CONSTITUTION OF THE SO-CALLED DITHIOURAZOLE OF MARTIN FREUND.

PART V. ISOMERISM OF HYDRAZODITHIODICARBONAMIDES, IMINOTHIOLTHIOBIAZOLES AND DI=R=IMINOTHIOBIAZOLES.

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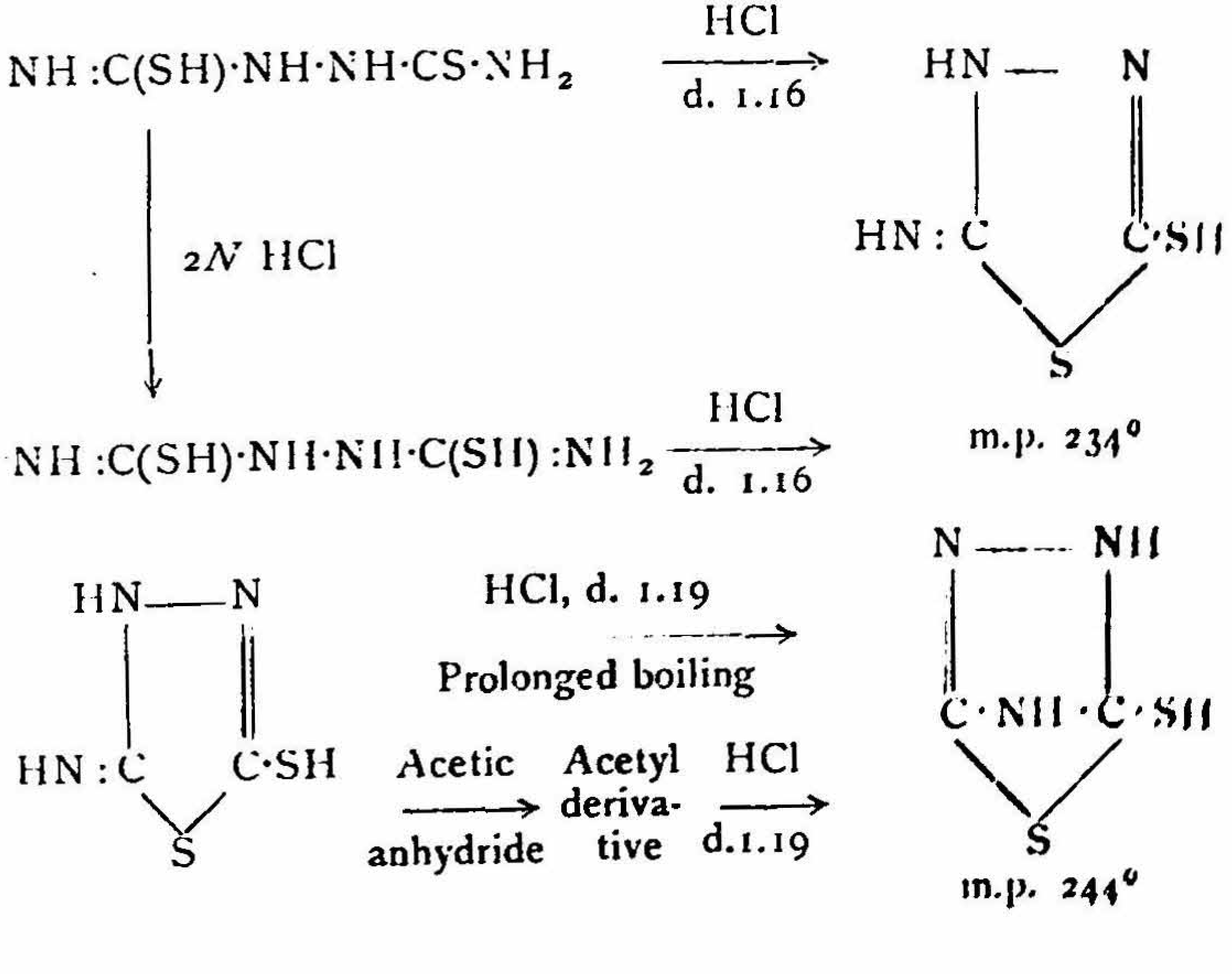
In part IV (*J. Amer. Chem. Soc.*, 1930, **52**, 4860) hydrazodithiodicarbonamide has been found to exist in two tautomeric forms,

