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On the Constitution of the Products Formed in the Reaction between 5-Aminotetrazole and Arenesulfonyl Chlorides

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The primary reaction products of acetylsulfanilyl chloride, *p*-toluenesulfonyl chloride, and other arenesulfonyl chlorides with 5-aminotetrazole have been shown to be arenesulfonylguanyl azides and not 5-sulfonamidotetrazoles. Under the influence of strong bases the sulfonylguanyl azides are rearranged to the isomeric 5-sulfonamidotetrazoles.

Three isomeric *p*-toluenesulfonylaminoguanidines have been prepared. 1-*p*-Toluenesulfonyl-3-aminoguanidine forms with nitrous acid an azide identical with the product of the reaction between *p*-toluenesulfonyl chloride and 5-aminotetrazole in pyridine. 1-Methyl-5-aminotetrazole does not react with *p*-toluenesulfonyl chloride, indicating that the point of attack of the sulfonyl chloride on 5-aminotetrazole is not the amino group, but the NH-group in the ring.

In 1941–1942 three compounds (A, B, and C) with the composition of an acetylsulfanilylaminotetrazole were described:

Compound A was obtained by Jensen [1] and by Tappi [2] by the reaction of 5-aminotetrazole with *p*-acetamidobenzenesulfonyl chloride in pyridine solution.

Compound B was obtained by Veldstra and Wiardi [3] by carrying out the condensation between 5-aminotetrazole and *p*-acetamidobenzenesulfonyl chloride in aqueous sodium carbonate solution.

Compound C was obtained by Tappi [2] and by Veldstra and Wiardi [4] by dissolution of compound A in 0.1 N sodium hydroxide and precipitation by acidification.

The mixed melting point of compounds B and C showed no depression, and only very small differences in crystal form and titration curves were noted, but Veldstra and Wiardi nevertheless considered the products to be different compounds. It should, however, be pointed out at once that we have found that compound A is the primary product also when the reaction is carried out in sodium carbonate solution; only by treatment with sodium

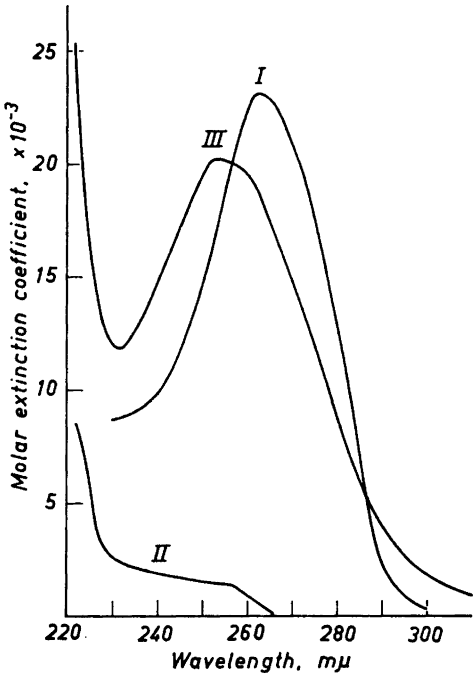


Fig. 1. Absorption spectra of *p*-acetamidobenzenesulfonylguanyl azide in methanol (I), 0.1 N methanolic HCl (II), and 0.1 N methanolic KOH (III).

hydroxide, which was used by Veldstra and Wiardi for purification, is it transformed into the higher melting compound. There is therefore no reason to assume that compounds B and C should be different, and actually we have found the infrared spectra of the two products to be completely identical. It may therefore be concluded that we need only consider the constitution of two compounds, A and B = C.

Jensen [1] found that alkaline hydrolysis of compound A resulted in a complete breakdown of the molecule with the formation of hydrazoic acid, HN_3. Mainly on this evidence the compound was formulated as the true 5-(acetylsulfanilamido)tetrazole (I; R = *p*-$CH_3CONHC_6H_4$), because from experience with other heterocyclic sulfanilyl derivatives it might be expected that a compound with the sulfanilyl group bound to one of the nitrogen atoms in the ring would easily hydrolyse into sulfanilic acid and 5-aminotetrazole, which is not transformed further under the conditions of the experiment.

