THE REACTION OF NITROUS ACID WITH 4-SUBSTITUTED-THIOSEMICARBAZIDES[1]

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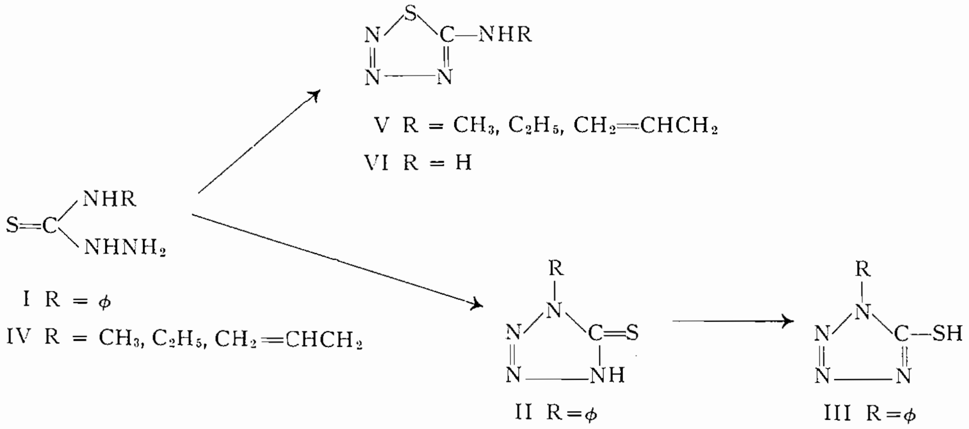
ABSTRACT

The reaction of nitrous acid with 4-alkyl- or 4-aryl-thiosemicarbazides, as well as the reaction of alkyl- or aryl-isothiocyanates with hydrazoic acid, leads to the identical 5-(substituted)amino-1,2,3,4-thiatriazole. This has been established by infrared absorption and chemical degradation studies. The reaction of the 5-(substituted)amino-1,2,3,4-thiatriazoles with aqueous bases leads to two competitive reactions: (1) degradation to an isothiocyanate and azide ion, and (2) isomerization to a 1-substituted-tetrazole-5-thiol, the extent of path (1) or (2) depending on the nature of the substituent. Path (1) predominates when the substituent is alkyl, whereas when the substituent is aryl both paths (1) and (2) occur, the relative proportion depending on the electrical nature of the aromatic group, path (2) increasing as the electronegativity increases. The 1-aryl-tetrazole-5-thiols were found to be thermally unstable at their melting points, degrading more or less violently to one mole proportion of pure nitrogen with the formation of sulphur and organic products of lower melting point as yet unidentified. Theories to account for these observations are presented and discussed.

INTRODUCTION

In 1895, Freund and Hempel (9) reported that when 4-phenylthiosemicarbazide (I) was treated with nitrous acid, a substance was produced to which the structure II was assigned. II was reported to be a stable compound, not decomposed by cold sulphuric acid or boiling hydrochloric acid. On melting, however, it decomposes more or less violently depending on the rate of heating. Freund and Hempel (9) reported that it could be recovered unchanged from cold alkaline solution, but on being heated, II was isomerized to a compound of different properties to which they assigned structure III. Structure III was supported by adequate chemical evidence (9). On the other hand, when R was an alkyl group (IV), Freund and Schwarz (11) assigned the structure V, on the basis of degradative evidence and of its marked instability in comparison



V R = CH_3, C_2H_5, $CH_2{=}CHCH_2$

VI R = H

I R = ϕ

IV R = CH_3, C_2H_5, $CH_2{=}CHCH_2$

II R=ϕ

III R=ϕ

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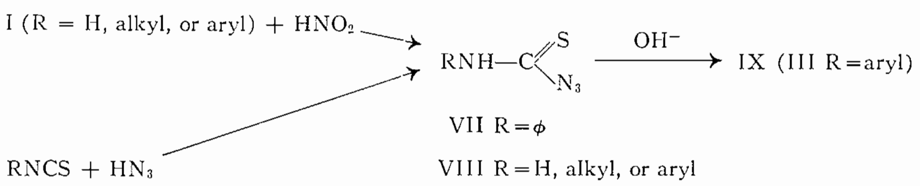
with structure II. Structures of type V were very similar in properties to that of VI obtained by the reaction of thiosemicarbazide with nitrous acid (10).

In 1913, Oliveri-Mandala and Noto (23) discovered that the reaction of hydrazoic acid with phenylisothiocyanate produced a compound, VII, that had properties very similar to those described for II. In continuation of these studies, Oliveri-Mandala (20, 21, 22) found that these compounds had properties more in conformance with a thiocarbamyl azide structure, VIII, and suggested that the initial diazotization products of thiosemicarbazides and their 4-alkyl- and 4-aryl-substitution products were identical with the condensation of an isothiocyanate with hydrazoic acid and that the differences observed by Freund (9, 10, 11) were not differences in structure but rather differences due to variations in stability depending on the nature of the R substituent. On the other hand, when VIII (R = aryl) was treated with bases, Oliveri-Mandala (20, 21) obtained the 1-aryl-tetrazole-5-thiols, IX, identical with the products described by Freund and Hempel (9).



