[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DE PAUL UNIVERSITY]

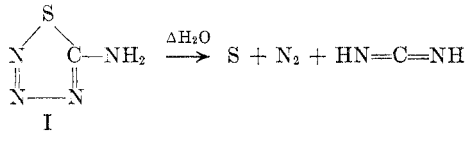
Reaction of 5-Amino-1,2,3,4-Thiatriazole with Benzylamine

EUGENE LIEBER AND C. N. PILLAI

Received April 25, 1957

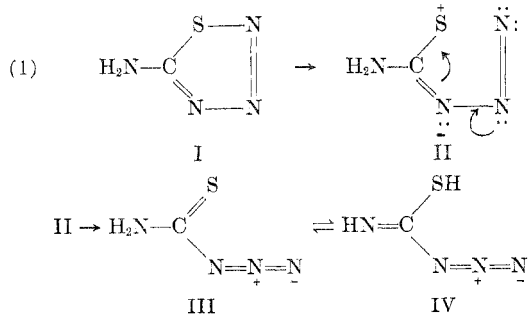
The reaction of 5-amino-1,2,3,4-thiatriazole with benzylamine proceeds by two modes, *viz.*, (*a*) a complete collapse of the ring with the elimination of sulfur, nitrogen, and cyanamid, the latter being isolated as benzylguanidine; and, (*b*) a decomposition to thiocyanic and hydrazoic acids, as evidenced by the isolation of benzylthiourea, *sym*-dibenzylthiourea and benzylammonium azide. The extent of modes (*a*) and (*b*) are dependent on the molar ratio of benzylamine, mode (*a*) predominating at low molar ratios, whereas mode (*b*) increases with increase in the mole ratio of benzylamine used. Mode (*a*) parallels the thermal degradation of 5-amino-1,2,3,4-thiatriazole and is ascribed to an explosive internal oxidation-reduction; whereas mode (*b*) is ascribed to a degradation of the anion of 5-amino-1,2,3,4-thiatriazole in which the azido ion is ejected. These theories are discussed.

One of the marked properties of 5-amino-1,2,3,4-thiatriazole (I) is the remarkable instability of its aqueous solution.[1] On standing at room temperature, even for a short period, the familiar whitish opalescence of colloidal sulfur sets in, the process being much accelerated by warming. One mole proportion of pure nitrogen is liberated along with the precipitation of sulfur and the formation of cyanamid:

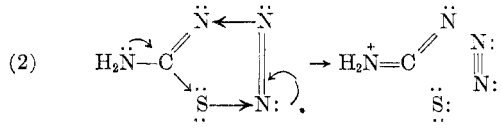


I

The above aqueous degradation is so startingly similar to the external reduction of an organic azide by hydrogen sulfide[2] as to suggest that the reaction proceeds by an internal oxidation-reduction involving the sulfur atom and the three sequentially linked nitrogen atoms of the heterocyclic ring. This can occur in one of two ways; *viz.* (1) a heterolytic bond breaking I to II (III and IV) in which



the internal oxidation-reduction takes place through the *geminal* thiol and azido groups[3] of structures III or IV; and, (2) an intramolecular oxidation-reduction movement of electrons *prior to the disintegration of the ring*, initiated by the movement of the lone pair of electrons of the 5-amino group into the ring followed by the ejection of a sulfur atom, a molecule of nitrogen, and the polarized form of cyanamid.



It should be noted that the thermal decomposition of I from the solid state exactly parallels its decomposition in water, the same products being obtained. Depending on the quantity involved, the thermal degradation of I proceeds more or less explosively. Freund and Schander[1] further showed that the same mode of degradation of I prevails in boiling aniline, the cyanamid being isolated as dicyandiamide. This has been confirmed in the present study.

Freund and Schander[1] observed that I was soluble in excess of aqueous alkali and could be recovered unchanged provided that the neutralization was immediately effected. Under these conditions they qualitatively reported the precipitation of a small quantity of sulfur and an odor of hydrazoic acid. By heating with aqueous alkali Freund and Schander[1] stated that the decomposition of I was more complete, and that on subsequent acidification, sulfur, hydrogen sulfide, and hydrazoic acid were formed. They failed to report the evolution of any gas on the reaction of I with aqueous alkali. We have confirmed these observations with the important exception that *sulfur precipitates prior to neutralization*. While this latter observation points to a similarity in the mode of decomposition in such disparate solvents as water, aqueous alkali, and aniline, the presence of sulfide and azide ions in the aqueous alkali points to a second mode of decomposition:

$$I + OH^- \rightarrow NCS^- + N_3^-$$

(1) M. Freund and A. Schander, *Ber.*, **29**, 2500 (1896).

