THIAZOLES

II. PREPARATION OF ALKYL-2-NITRAMINOTHIAZOLES[1,2]

By Sidney Kasman[3] and Alfred Taurins

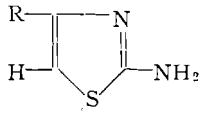
ABSTRACT

1-Chloro-3-methyl-2-butanone and 2-amino-4-*iso*propylthiazole have been synthesized. The mononitration of 2-aminothiazole and five alkyl-2-aminothiazoles in the 2-amino group has been carried out with absolute nitric acid in concentrated sulphuric acid at low temperatures ranging from 0° to −10°. 2-Nitramino- and alkyl-2-nitramino-thiazoles are crystalline, stable compounds. The dinitration of some alkyl-2-aminothiazoles under the same conditions lead to the formation of alkyl-2-nitramino-5-nitrothiazoles. The rearrangement of 2-nitraminothiazole to 2-amino-5-nitrothiazole was studied in the presence of mesitylene for the first time.

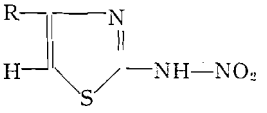
A previous paper (10) of this laboratory described the further nitration of 2-nitramino-5-nitrothiazole with a mixture of 99–100% nitric acid in acetic anhydride. In the same article a summary of previous investigations on the exceptional formation of the dinitration products was given.

The objective of this work was to study the nitration of 2-aminothiazole and several alkyl-2-aminothiazoles under conditions at which the nitration would occur only in the amino group without substituting the hydrogen in the 5-position. The nitrating agent used was absolute nitric acid and the reaction medium was concentrated sulphuric acid. After the completion of this investigation (8) a paper by Dickey, Towne, and Wright (2) appeared dealing partly with the same problem. These authors nitrated 2-aminothiazole in systems containing up to 30% water.

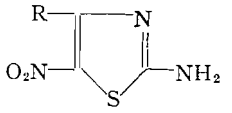
We expected that selective mononitration of the 2-amino group would be favored by the use of a limited quantity of nitric acid, by short reaction time, and by low reaction temperature. The addition of nitric acid to the 2-aminothiazole (I), instead of the reverse, should also foster mononitration through the absence of an excess of nitric acid. It was soon found that one or two excess equivalents of nitric acid were not harmful and increased the yields, that reaction times of the order of a few minutes to an hour were satisfactory, and that the critical factor was the reaction temperature. The working region was found to lie between −10° and 0°.



I: R = H
IV: R = CH_3
VII: R = C_2H_5
X: R = *i*-C_3H_7



II: R = H
V: R = CH_3
VIII: R = C_2H_5
XI: R = *i*-C_3H_7



III: R = H
VI: R = CH_3
IX: R = C_2H_5
XII: R = *i*-C_3H_7

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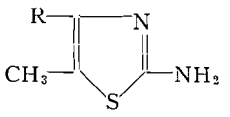
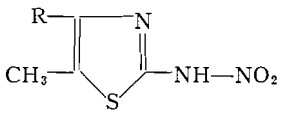
[2]*Part I of this series by S. J. Viron and A. Taurins, Can. J. Chem. 31: 885. 1953.*

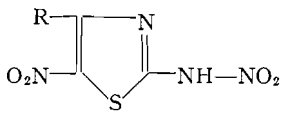
[3]*Holder of a Canadian Industries (1954) Limited Scholarship, 1953–1954.*



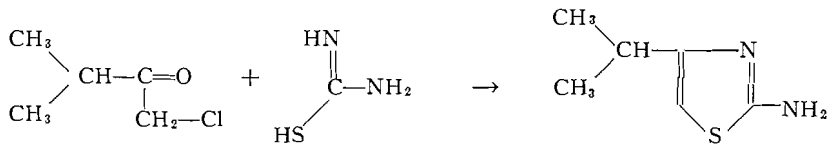
XIII: R = H
XV: R = CH_3



XIV: R = H
XVI: R = CH_3



XVII: R = CH_3
XVIII: R = i-C_3H_7



XIX X

Solutions obtained in this way by the nitration of 2-aminothiazole were invariably found to precipitate a product when poured onto ice. After purification, it was demonstrated to be 2-nitraminothiazole (II) unnitrated in the ring. The 2-nitraminothiazole was found to be a nearly white crystalline solid, acidic to litmus, slightly soluble in water, and quite soluble in dilute sodium hydroxide solution, from which it precipitated on acidification. It gave a positive Franchimont test (5) and deflagrated or exploded when heated to the melting point. The 2-nitraminothiazole was always accompanied by a small amount of 2-amino-5-nitrothiazole (III). This coproduct was precipitated from the acid filtrate by treatment with excess alkali.