The present investigation is part of a general study of azole chemistry with the specific object of resolving the conflicts concerning the structure of the initial diazotization products of 4-alkyl- and 4-aryl-thiosemicarbazides.

EXPERIMENTAL[5,6]

1,3-Diaryl-2-thioureas, RNHC(S)NHR.—These were prepared by refluxing an alcoholic solution of the arylamine with carbon disulphide until the evolution of hydrogen sulphide ceased. On cooling, the product crystallizes and is purified by recrystallization from alcohol. The following gives the R, % yield, m.p., and literature m.p.: benzyl, 90, 147–148°, 147–148° (27); *o*-tolyl, 53, 158–159°, 161° (7); *p*-tolyl, 63, 177–178°, 177° (3); *p*-anisyl, 95, 185–186°, 186.5° (7); *o*-anisyl, 82, 132–133°, 134° (8); *p*-hydroxyphenyl, 95, 223.5–224°, 223–224° (7).

Organic isothiocyanates, RNCS.—Of these R = CH_3, C_2H_5, $n\text{-}C_4H_9$, $n\text{-}C_7H_{15}$, phenyl, and allyl are commercially available. R = *p*-tolyl, *o*-tolyl, *o*-anisyl, and *p*-anisyl were prepared by refluxing the corresponding thiourea with acetic anhydride by the method of Werner (28). This method, however, gave only a very poor yield for R = benzyl, which was best prepared by the method of Moore and Crossley (19) in 75% yield. R = $4\text{-Cl-}C_6H_4$ was prepared in 32% yield, based on *p*-chloroaniline, from 1-(4-chlorophenyl)-3-phenyl-2-thiourea (from *p*-chloroaniline and phenylisothiocyanate) by steam distilling in the presence of sulphuric acid by the method of Chattaway, Hardy, and Watts (5), m.p. 40–45°, b.p. 110–115° at 4 mm. Refluxing 1,3-di-(*p*-hydroxyphenyl)-2-thiourea with acetic anhydride leads to *p*-acetoxy-phenylisothiocyanate (16), non-volatile with steam, purified by vacuum fractional distillation, the fraction being collected

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[5] *All melting points are uncorrected.*

[6] *Microanalyses by Dr. C. Weiler and Dr. F. B. Strauss, Oxford, England.*

at 167–175° at 8 mm., 58 g. (84%) from 93 g. of the thiourea; solidifies on cooling, recrystallized from ethanol, m.p. 33.5–34.5°. Anal. Calc. for $C_9H_7NO_2S$: N, 7.25; S, 16.6. Found: N, 7.28; S, 16.5.

4-Substituted-thiosemicarbazides (*Table I*).—All of the isothiocyanates readily underwent hydrazination to form the corresponding 4-substituted-thiosemicarbazide, purification being effected by repeated recrystallization from ethanol. The products so prepared are summarized in Table I. Para-acetoxyphenylisothiocyanate was found to undergo hydrazinolysis as well as hydrazination.

TABLE I

4-SUBSTITUTED-THIOSEMICARBAZIDES

RNHC(S)NHNH$_2$ R =	% Yield	M.p., ° C. Found	M.p., ° C. Reported	Formula	Calc.	Found
CH_3	93	136.5–137	137–138[a]	$C_2H_7N_3S$	39.98	40.00
C_2H_5	87	83.5–84	84[b]	$C_3H_9N_3S$	35.25	35.20
C_3H_6[c]	86	96.5–97	88–89[a]	$C_4H_9N_3S$	32.02	32.40
n-C_4H_9	89	74–74.5	70[d]	$C_5H_{12}N_3S$	28.54	28.40
n-C_7H_{15}	92	53–54	54–55[e]	$C_8H_{18}N_3S$	22.20	22.60
$C_6H_5CH_2$	70	129.5–130.5	130[e]	$C_8H_{10}N_3S$	23.30	23.40
4-$CH_3C_6H_4$	95	137	137[f]	$C_8H_{10}N_3S$	23.30	23.00
2-$CH_3C_6H_4$	98	148	148[g]	$C_8H_{10}N_3S$	23.30	23.20
4-$CH_3OC_6H_4$	95	150–151	144[h]	$C_8H_{10}N_3OS$	21.31	21.20
2-$CH_3OC_6H_4$	95	154	156[g]	$C_8H_{10}N_3OS$	21.31	21.20
4-ClC_6H_4	95	180	180[h]	$C_7H_7ClN_3S$	20.84	20.60[i]