(2) Hydrogen sulfide reduces guanylazide nitrate to guanidine and nitrogen, sulfur being precipitated, J. Thiele, *Ann.*, **270**, 1 (1892).

(3) A very closely related example is the spontaneous decomposition of azidothiocarbonic acid, $HSC(S)N_3$ to thiocyanic acid, nitrogen, and sulfur [H. E. Williams, *Cyanogen Compounds*, Edward Arnold and Co., London, 1949, page 321]. A reexamination of the structure of azidodithiocarbonates is in progress in this laboratory.

followed by alkaline hydrolysis of the thiocyanate ion to sulfide ion and ammonia. It was the objective of this investigation to explore this latter mode of decomposition by a study of the decomposition of I in benzylamine as solvent.

When a mixture of one mole proportion each of I and benzylamine was warmed on the steam bath a vigorous reaction ensued with copious evolution of nitrogen followed by the precipitation of sulfur in 70% yield and the isolation of benzylguanidine also in 70% yield. As the mole proportion of the benzylamine increased, the violence of the reaction, under the same initial conditions, moderated. This was paralleled by a decrease in the yield of sulfur. The products isolated depended on the method of working up the reaction mixture. Benzylammonium azide, a new compound, was readily isolated by sublimation from the reaction mixture due to the heat of reaction. The yield increased from 27 to 85% as the mole proportion of benzylamine to I increased from 2 to 4. The isolation of benzylammonium azide indicated that the following mode of decomposition was taking place:

$$I \rightarrow HNCS + HN_3$$

and that the reaction products of benzylamine and thiocyanic acid should also be present. Again, the method of recovery determined the type of product isolated. By heating a 1:4 mole mixture of I and benzylamine at the boiling point of benzylamine (185°), the only product isolated was 1,3-dibenzyl-2-thiourea, the benzylammonium azide being lost by thermal decomposition. Under milder conditions of reaction, and the removal of the excess benzylamine by steam distillation, sulfur, benzylthiourea, 1,3-dibenzyl-2-thiourea and benzylammonium azide were all isolated from the reaction mixture. The experimental results show that I undergoes two modes of decomposition:

$$\text{I} \begin{cases} \xrightarrow{(a)} S + N_2 + HN{=}C{=}NH \\ \xrightarrow{(b)} HNCS + HN_3 \end{cases}$$

mode (*a*) being the same as in its thermal decomposition from the solid state, whereas mode (*b*) is initiated under environmental conditions that will create the anion of I (Structure V, Chart I) which then undergoes a heterolytic bond breaking to structure VI, the conjugate base of III or IV. The thiocyanic acid (VII) thus produced reacts with the benzylamine to initially produce the monobenzylated product (VIII) which in turn undergoes reaction with the excess of benzylamine to produce the dibenzylated product (IX). This latter point was demonstrated independently by heating an authentic sample of benzylthiourea (VIII) with benzylamine. The change in the mode of decomposition from (*a*) to (*b*) with increasing molar proportion of benzylamine can be simply accounted for by an increase in the proportion of the anion (V) as a greater quantity of I dissolves in the solvent medium.

EXPERIMENTAL[4,5]

5-Amino-1,2,3,4-thiatriazole (I) was prepared by a modification[6] of the method of Freund and Schander.[1]

Decomposition of I *in water.* The observations reported by Freund and Schander[1] were confirmed. A weighed sample of I gave very nearly one mole proportion of a gas. A mass spectrometric analysis[7] showed the gas to be pure nitrogen.

