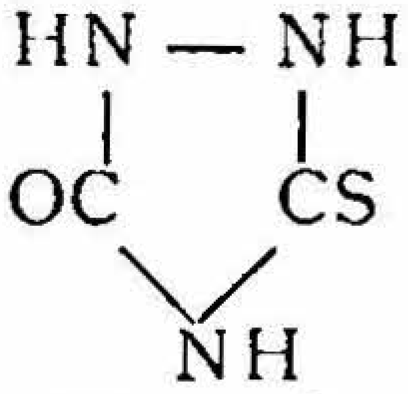
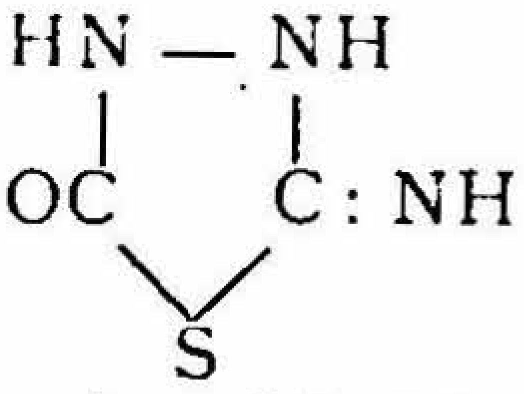
PART VI. ISOMERISM OF HYDRAZOMONOTHIODICARBONAMIDES, IMINOTHIOBIAZOLONES AND MONOTHIOURAZOLES.

By S. L. Janniah and P. C. Guha.

Freund and Schander (*Ber.*, 1896, **29**, 2506), by heating the hydrazide NH_2-CS-NH-NH-CO-NH_2 with concentrated hydrochloric acid obtained a compound, $C_2H_3ON_3S$, to which they ascribed the monothiourazole formula. Busch and Lotz (*J. pr. Chem.*, 1914, **90**, ii, 257) have shown Freund's monothiourazole to be 3-imino-4 :1 :2-thiobiazole-5-one



(Freund)



(Busch and Lotz)

Arndt, Milde, and Tschenscher (*Ber.*, 1922, **55**, 341) found that of the two isomeric hydrazides,

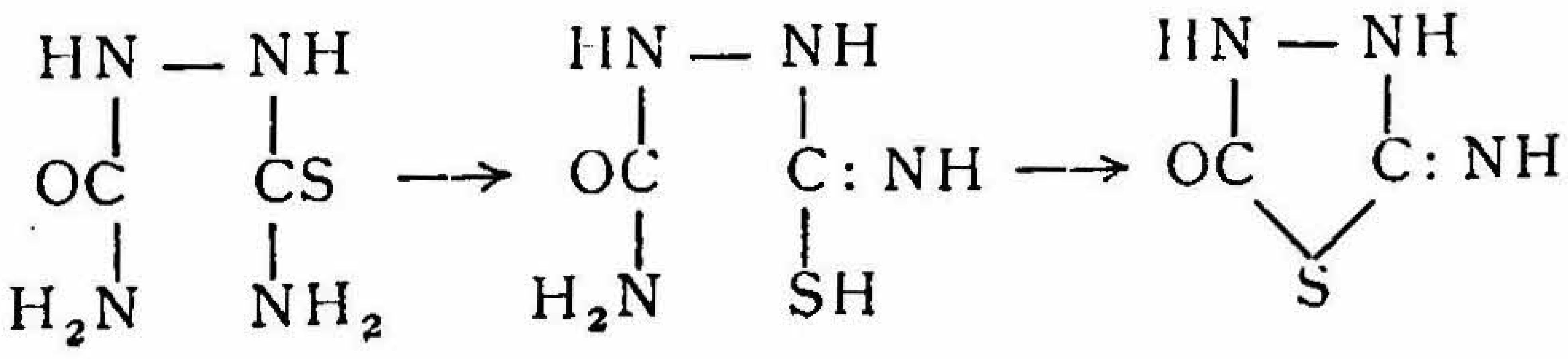
$NHPh$-CO-NH-NH-CS-NH_2 and $NHPh$-CS-NH-NH-CO-NH_2

the former gave thiourazole (m.p. 206°) and 4-phenylthiourazole, and the latter phenylthiourazole, on being boiled with a solution of sodium hydroxide.