[a] *Pulvermacher, Ber.* ***27****, 622 (1894).*
[b] *Freund and Schwarz, Ber.* ***29****, 2483 (1896).*
[c] *Allyl.*
[d] *Hogarth and Young, J. Chem. Soc. 1582 (1950).*
[e] *Baird, Burns, and Wilson, J. Chem. Soc. 2527 (1927).*
[f] *Guha and Ray, J. Am. Chem. Soc.* ***47****, 387 (1925).*
[g] *Fromm, Soffner, and Frey, Ann.* ***434****, 285 (1923).*
[h] *Busch and Ulmer, Ber.* ***35****, 1714 (1902).*
[i] *Calc.:* S, *15.91;* Cl, *17.59. Found:* S, *15.50;* Cl, *17.75.*

4-(p-Hydroxyphenyl)-thiosemicarbazide.—To a solution of 54 g. (0.28 mole) of *p*-acetoxyphenylisothiocyanate in 200 ml. of ethanol was added 15 ml. of 95% hydrazine hydrate diluted with 10 ml. of water. The mixture was shaken for a few minutes and cooled. The precipitate was recovered by filtration. Yield, 40 g. (80%); recrystallized from ethanol, m.p. 170–171° (decomp.). Anal. Calc. for $C_7H_9N_3SO$: C, 45.86; H, 4.95; N, 22.94; S, 17.50. Found: C, 45.68; H, 4.94; N, 23.60; S, 17.40.

1-Benzylidene-4-(p-hydroxyphenyl)-thiosemicarbazide.—From 1 g. of 4-(*p*-hydroxyphenyl)-thiosemicarbazide and 1 g. of benzaldehyde in ethanol in the presence of nitric acid. Recrystallized three times from ethanol and dried at 100° at 4 mm.; m.p. 184–185°. Anal. Calc. for $C_{14}H_{13}N_3SO$: C, 61.95; H, 4.83; N, 15.50; S, 11.82. Found: C, 61.53; H, 4.56; N, 15.30; S, 11.60.

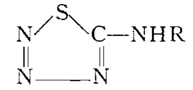
4,4-Dimethylthiosemicarbazide.—From 70 g. (0.39 mole) of N,N-dimethylthiocarbamylthioglycolic acid, m.p. 144–146° (13), 7 g. of sodium hydroxide in 170 ml. of water, and 35 ml. of 85% hydrazine hydrate. Recrystallized from water, m.p. 151–152° (reported (13) value is 156–157°).

1-Benzylidene-4,4-dimethylthiosemicarbazide.—Recrystallized from ethanol, m.p. 161–162°. Anal. Calc. for $C_{10}H_{13}N_3S$: N, 20.28; S, 15.48. Found: N, 20.50; S, 15.50.

The reaction of 4-substituted-thiosemicarbazides with nitrous acid, 5-(substituted)amino-1,2,3,4-thiatriazoles (*Table II*).—The preparation of 5-anilino-1,2,3,4-thiatriazole was

TABLE II

5-(SUBSTITUTED)AMINO-1,2,3,4-THIATRIAZOLES



R^i=	% Yield	M.p., ° C.		Formula	Analysis							
					% C		% H		% N		% S	
		Found	Reported		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
CH_3	60	93–96	96[c]	$C_2H_4N_4S$					48.25	48.40	27.61	27.50
C_2H_5	62	66–67	66–67[c]	$C_3H_6N_4S$					43.05	42.70	24.64	24.84
n-C_4H_9[a]	80	40–41	—	$C_5H_{10}N_4S$	37.93	37.96	6.37	6.31	35.42	35.60	20.27	20.50
n-C_7H_{15}[a]	97	75–75.5	—	$C_8H_{16}N_4S$	47.95	48.33	8.05	7.92	27.98	27.60	16.01	15.80
C_6H_5	89	142–143	142–145[d]	$C_7H_6N_4S$	47.15	47.10	3.40	3.51	31.45	31.60	18.00	17.60
4-$CH_3C_6H_4$	94	142–144	140–144[e]	$C_8H_8N_4S$	50.00	50.22	4.17	4.39	29.17	28.90	16.67	16.90
2-$CH_3C_6H_4$	90	114–115	120[f]	$C_8H_8N_4S$	50.00	50.11	4.17	4.40	29.17	29.00	16.67	16.50
4-$CH_3OC_6H_4$[a]	85	136–137	—	$C_8H_8N_4OS$	46.12	46.24	3.87	3.91	26.92	27.10	15.40	15.00
$C_6H_5CH_2$[a]	90	80.5–81	—	$C_8H_8N_4S$	50.00	50.07	4.17	4.25	29.17	29.00	16.67	16.70
4-ClC_6H_4[a,g]	75	147–148	—	$C_7H_5ClN_4S$	39.50	40.54	2.39	2.16	26.35	26.00	15.08	15.18
$(CH_3)2$[a,b]	31	49–51	—	$C_3H_6N_4S$	27.66	27.90	4.65	4.53	43.05	42.80	24.64	24.40
$CH_2{=}CHCH_2$	72	53–53.5[h]	54[c]	$C_4H_6N_4S$	33.78	33.81	4.26	4.47	39.42	39.41	22.56	22.65
2-$CH_3OC_6H_4$[a]	85	89–90	—	$C_8H_8N_4OS$	46.12	46.29	3.87	3.96	26.92	26.60	15.40	15.45

