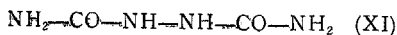
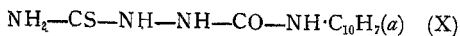
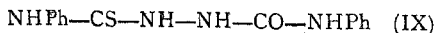
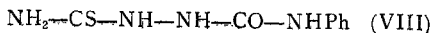
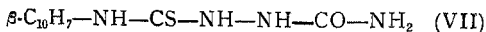
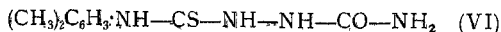
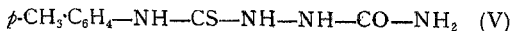
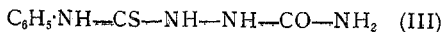
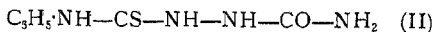
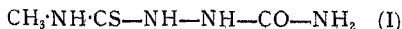


II.—RING CLOSURE OF HYDRAZO-MONOTHIODICARBONAMIDES WITH ACETIC ANHYDRIDE: FORMATION OF IMINOTHIOLIAZOLONES AND IMINOTHIOLTRIAZOLES.¹

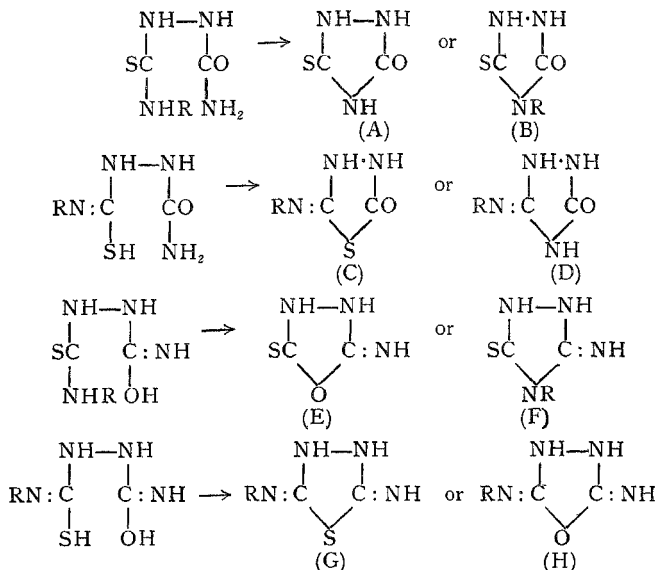
By Praphulla Chandra Guha and Tarani Kanta Chakraborty.

The ring-closing action of acetic anhydride upon hydrazo-dithiocarbamide and its substituted derivatives has been studied by one of us (Guha, *J. Amer. Chem. Soc.*, 1923, **45**, 1036) where it has been shown that the reaction takes place with elimination of sulphuretted hydrogen yielding 2 : 5-diamino-1 : 3 : 4-thiadiazoles. In the present paper, the ring-closure of the following substituted hydrazodicarbonylamides with acetic anhydride has been studied of which I-VII are substituted in the thiocarbonylamide group, VIII and X are substituted in the carbonylamide group, IX is substituted both ways and XI is an unsubstituted dicarbonylamide.



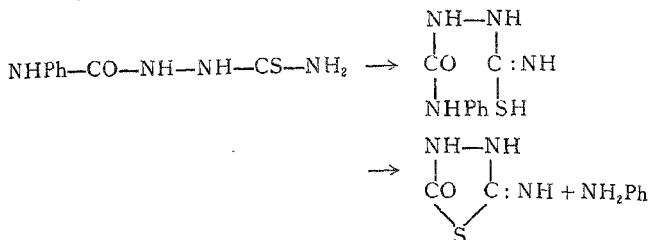
¹ Reprinted from the *Journal of the Indian Chemical Society*, 1929, 6, 99.

Monosubstituted hydrazo-monothiodicarbonamides of the type $\text{NHR}-\text{CS}-\text{NH}-\text{NH}-\text{CO}-\text{NH}_2$ might react in the following four different ways to yield one or more cycloids of the type A to H.