While attempting the ring-closure of hydrazomonothio- (and dithio-) dicarbonamides with acetic anhydride, Guha (*J. Amer. Chem. Soc.*, 1923, **45**, 1036) found that the hydrazide

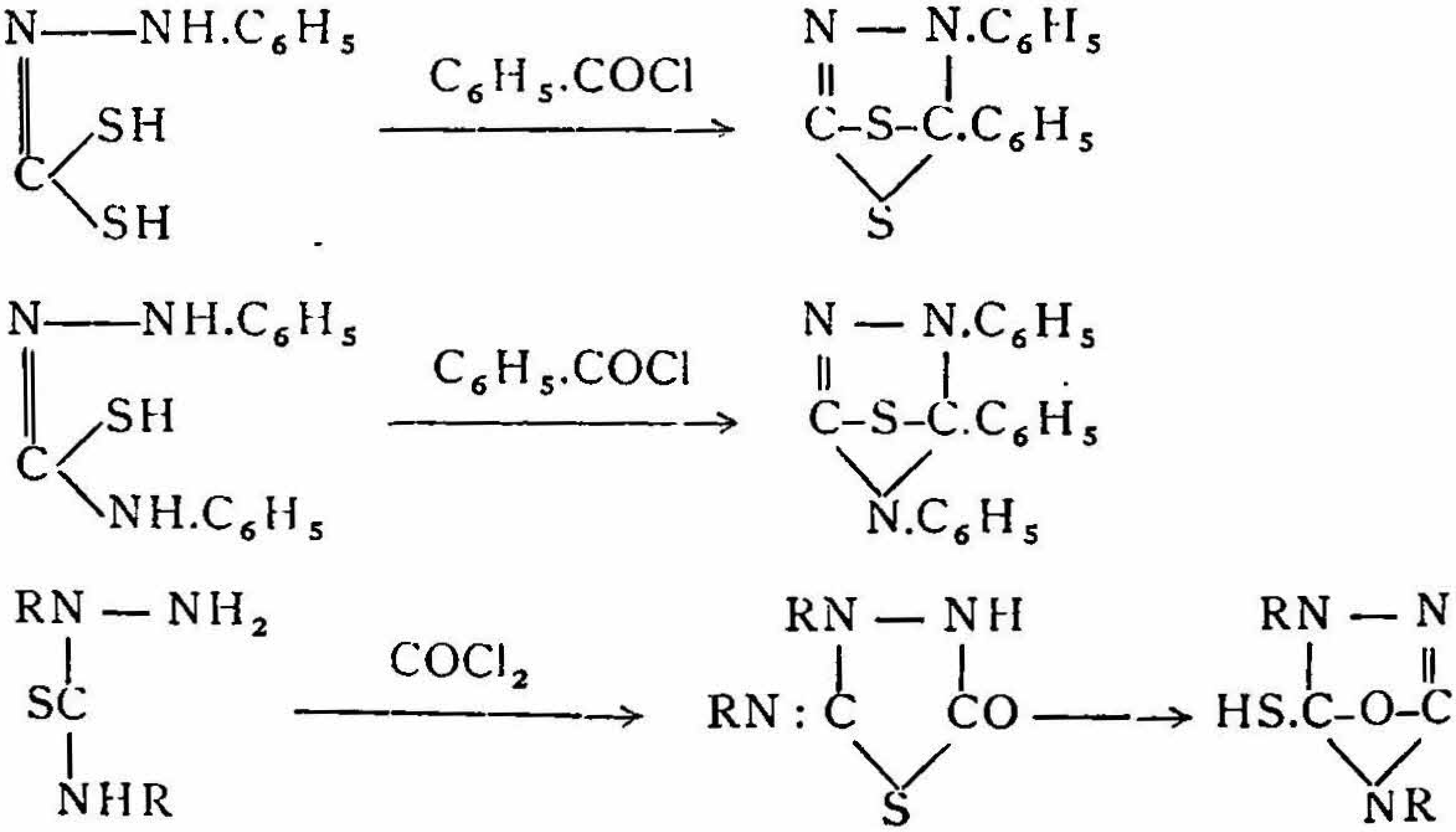
NH_2-CS-NH-NH-CO-NH_2

instead of giving 3 :5-diiminotetrahydro-4 :1 :2-thiobiazole according to the general rule holding good in the case of the hydrazodithiodicarbonamides, gave ketoiminothiodiazole m.p. 235°, thus :



and that his compound was quite different from Freund's compound (m.p. 177°).