Jensen and Hansen [5] formulated compound B as 1-acetylsulfanilyl-5-aminotetrazole (II), but Veldstra and Wiardi [4] adduced convincing evidence that their compound B was actually 5-(acetylsulfanilamido)tetrazole. In electrometric titrations this compound behaves as a dibasic acid, which is only compatible with formula I, the acidic groupings being $-SO_2NH-$ and $-NH-$ in the tetrazole ring.

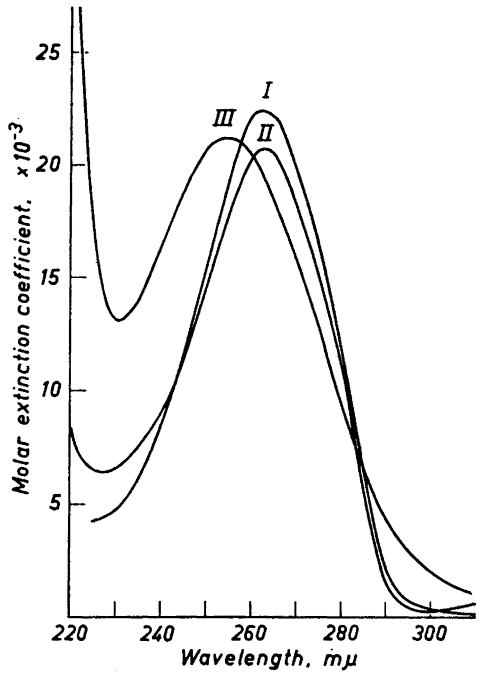
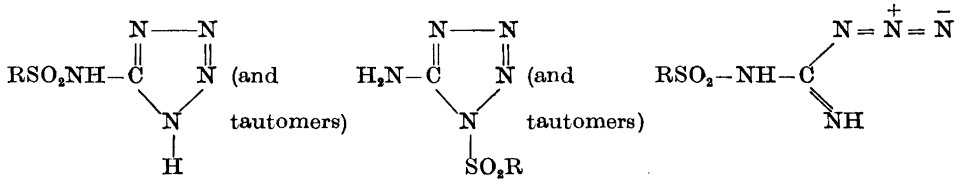


Fig. 2. Absorption spectra of 5-(*p*-acetamidobenzenesulfonamido)tetrazole in methanol (I), 0.1 N methanolic HCl (II), and 0.1 N methanolic KOH (III).



I II III

In 1952 Jensen and Hansen [6] showed that compound A could also be prepared from acetylsulfanilylaminoguanidine and nitrous acid. Although the compound was still tentatively formulated as 5-acetylsulfanilamidotetrazole, it was announced that a closer examination of the isomeric compounds was in progress. This soon led us to the conclusion that compound A is actually an azide (III). These experiments were mainly carried out with *p*-toluenesulfonyl derivatives instead of the acetylsulfanilyl derivatives because the latter are more difficult to purify and have poorly defined melting points.

The conclusion that the product formed from 5-aminotetrazole and sulfonyl chlorides in pyridine solution are sulfonylguanyl azides is based on the following arguments: 1) The infrared spectra of these compounds show the characteristic absorption band at 4.67 μ characteristic of the azide group. 2) The