$$NH_2\text{-CS-NH-NH-C(SH)}:NH$$

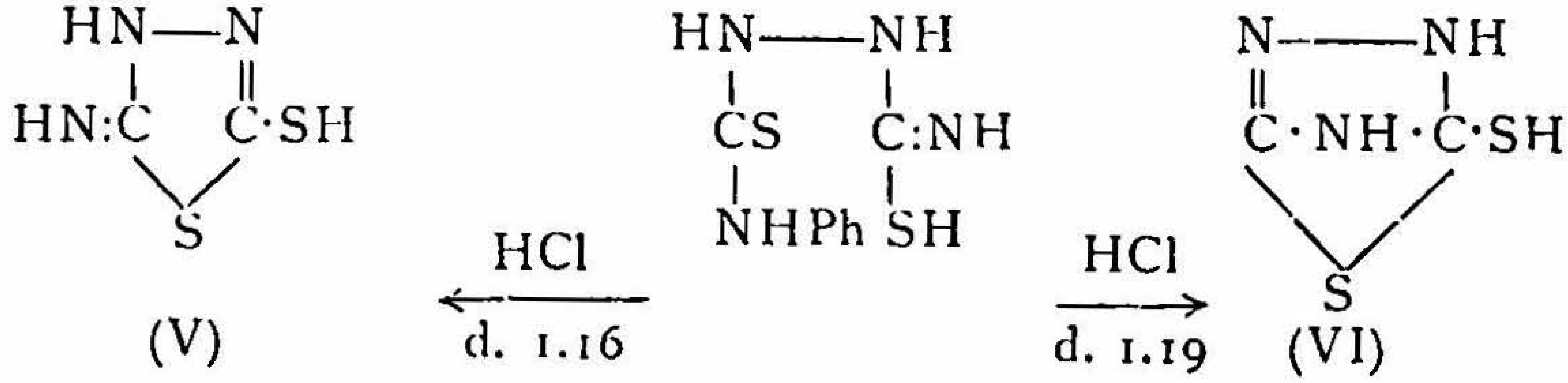
$$\text{and } NH:\text{C(SH)-NH-NH-C(SH)}:NH,$$

and their interconvertibility established. Iminothiolthiobiazole has been isolated as an intermediate compound during the formation of Freund's so-called dithiourazole (*Ber.*, 1895, **28**, 946) which has been shown to be *endo*iminothiolthiobiazole; the latter has been found to be formed either by the prolonged action of hydrochloric acid (d. 1.19) on either the hydrazide or the iminothiolthiobiazole, or by acetic anhydride treatment of the thiobiazole with subsequent deacetylation.



NH_2-CS-NH-NH-CS-NH_2

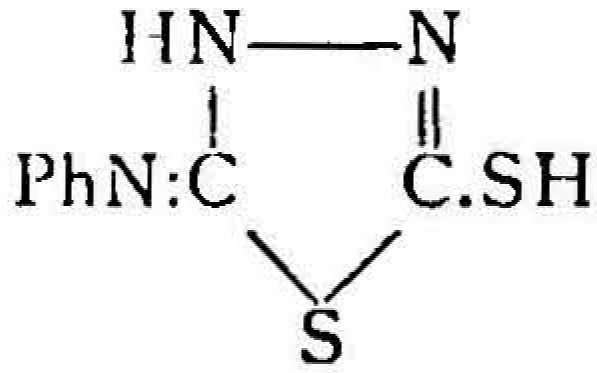
The reaction evidently proceeds in the following manner :