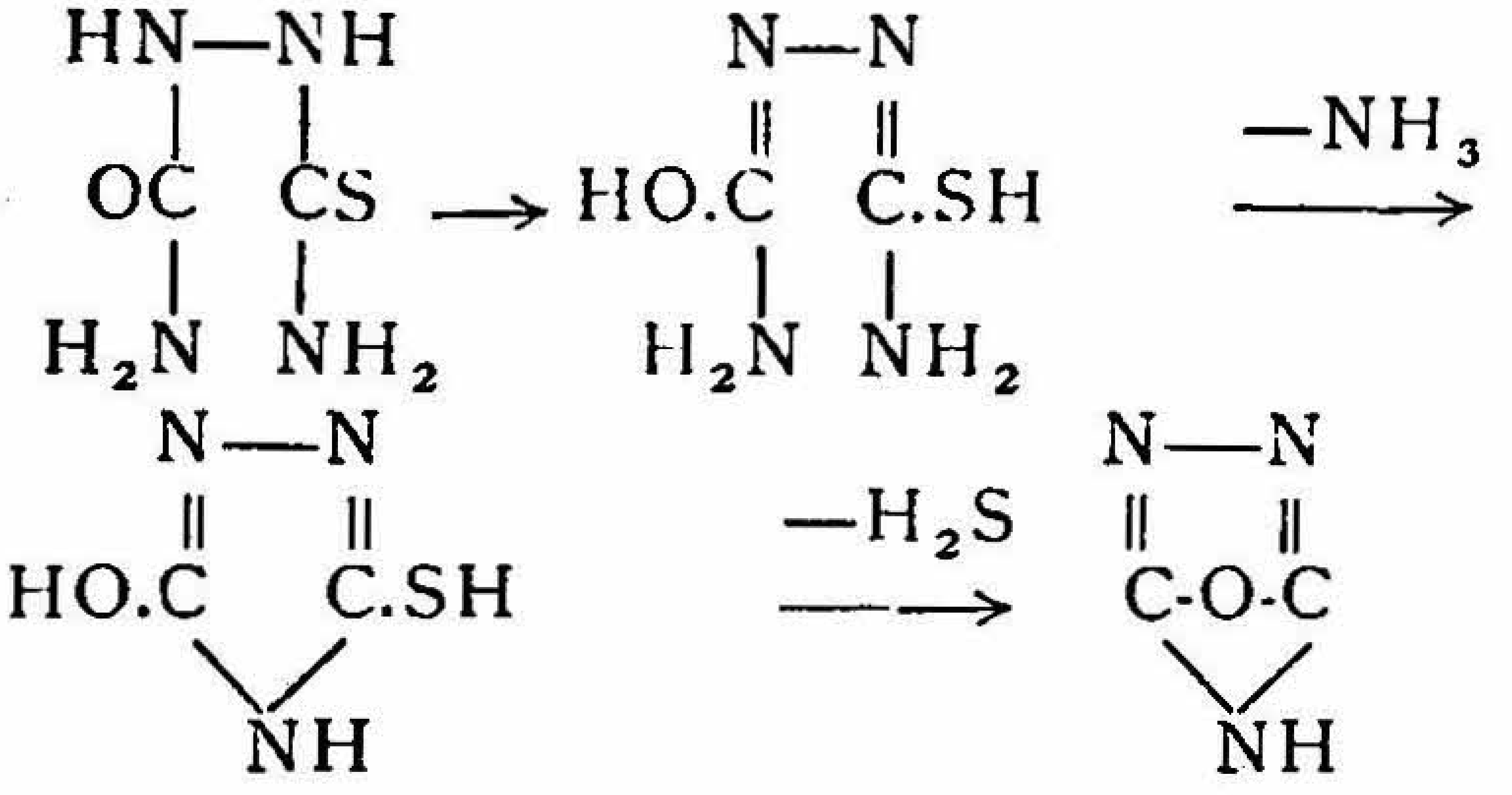
Guha and Sen (*J. Ind. Chem. Soc.*, 1927, **4,** 43) obtained by the action of urea upon substituted thiosemicarbazides four types of compounds namely, 3-R-5-keto-3-thioldihydro-4 :1 :2-triazole, 5-keto-3-R-aminodihydro-4 :1 2-thiobiazole, 4-R-3-thiol-5-R-amino-4 :1 :2-triazole and 3 :5-*endo*xy-4 :1 :2-triazole. Of the above four types, ketothioltriazoles have been prepared also by Freund and Schneider, Arndt and his collaborators (*loc. cit.*) and by Fromm and Nehring *Ber.*, 1923, **56**, 1370) ketoaminothiobiazoles by Busch (*Ber.*, 1901, **34**, 320, 2328 ; 1902, **35**, 973 ; 1904, **37**, 2333 ; 1909, **42**, 4763 ; 1911, **44,** 561, 1580) and by Nirdlinger and Acree (*J. Amer. Chem. Soc.*, 1922, **44,** 224). Lastly, though Schneider (*J. pr. Chem.*, 1890, **67,** 263), Marckwald (*Ber.*, 1892, **25,** 3113 ; 1896, **29,** 2923), Busch (*loc. cit.*) and Nirdlinger and Acree have prepared the derivatives of *endo*xy-, *endo*thio-, and *endo*iminotriazoles and thiobiazoles by methods fundamentally different from that of Guha, e.g :—



the parent *endo*xytriazole was prepared for the first time by Guha and Sen. Guha and Chakraborti (*J. Ind. Chem. Soc.*, **6**, 99-110) while studying the ring-closure of hydrazomonothiodicarbonamide and its mono- and *sym*-di-substitution products with acetic anhydride, obtained iminothiobiazolones and iminothioltriazoles.