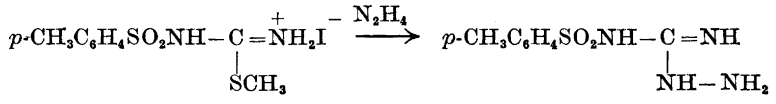
compounds are formed from guanyl hydrazides and nitrous acid. 3) Their properties are those characteristic of azides; especially, they may be hydrolysed to give hydrazoic acid or reduced by hydrogen sulfide or catalytically to give sulfonylguanidines. The reducibility by hydrogen sulfide is a common property of guanylazides [7]. The substances formed from the azides by treatment with bases have quite different properties: They can neither be hydrolysed nor reduced, and in contrast to the azides they form slightly soluble silver salts, a characteristic property of tetrazoles which are unsubstituted in the 1-position. They are weak acids without basic properties, whereas the azides are weak bases without acid properties, as shown by the change of the ultraviolet spectra by addition of hydrochloric acid or potassium hydroxide (Figs. 1 and 2). A comparison of the properties of the azides and tetrazoles is shown in Table 1.

These results show that compounds obtained by condensation of 5-aminotetrazole with sulfonyl chlorides in pyridine are sulfonylguanyl azides and not sulfonylaminotetrazoles. This does not only apply to the acetylsulfanilyl derivative, but also to a *p*-toluenesulfonyl derivative prepared by Dahlbom and Ekstrand [8] and to a *p*-nitrobenzenesulfonyl derivative prepared by Roblin *et al.*[9], who by catalytic hydrogenation of their product obtained sulfanilylguanidine instead of the expected sulfatetrazole. We have now shown that in both cases are the true 5-sulfonamidotetrazoles obtained by treatment of the azide with sodium hydroxide. We have further studied the reaction between β-napthalenesulfonyl chloride and 5-aminotetrazole in pyridine. Also in this case the primary product is the azide, which by treatment with sodium hydroxide is rearranged to the isomeric tetrazole. We encountered, however, difficulties in obtaining analytically pure preparations, and therefore the naphthalenesulfonyl derivatives were not investigated further.

Table 1.

Azides (III)	*Tetrazoles (I)*
1. Formed as primary products from 5-aminotetrazole and sulfonyl chlorides or from aminoguanidines and nitrous acid.	1. Formed by rearrangement of the azides by means of bases, therefore also by the reaction of 5-aminotetrazole with sulfonyl chlorides in the presence of strong bases.
2. Have basic properties and are dissolved in strong acids with salt formation (titration, UV-spectra), but are transformed into tetrazoles by bases.	2. Have no basic properties (insoluble in aqueous acids, UV-spectra of an alcoholic solution not changed by addition of hydrochloric acid).
3. No precipitate with Ag^+.	3. White precipitate with Ag^+.
4. Form sulfonylguanidines on catalytic hydrogenation.	4. Unchanged by catalytic hydrogenation.
5. Reduced by hydrogen sulfide to sulfonylguanidines with precipitation of sulfur.	5. Not reduced by hydrogen sulfide.
6. Concentrated hydrochloric acid slowly splits off the sulfonyl group with the formation of a sulfonyl chloride or sulfonic acid.	6. Not changed on standing with concentrated hydrochloric acid.
7. Hydrazoic acid is formed by hydrolysis with a strong base.	7. Unchanged by boiling with a strong base.

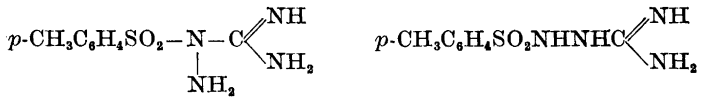
The compound 1-acetylsulfanilyl-3-aminoguanidine, which forms acetylsulfanilylguanyl azide on reaction with nitrous acid, has been prepared in several different ways [6,10,11]. We have prepared the corresponding 1-*p*-toluenesulfonyl-3-aminoguanidine in the following unambiguous way:



IV

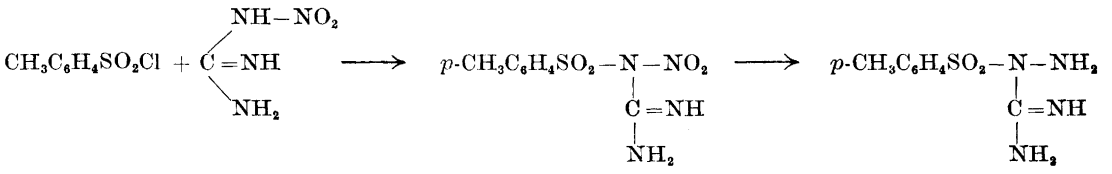
With nitrous acid this hydrazide gives *p*-toluenesulfonylguanyl azide identical with the product of the reaction between *p*-toluenesulfonyl chloride and 5-aminotetrazole in pyridine solution.