(V) (VI)

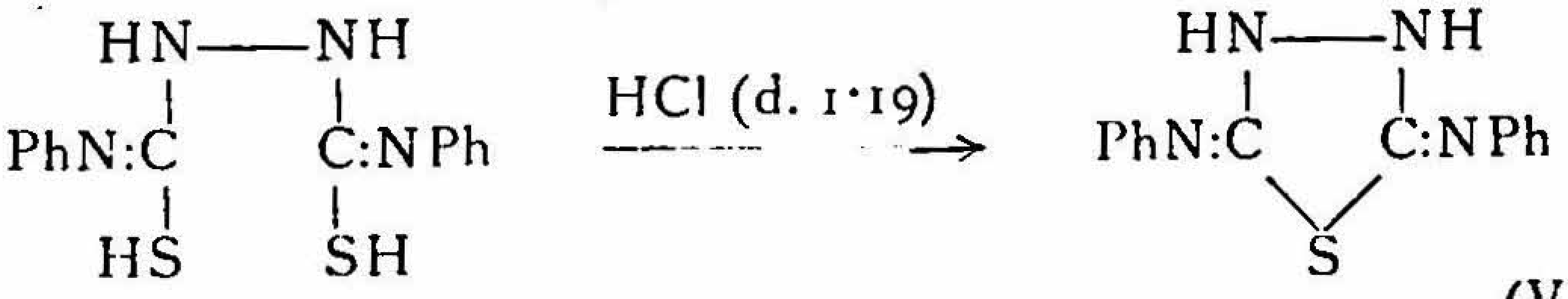
The literature does not appear to describe the action of acids upon the mono-substituted hydrazodithiodicarbonamides.

The symmetrical disubstituted hydrazides have given interesting results. Freund and Imgart (*Ber.*, 1895, **28**, 946) obtained by the action of hydrochloric acid upon diphenylhydrazodithiodicarbonamide an alkali-soluble compound, $C_8H_7N_2S_2$, melting at 210° which they called phenyldithiourazole, proved subsequently by Guha to be 3-thiol-5-phenylimino-4 :1 :2-thiobiazole (VII).



(VII)

It has now been found, however, that this thiobiazole is formed in good yield only when the hydrazide is treated with hydrochloric acid (d. 1.16) and not with concentrated acid (d. 1.19), in which case an alkali-insoluble compound, $C_{14}H_{12}N_4S$, m.p.249° is obtained as the main product. This contains two phenyl groups, and the sulphur atom is a member of the ring. It is therefore formed by the elimination of a molecule of hydrogen sulphide from the diphenylhydrazide thus :