The present investigation is a continuation of the work described in parts IV and V, undertaken with the expectation that interesting cases of isomerism amongst the hydrazomonothiodicarbonamides, as also amongst the thiobiazoles and triazoles obtained from them by ring-closure might yet arise, and these have been found.

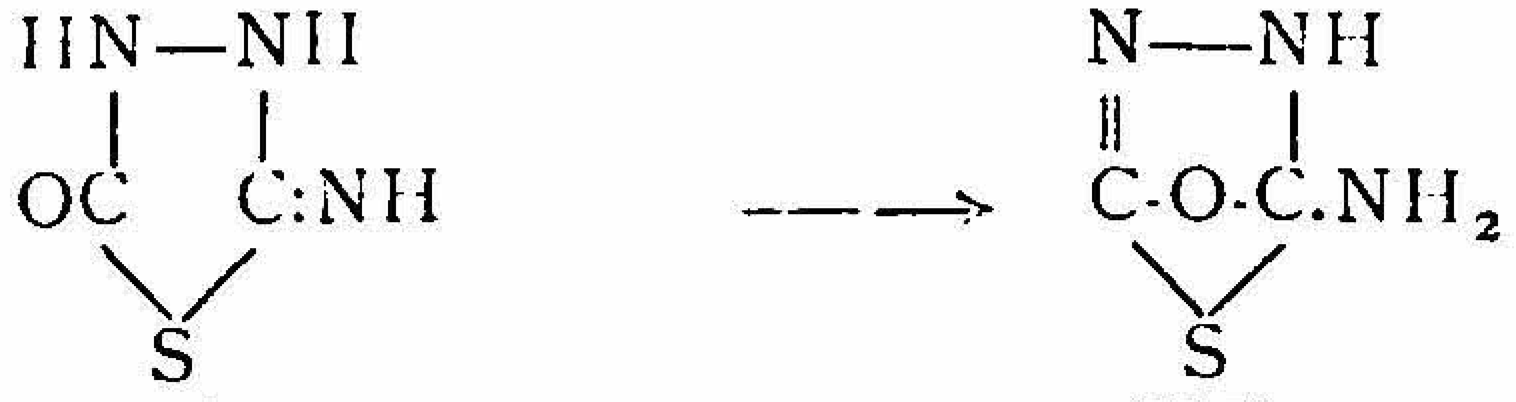
Our first attempt was to study the effect of 2*N* hydrochloric acid upon hydrazomonothiodicarbonamide, but this failed to give an isomer; under the various conditions tried only thiosemicarbazide hydrochloride (m.p. 190°) could be obtained. With boiling 5*N* hydrochloric acid, however, the hydrazide gave a substance, C_2HON_3, m.p. 255°, identical with 3:5-*endo*xy-4:1:2-triazole prepared by Guha and Sen (*J. Ind. Chem. Soc.*, 1927, **4**, 43). The reaction evidently takes the following course:—



(I)

By repeating Freund's experiment with hydrochloric acid (d. 1.16) under varied experimental conditions it has now been found that iminothiobiazolone, m.p. 177°, is formed in poor yield; and with concentrated hydrochloric acid (d. 1.19) both compounds (m.p. 177° and 235°) are produced, the latter due to its pronounced basic property remaining in the acidic mother liquor after the separation of the former.

This thiobiazolone (m.p. 177°) gives with acetic anhydride an acetyl derivative (m.p. 295°) which on being hydrolysed with concentrated hydrochloric acid gives a hydrochloride (m.p. 107-108°), and a free base (m.p. 235°) identical with the corresponding compounds obtained from hydrazomonothiodicarbonamide with acetic anhydride (Guha, *J. Amer. Chem. Soc.*, 1923, **45**, 1036). The substance has the composition, $C_2H_3ON_3S$, and is therefore isomeric with the substance melting at 177°. It is insoluble in alkali, remains unchanged on mercuric oxide treatment, and forms compounds with phenyl *iso*cyanate, phenyl mustard oil, and benzaldehyde. It is thus clear that (1) the sulphur atom is a member of the ring, and (2) an amino-group is present. All these facts give further support to the *endo*aminothiobiazole structure (III) ascribed to compound, m.p. 235° (compare part IV, 4863). It appears very probable that by the action of concentrated hydrochloric acid the hydrazide is first converted into iminothiobiazolone, m.p. 177° (II) which then rearranges itself into the *end*-oxyaminothiobiazole, m.p. 235° (III) :—



(II) (III).

Mono-substituted hydrazides of the type,

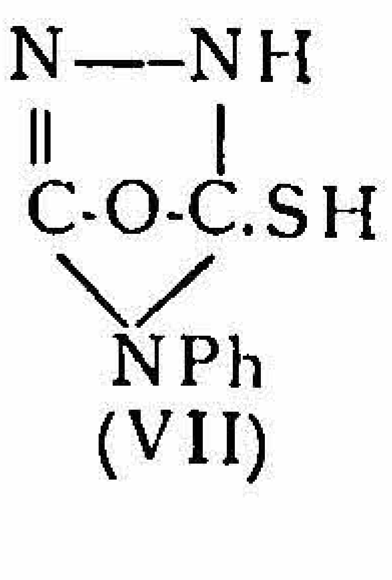
NH_2-CO-NH-NH-CS-NHR (R = Ph, Me, Allyl).

give the corresponding isomeric hydrazides (IV, V, VI) with 2*N* hydrochloric acid similar to those described in parts IV and V.