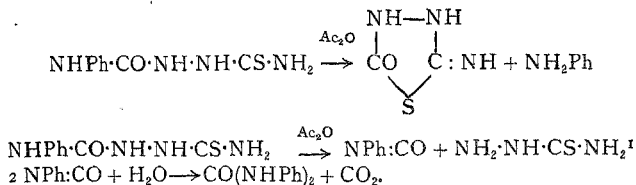


But the compounds actually isolated correspond to the general formula $\text{C}_2\text{H}_2\text{RON}_3\text{S}$ and so cannot possess the structure represented by formulae A, D, E, F, G or H, F and G being free from oxygen, D and H being free from sulphur, A and E being free from the group R. So the formula must be B or C, and as the compounds are not mercaptans only C meets all the points. The acetyl derivatives of the substituted iminothiobiazolones are invariably obtained from the hydrazides I-VI which on deacetylation give the free R-iminothiobiazolones. Besides the formation of the acetyl-R-iminothiobiazolones, indication is given as to the formation of other products and the actual isolation of more than one has been possible with the hydrazides II, III and V. It is worth mentioning that one product from the hydrazide V happens to be an iminothioltriazole of type F. The hydrazide VII is completely decomposed with the regeneration of β -naphthyl *is*othiocyanate almost in a quantitative yield,

The hydrazide VIII under mild treatment gives mono- and diacetyl derivatives of iminothiobiazolone. The ring closure is evidently effected with elimination of aniline, thus :—

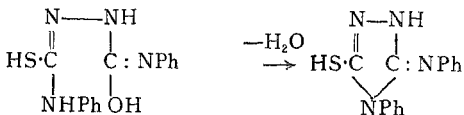


When boiled with acetic anhydride over a free flame, the hydrazide is decomposed yielding diphenylurea, acetanilide, a trace of mono-acetyliminothiobiazolone and two compounds melting at 92–93° and 115° respectively. The formation of acetyliminothiobiazolone, diphenylurea and acetanilide can be explained thus :—



The formation of unsubstituted iminothiobiazolone in the present instance and of substituted iminothiobiazolones with the hydrazides containing substituted thiocarbamide groupings is significant.

The behaviour of the *sym*-disubstituted hydrazide, NPh·CS·NH·NH·CO·NPh appears to be peculiar, as instead of yielding the expected iminothiobiazolone derivatives, it gives 1-*N*-phenyl-2-phenylimino-5-thiol-dihydro-1 : 3 : 4-triazole, thus :—



¹ The analytical values of the compound, m.p. 92–93°, agree fairly well with those of diacetyl thiosemicarbazide (Calc. N, 24.28; S, 18.5. Found: N, 24.70; S, 18.67 per cent.).

When boiled with acetic anhydride, the hydrazide yields diphenyl-urea as the main product. The hydrazide IX, like VII, is easily decomposed and the α -naphthyl *isocyanate* so formed reacts readily with water to give di- α -naphthylcarbamide.

Hydrazodicarbonamide (XI) is unaffected even when boiled with acetic anhydride for several days, but when the mixture is heated in a sealed tube at 200° is decomposed into various products amongst which carbon dioxide and *sym*-diacetylhydrazine have been identified.

EXPERIMENTAL.

Hydrazodicarbo-monothiomethylamide (I).

Semicarbazide hydrochloride (5.6 g.) was dissolved in the least quantity of water and sodium carbonate (2.7 g.) added. Molecular proportion of methyl mustard oil dissolved in the least quantity of alcohol was added and the mixture was warmed. Within a minute or two the hydrazide separated, and was crystallised from alcohol, melting at 212° ; the yield was quantitative (Found: N, 37.62. $C_3H_8ON_4S$ requires N, 37.84 per cent.).

2-Methylimino-4-acetyl-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole.

The above hydrazide (5 g.) was heated with a slight excess of acetic anhydride, the hot clear solution poured into 100–120 c. c. of cold water and the aqueous solution boiled for some time when an oily product separated which, however, solidified after 24 hours. It was filtered, washed with ether and crystallised from alcohol. It is very slightly soluble in water and in acid; alkali decomposes it producing a faint smell of *isocyanide*; m.p. 197° , yield 1.5 gms. (Found: N, 24.02. $C_5H_7O_2N_3S$ requires N, 24.3 per cent.).