[a] *New compounds.*

[b] $R = CH_3$, $H = CH_3$.

[c] *Freund and Schander, Ber.* **29**, *2491 (1896).*

[d] *Freund and Hempel, Ber.* **28**, *74 (1895).*

[e] *Oliveri-Mandala, Gazz. chim. ital.* **44**, *I, 670 (1914).*

[f] *Oliveri-Mandala, Gazz. chim. ital.* **51**, *II, 195 (1921).*

[g] *Calc.* % Cl, *16.68; Found* % Cl, *16.38.*

[h] *Recrystallization must be made from non-aqueous solvents in order to avoid decomposition; a mixture of ether – petroleum ether was found best.*

[i] *All products showed the absence of the azido-group frequency in the infrared.*

typical. To a stirred and cooled mixture of 16.7 g. (0.10 mole) of 4-phenylthiosemicarbazide and 76 ml. of 15% hydrochloric acid was added 6.9 g. (0.10 mole) of sodium nitrite in 50 ml. of water. The white powdery material, which rapidly turns pale pink, was filtered. Yield, 16 g. (89%), m.p. 136–137° (decomp.). Recrystallization from methanol yields colorless needles, m.p. 142–143° (decomp.).

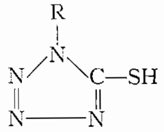
Reaction of nitrous acid with 4-phenylthiosemicarbazide in different acid environments.—Diazotizations were carried out in 50% aqueous acetic acid, in anhydrous acetic acid, and in hydrochloric acid of pH 3 and 5, respectively. In all cases a product melting at 142–143° was obtained. Mixed melting points showed all the products to be identical with 5-anilino-1,2,3,4-thiatriazole obtained above.

Reaction of phenylisothiocyanate and hydrazoic acid.—A mixture of 13.5 g. (0.1 mole) of phenylisothiocyanate and 6.5 g. (0.1 mole) of sodium azide was cooled to 0° and 25 ml. of 4 *N* hydrochloric acid added over a period of 30 minutes. After the addition of the acid, the reaction mixture was warmed on the water bath for 30 minutes and then cooled in an ice bath. The product was recrystallized from ethanol, m.p. 142°; no depression of m.p. with 5-anilino-1,2,3,4-thiatriazole. An infrared analysis showed the absence of the azido-group frequency.

Reaction of methylisothiocyanate and hydrazoic acid.—Hydrazoic acid from 2 g. (0.03 mole) of sodium azide was distilled into a solution of 2 g. (0.02 mole) of methylisothiocyanate in 25 ml. of ethanol. When the mixture was cooled, after concentration under

TABLE III

1-SUBSTITUTED-TETRAZOLE-5-THIOLS



R =	% Yield	M.p., ° C.		Formula	Analysis							
					% C		% H		% N		% S	
		Found	Reported		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
C_6H_5	34	148–148.5	147–150[a]	$C_7H_6N_4S$	47.15	47.33	3.40	3.61	31.45	31.40	18.00	17.70
4-$CH_3C_6H_4$	30	150	150–151[b]	$C_8H_8N_4S$	50.00	50.41	4.17	4.17	29.17	28.90	16.67	16.20
2-$CH_3C_6H_4$	22	121–123	129[c]	$C_8H_8N_4S$	50.00	50.18	4.17	4.38	29.17	28.80	16.67	16.60
4-$CH_3OC_6H_4$[d]	30	150	—	$C_8H_8N_4OS$	46.12	46.19	3.87	4.02	26.92	27.00	15.40	15.30
2-$CH_3OC\ H_4$[d]	24	139–140	—	$C_8H_8N_4OS$	46.12	46.38	3.87	4.08	26.92	26.60	15.40	15.15
$C_6H_5CH_2$[d] $_6$	25	138–139	—	$C_8H_8N_4S$	50.00	50.21	4.17	4.33	29.17	29.20	16.67	16.64
4-ClC_6H_4[d, e]	37	156–157	—	$C_7H_5ClN_4S$	39.50	38.85	2.39	2.18	26.35	26.20	15.08	15.60
4-HOC_6H_4	None											
CH_3	None											
n-C_7H_{15}	None											

[a] *Freund and Hempel, Ber.* ***28****, 74 (1895).*

[b] *Oliveri-Mandala, Gazz. chim. ital.* ***44****, I, 670 (1914).*

[c] *Oliveri-Mandala, Gazz. chim. ital.* ***51****, II, 195 (1921).*

[d] *New compounds.*

[e] *Calc.* % Cl, *16.68. Found* % Cl, *16.40.*

reduced pressure, colorless crystals were obtained which were recrystallized from ethanol, m.p. 96°; no depression of the melting point with 5-methylamino-1,2,3,4-thiatriazole. An infrared analysis showed the absence of the azido-group frequency.