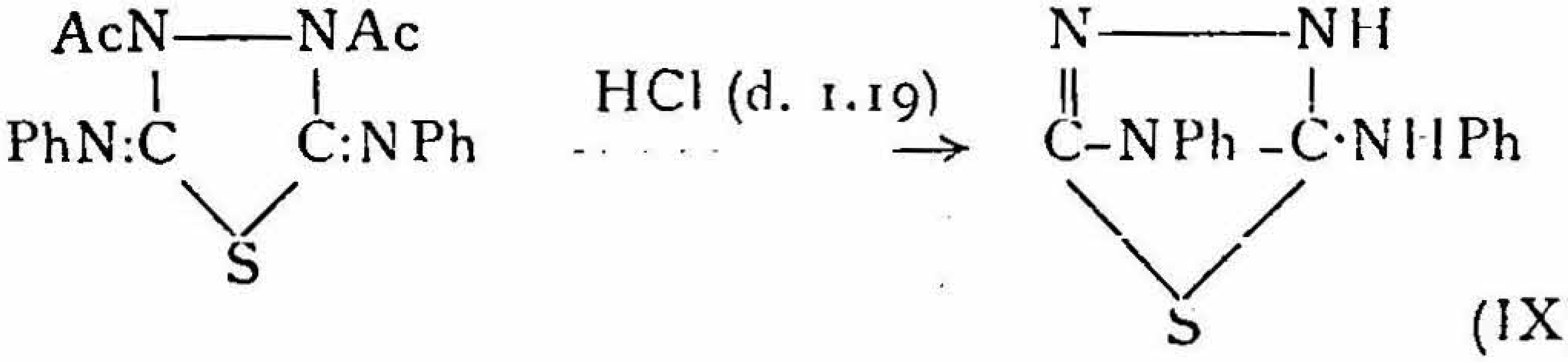


(VIII)

Identity of this (VIII) with that obtained by Guha from diphenylhydrazodithiodicarbonamide and acetic anhydride (*J. Amer. Chem. Soc.*, 1923, **45**, 1036) has been established.

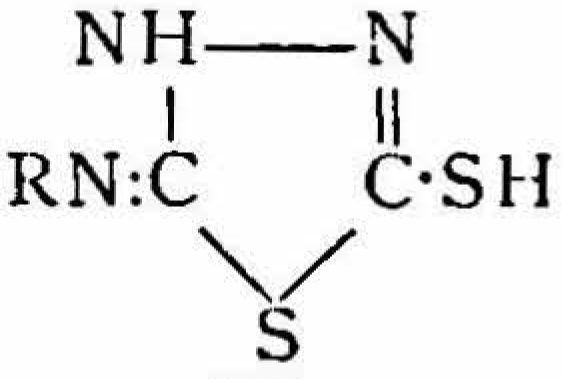
It is, however, interesting to note that the acetyl derivative (m.p. 224°) of 3 :5-diphenyliminthiobiazole, whether obtained from the diphenylhydrazide or the thiobiazole by the action of acetic anhydride, regenerates the same thiobiazole melting at 249° when treated with dilute hydrochloric acid (1 :1). If concentrated hydrochloric acid (d. 1.19) is used as hydrolysing agent, an alkali-insoluble thiobiazole (IX) melting at 208° and isomeric with (VIII) and with the thiobiazole, m.p.249°, is obtained. This product has escaped previous workers because they used less concentrated hydrochloric acid Since Guha employed hydrochloric acid of which the strength is not mentioned, it is probable that his sample was mixed with a trace of the 208° variety, thus accounting for the slightly lower melting point (viz., 247°) recorded for the 249° variety.

Compounds (VIII) and (IX) contain two phenyl groups and one sulphur atom ; they are insoluble in alkali, do not form disulphides and are not desulphurised by mercuric oxide. Guha (*J Amer. Chem. Soc.*, 1923, **45**, 1040) has already proved the constitution of the thiobiazole (VIII) and shown it to be 3 :5-diphenylimino-4 :1 :2-thiobiazole. By analogy with the compounds discussed in part IV, the new thiobiazole melting at 208° is in all probability, 2 :3-dihydro-3-anilino-3 :5-*endo*phenylimino-4 :1 :2-thiobiazole, formed from the acetyl derivative of compound (VIII) by molecular rearrangement during hydrolysis with acid (d. 1.19) :—

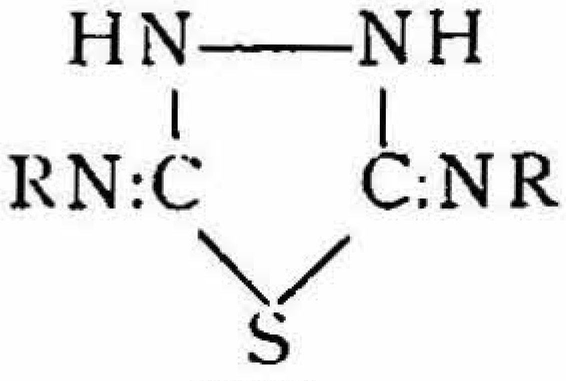


(IX)