$NHPh$-CS-NH-NH-CO-NH_2 (IV) CH_3·NH-CS-NH-NH-CO-NH_2 (V)

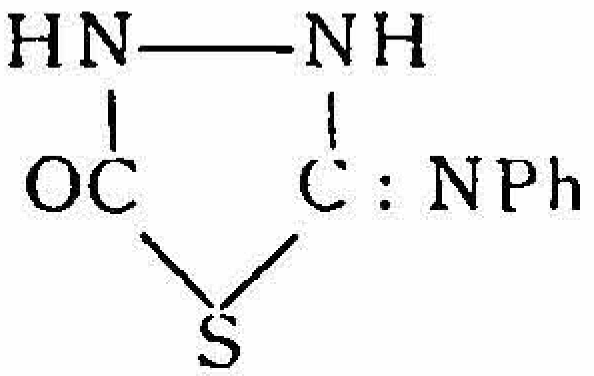
C_3H_5·NH-CS-NH-NH-CO-NH_2 (VI)

Although hydrochloric acid of different strength (d. 1.16 and 1.19) produces different thiobiazoles in the case of the mono- and di-substituted hydrazodithiodicarbonamides, their effect as ring-closing agents on the hydrazides of the monothio-series is similar. Strong hydrochloric acid brings about a ring-closure in the hydrazide (IV) producing a compound (m.p. 184°) of the empirical formula, $C_8H_7ON_3S$. This is soluble in dilute alkali, gives a thiomethyl ether, m.p. 90-91°, and a disulphide, m.p. 196°. These properties eliminate the possibility of the compound being 3-phenylimino-5-keto-4 :1 :2-thiobiazole (m.p. 246°) synthesised by Guha and Sen (*J. Ind. Chem. Soc.*, 1927, **4**, 44) by the action of urea on phenylthiosemicarbazide. It therefore follows that the substance under consideration must be a triazole containing a thiol group. 4-phenylthiourazole (m.p. 196°) of Arndt (*Ber.*, 1922, **55**, 341), obtained by the action of alkali on the same hydrazide has a mercaptanic group (thiomethyl ether m.p. 208°, disulphide, m.p. 285°), and is evidently a different substance. There thus remains the only alternative *endo*-formula (VII) for the substance melting at 184°, viz., 3-thiol-3 :5-*endo*xy-2 :3-dihydro-4-phenyl-4 :1 :2-triazole,

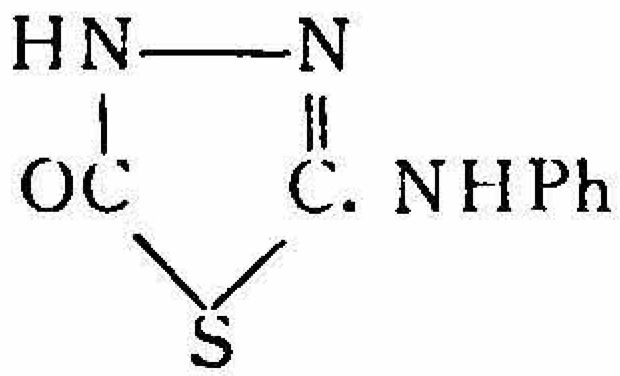


(VII)

Compound (VII) gives with acetic anhydride a diacetyl derivative (m.p. 213-214°) which on deacetylation gives a substance (m.p. 206°) having the same composition ($C_8H_7ON_3S$) as the parent *endo*xytriazolethiol but without mercaptanic properties. Thus compound (VII) after acetylation and deacetylation is no longer a triazole, and must have been changed into a substance with the sulphur atom in the ring. The diacetyl derivative (m.p. 214°) and the deacetylated compound (m.p. 206°) have been proved identical with the corresponding compounds obtained by Guha and Chakraborti from the hydrazide by the action of acetic anhydride (*loc. cit.*). To distinguish their compound, m.p. 206°, from that having m.p. 246° (Guha and Sen, *loc. cit.*) Guha and Chakraborti ascribed a ketophenyliminotetrahydrothiobiazole structure to the former as distinct from the ketophenylaminodihydrothiobiazole structure of the latter