The method described for the preparation of 2-nitraminothiazole was found to be applicable to a number of alkyl-substituted thiazoles. At first, 2-amino-4-methylthiazole (IV) (3) was mononitrated to 4-methyl-2-nitraminothiazole (V) in cold sulphuric acid using one equivalent of nitric acid. The reaction was quenched after 15 min. to obtain 56% yield of (V) and 40% of 2-amino-4-methyl-5-nitrothiazole (VI). Lower reaction temperatures favored the formation of the nitramine (V), while higher temperatures favored the formation of the 5-nitro compound (VI).

The next homologous compound, 2-amino-4-ethylthiazole (VII) (9), was nitrated by the same method for 15 min. The unreacted nitric acid was destroyed with absolute alcohol and the reaction was quenched on ice. The yield of 4-ethyl-2-nitraminothiazole (VIII) was 42%, and of 2-amino-4-ethyl-5-nitrothiazole (IX), 4.8%. In another experiment the reaction mixture was stirred for one hour before quenching the reaction. No nitramine could then be isolated, but a 68% yield of (IX) was obtained. These two nitration experiments demonstrated the rearrangement of the nitramine (VIII) into amino-nitro compound (IX), and its importance in the formation of 2-amino-5-nitrothiazoles.

We synthesized for the first time 2-amino-4-*iso*propylthiazole (X) by condensing 1-chloro-3-methyl-2-butanone with thiourea. The 1-chloro-3-methyl-2-butanone (XIX) was prepared in 38% yield by the action of diazomethane on 2-methylpropionyl chloride, followed by treatment with dry hydrogen

chloride. Mononitration of 2-amino-4-*iso*propylthiazole (X) in cold sulphuric acid gave a 37% yield of pure 4-*iso*propyl-2-nitraminothiazole (XI) and a 32% yield of 2-amino-4-*iso*propyl-5-nitrothiazole (XII).

As an example of a 2-amino-5-alkylthiazole, 2-amino-5-methylthiazole (XIII) gave on nitration, at best, a 22% yield of 5-methyl-2-nitraminothiazole (XIV) when the unreacted nitric acid was destroyed with alcohol. The mononitration of 2-amino-4,5-dimethylthiazole (XV) (4, 7) tended to give gummy products, but a small amount of 4,5-dimethyl-2-nitraminothiazole (XVI) was isolated.

Dinitration

The dinitration of two 2-amino-4-alkylthiazoles was carried out in concentrated sulphuric acid at low temperature using 2.2 to 2.4 equivalents of absolute nitric acid. The nitration of 2-amino-4-methylthiazole (IV) gave a 41% yield of pure 4-methyl-2-nitramino-5-nitrothiazole (XVII) and a 34% yield of 2-amino-4-methyl-5-nitrothiazole (VI). Under similar conditions 2-amino-4-*iso*propylthiazole (X) gave 2-nitramino-5-nitro-4-*iso*propylthiazole (XVIII) (45% yield), which was accompanied by a 13% yield of 2-amino-4-*iso*propyl-5-nitrothiazole (XII).

Rates of Nitration

In order to compare qualitatively the rates of nitration of the 2-amino group and hydrogen atom in the 5-position, a sample of 2-aminothiazole was nitrated at −5° and aliquots of the cold reaction mixture were withdrawn 7 and 67 min. after the addition of nitric acid was completed. After removal, these two aliquots were promptly quenched on ice. The precipitated 2-nitraminothiazole (II) was filtered off and crystallized from 95% ethanol. The yields were corrected for solubility in cold 95% ethanol (0.55 gm./100 ml.). The acid filtrates were rendered alkaline and the precipitated 2-amino-5-nitrothiazole (III) was crystallized from 95% ethanol. The results are listed in Table I.