Hydrolysis to the thiodiazole.—Two grams of the above acetate were boiled with strong hydrochloric acid for about three minutes, becoming dissolved and on evaporation yielding the free basic thiodiazole. It was filtered and further purified by crystallisation from water, m.p. 232° (Found: N, 31.57. $C_3H_5N_3OS$ requires N, 32.06 per cent.).

Hydrazomonothioallyldicarbonamide (II).

Semicarbazide hydrochloride (5 g.) was dissolved in water, treated with anhydrous sodium carbonate (2.4 g.) and boiled on a water-bath with an alcoholic solution of allyl mustard oil (4.5 g.) for five minutes

when crystals of the hydrazide began to separate as shining plates. The reaction was complete within ten minutes. The hydrazide was purified by crystallisation from alcohol; m.p. 202° (Found; N, 32.52. $C_5H_{10}ON_4S$ requires N, 32.18 per cent.).

2-Allylimino-3-acetyl-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole.

A few grams of the hydrazide were just covered with acetic anhydride and heated under reflux over a small free flame until a clear solution was obtained. On pouring the solution into water, an oil separated which solidified on keeping under water for a few days. The yield of the solid was very small and the presence of a considerable quantity of mustard oil was detected, showing that the major portion of the hydrazide had undergone decomposition. The solid was washed with ether and crystallised from alcohol; m.p. 137° . The yield was so small that no further investigation of the substance was possible.

The experiment was repeated by heating the hydrazide with acetic anhydride on a water-bath instead of over a free flame; the resulting oil soon solidified yielding a much greater quantity of the substance. It was washed with ether, and on attempting crystallisation from rectified spirit was found to be a mixture of two substances. The solid was dissolved by heating with 60 per cent. alcohol and filtered while hot. The filtrate yielded on cooling a crystalline substance, representing about 90 per cent. It was again crystallised from rectified spirit; m.p. 171° (Found: N, 21.33; S, 15.65. The monoacetyl compound, $C_7H_9O_2N_3S$ requires N, 21.11; S, 16.08 per cent.).

The substance dissolves in cold dilute alkali but is not acted on by oxidising agents such as iodine solution or hydrogen peroxide. It was deacetylated by heating with moderately strong hydrochloric acid when it dissolved, yielding on concentration crystals of the free thiodiazole; m.p. 210° (Found: N, 26.83. $C_5H_7ON_3S$ requires N, 26.75 per cent.).

The mother-liquor was concentrated on a water-bath to very small bulk, filtered and allowed to cool when a white crystalline substance separated, m.p. 269° , and sparingly soluble in cold alkali, but more in hot, giving the smell of isocyanide. The yield was only 0.05 g. and so it could not be analysed.

Hydrazomonothiophenyldicarbonamide (III) and acetic anhydride. Formation of 2-Phenylimino-3-acetyl-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole and 2-Phenylimino-3:4-diacetyl-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole.

The hydrazide, $NH_2 \cdot CO \cdot NH \cdot NH \cdot CS \cdot NHPh$, prepared according to the method of Arndt, Milde and Tschenscher (*Ber.*, 1922, 55, 349)

was heated over a small flame with acetic anhydride sufficient to cover it, in presence of a little well powdered fused sodium acetate. The clear solution thus obtained was poured into water when an oil with a strong smell of phenyl mustard oil separated and solidified on keeping under water for a few days. The yellow solid was washed successively with rectified spirit and ether, dissolved in boiling dilute alcohol, the solution filtered and the filtrate allowed to stand for some time while a good quantity of crystals separated. They were filtered, and the mother-liquor on concentration gave another crop of crystals of different shape and appearance from the former. The two portions were separately collected and gave different and fairly sharp melting points ($210-211^\circ$) and ($171-172^\circ$) respectively. After recrystallisation from dilute alcohol, the first portion melted at 213° and was the diacetyl compound (Found: N, 15.47. $C_{12}H_{11}O_3N_3S$ requires N, 15 per cent.). The second portion melted at 173° and was the monoacetyl compound (Found: N, 18.01. $C_{10}H_9O_2N_3S$ requires N, 17.95 per cent.).