Greer *et al.*[11] have prepared the three possible structural isomers of sulfanilylaminoguanidine. Similarly, three structural isomers of *p*-toluenesulfonylaminoguanidine are possible, *viz.* in addition to the above-mentioned isomer, IV, the following two:



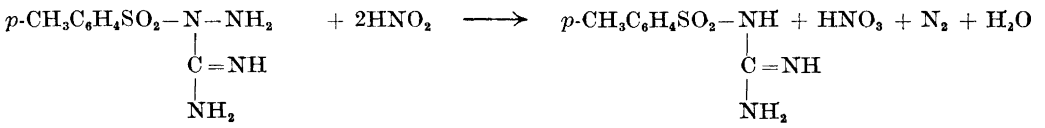
V VI

The isomer V was prepared from nitroguanidine in a way analogous to that in which Greer *et al.* prepared the corresponding sulfanilylaminoguanidine;

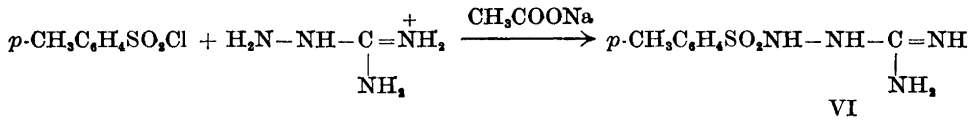


VII V

This isomer reacts with nitrous acid with formation of *p*-toluenesulfonylguanidine:



The third isomer, VI, was obtained by sulfonylation of aminoguanidine in aqueous solution at pH 6, *i.e.* by sulfonylation of the aminoguanidinium ion:

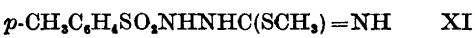


VI

The *p*-toluenesulfonylaminoguanidine is a much weaker base than aminoguanidine and is mainly present in the uncharged state at pH 6; it crystallises from the solution on cooling.

From the reaction between *p*-toluenesulfonyl chloride and aminoguanidine in pyridine solution, or in aqueous solution with the addition of sodium carbonate, we did not succeed in obtaining a pure substance. Analyses indicated that the products always contained a considerable amount of a disulfonyl derivative. With nitrous acid, however, the reaction products gave a certain amount of pure *p*-toluenesulfonylguanyl azide and so must have contained the monosulfonylderivative IV. As would be expected, sulfonylation of *free* aminoguanidine therefore takes place first in the =NH group, followed probably by sulfonylation in the hydrazine group.

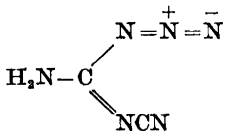
We tried to prepare the isomer VI also by treatment of *p*-toluenesulfonyl-*S*-methylisothiosemicarbazide [XI] with ammonia. However, instead



XI

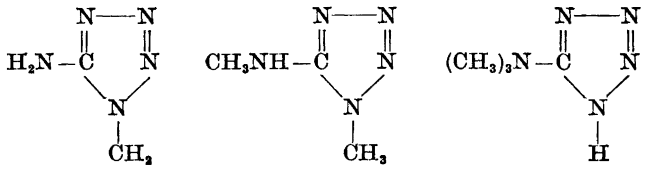
of the formation of an aminoguanidine a McFadyen-Stevens reaction took place with formation of *p*-toluenesulfinic acid. This reaction has been subjected to a closer examination which will be published in another paper.