1-Substituted-tetrazole-5-thiols (*1-substituted-5-thiatetrazolones*) (*Table III*).—The procedure used for the preparation of 1-phenyltetrazole-5-thiol was typical. A mixture of 2.2 g. (0.012 mole) of 5-anilino-1,2,3,4-thiatriazole and 25 ml. of 10% aqueous sodium hydroxide (4 moles) was refluxed for several minutes. The solution, which was at first a green color, turned yellow and turbid. On acidification, hydrogen sulphide was liberated and a faint yellow crystalline material precipitated. Recrystallization was effected from ethanol.

Alkaline steam degradation of 5-anilino-1,2,3,4-thiatriazole.—A mixture of 9 g. (0.05 mole) of 5-anilino-1,2,3,4-thiatriazole, 9 g. (0.23 mole) of sodium hydroxide, and 250 ml. of water was steam distilled. The steam distillation was continued for a period of 1 to 2 hours in order to make certain that no further steam-volatile degradation products were being produced. Aniline, identified by conversion to benzanilide, m.p. 161°, was found in the distillate. Acidification of the residue in the distillation flask gave the familiar odor of hydrogen sulphide and a crystalline precipitate, which after recrystallization from ethanol melted at 148°. It was identified as 1-phenyltetrazole-5-thiol by mixed melting point with an authentic specimen. Hydrazoic acid was also identified in the steam distillation residue by distilling the acidified mixture into a solution of ferric chloride. The characteristic blood-red coloration (6) due to the ferric–azide ion complex resulted. When the experiment was repeated in the presence of a stoichiometric quantity of sodium hydroxide, the distillate contained initially phenylisothiocyanate followed by 1,3-diphenyl-2-thiourea, identified by its m.p. of 154° (12) and analysis.

Anal. Calc. for $C_{13}H_{12}N_2S$: C, 68.37; H, 5.30; N, 12.28; S, 14.05. Found: C, 68.15; H, 5.37; N, 12.00; S, 13.90. The residue, on acidification, again yielded 1-phenyltetrazole-5-thiol, hydrogen sulphide, and hydrazoic acid. The 1-phenyltetrazole-5-thiol, recovered from the residue of the alkaline steam degradation, was resubmitted to steam distillation in the presence of 4 moles of sodium hydroxide over a period of 1 hour. No volatile product of any type was found in the distillate and the 1-phenyltetrazole-5-thiol was recovered unchanged and in quantitative yield. Neither hydrogen sulphide nor hydrazoic acid could be detected.

Thermal behavior of 1-phenyltetrazole-5-thiol.—On melting at 147–148°, 1-phenyltetrazole-5-thiol undergoes a marked decomposition with evolution of a gas and the development of a yellow coloration. On cooling, a grease-like substance of lower melting point was obtained. Quantitative experiments were carried out by mixing weighed quantities of 1-phenyltetrazole-5-thiol with white sand, in order to moderate the violence of the decomposition, and collecting the evolved gas over concentrated potassium hydroxide solution. Replicate runs showed that very nearly 1 mole of gas was liberated per mole of 1-phenyltetrazole-5-thiol. Mass spectrometric analysis[7] of the evolved gas showed it to be pure nitrogen. Sulphur was isolated and identified. A white crystalline material has been isolated whose identity is as yet unknown. Studies on the identity of this product are in progress.

The reaction of 5-(substituted)amino-1,2,3,4-thiatriazole with hydrogen sulphide.—Aqueous solutions of 5-methylamino-, 5-*n*-heptylamino-, and 5-anilino-1,2,3,4-thiatriazole, respectively, were saturated with hydrogen sulphide and allowed to stand overnight, at room temperature, under a slight excess pressure of hydrogen sulphide. All of the thiatriazoles were recovered quantitatively and unchanged.

Potentiometric titrations of 1-(substituted)phenyltetrazole-5-thiols.—The apparent acidic dissociation constants were determined by potentiometric titration in 50% aqueous ethanol using a photovolt pH meter. The titration curves for the compounds studied were of the moderately strong acid type. The data obtained for 1-*p*-chlorophenyl-, 1-phenyl-, and 1-*p*-methoxyphenyl- were, respectively, in pK_a units 3.3, 3.4, and 3.4.