2-Phenylimino-5-ketotetrahydro-1:3:4-thiadiazole.

The above acetyl compounds were separately hydrolysed with strong hydrochloric acid. A crystalline white precipitate was slowly produced from each solution on adding water and was crystallised from dilute alcohol, melting at 206° . It slowly dissolves in cold dilute alkali with the development of a pale green colour and the disagreeable smell of isocyanide (Found: N, 21.98. $C_8H_7ON_3S$ requires N, 21.76 per cent.).

The hydrazide was also heated with acetic anhydride in presence of a small quantity of fused sodium acetate on a water-bath instead of over a free flame, with greatly increased yield. Only a small fraction of the hydrazide was acted on during a period of two hours. Only the monoacetyl compound was obtained in this way.

Hydrazomonothio-ortho-tolyldicarbonamide (IV).

Semicarbazide hydrochloride (5 g.) dissolved in the least quantity of water was treated with anhydrous sodium carbonate (2.4 g.) and heated under reflux with *o*-tolyl mustard oil (6.6 g.) for twenty minutes while the hydrazide separated as a white solid. It was crystallised from alcohol; m.p. 201° with decomposition (Found: N, 25.12. $C_9HO_{12}N_4S$ requires N, 25.00 per cent.).

2-O-Tolylimino-3-acetyl-5-keto-2:3:4:5-tetrahydro-1:3:4-thiadiazole.

The above hydrazide was covered with acetic anhydride in presence of a little powdered fused sodium acetate and carefully heated

with a small flame until the reaction commenced, yielding a clear solution which gave an oily product on being poured into water. After 24 hours' standing the solidified oil was washed well with alcohol and ether and crystallised from rectified spirit; m.p. 183° (Found: N, 17.10. $C_{11}H_{11}O_2N_3S$ requires N, 16.87 per cent.).

2-o-Tolylimino-5-ketotetrahydro-1:3:4-thiodiazole.

The above acetyl compound was boiled under reflux with fuming hydrochloric acid but was not dissolved. The solid product was washed with water, dried and crystallised from a large quantity of dilute alcohol; m.p. 210° (Found: N, 20.44. $C_9H_9ON_3S$ requires N, 20.29 per cent.).

Hydrazomonothio-p-tolyldicarbonamide (V).

Semicarbazide hydrochloride (5 g.) dissolved in the least quantity of water was treated with anhydrous sodium carbonate (2.4 g.) and boiled under reflux with *p*-tolyl mustard oil (6.6 g.). After 15 minutes, crystals of the hydrazide began to separate and the reaction came to an end after about half an hour. It was crystallised from alcohol; m.p. 192° (Found: N, 25.32. $C_9H_{12}ON_4S$ requires N, 25.00 per cent.).

Hydrazomonothio-p-tolyldicarbonamide and acetic anhydride. Formation of 2-p-Tolylimino-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole and p-Tolyl-2-imino-5-thiol-3-acetyl-2:3-dihydro-1:3:4-triazole.

The clear solution obtained within a few minutes' heating was poured into cold water and allowed to stand overnight. Next morning the oil was found to have partially solidified with a layer of crystals deposited over it. The white solid that came from the aqueous solution was carefully collected and crystallised from rectified spirit; m.p. 247° . It was 2-*o*-tolylimino-5-keto-2:3:4:5-tetrahydro-1:3:4-thiodiazole, insoluble in alkali and remaining unchanged on being boiled with fuming hydrochloric acid pointing to the fact that there was no acetyl group present (Found: N, 20.61. $C_9H_9ON_3S$ requires N, 20.29 per cent.). The solidified oil was washed carefully with ether and crystallised twice from rectified spirit; m.p. 154° . It readily dissolves in alkali from which acid precipitates it. It is acted on by ferric chloride, hydrogen peroxide and iodine solution. It is 2-*o*-tolylimino-3-acetyl-5-thiol-2:3-dihydro-1:3:4-triazole (Found: N, 21.97; S, 12.83. $C_{11}H_{12}ON_4S$ requires N, 22.58; S, 12.90 per cent.). As the quantity was very small it could not be deacetylated with hydrochloric acid,

Hydrazomonothio-xylyldicarbonamide (VI).