The formation of azides in the reaction between hydrazides and nitrous acid is, of course, well known, and the ring closure of guanyl azides to tetrazoles is a general way of preparing tetrazoles. The splitting of the tetrazole ring to give guanyl azides under the influence of sulfonyl chlorides is, however, a remarkable reaction, although it is not quite unprecedented. Hart [12] found, *e.g.*, that cyanogen bromide and 5-aminotetrazole react to give the following azide:



The reaction between 5-aminotetrazole and acetyl chloride or benzoyl chloride in pyridine solution gives the known compounds 5-acetamidotetrazole and 5-benzamidotetrazole, prepared by Thiele and Ingle [13] in another way. These compounds are true tetrazoles: They are neither hydrolysed by concentrated hydrochloric acid nor reduced by hydrogen sulfide or catalytically. With silver nitrate solution they give a white precipitate. Thus carboxylic acid chlorides are not able to split aminotetrazole in contrast to sulfonyl chlorides.

We have further studied the reaction of *p*-toluenesulfonyl chloride with the following aminotetrazoles:



VIII IX X

1-Methyl-5-aminotetrazole (VIII) was prepared from 5-aminotetrazole and diazomethane or from 1-methyl-3-aminoguanidine and nitrous acid by ring closure of the azide formed. It has earlier been prepared by methylation of aminotetrazole [14,15], from methylthiourea, sodium azide and lead oxide [16], and from methyl *iso*thiocyanate and hydrazoic acid [17]. In all these ways the same methyltetrazole is obtained. The assignment of structure VIII to this compound is undoubtedly correct because it has no acidic character and gives no precipitate with silver nitrate solution.

The two dimethyl derivatives of 5-aminotetrazole (IX and X) were prepared from the appropriate dimethylaminoguanidines in the same way as 5-aminotetrazole from aminoguanidine. The structures of the two dimethyl derivatives follow unambiguously from their mode of preparation. Compound X gives a precipitate with silver nitrate, whereas IX does not, in accordance with their formulae.

1-Methyl-5-aminotetrazole and 1-methyl-5-methylaminotetrazole are unaffected by *p*-toluenesulfonyl chloride in pyridine solution. Both could be recovered unchanged. In contrast 5-dimethylaminotetrazole reacted with *p*-toluenesulfonyl chloride with the formation of *NN*-dimethylhydrazine. A study of this reaction will be published in another paper.

These results seem to indicate that the point of attack of the sulfonyl chloride is the NH-group in the tetrazole ring. Probably the primary reaction product is the 1-sulfonyltetrazole (II), which is immediately rearranged to an azide because of the strong electrophilic character of the sulfonyl group. The presence of the 5-amino group is necessary to produce a sufficiently high electron density in the tetrazole ring. Tetrazole itself does not react with *p*-toluenesulfonyl chloride in pyridine — neither could its silver salt be induced to react with *p*-toluenesulfonyl chloride. With the less electrophilic acyl group, RCO, no opening of the ring takes place. If a 1-acyl derivative is formed also in this case as the primary product, it is rearranged into a 5-acylamino derivative by an acyl migration.

This work was completed in the year 1952. In a recent publication [18], Nagy *et al.* have come to the same conclusion concerning the structure of the product formed in the reaction between 5-aminotetrazole and acetylsulfanilyl chloride in pyridine.

EXPERIMENTAL

p-*Acetamidobenzenesulfonylguanyl azide.* (III; R = p-$CH_3CONHC_6H_4$) Prepared by condensation of anhydrous 5-aminotetrazole and p-acetamidobenzenesulfonyl chloride in pyridine according to Jensen [1] and Jensen and Hansen [5], this compound was obtained as a colourless powder with m.p. 166°C after recrystallisation from acetone + water. (Found: C 38.28; H 3.73; N 29.54; S 11.20. Calc. for $C_9H_{10}N_6O_3S$: C 38.29; H 3.57; N 29.78; S 11.36.)