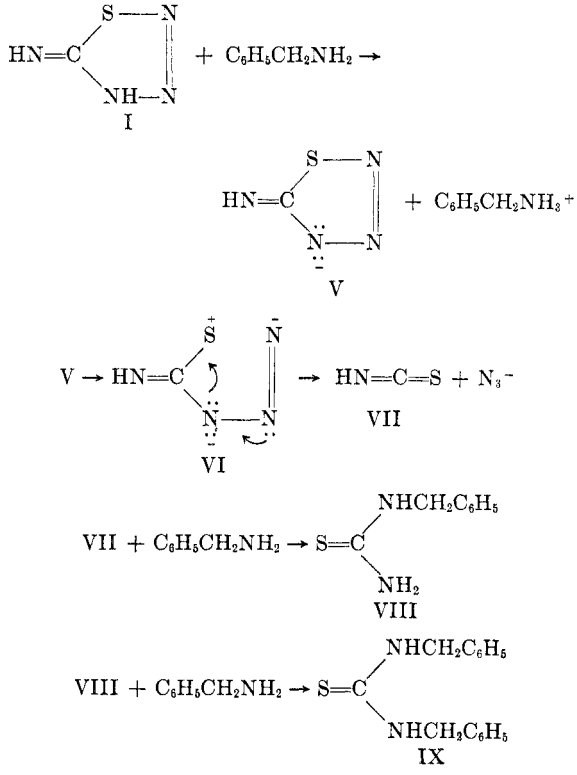


CHART I: Reaction of 5 Amino-1, 2, 3, 4-Thiatriazole in Excess Benzylamine

Reaction of I *with aqueous sodium hydroxide.* On warming I in 4% aqueous sodium hydroxide, sulfur was precipitated without the evolution of a gas. Acidification of the solution resulted in the evolution of hydrogen sulfide and hydrazoic acid, the latter being detected by the blood-red coloration it produces with a solution of ferric chlorides.[8]

Reaction of I *with aniline.* A mixture of 2 g. of I and 5 g. of aniline was boiled until the evolution of gas ceased. The mixture was diluted with 5 ml. of ethanol and the precipitated sulfur removed by filtration. The ethanol was removed by evaporation, whereupon the addition of ether precipitated a white crystalline material, m.p. 209–210°. It was

(4) All melting points are uncorrected.

(5) Microanalyses by Dr. C. Weiler and Dr. F. B. Strauss, Oxford, England.

(6) E. Lieber, E. Oftedahl, C. N. Pillai, and R. D. Hites, *J. Org. Chem.*, **22**, 441 (1957).

(7) Consolidated Engineering Corporation, Pasadena, Calif.

(8) L. M. Dennis and A. W. Browne, *J. Am. Chem. Soc.*, **26**, 577 (1904).

identified as dicyandiamide by mixed melting point technique.

Reaction of I *with benzylamine.* (*a*) *One molar proportion of benzylamine.* A mixture of 1.02 g. (0.01 mole) of I and 1.07 g. (0.01 mole) of benzylamine was heated on a steam bath. A violent reaction, reminiscent of the behavior of I on melting,[3] took place. After 5 min. heating the evolution of gas had practically ceased. The mixture in the flask was mixed with 5 ml. of ethanol and cooled. The yellow precipitate, after filtration and washing with ether, was identified as sulfur, yield 0.24 g. (70%). The mother liquor was evaporated at room temperature to remove the ethanol, and the resulting oil washed thoroughly with ether to remove any unreacted benzylamine. A pale yellow sirup, yield, 1.1 g. (73%), was obtained. The oil was found to be very soluble in water and to yield a strongly basic solution. It could not be induced to crystallize. It was identified as *benzylguanidine* by conversion to the corresponding picrate and nitrate.

Benzylguanidine picrate was obtained by reaction of the pale yellow sirup obtained above with an aqueous solution of picric acid. Recrystallized from ethanol, m.p. 185–186°. This compound has been reported to melt at 185.5[9] and at 190–191°.[10] Accordingly, it was analyzed.

Anal. Calcd. for $C_{14}H_{14}N_6O_7$: C, 44.43; H, 3.73; N, 22.23. Found: C, 44.91; H, 3.93; N, 22.20.

Benzylguanidine nitrate was obtained by reaction of the pale yellow sirup obtained above with an aqueous solution of nitric acid. The nitrate salt on recrystallization from water melted at 151–152°. This compound has been reported to melt at 149–150°[10] and at 165°.[9]

Anal. Calcd. for $C_8H_{12}N_4O_3$: C, 45.25; H, 5.70; N, 26.41. Found: C, 44.96; H, 5.88; N, 26.6.