TABLE I

Aliquot	Yield of 2-nitraminothiazole(II)	Yield of 2-amino-5-nitrothiazole (III)
1	1.95 gm.; 37.4%	0.16 gm.; 3.1%
2	1.72 gm.; 33.0%	0.16 gm.; 3.1%
3	None	2.14 gm.; 52.7%

This experiment shows that at −5° the rate of formation of 2-nitraminothiazole is quite high and involves an equilibrium reaction. Under the same conditions the process which forms 2-amino-5-nitrothiazole does not proceed at a significant rate. The small initial yield of 2-amino-5-nitrothiazole must have been formed under conditions peculiar to the beginning of the reaction. Otherwise the yield of (III) would be expected to increase markedly in one hour over the 3% found after only seven minutes, since nuclear nitro groups are introduced in an irreversible reaction. Local heating was unavoidably

produced during the dropwise addition of nitric acid solution to the reaction mixture. It was probably due to the exothermic nature of the nitration reaction and to the heat of dilution of nitric acid in sulphuric acid.

In another nitration, two equivalents of nitric acid were used, and 6.4% of 2-amino-5-nitrothiazole was isolated, supporting the view that transient high temperatures were responsible for the initial formation of this nitration product.

The residual solution, the third aliquot of the first batch, was warmed gently. Its temperature rose suddenly to 140° and then dropped rapidly. In this process all of the 2-nitraminothiazole, as well as some of the hitherto unreacted 2-aminothiazole, appeared in highly augmented yield (52.7%) of 2-amino-5-nitrothiazole. This result indicates the high activation energy and great temperature dependence of the nuclear nitration reaction.

Another pair of nitration experiments was carried out with 2-amino-4-ethylthiazole (VII) at temperature below 0°, with one equivalent of nitric acid. Five minutes after the nitric acid was added, 42% of 4-ethyl-2-nitraminothiazole (VIII) and 4.8% of 2-amino-4-ethyl-5-nitrothiazole (IX) were isolated. After 65 min. at 0°, only (IX) in 68% yield could be isolated. The +Is effect of the 4-ethyl group has undoubtedly activated the 5-position to nitronium ion attack, as compared with the 5-position of 2-aminothiazole. Nevertheless, the rate of nuclear nitration is still very slow compared with the rate of nitration of the 2-amino group. The final isolation of only 2-amino-4-ethyl-5-nitrothiazole is another example of a slow irreversible nuclear nitration reaction prevailing over a fast reversible nitration reaction of the amino group.

Rearrangement Experiments

The rearrangement of 2-nitraminothiazole to 2-amino-5-nitrothiazole when added to concentrated sulphuric acid was observed to proceed readily. The mechanism of the acid-catalyzed rearrangement of aromatic nitramines has not been extensively investigated, and some uncertainty remains in the interpretation of results. Bradfield and Orton (1) measured photometrically the rate of isomerization of 2-bromo-4-methyl-1-nitraminobenzene to 6-amino-2-bromo-4-methylnitrobenzene. Hughes and Jones (6) studied the rearrangement of nitraminobenzene in acidic medium in the presence of a foreign substance which can be easily nitrated. They added 1,4-dimethylbenzene, phenol, or dimethylaniline, which were nitrated by the rearranging nitramine. They found that the compounds mentioned above gave complicated nitration mixtures when used as the foreign substance.

We made a search for a compound which could be easily nitrated to yield only one mononitration product which would be steam-volatile for easy separation and solid for easy purification. We found that 1,3,5-trimethylbenzene (mesitylene) satisfied these criteria. To ensure the formation of only mononitromesitylene, *two* molar equivalents of mesitylene were suspended in stirred concentrated sulphuric acid at 0° and one molar equivalent of 2-nitraminothiazole was added in portions. From the diluted reaction mixture, an oily solid was separated by steam distillation. The solid was filtered from the oil which was reduced with tin and hydrochloric acid and acetylated with

acetic anhydride. When it had been purified, the original solid proved, surprisingly, to be 2,4-dinitro-1,3,5-trimethylbenzene.

Since mesitylene was present in excess during the rearrangement and since a nitro group tends to deactivate an aromatic ring, it is difficult to account for the exclusive formation of dinitromesitylene. If nitromesitylene is much more soluble in sulphuric acid than mesitylene, it is understandable that the homogeneous reagent reacts more quickly than the heterogeneous one.

The nitration of added mesitylene leaves little doubt that in the rearrangement of 2-nitraminothiazole, an intermolecular mechanism is important.

