18.66; S, 64.00. Found: C, 15.73; N, 18.30; S, 64.13.

New Varieties of 2-Thio-5-imino-tetrahydro-thiodiazole or 2-Thiol-5-amino-thiodiazole.—Freund's dithio-urazole (m. p. 245°) on standing for about 2 months was found to melt at 232°. Both of the above varieties on being heated in sealed tubes at 150° with conc. hydrochloric acid for 3 hours gave brownish-yellow rectangular crystals, melting at 224°.

Analyses. Calc. for $C_2H_3N_3S_2$: C, 18.04; H, 2.26; S, 48.11. Found: (comp. m. p. 232°) C, 17.80; H, 2.51; S, 48.38; (comp. m. p. 224°) C, 18.39; H, 2.72; S, 47.88.

De-acetylation of Acetyl-phenylimino-thio-thiodiazole.—Acetyl-phenylimino-thio-thiodiazole was boiled with a 10% solution of potassium hydroxide for 15 minutes. The solution was filtered and hydrochloric acid was added to it. A precipitate was thus obtained which was purified by crystallization from dil. alcohol in dull-yellow needles, m. p. 207°.

Analyses. Subs., 0.1132: CO_2, 0.1893; H_2O, 0.0388. Subs., 0.1034: $BaSO_4$, 0.2269. Calc. for $C_8H_7N_3S_2$: C, 45.94; H, 3.35; S, 30.63. Found: C, 45.61; H, 3.81; S, 30.12.

A New Variety of Acetyl-phenylimino-thio-tetrahydro-thiodiazole.—The mono-acetyl compound, m. p. 244° (not 252° as described by Freund and Imgart[2]) on standing for several weeks melted at 236°. It was twice crystallized from alcohol and the melting point after each crystallization was unchanged.

The same variety of acetyl-phenylimino-thio-tetrahydro-thiodiazole was obtained by heating the diacetyl compound for only 5 minutes at 175°. The diacetyl compound melted at 156° (and not at 176° as described by Freund and Imgart) and again solidified at 162°. The temperature was then raised to 175° and kept there for 5 minutes. The compound was then crystallized from alcohol, when it melted at 236°.

Analyses. Subs., 0.1717: CO_2, 0.2965; H_2O, 0.0621. Subs., 0.1010: $BaSO_4$, 0.1848. Calc. for the mono-acetyl compound, $C_{10}H_9ON_3S_2$: C, 47.80; H, 3.59; S, 25.50. Found: C, 47.10; H, 4.03; S, 25.13.

The above mono-acetyl compound as prepared by either of the above mentioned methods gave identical analytical results and the same mixed melting point, 236°

The author takes this opportunity of expressing his sincere thanks to Sir P. C. Rây and Dr. P. C. Mitter for the kind interest they have taken during the progress of the work.

CALCUTTA, INDIA