(*b*) *Two-mole proportion of benzylamine.* A mixture of 5.1 g. (0.05 mole) of I and 10.7 g. (0.1 mole) of benzylamine was warmed on the steam bath. The mixture which contained undissolved I, began to undergo visible reaction almost immediately, as evidenced by vigorous effervescence and frothing, accompanied by the deposition of light glistening crystals in the upper cooler portion of the reaction flask. The evolution of gas was complete in approximately 10 min. The reaction mixture was diluted with 20 ml. of ethanol and cooled. The yellow crystalline sulfur was removed by filtration, yield, 0.5 g. (31%). The filtrate was mixed with enough ether to produce a milky appearance and stored in the refrigerator for several hours. The colorless crystals which had separated were filtered and washed with ether. It was identified as *benzylammonium azide*, yield 2 g. (27%). It was purified by reprecipitation from ethanolic solution with ether, m.p. 156–157°.

Anal. Calcd. for $C_7H_{10}N_4$: C, 55.96; H, 6.71; N, 37.33. Found: C, 56.61; H, 6.84; N, 36.80.

The identification was completed by mixture melting point technique with an authentic specimen of *benzylammonium azide* prepared by distilling hydrazoic acid into an ethanolic solution of benzylamine and precipitating with ether.

Benzylammonium picrate, prepared by double decomposition of *benzylammonium azide* with picric acid solution, was recrystallized from aqueous ethanol, m.p. 194°.

Anal. Calcd. for $C_{13}H_{12}N_4O_7$: N, 16.67. Found: N, 16.30.

(*c*) *Four-mole proportion of benzylamine.* A mixture of 5.1 g. (0.05 mole) of I and 21.4 g. (0.2 mole) of benzylamine was heated on the steam bath. There was a slight, but detectable, effervescence and the solution, which was originally clear, became thick with white crystalline material. The mixture was cooled and diluted with 10 ml. of ether. The glistening platelike crystals weighed 6.4 g. (85%) and were identified as benzylammonium azide. The ether was removed from the filtrate by distillation and the residue steam-distilled in order to remove the excess of benzylamine. The aqueous solution in the distilling flask was filtered to remove about 0.1 g. (about 5%) of sulfur. The filtrate was concentrated by evaporation of the water on a steam bath until a sirupy residue was obtained and cooled. The crystalline precipitate obtained was recrystallized twice from ethanol to yield 3 g. (25%), m.p. 147–148°. It was identified as *1,3-dibenzyl-2-thiourea* by mixed melting point with an authentic specimen.[11]

The mother liquor resulting from the recovery of the 1,3-dibenzyl-2-thiourea was concentrated on the steam bath. A crystalline material was obtained which, on recrystallization from hot water, melted at 161–162°. It was identified as *benzylthiourea*, yield 1 g. (12%), by mixed melting technique with an authentic specimen prepared from benzylisothiocyanate and ammonia.

Direct preparation of 1,3-dibenzyl-2-thiourea from I. A mixture of 1.02 g. (0.01 mole) of I and 4.32 g. (0.04 mole) of benzylamine was heated on the steam bath until evolution of gas had ceased (about 5 min.) and then boiled for 10 min. The thick dark sirup was cooled and diluted with 5 ml. of ether. On cooling in the refrigerator overnight, a quantity of pale yellow crystals had precipitated. Recrystallization from ethanol yielded 0.5 g. (20%) of material, m.p. 147–148°. Mixed melting point with an authentic specimen[11] of 1,3-dibenzyl-2-thiourea gave no depression.

Reaction of benzylthiourea with benzylamine. A mixture of 0.9 g. (0.05 mole) of benzylthiourea (from benzylisothiocyanate and ammonia) and 0.9 g. (0.08 mole) of benzylamine was boiled for 5 min. After cooling, the product was recovered as described above; yield about 0.3 g. (about 20%), m.p. 147–148°; no depression of melting point with an authentic specimen of 1,3-dibenzyl-2-thiourea.

Acknowledgment. The authors gratefully acknowledge the receipt of research grants from the Eli Lilly Company, Indianapolis, Ind., and the Research Corporation, New York, N. Y., which made this study possible.

CHICAGO 14, ILL.

(9) T. L. Davis, and R. C. Elderfield, *J. Am. Chem. Soc.*, **54**, 1499 (1932).

(10) H. King and I. M. Tonkin, *J. Chem. Soc.*, 1063 (1946).

(11) H. G. Underwood, and F. B. Dains, *J. Am. Chem. Soc.*, **57**, 1768 (1935).