EXPERIMENTAL

2-Nitraminothiazole (II)

(*a*) To 30 ml. of concentrated sulphuric acid was added 21.0 gm. (0.21 mole) of 2-aminothiazole (I) in portions, while stirring and cooling. The temperature was kept below 0° by intermittent cooling with a dry ice – alcohol bath. About 15 ml. of concentrated sulphuric acid was cooled to −30° and 9.2 ml. (13.9 gm., 0.22 mole) of absolute nitric acid was added to it. The mixture was stirred as it warmed up and became fluid. The mixed acid solution was added dropwise to the stirred amine sulphate mixture during 15 min. The reaction temperature was maintained at 0±3°. The solution was then stirred for 55 min. at 2–3° and poured onto 65 gm. of chipped ice. The resulting creamy precipitate was filtered off under suction and crystallized immediately from 300 ml. of 95% alcohol. The crystals were in the form of needles. The pure crystalline 2-nitraminothiazole (II) exploded at 204.7°. The yield was 7.2 gm. (23.7%).

A 0.1478 gm. sample of (II) required 10.95 ml. of 0.0926 *N* sodium hydroxide solution for neutralization. Equiv. wt. Calc. for $C_3H_3O_2N_3S$: 145.1. Found: 145.7. Anal. Calc. for $C_3H_3O_2N_3S$: C, 24.82; H, 2.08%. Found: C, 25.11; H, 2.29%.

(*b*) In another preparation, 5.00 gm. (0.05 mole) of (I) in sulphuric acid was nitrated with 4.17 ml. (6.30 gm., 0.10 mole) of nitric acid in sulphuric acid. The mixed acid was added during 55 min. while the reaction temperature was kept below 0°. After the nitric acid was added, stirring and cooling was continued for two min. and then 5 ml. of methanol was run in during eight minutes, while the temperature was kept below 0°. Stirring was continued for another two minutes and the reaction mixture was poured onto 25 gm. of chipped ice. The precipitated nitramine (II) was filtered off, boiled with 120 ml. of water and some active charcoal, and gravity filtered while hot. This yielded 3.21 gm. of pure dried product (44.3%), m.p. 204.7°. Rendered just alkaline with concentrated ammonia, the diluted sulphuric acid filtrate precipitated 0.56 gm. of 2-amino-5-nitrothiazole (III), which after crystallization from alcohol melted at 195°.

4-Methyl-2-nitraminothiazole (V)

To a stirred mixture of 11.4 gm. (0.10 mole) 2-amino-4-methylthiazole (IV) in 15 ml. of sulphuric acid cooled to −8° was added 4.35 ml. (6.61 gm., 0.105 mole) of nitric acid in 7 ml. of sulphuric acid during 50 min. The reaction mixture was then stirred five minutes at 5° and poured onto 35 gm. of chipped

ice. The resulting sludgy precipitate was extracted with 150 ml. of boiling 95% alcohol and filtered while hot. The filtrate was reboiled with charcoal and filtered to give a deep red filtrate. The resulting matted needles were filtered off and the filtrate was reboiled and passed through the sludge again. A second crop of needles was obtained on cooling. The filtrate was reduced to 60 ml., cooled in ice, and diluted with 25 ml. of water. A third crop was obtained. The combined nitramine product weighed 8.96 gm. (56.4%) when dry. Crystallized from 10% acetic acid, 4-methyl-2-nitraminothiazole (V) melted at 190° with decomposition. Anal. Calc. for $C_4H_5O_2N_3S$: C, 30.18; H, 3.14%. Found: C, 30.27; H, 3.29%.

The dilute sulphuric acid filtrate yielded 6.32 gm. (39.8%) of 2-amino-4-methyl-5-nitrothiazole (VI). After two crystallizations from 50% alcohol, it melted at 218–219° with decomposition.

4-Ethyl-2-nitraminothiazole (VIII)

A solution of 0.83 ml. (1.26 gm.; 0.02 mole) nitric acid in 1 ml. of sulphuric acid was added to a stirred solution of 2.56 gm. of 2-amino-4-ethylthiazole (VII) in 5 ml. of sulphuric acid at −5° during five minutes. The mixture was stirred for five minutes below 0° and then poured onto 18 gm. of chipped ice. The precipitate of nitramine was crystallized from 150 ml. of 7% acetic acid to yield 1.46 gm. (42.1%) of pure 4-ethyl-2-nitraminothiazole (VIII), melting at 190° with decomposition. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.61; H, 3.96%.