Semicarbazine hydrochloride (5 g.) dissolved in a small quantity of water was treated with anhydrous sodium carbonate (2.4 g.) and boiled under reflux with xylyl mustard oil (7.2 g.) in about 200 c.c. alcohol. Within half an hour the reaction was complete and the separated solid was crystallised from alcohol, m. p. 200° with decomposition (Found: N, 23.81. $C_{10}H_{14}ON_4S$ requires N, 23.53 per cent.).

2-Xylylmino-3-acetyl-5-keto-2 : 3 : 4 : 5-tetrahydro-1 : 3 : 4-thiodiazole.—The hydrazide was treated as usual with fused sodium acetate and acetic anhydride and within two minutes a clear solution was obtained which was poured into water. An oil separated smelling strongly of mustard oil and solidified after 24 hours. It was washed with ether and crystallised from rectified spirit, m. p. 218° (Found: N, 16.00. $C_{12}H_{13}O_2N_3S$ requires N, 15.97 per cent.).

Hydrolysis.—The above acetyl compound was boiled for half an hour under reflux with fuming hydrochloric acid, and the product crystallised from rectified spirit; m.p. 232°. The substance slowly dissolved in cold dilute alkali with a pinkish colour which disappears on boiling but reappears on cooling (Found: N, 18.68. $C_{10}H_{11}ON_3S$ requires N, 19.00 per cent.).

Hydrazo-monothio-β-naphthylldicarbonamide (VII).

β-Naphthyl mustard oil (5 g.) was dissolved in alcohol by warming and to this was added an aqueous solution of semicarbazide hydrochloride (3 g.) treated previously with anhydrous sodium carbonate (1.4 g.). The mixture was then gently boiled under reflux for about 10 minutes and the separated hydrazide after washing with alcohol was crystallised from a large volume of the same solvent; m.p. 210° (decomp.) (Found: N, 21.10. $C_{12}H_{12}ON_4S$ requires N, 21.54 per cent.).

The hydrazide on being heated with acetic anhydride (though extremely carefully) decomposed completely. Among the decomposition products almost the calculated quantity of β-naphthyl mustard oil was isolated and identified.

Hydrazomonothio-phenyldicarbonamide (VIII) and acetic anhydride.

Formation of 2-Imino-3-acetyl-5-keto-2 : 3 : 4 : 5-tetrahydro-1 : 3 : 4-thiodiazole and 2-Imino-3 : 4-diacetyl-5-keto-2 : 3 : 4 : 5-tetrahydro-1 : 3 : 4-thiodiazole.

Hydrazomonothio-phenyldicarbonamide, $NHPh \cdot CO \cdot NH \cdot NH \cdot CS \cdot NH_2$, prepared from phenyl isocyanate and

thiosemicarbazide according to Freund and Schauder (*Ber.*, 1896, 29, 2510) was treated with acetic anhydride in the usual way. The solid obtained from the oil after 24 hours was crystallised from rectified spirit, m.p. 275° (Found: N, 26.52, 26.72; S, 19.90. The monoacetyl compound, $C_4H_5O_2N_3S$ requires N, 26.42; S, 20.13 per cent.).

The solution after the separation of the solidified oil was concentrated to small bulk, and steam passed through it until the solution was almost free from acetic acid. The volume was again considerably reduced by evaporating on a water-bath and crystals came out on cooling; these were recrystallised from a mixture of water and alcohol, m.p. 160° (Found: N, 21.04. The diacetyl compound, $C_9H_7O_4N_3S$ requires N, 20.90 per cent.). The free thiodiazole derivatives could not be prepared by deacetylation with hydrochloric acid for want of sufficient quantity of the acetyl derivatives.

In another experiment the hydrazide was boiled with excess of acetic anhydride for about 10 minutes and the clear solution found to smell of phenyl isocyanate. The reaction mixture on being poured into water gave an oil which solidified on standing, and from which diphenylurea and acetanilide were isolated. The aqueous solution was evaporated to a syrup and kept in a desiccator containing potassium hydroxide under vacuum for two to three days when it was found not to solidify. It was then dissolved in water, steamed until free from acetic acid and evaporated almost to dryness. On cooling a solid separated which was found to be partially soluble in sodium hydroxide solution. This alkaline solution after acidification was evaporated to dryness, extracted with absolute alcohol and the alcoholic extract gave on concentration and cooling a crystalline mass, m.p. 92-93° (Found: N, 24.7; S, 18.67 per cent.).