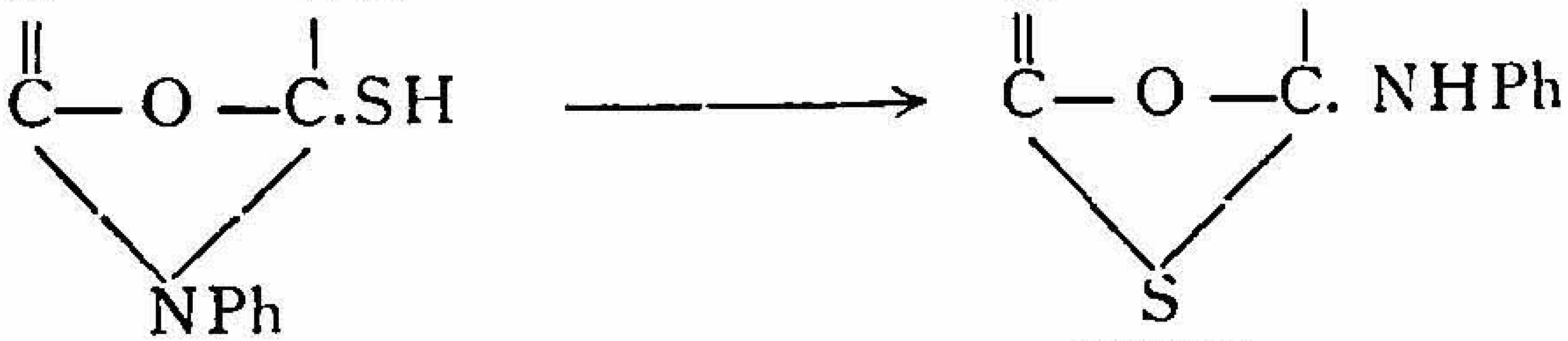


(m.p. 206°, Guha and Chakraborti)



(m.p. 246°, Guha and Sen)

Seeing that both compounds (m.p. 206° and 246°) are quite stable and show no sign of interconvertibility under ordinary conditions, unexpectedly from the tautomeric nature of the above formulae, and from analogy with the *endo*-isomers of the thiobiazoles and triazoles obtained from the hydrazomono- and dithiodicarbonamides, it is now proposed to attribute an *endo*-formula, namely, 3-phenylamino-3 :5-*endo*xy-4 :1 :2-thiobiazole, to the compound melting at 206° ; and its formation from compound (VII) is explained on the assumption that an interchange of position between NPh and S takes place :—

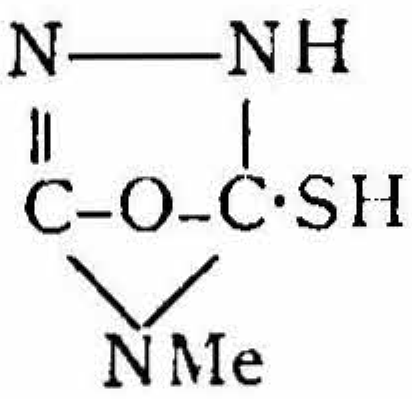


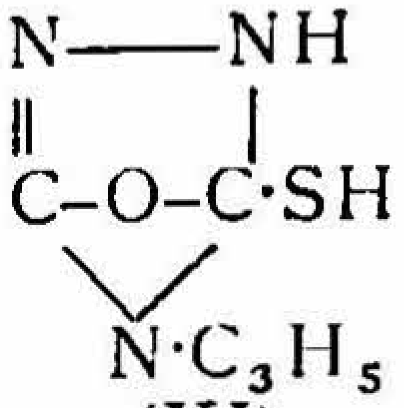
(VII) (VIII)

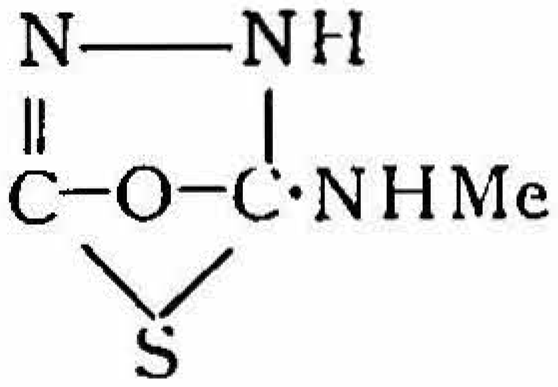
Methyl- and allyl-substituted hydrazomonothiodicarbonamides,

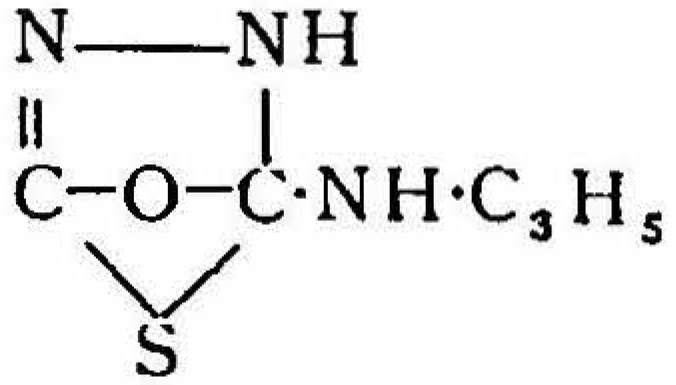
$$NH_2\text{-}CO\text{-}NH\text{-}NH\text{-}CS\text{-}NHR \qquad (R = Me, Allyl),$$

by the action of concentrated hydrochloric acid and acetic anyhdride, have yielded the corresponding methyl and allyl substituted *endo*xythioltriazoles (IX and XI) and *endo*xy-R-iminothiobiazoles (X and XII) respectively :


(IX)


(XI)


(X)


(XII)

EXPERIMENTAL.