The sulphuric acid filtrate was made alkaline with concentrated ammonia. The precipitate was filtered off and dried to obtain 0.27 gm. (4.8%) of 2-amino-4-ethyl-5-nitrothiazole (IX). After two crystallizations from 50% alcohol it melted at 197.5° with decomposition. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.83; H, 3.98%.

2-Methylpropionyl Chloride

A solution of 106 gm. (1.20 moles) of *iso*butyric acid and 161 gm. (1.35 moles) of thionyl chloride was heated under reflux for one hour and then slowly distilled. The product collected between 86° and 92° weighed about 150 gm. and was obviously contaminated with thionyl chloride. The product was refluxed for two hours with 15 gm. (0.12 mole) of benzoic acid and distilled. The procedure was carried out two more times, finally yielding 90.3 gm. (70.5%) of 2-methylpropionyl chloride, boiling at 92–94°.

1-Chloro-3-methyl-2-butanone (XIX)

Diazomethane was generated in the usual way from 100 gm. (0.97 mole) of nitrosomethylurea and dried over potassium hydroxide pellets. The solution was cooled with ice and stirred while 2-methylpropionyl chloride was added dropwise. The solution was allowed to stand for one hour at 5°. Dry hydrogen chloride was then bubbled through the solution for one hour and the ether was distilled off. The residual oil was distilled over at about 60 mm. pressure and then fractionally distilled at atmospheric pressure. The fraction boiling at

149–152° weighed 17.48 gm. (38%). Attempts to prepare the oxime were unsuccessful. The pale yellow liquid had a specific gravity of 1.022 gm./cc. at 28° and a refractive index, n_D^{28} 1.4252. M_D Calc., 30.17. Found, 30.18.

2-Amino-4-isopropylthiazole (*X*)

A mixture of 16.25 gm. (0.135 mole) of 1-chloro-3-methyl-2-butanone, 10.7 gm. (0.140 mole) of thiourea, and 11 ml. of 95% alcohol was warmed under reflux on the steam bath. After a few minutes, a vigorous exothermic reaction occurred. Heating was continued for one hour under reflux and then the condenser was removed to permit alcohol to escape. The residue was made alkaline with concentrated ammonia, diluted with water, filtered to remove an insoluble scum, and extracted with three 35-ml. portions of ether. The extracts were dried over anhydrous magnesium sulphate and distilled to remove ether. The residue was distilled under vacuum to give a readily crystallizing pale yellow oil. Yield 14.88 gm. (77.5%), melting at 48–50°. Picrate: m.p. 216–217° decomp. Anal. Calc. for $C_{12}H_{23}O_7N_5S$: C, 38.83; H, 3.53%. Found: C, 38.96; H, 3.83%.

2-Acetamido-4-isopropylthiazole

A mixture of 1.42 gm. (0.01 mole) of 2-amino-4-*iso*propylthiazole and 3 ml. (3.24 gm., 0.03 mole) of acetic anhydride was warmed briefly on the steam bath to obtain a solution. After it had been left for four hours at room temperature, the solution was poured onto 5 gm. of chipped ice and the resulting white granular precipitate was filtered off and dried. It weighed 1.70 gm. (93.5%). One crystallization from 50% alcohol improved the melting point from 143–144° to 145.8–146.5°. Anal. Calc. for $C_8H_{12}ON_2S$: C, 52.16; H, 6.57%. Found: C, 52.37; H, 6.66%.

4-Isopropyl-2-nitraminothiazole (*XI*)

A solution of 1.45 ml. (2.20 gm., 0.035 mole) of nitric acid and 2 ml. of sulphuric acid was added during 14 min. to a stirred mixture of 4.26 gm. (0.03 mole) of 2-amino-4-isopropylthiazole (X) and 5 ml. of sulphuric acid at −25°. Stirring was continued for 10 min. at −20° and then an excess (2 ml.) of absolute alcohol was cautiously added at −15°. The reaction mixture was rinsed onto 30 gm. of supercooled, chipped ice and the resulting precipitate was filtered off and rinsed with alcohol. It was crystallized from 140 ml. of 50% alcohol to obtain 2.10 gm. (37%) of (XI) in the form of golden needles, melting at 185° with decomposition. Equiv. wt. Calc. for $C_6H_9O_2N_3S$: 187. Found: 184. Anal. Calc. for $C_6H_9O_2N_3S$: C, 38.50; H, 4.85%. Found: C, 38.22; H, 5.07%.