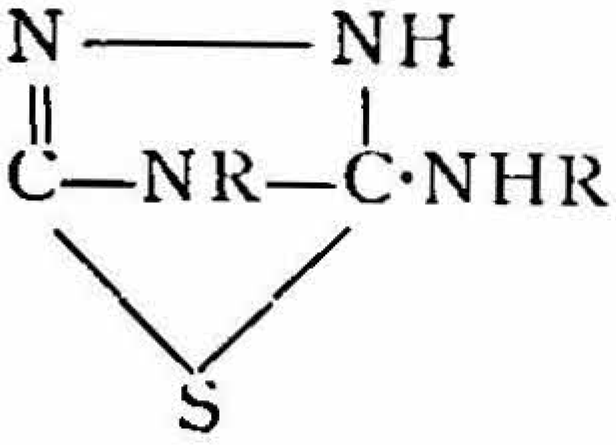
Di-*o*-tolylhydrazodithiodicarbonamide resembles its phenyl analogue and yields three thiobiazole compounds X, XI and XII :—



(X)



(XI)



(XII) (R = *o*-tolyl)

EXPERIMENTAL.

Isomer of dimethylhydrazodithiodicarbonamide (I).—Dimethylhydrazodithiodicarbonamide (5 g.), prepared according to the method of Freund (*Ber.*, 1895, **28**, 946), was dissolved in 2*N* hydrochloric acid (100 c.c.) over a small flame and the solution boiled for exactly ten minutes. On slow cooling minute needles separated and were recrystallised from hot water in colourless needles, m.p. 198°, the yield being almost quantitative. This substance was found to be more readily soluble in alkali than the parent hydrazide (m.p. 224°) and the analytical values were the same (Found : N, 31.6 ; S, 36.0 ; $C_4H_{10}N_4S_2$ requires N, 31.4 ; S, 35.9 per cent.). The absorption spectra of both have been studied in aqueous solutions.

Isomer of monophenylhydrazodithiodicarbonamide (II).—Experimental procedure was that adopted in the case of the unsubstituted hydrazide (*J. Amer. Chem. Soc.*, 1930, **52**, 4864). The crystalline solid obtained on cooling the solution from 3 g. of the hydrazomonophenyldithiodicarbonamide (m.p. 180°) in 2*N* acid (80 c.c.) was filtered, washed with water and recrystallised from dilute alcohol, m.p. 162° ; yield, 1.6 g. (Found : N, 24.9 ; S, 28.5. $C_8H_{10}N_4S_2$ requires N, 24.7 ; S, 28.31 per cent.).

Action of strong hydrochloric acid on monophenylhydrazodithiodicarbonamide : Formation of compounds V *and* VI.—No phenylthiobiazole could be obtained from the hydrazide by treating it with hydrochloric acid of various higher concentrations in the manner described in part IV ; aniline was liberated in all cases together with a small quantity of phenyl mustard oil. Only iminothiolthiobiazole (m.p. 234°) was obtained as the final product with hydrochloric acid (d. 1.16) and *endo*iminothiolthiobiazole (m.p. 244°) with acetic anhydride followed by deacetylation with hydrochloric acid (d. 1.19) or direct treatment with the latter (Found : N, 31.5 ; S, 47.9. $C_2H_3N_3S_2$ requires N, 31.6 ; S, 48.1 per cent.).

Isomer of diphenylhydrazodithiodicarbonamide (III).—Diphenylhydrazodithiodicarbonamide (m.p. 187°) on treatment with 2*N* hydrochloric acid gave an isomeric hydrazide, which on recrystallisation from hot dilute alcohol melted sharply at 173°. The mixed melting point of the two hydrazides was quite indefinite, gradually rising from 155° to about 180° (Found : N, 18.6 ; S, 21.23. $C_{14}H_{14}N_4S_2$ requires N, 18.54 ; S, 21.19 per cent.)