Hydrazomonothiodicarbonamide and 5N *hydrochloric acid* : *Formation of* 3 :5-*endoxy*-4 :1 :2-*triazole* (I).—The hydrazide (m.p. 220° ; 5 g.) was heated with the acid (50 c.c.) and the clear solution thus obtained was boiled during half an hour, when hydrogen sulphide and a small quantity of sulphur separated. The clear solution on cooling gave a small quantity of white crystalline solid, increased on concentrating the mother liquor. This crystallised from hot water, m.p. 255° ; yield, about 2 g. The substance was insoluble in alkali and was identical with the *endo*xytriazole (m.p. 255°) of Guha and Sen (*loc. cit.*) (Found : N, 50.85 ; C_2HON_3 requires N, 50.6 per cent.).

Hydrazomonothiodicarbonamide and concentrated hydrochloric acid (d. 1.19) : *Formation of* 3-*imino*-5-*keto*-4 :1 :2-*thiobiazole*.—The hydrazide (5 g.) was boiled vigorously with the acid (25 c.c.) during half an hour when sulphuretted hydrogen was evolved profusely. On cooling, a very small quantity of a crystalline solid separated which crystallised from hot water, m.p. 255°, and was identical with the *endo*xytriazole obtained above. The mother liquor on concentration gave a little more of the *endo*xytriazole and the filtrate from the latter on being evaporated to dryness left a white residue which crystallised from a small quantity of water, m.p. 177°. The yield was only about 0.5 g., but the hydrazide, when gently boiled with hydrochloric acid (d. 1.19) for only 15 minutes, gives a better yield of 177° compound (Found : N, 36.3 ; S, 27.5. $C_2H_3ON_3S$ requires N, 35.9 ; S, 27.35 per cent.).

Iminothiobiazolone and acetic anhydride.—The pale yellow solution obtained on heating the substance with acetic anhydride, on being boiled for a quarter of an hour, gave a brownish yellow solid which crystallised from water, m.p. 295°.

The free base: *3-Amino-3:5-endoxy-2:3-dihydro-4:1:2-thiobiazole* (III).—The acetyl derivative dissolved in gently boiling concentrated hydrochloric acid and deposited the hydrochloride on cooling; this crystallised from dilute hydrochloric acid, m.p. 107°, and gave the free base with sodium carbonate, m.p. 235° (Found: N, 36.15; S, 27.4. $C_2H_3ON_3S$ requires N, 35.9; S, 27.35 per cent.).

The identity of the acetyl derivative, the hydrochloride and the free base with the corresponding compounds of Guha (*loc. cit.*) was established. The free base gave compounds with phenyl *iso*cyanate m.p. 228°; with phenyl mustard oil, m.p. 256°; and with benzaldehyde m.p. 216°.

Isomer of phenylhydrazomonothiodicarbonamide (IV; m.p. 200°).—Procedure adopted in the case of hydrazodithiodicarbonamide (part IV, 8) was followed. The crystalline solid obtained on cooling the solution of the hydrazide in 2*N* hydrochloric acid, was filtered, washed, and recrystallised from dilute alcohol, m.p. 175° (Found: N, 26.5; S, 15.1. $C_8H_{10}ON_4S$ requires N, 26.6; S, 15.25 per cent.).

Phenylhydrazomonothiodicarbonamide and concentrated hydrochloric acid (d. 1.19): *Formation of 3-thiol-3:5-endoxy-4-phenyl-2:3-dihydro-4:1:2-triazole* (VII).—The hydrazide was boiled with the acid for fifteen minutes when from the clear solution a white solid began to separate; it crystallised from dilute alcohol, m.p. 184°, is soluble in alkali, gives a disulphide with iodine, m.p. 196°, and a thiomethyl ether, m.p. 90-91° (Found: N, 21.9; S, 16.3. $C_8H_7ON_3S$ requires N, 21.75; S, 16.5 per cent.).

The *diacetyl* derivative crystallised from dilute alcohol, m.p. 213-214° (Found: N, 15.0; S, 11.3. $C_{12}H_{11}O_3N_3S$ requires N, 15.2; S, 11.5 per cent.).