2-Amino-4-isopropyl-5-nitrothiazole (*XII*)

The dilute sulphuric acid filtrate was made alkaline with an excess of concentrated ammonia and the resulting precipitate of (XII) was filtered off and dried. Crude yield: 1.82 gm. (32.4%). After three crystallizations from 50% alcohol, a pure compound, melting at 230–231° with decomposition, was obtained. Anal. Calc. for $C_6H_9O_2N_3S$: C, 38.50; H, 4.85%. Found: C, 38.70; H, 4.80%.

4-Isopropyl-2-nitramino-5-nitrothiazole (XVIII)

A solution of 4.00 ml. (6.04 gm., 0.096 mole) nitric acid in 3 ml. of sulphuric acid was added during seven minutes to a stirred mixture of 5.68 gm. (0.04 mole) 2-amino-4-*iso*propylthiazole (X) in 7 ml. sulphuric acid at −17°. The red solution was stirred for 1.2 hr. while immersed in an ice-water bath, which was then removed. The reaction temperature rose to 30° and was reduced by ice cooling. The mixture was then stirred for 4.7 hr. without cooling. An excess of absolute alcohol was added cautiously and the reaction mixture was poured onto 40 gm. of chipped ice. A gummy substance resulted, which was removed and boiled with 300 ml. water. The hot mixture was filtered and the filtrate was cooled. A yellow crystalline precipitate formed and was filtered off. The filtrate was reboiled with the residue to obtain a second crop of crystalline product. The combined yield was 4.17 gm. (45.0%). One crystallization from 220 ml. of 10% acetic and one crystallization from 300 ml. of 1.2 *N* hydrochloric acid gave product (XVIII), which melted with decomposition at 144°. Equiv. wt. Calc. for $C_6H_8O_4N_4S$: 232.2. Found: 231.2. Anal. Calc. for $C_6H_8O_4N_4S$: C, 31.03; H, 3.47%. Found: C, 31.15; H, 3.52%.

5-Methyl-2-nitraminothiazole (XIV)

To a stirred solution consisting of 4.56 gm. (0.04 mole) of 2-amino-5-methylthiazole (XIII) in 8 ml. of concentrated sulphuric acid cooled below −15°, was added a solution of 1.98 ml. (3.00 gm., 0.0475 mole) nitric acid in 2 ml. sulphuric acid during 10 min. The resulting solution was stirred and maintained below −10°, while 2 ml. of absolute alcohol was cautiously added to destroy unreacted nitric acid. The solution was quickly rinsed onto 30 gm. of chipped ice. The yellow precipitate that formed was filtered off, rinsed free of acids with water, and vacuum dried. The yield of the product melting at 195–196° with decomposition was 1.39 gm. (21.8%). One crystallization from 5% acetic acid improved the melting point to 198–199° with decomposition. The compound (XIV) could be induced to explode at 202° when heated rapidly. Anal. Calc. for $C_4H_5O_2N_3S$: C, 30.18; H, 3.14%. Found: C, 30.35; H, 3.24%.

4,5-Dimethyl-2-nitraminothiazole (XVI)

A solution of 2.56 gm. (0.02 mole) of 2-amino-4,5-dimethylthiazole (XV) in 4 ml. of sulphuric acid was cooled below −5°. Nitric acid (0.92 ml., 1.39 gm., 0.032 mole) dissolved in 1 ml. of sulphuric acid was added dropwise to the above solution with stirring during 10 min. About 0.5 ml. of absolute alcohol was then added cautiously to destroy unreacted nitric acid and the reaction mixture was rinsed onto 10 gm. of chipped ice. The precipitate that formed after a few minutes was rinsed with water and crystallized from 15% acetic acid. On cooling, a small granular precipitate of nitramine formed. The compound (XIV) exploded on heating at 192°. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.85; H, 4.08%.