DISCUSSION

The most important observation arising from this study is the fact that all of the initial diazotization products summarized in Table II, as well as identical substances produced by the reaction of phenyl- and methyl-isothiocyanates with hydrazoic acid, show no azido-group frequency in the infrared. This at once eliminates the assertion of Oliveri-Mandala (20, 21, 22, 23) that the products of the above reaction are thiocarbamyl azides, VII and VIII, in spite of the almost overwhelming chemical evidence in favor of this hypothesis. The most important of this chemical evidence is the formation of the azide and sulphide ions by alkaline degradation. Thus, the alkaline degradation of VIII (R = H) (10) corresponds almost exactly to that of guanyl azide nitrate (25) in which the azido-group frequency in the infrared is quite marked (17). On the other hand, the inertness of VII and VIII to hydrogen sulphide is in agreement with the infrared spectroscopy data. The facile reducibility of the azido-group by hydrogen sulphide has been frequently demonstrated (14, 18, 25, 26). Freund (9) placed a great deal of stress on his observation that the initial diazotization product of I showed marked stability

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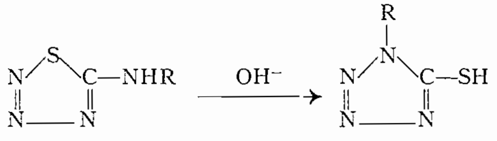
[7] *Consolidated Engineering Corporation, Pasadena, California.*

in alkaline medium[8] and on this basis assigned the structure II to his product. Unfortunately, Freund's (9) observations and deductions were incorrect and incomplete.

The present study has shown that from the infrared absorption spectroscopy and the chemical properties the initial diazotization products of 4-alkyl- and 4-aryl-thiosemicarbazides, as well as the alkyl- and aryl-isothiocyanate – hydrazoic acid reaction products, are best represented as possessing the 1,2,3,4-thiatriazole ring structure, X, regardless of whether R is represented as hydrogen,[9] alkyl, or aryl. The most significant



X XI

observation arising out of the conversion of X (R = ϕ) to XI (R = ϕ) is the fact that on warming in alkali, the odor of phenylisothiocyanate is almost immediately discernible and that on acidifying the alkaline mixture, in order to isolate the tetrazole XI, hydrogen sulphide is abundantly present. Further, XI was obtained in much less than stoichiometric yield (Table III). Since these observations indicated that some extensive degradation of X was taking place, the experiments were repeated in such a manner that the volatile degradation products could be collected and identified. All of the results can be interpreted on the basis that the initial reaction involves the degradation of X to phenylisothiocyanate and hydrazoic acid:

$$\mathrm{X(R} = \phi) + \mathrm{OH^-} \longrightarrow \phi\mathrm{NCS} + \mathrm{N_3^-} + \mathrm{H_2O},$$

followed by the basic hydrolysis of the phenylisothiocyanate:

$$\phi\mathrm{NCS} + \mathrm{H_2O} + 2\mathrm{OH^-} \longrightarrow \phi\mathrm{NH_2} + \mathrm{SH^-} + \mathrm{HCO_3^-}.$$

In the presence of one mole proportion of sodium hydroxide, the hydrolysis of the phenylisothiocyanate is somewhat retarded owing to the consumption of the base by the formation of the azide ion. That alkaline hydrolysis does occur is evidenced by the formation of 1,3-diphenyl-2-thiourea, XII:

$$\phi\mathrm{NCS} + \phi\mathrm{NH_2} \longrightarrow \underset{\mathrm{XII}}{\phi\mathrm{NHC(:S)NH}\phi}$$

found in both the residue and the steam distillate.[10] In the presence of a large excess of sodium hydroxide, aniline is the only volatile product. This could arise solely from the phenylisothiocyanate or by alkaline hydrolysis of XII:

$$\mathrm{XII} + \mathrm{H_2O} + 2\mathrm{OH^-} \longrightarrow 2\phi\mathrm{NH_2} + \mathrm{HCO_3^-} + \mathrm{HS^-}.$$

In either case, on acidification of the steam distillation residue, the additional volatile products are due to the neutralization of the azide, bicarbonate, and bisulphide ions, the non-volatile residue XI (R = ϕ), of course, arising from the same cause. XI (R = ϕ), isolated from these alkaline steam degradation studies, is identical with the so-called

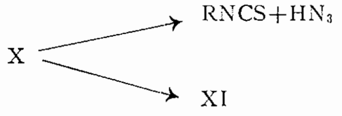
[8] *It is interesting to point out that Freund and Hempel (9) in preparing a large quantity of III (R = ϕ) by digestion with aqueous sodium carbonate, at 50–60°, found 1,3-diphenyl-2-thiourea (reporting a m.p. of (150°) in the residue and indicated that the odor of phenylisothiocyanate was discernible and that at the same time aniline appeared. However, they completely disregarded the significance of these observations.*