3-Phenylamino-3:5-endoxy-2:3-dihydro-4:1:2-thiobiazole (VIII).—The above diacetyl derivative was boiled with concentrated hydrochloric acid and the cooled solution diluted with water when a crystalline white solid separated out slowly and was recrystallised from dilute alcohol, m.p. 206°. It is insoluble in cold dilute alkali, but on boiling the solution becomes pale green and liberates phenyl mustard oil. It is not desulphurised with mercuric oxide (Found: N, 21.95; S, 11.95. $C_8H_7ON_3S$ requires N, 21.7; S, 11.4 per cent.). It is identical with Guha and Chakraborti's compound obtained by the action of acetic anhydride directly on the hydrazide (*loc. cit.*).

Isomer of methylmonothiohydrazodicarbonamide (V; m.p. 212°).—The isomeric hydrazide obtained by the action of 2*N* hydrochloric acid melted at 168° (Found: N, 37.7; S, 21.45. $C_3H_8ON_4S$ requires N, 37.8; S, 21.6 per cent.).

3-*Thiol*-3:5-endo*xy*-4-*methyl*-4:1:2-*triazole* (IX).—The clear solution obtained by boiling the hydrazide with concentrated hydrochloric acid (d. 1.19) gave a solid on cooling which crystallised from dilute alcohol, m.p. 182°. It was soluble in cold dilute alkali, and with iodine gave a disulphide, m.p. 265° (Found: N, 31.6; S, 24.3. $C_3H_5ON_3S$ requires N, 32.06; S, 24.4 per cent.).

The *acetyl* derivative obtained from compound (IX) crystallised from dilute alcohol, m.p. 196-197° (Found: N, 24.05; S, 18.4. $C_5H_7O_2N_3S$ requires N, 24.3; S, 18.5 per cent.).

3-*Methylamino*-3:5-endo*xy*-2:3-*dihydro*-4:1:2-*thiobiazole* (X).—The above acetyl derivative with boiling concentrated hydrochloric acid (d. 1.19) gave on cooling a small quantity of a crystalline solid increased on concentration; it crystallised from aqueous alcohol, m.p. 232°, and was insoluble in cold dilute alkali (Found: N, 31.85; S, 24.45. $C_3H_5ON_3S$ requires N, 32.06; S, 24.4 per cent.).

Isomer of allylhydrazomonothiodicarbonamide (m.p. 190°; VI).—The isomeric hydrazide after crystallisation from alcohol melted at 192°. The difference between the melting points of the two isomeric hydrazides was only 2°, but a melting point of the mixture was 8-9° lower (Found: N, 32.42. $C_5H_{10}ON_4S$ requires N, 32.18 per cent.).

3-*Thiol*-3:5-endo*xy*-4-*allyl*-2:3-*dihydro*-4:1:2-*triazole* (XI).—The above hydrazide treated with concentrated hydrochloric acid as with the other hydrazides gave a product crystallising from dilute alkali; the disulphide melted at 174° (Found: N, 26.6; S, 20.3. $C_5H_7ON_3S$ requires N, 26.75; S, 20.4 per cent.).

The *acetyl* derivative from the triazole (X) and acetic anhydride had m.p. 171° (Found: N, 21.3; S, 15.74. $C_7H_9ON_3S$ requires N, 21.11; S, 16.08 per cent.).

3-*Allylamino*-3:5-endo*xy*-2:3-*dihydro*-4:1:2-*thiobiazole* (XII.)—The acetyl derivative was deacetylated by boiling concentrated hydrochloric acid, and the solution on concentration deposited the free *end*oxytriazole as a white solid which crystallised from dilute alcohol, m.p. 210-211°. The substance is insoluble in cold dilute alkali (Found: N, 26.7; S, 20.32. $C_5H_7ON_3S$ requires N, 26.75; S, 20.4 per cent.).

SUMMARY.

The isomeric form of hydrazomonothiodicarbonamide could not be obtained, owing to ready decomposition; but isomers of the substituted hydrazides have been isolated. Besides Freund's iminothiobiazolone, m.p. 177°, the unsubstituted hydrazide has yielded 3 :5-*end*-oxytriazole, m.p. 255° (I) and 3 :5-*end*oxy-3-aminothiobiazole, m.p. 235° (III) on treatment with hydrochloric acid of different concentration.

Hydrochloric acid (d.1.16 and 1.19) behaved similarly in effecting ring-closure of the mono-substituted hydrazides of this series, giving rise to *end*oxytriazole-thiols VII, IX and XI which in their turn were converted by acetylation followed by hydrolysis into *end*oxythiobiazoles VIII, X and XII by an interchange of position between the group NR of the nucleus and the sulphur atom.

Department of Organic Chemistry,
Indian Institute of Science,
Bangalore.

[Accepted, 18-1-33.]

PRINTED AND PUBLISHED BY V. M PHILIP, AT THE DIOCESAN PRESS MADRAS.—1933. 7314.