The alkali insoluble solid on repeated fractional crystallisation from spirit yielded two compounds melting respectively at 115° and 296°. The former on analysis gave C, 42.61; H, 5.01, and the latter gave S, 19.2; N, 26.72 ($C_4H_5O_2N_3S$ requires S, 20.13; N, 26.42) and is evidently identical with acetyl iminothiobiazolone of Guha (*J. Amer. Chem. Soc.*, 1923, 55, 1042).

Hydrazomonothio-sym-diphenyldicarbonamide (IX) and acetic anhydride. Formation of 1-Phenyl-2-phenylimino-5-thiol-2:3-dihydro-1:3:4-triazole.

Hydrazomonothio-sym-diphenyldicarbonamide, was prepared from 4-phenylthiosemicarbazide and phenyl isocyanate. The solidified oil

obtained after the usual treatment was washed with ether and crystallised twice from alcohol. It melted at 208°. The substance was soluble in alkali and unchanged by boiling with strong hydrochloric acid, showing that no acetyl group was present (Found: N, 21.06. $C_{14}H_{12}N_4S$ requires N, 20.90 per cent.). On heating with excess of acetic anhydride for about ten minutes the main product was diphenylurea, m.p. 236° mixed with a small quantity of the alkali soluble substance, m.p. 208°.

Hydrazomonothio- α -naphthylidicarbonamide (X).

Thiosemicarbazide (4 g.) dissolved in the least quantity of boiling water was treated with a few drops of acetic acid; to this was gradually added α -naphthyl isocyanate (7.4 g.) in about 200 c.c. of absolute alcohol. A vigorous reaction took place instantaneously, the hydrazide came out as a white solid and was crystallised from rectified spirit; m.p. 213° (Found: N, 21.68. $C_{12}H_{12}ON_4S$ requires N, 21.54 per cent.).

Hydrazomonothio- α -naphthylidicarbonamide and acetic anhydride.

The hydrazide was covered with acetic anhydride in presence of a little powdered fused sodium acetate and gently heated to boiling for about five minutes; the turbid solution was poured into water through a filter. The separated oil was stirred vigorously for ten minutes with hot water and within an hour or so the oil solidified, being freed from tar by washing successively with acetone, ether and benzene. It was then crystallised twice from boiling pyridine; m.p. 293°. The compound contains no sulphur, is insoluble in acid and alkali and in all solvents excepting boiling pyridine (Found: N, 9.18 per cent.). It is therefore *sym*- α : α' -dinaphthyl urea (Cal. N, 8.97 per cent.).

Hydrazodicarbonamide (XI) and acetic anhydride: Formation of sym-Diacetylhydrazine.

Hydrazodicarbonamide (10 g.) prepared according to the method of Thiele (*Annalen*, 1892, 271, 127) was heated with 30-40 c.c. of pure acetic anhydride in a sealed tube at 200° in an oil-bath for two hours when all dissolved. On opening the tube carbon dioxide escaped under great pressure. The solution was filtered from a small quantity of hydrazodicarbonamide and steam passed for four hours to remove acetic acid. The solution was then evaporated to a brown syrup on the water-bath, dissolved in acetone and boiled under reflux for thirty minutes with animal charcoal. After filtration and concentration,

excess of ether was added to the cold syrup under vigorous stirring when a beautiful crystalline mass separated. It was purified by precipitating again from an acetone solution and finally crystallised from benzene; m.p. 139° (yield, 4 gms.). It was proved to be *sym*-diacetylhydrazine (m.p. 138°) and on being heated with strong hydrochloric acid gave hydrazine dihydrochloride, m.p. 200° .

Our thanks are due to Mr. Sreekumaran Unni Nair for some preliminary work in connection with this paper.

The University, Dacca.
Department of Organic Chemistry,
Indian Institute of Science,
Bangalore.

[Accepted, 30-5-29.]