Diphenylhydrazodithiodicarbonamide and hydrochloric acid (d. 1.16) ; *Formation of 3-thiol-1 :5-dihydro-5-phenylimino-4 :1 :2-thiobiazole* (VII).—The hydrazide (3 g.) soon dissolved in the boiling acid

(20 c.c.), but after 3-4 minutes some reddish-brown, oily drops separated with odour of phenyl mustard oil; after about ten minutes the solution became turbid and a white solid separated rapidly on cooling. This was filtered, well pressed, washed with a little water and ether to remove mustard oil, and finally recrystallised from 95 per cent. alcohol, m.p. 219°. Yield, 1.8 g. It dissolved easily in cold dilute alkali (Found: N, 20.4; S, 30.2. $C_8H_7N_3S_2$ requires N, 20.1; S, 30.6 per cent.).

3:5-*Diphenylimino-2:3:5:1-tetrahydro-4:1:2-thiobiazole* (VIII). Diphenylhydrazodithiodicarbonamide (3 g.) dissolved when gently heated with concentrated acid (d. 1.19, 20 c.c.); after boiling over a small flame for nearly fifteen minutes a very small quantity of phenyl *iso*thiocyanate was liberated. The clear, filtered solution when cold gave a curdy white solid which after being washed with water and ether was crystallised from 95 per cent. alcohol, m.p. 249° (decomp.). Yield, 1.2 g. The substance was insoluble in cold dilute alkali but was decomposed when boiled with sodium hydroxide solution liberating phenyl *iso*cyanide. It did not give any disulphide with iodine, which was not even decolorised, and could not be desulphurised by mercuric oxide (Found: N, 21.2; S, 11.6. $C_{14}H_{12}N_4S$ requires N, 20.9; S, 11.9 per cent.). The strongly acid filtrate on being neutralised with dilute ammonia gave a small quantity of the alkali-soluble phenyliminothiolthiobiazole melting at 219°.

The *diacetyl* derivative, prepared by heating the diphenyliminothiodiazole, m.p. 249°, with acetic anhydride, crystallised from hot water acidified with acetic acid, m.p. 224°. It is identical with that obtained by treating the diphenylhydrazodithiodicarbonamide (m.p. 187°) with acetic anhydride (Found: N, 16.2; S, 8.9. $C_{18}H_{16}O_2N_4S$ requires N, 15.9; S, 9.09 per cent.).

Hydrolysis of the diacetyl derivative with 5N *hydrochloric acid: Formation of compound* (VIII).—The diacetyl derivative dissolved after about five minutes in the boiling acid the solution becoming turbid during the next ten minutes. After crystallisation from alcohol the product was found to be the diphenyliminothiobiazole, m.p. 249°.

The endo*phenyliminothiobiazole* (IX).—When the diacetyl derivative was hydrolysed by concentrated hydrochloric acid (d. 1.19) the solution did not become turbid as with 5*N* acid, although the boiling was prolonged for about twenty minutes. Drops of phenyl mustard oil separated, and the solution on cooling deposited white crystals which separated from absolute alcohol in cubes, m.p. 208°. It was insoluble in sodium hydroxide solution, but decomposed on boiling with the alkali and could not be desulphurised by mercuric oxide (Found: N, 21.15; S, 11.7. $C_{14}H_{12}N_4S$ requires N, 20.9; S, 11.9 per cent.).