[9] *The chemistry of 5-amino-1,2,3,4-thiatriazole will be reported in a separate communication.*

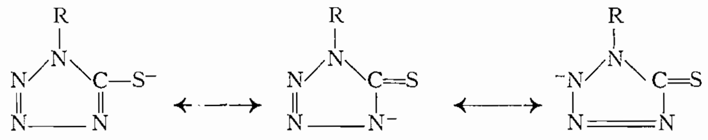
[10] *Independent experiments have shown that the reaction of alkyl- or aryl-isothiocyanates with one to two molar proportions of aqueous sodium hydroxide leads to substantial yields of symmetrical disubstituted thioureas. This work will be reported in a separate communication.*

base-tautomerized II (R = φ) of Freund (9) and to the base-tautomerized phenylisothiocyanate – hydrazoic acid reaction product, IX, of Oliveri-Mandala (20, 21).

The presence of XI (R = φ) in the alkaline steam degradation of X (R = φ) can be accounted for on the basis that two competitive reactions are taking place:



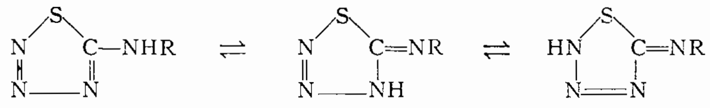
and that the driving force leading to XI depends on the stabilization afforded by the anion of XI in the alkaline medium, XIII and XIV (R = aryl):


XIII XIV

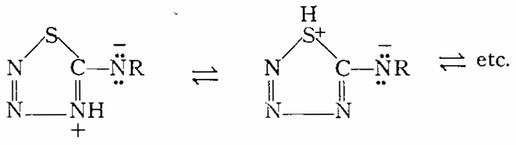
This was demonstrated by the fact that when the 1-phenyltetrazole-5-thiol (XI, R = φ), recovered from the initial alkaline steam degradation, was resubmitted to steam distillation in the presence of a large excess of sodium hydroxide, it was recovered quantitatively unchanged and no volatile product of any type was detectable in the steam distillate. These facts lead immediately to the conclusion that the initial diazotization products of 4-arylthiosemicarbazides cannot possess the tetrazole ring structure as demanded by the structural assignment II (R = aryl) of Freund (9) since its anion, XIV, is identical with the anion of III (R = aryl) and should exhibit the same stability in alkaline medium.

The conclusion that both the initial diazotization products of 4-substituted-thiosemicarbazides and the isothiocyanate – hydrazoic acid reaction products are 5-(substituted)-amino-1,2,3,4-thiatriazoles (structure X) clarifies many of the observations recorded in the literature and in this communication. Some of these points will now be considered.

While structure X can now be assigned to the initial diazotization products of 4-substituted-thiosemicarbazides, the high melting points and crystalline character can best be explained by assuming that X may not exist only as a tautomeric mixture of two or more forms:

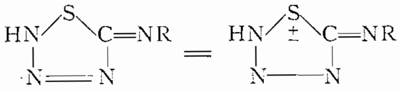


but more probably in zwitterion form:



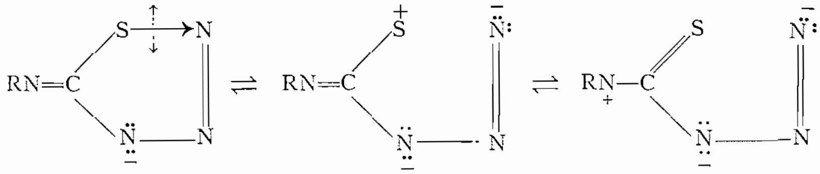
In view of the large number of such charged structures which can be written for

5-(substituted)amino-1,2,3,4-thiatriazoles, it is not inappropriate to consider a mesoionic structure (1):



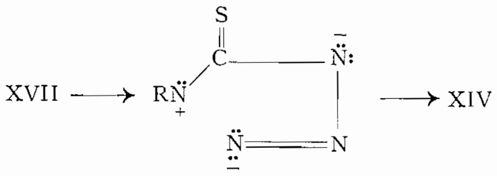
as a possibility.[11]

The basic degradation of the 5-(substituted)amino-1,2,3,4-thiatriazoles can readily be accounted for on the basis that the anion produced, XV, undergoes heterolytic cleavage to XVI. The positive (+) charge resulting from this ring opening can then be distributed between the sulphur and nitrogen atoms, as in XVI and XVII, the contribution of each of these high energy forms being dependent on the electrical character of the substituent R:



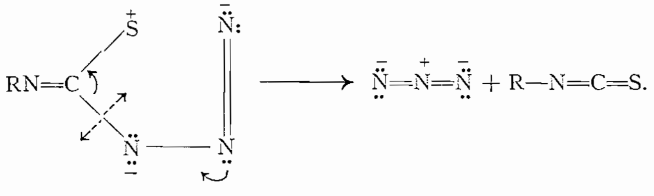
XV XVI XVII

This is due to the fact that it would be more natural for the positive (+) charge to reside on the sulphur atom rather than on the nitrogen atom because of the greater electronegativity of the nitrogen over sulphur. However, if the electron density of the 5-amino nitrogen atom is decreased by the electron-withdrawing ability of the substituent R, the structure XVII should make a marked contribution to the ground state of the anion, XV. Structure XVII has exactly the charge distribution needed for the formation of the tetrazole ring, which is readily accomplished by the rotation of the azido-group about the carbon atom to produce structure XVIII:



XVIII

which on ring closure produces the anion of the 1-(substituted)-5-thiatetrazolone, structure XIV being equivalent to structure XIII. On the other hand, the anion structure XVI can readily stabilize itself by the ejection of the more stable azido ion in the following manner:



XVI

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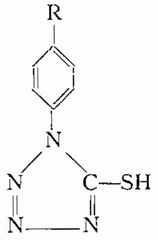
[11] *Spectral, absorption studies in the U.V. region are in progress. Surprisingly, 5-amino-1,2,3,4-thiatriazole shows a very strong absorption maximum at 267 mμ, while the introduction of a* CH_3^- *in the 5-amino position causes a marked bathochromic shift. Similar evidence (15) has been used to show the mesoionic character of 2-methyl-5-alkylaminotetrazoles, which has been also verified by X-ray crystal structure analysis (4).*

These considerations lead to the prediction that the tetrazole formation will be favored if R is electronegative, whereas isothiocyanate and azido ion formation will be favored if R is electropositive. This theory is approximately confirmed by the yields of 1-(substituted)-tetrazole-5-thiols summarized in Table III. Note that when R is alkyl or the phenoxide ion, the formation of tetrazole is excluded and that as the electronegativity of R increases there is an approximate trend of increasing tetrazole formation. This is brought out more clearly by a comparison of the following parasubstituted R substituents:

XVIII R	% Yield of 1-R-tetrazole-5-thiol
(4) $^{-}OC_6H_4$	None
4-$CH_3OC_6H_4$	24
4-$CH_3C_6H_4$	30
4-HC_6H_4	34
4-ClC_6H_4	37

In spite of the complexity of the reactions taking place in alkaline medium, the correlation is reasonably good.

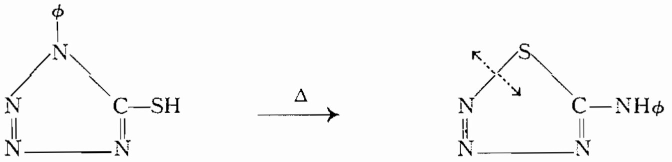
Freund and Hempel (9) on the basis of qualitative observations reported that 1-phenyltetrazole-5-thiol, III (R = ϕ), possessed strong acidic properties and attributed this to the mercapto-group. The present investigation has confirmed this quantitatively by potentiometric titration of a series of 1-(substituted)phenyltetrazole-5-thiols with the following results:



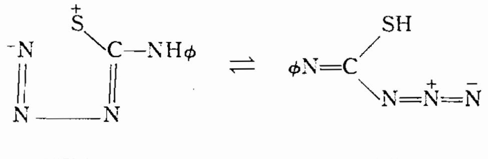
R = CH_3O pK_a = 3.4
H 3.4
Cl 3.3

The lack of response in acidity to the inductive effect of the R substituent is surprising in view of the fact that Schwarzenback and Egli (24) found a marked effect of groups on the dissociation of metasubstituted phenylthiols.

The unexpected thermal instability of 1-phenyltetrazole-5-thiol should be noted in view of the marked stability that has previously been reported (2) for the tetrazole ring system. So violent is the degradation at the melting point of the substance that it must be moderated by initially mixing the substance with sand before it can be studied quantitatively. One mole proportion of pure nitrogen is evolved and sulphur is precipitated. The violence of the thermal decomposition suggests the hypothesis that isomerization to the thiatriazole takes place at the melting point:



followed by a heterolytic bond breaking to produce structure XIX:



XIX XX

which is equivalent to phenylthiocarbamyl azide, XX. The presence of the thiol- and azido-groups then leads, at the temperature involved, to an explosive internal oxidation–reduction involving these two groups, producing nitrogen and sulphur. It is possible that this rapid internal oxidation–reduction may take place before isomerization to the thiatriazole ring has taken place. This is comparable to the relatively easy external reduction of the azido-group by hydrogen sulphide (14, 18, 26), the products being the same. A general investigation of the thermal behavior of 1-substituted-tetrazole-5-thiols is in progress.

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