Study of the Mechanism of Nitration of 2-Aminothiazole

To a mixture of 10.0 gm. (0.10 mole) of 2-aminothiazole and 15 ml. of sulphuric acid was added 4.35 ml. (6.16 gm., 0.105 mole) of nitric acid in 5 ml. of

sulphuric acid during 10 min. with stirring and cooling to keep the temperature at −5°. After seven minutes, 10 ml. of the solution was pipetted into 10 gm. of chipped ice. The precipitated nitramine was filtered off and crystallized from 70 ml. of 95% alcohol. The purified product weighed 1.57 gm. A saturated solution of 2-nitraminothiazole was found to contain 0.55 gm. of nitramine per 100 ml. of solution. The product must then have contained 0.55 gm. × 0.70 = 0.38 gm. more nitramine before crystallization. Corrected yield 1.57 gm. +0.38 gm. = 1.95 gm. The aliquot was about 0.36 of the total reaction mixture, so when the aliquot was withdrawn there must have been 1.95 gm. ÷ 0.36 = 5.42 gm. of nitramine present, i.e. 37.4% of the thiazole present. Neutralization of the sulphuric acid filtrate gave crude 2-amino-5-nitrothiazole which after one crystallization from alcohol weighed 0.16 gm. dry (3.1%). Similarly, a second aliquot removed 67 min. after the nitric acid was added gave 1.72 gm. (33.0%) of nitramine and 0.16 gm. (3.1%) of 2-amino-5-nitrothiazole. The residual reaction mixture, 0.28 (1 − 0.36 × 2 = 0.28) of the whole, was then warmed gently on the steam bath. The temperature rose suddenly to 140° and the mixture became quite dark. It was warmed an additional 30 min. and then quenched by pouring onto 10 gm. of chipped ice. No nitramine precipitated. On neutralization with ammonia, a precipitate of 2-amino-5-nitrothiazole formed that weighed 2.14 gm. (52.7%) after one crystallization from alcohol. Corrections for solubility were not made to the weights of 2-amino-5-nitrothiazole.

Rearrangement of 2-Nitraminothiazole

To 4.7 ml. of concentrated sulphuric acid, cooled to 0°, was added 2.76 gm. (0.019 mole) of 2-nitraminothiazole, in portions. Local heating could not be avoided as the nitramine came in contact with the acid. After 10 min., the solution was poured onto 8 gm. of ice. A small precipitate (0.10 gm. dry) formed. It was filtered off and the filtrate was made alkaline with concentrated ammonia. The precipitate of 2-amino-5-nitrothiazole weighed 1.37 gm. dry (49.5%) and was pure after one crystallization from 30 ml. 10% acetic acid.

Rearrangement of 2-Nitraminothiazole in the Presence of Mesitylene

Mesitylene (3.31 gm., 0.276 mole) was suspended in 10 ml. of concentrated sulphuric acid by agitation and the mixture was kept near −5°. During 20 min., 2.0 gm. (0.138 mole) of 2-nitraminothiazole (II) was added in small portions. The mixture was then surrounded with an ice-water bath and stirred for 10 hr. The reaction mixture was then diluted to 100 ml. with water and steam distilled until 300 ml. of distillate containing a yellow solid had collected. The distillate was extracted with three 50-ml. portions of ether and the extract was dried (over anhydrous magnesium sulphate) and evaporated. An oily crystalline solid remained. The crystals were filtered from the oil and weighed 0.20 gm. Sublimation at 100° and 1 mm. pressure gave 0.10 gm. of a pale yellow solid melting at 77–83°. Crystallized from 95% alcohol the product melted at 85.0–85.5°. Reported for 2,4-dinitro-1,3,5-trimethylbenzene: m.p. 84°. The oil that was obtained was warmed on the steam bath for several hours with excess of powdered tin and hydrochloric acid. The solution was filtered

from the tin, made alkaline with excess of sodium hydroxide, and filtered from the white precipitate. The precipitate and filtrate were separately extracted with ether and the combined extracts were evaporated nearly dry. The residue was treated with acetic anhydride. Immediately, a precipitate of fine needles formed; m.p. 330–334° decomp. Sublimation at 190° and 0.2 mm. pressure did not improve the melting point. One crystallization from absolute alcohol raised the melting point to 344–346° with decomposition. Reported for 1,3-diacetamido-1,3,5-trimethylbenzene: m.p. 320–325°. Anal. Calc. for $C_{13}H_{18}O_2N_2$: C, 66.64; H, 7.74%. Found: C, 66.48; H, 7.87%.

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