*Isomer of di-*o*-tolylhydrazodithiodicarbonamide* (IV).—On treatment with 2*N* hydrochloric acid, the ordinary hydrazide (m.p. 171°) yielded the isomeric compound, obtained from dilute alcohol as minute, colourless crystals m.p. 178°. The melting point of a mixture with the original hydrazide ranged from about 162° to 176° (Found: N, 16.8; S, 19.2. $C_{16}H_{18}N_4S_2$ requires N, 16.99; S, 19.4 per cent.).

o-*Ditolylhydrazodithiodicarbonamide and strong hydrochloric acid* (d. 1.16): *Formation of 3-thiol-5:1-dihydro-5-tolylimino-4:1:2-thiobiazole* (X).—The hydrazide soon dissolved in the hot acid and further boiling of the solution gave a white solid with a few drops of tolyl mustard oil. At this stage the mixture was allowed to cool and the solid washed with water and then with a little ether; it crystallised from 95 per cent. alcohol in minute, colourless prisms m.p. 195°. This thiobiazole was readily soluble in cold dilute alkali and decolourised iodine with the formation of a disulphide (Found: N, 19.1; S, 28.4. $C_9H_9N_3S_2$ requires N, 18.8; S, 28.7 per cent.).

3:5-*Di-*o*-tolylimino-2:3:5:1-tetrahydro-4:1:2-thiobiazole* (XI).—On heating, di-*o*-tolyl-hydrazodithiodicarbonamide soon dissolved in boiling concentrated hydrochloric acid (d. 1.19) and a very small quantity of the *iso*thiocyanate was liberated. The clear solution gave on cooling a white solid, which after being washed with water and ether was crystallised from 95 per cent. alcohol, m.p. 217° (decomp.) (Found: N, 19.2; S, 11.1. $C_{16}H_{16}N_4S$ requires N, 18.9; S, 10.8 per cent.). The substance was insoluble in cold dilute alkali, but decomposed on boiling and did not give a disulphide. As in the case of the diphenylhydrazide the acid filtrate from the foregoing substance on neutralisation gave a white solid which crystallised from alcohol, m.p. 195° and was identical with the alkali-soluble thiobiazole (X).

The *diacetyl* derivative from the above thiobiazole (m.p. 217°) after crystallisation from dilute acetic acid melted with decomposition at 262° (Found; N, 14.4; S, 8.2. $C_{20}H_{20}O_2N_4S$ requires N, 14.7; S, 8.4 per cent.).

Hydrolysis of the diacetyl derivative with 5N *hydrochloric acid*: *Formation of* 3:5-*ditolyliminothiobiazole* (XI).—The boiling acid dissolved the diacetyl derivative in about five minutes, and after another ten minutes the clear solution became turbid; when cold, the solid product was filtered, washed, and recrystallised from alcohol, m.p. 217°, being identical with the di-*o*-tolyliminothiobiazole.

Hydrolysis with concentrated acid (d. 1.19): *Formation of* 2:3-*dihydro-3-tolylimino-3:5-*endo-o-*tolylimino-4:1:2-thiobiazole* (XII).—The clear solution obtained on boiling the diacetyl derivative with the acid deposited white cubic crystals on cooling. These after recrystallisation from absolute alcohol melted at 133°. It was insoluble in cold dilute alkali but decomposed on boiling and did not decolourise iodine (Found: N, 18.8; S, 11.0. $C_{16}H_{16}N_4S$ requires N, 18.9; S, 10.8 per cent.).

It is to be mentioned that both of the isomeric monophenyl, diphenyl- and di-*o*-tolylhydrazodithiodicarbonamides have been found to yield identical compounds on treatment with hydrochloric acid of density 1.16 and 1.19, and acetic anhydride respectively.

SUMMARY

The action of 2*N* hydrochloric acid on mono- and di-substituted hydrazodithiodicarbonamides is the same as on the unsubstituted hydrazide in giving the corresponding isomers. Stronger acids eliminate the amine from the mono-substituted hydrazide yielding the isomeric iminothiol- and *endo*iminothiolthiobiazoles (V) and (VI).

In the case of disubstituted hydrazides, hydrochloric acid (d. 1.16) gives the alkali-soluble R-iminothiolthiobiazole (VII) as the main product; concentrated acid (d. 1.19) on the other hand yields isomeric 3:5-di-R-iminothiobiazole (VIII) and 3:5-*endo*-R-imino-3-R-iminothiobiazole (IX).

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