This compound is also obtained from 5-aminotetrazole and p-acetamidobenzenesulfonyl chloride in sodium carbonate solution according to the directions of Veldstra and Wiardi [3], but *without* treatment with sodium hydroxide. From 2 g of 5-aminotetrazole we obtained 3.45 g of crude product with m.p. *ca.* 156°C. Recrystallisation from ethanol raised the melting point to 165–166°C; no depression on admixture of the foregoing product.

The same compound is finally obtained from 4-acetylsulfanilylaminoguanidine and nitrous acid (*cf.* Jensen and Hansen [6], who give a slightly higher m.p., which was determined on a preheated block).

The compound does not yield a precipitate with silver nitrate; it is insoluble in 4 N hydrochloric acid, but dissolves in concentrated hydrochloric acid; when this solution was evaporated after standing for three days, a solid residue was obtained, and when this was recrystallised from water, colourless crystals formed; they were identified as sulfanilic acid. An aqueous solution of the compound is reduced by hydrogen sulfide with formation of sulfur, and it is reduced catalytically to acetylsulfanilylguanidine: A solution of 0.20 g in 30 ml ethanol to which was added 20 mg of PtO_2 was hydrogenated at room temperature and 1 atm. until the calculated amount of hydrogen had been absorbed. The solution was filtered and evaporated to dryness. Yield 0.18 g acetylsulfanilguanidine with m.p. 255°C; after recrystallisation from water m.p. 263–265°C; no depression on admixture of an authentic sample of acetylsulfanilylguanidine. (Found: C 39.41; H 5.14; N 20.42. Calc. for $C_9H_{12}N_4O_3S{\cdot}H_2O$: C 39.16; H 5.41; N 20.52.)

5-Acetylsulfanilamido tetrazole (I; R = p–$CH_3CONHC_6H_4$). Prepared according to Veldstra and Wiardi [3,4] by condensation of p-acetylaminobenzenesulfonyl chloride (16.8 g) with a solution of 5-aminotetrazole (6 g) and sodium carbonate (7.4 g) in water (70 ml). The crude product was dissolved in 0.2 N sodium hydroxide, precipitated with hydrochloric acid, and recrystallised from water. M.p. 205–206°C. Prepared in this way the compound contains approximately 1.5 moles water of crystallisation, which is given off by storage over phosphorus pentoxide or by heating to 170–180°C. (Found: C 35.11; H 4.26; N 27.25; S 10.30; H_2O 8.93. Calc. for $C_9H_{10}N_6O_3S.1\frac{1}{2}H_2O$:C 34.94; H 4.24; N 27.17; S 10.36; H_2O 8.73.)

The same compound was obtained by dissolving p-acetamidobenzenesulfonylguanyl azide in sodium hydroxide and precipitating with hydrochloric acid or by prolonged treatment of the azide with sodium carbonate: 0.3 g of the azide was stirred with a solution of 2 g of sodium carbonate in 20 ml of water; after 12 h the mixture was heated slowly to 50°C and kept at this temperature until practically all had dissolved. The solution was filtered and acidified with hydrochloric acid. The precipitate which separated was recrystallised from water. M.p. 215–216°C, mixed m.p. on addition of the foregoing product 204–206°C. The product was analysed after drying to constant weight over phosphorus pentoxide. (Found: C 38.72; H 3.66; N 28.91; S 11.26. Calc for $C_9H_{10}N_6O_3S$: C 38.29; H 3.57; N 29.78; S 11.36.)

In contrast to the azide, this compound gives a precipitate with silver nitrate, is insoluble in concentrated hydrochloric acid, and is not reduced by hydrogen sulfide or catalytically: 0.2 g was dissolved in 50 ml of ethanol, 20 mg of PtO_2 was added, and the solution was treated with hydrogen for 24 h. The compound was recovered unchanged, m.p. 214–216°C, 210–211°C after mixing with the starting product. (Found: S 10.34. Calc. 10.36.)

p-*Toluenesulfonylguanyl azide* (III; R = p–$CH_3C_6H_4$). Prepared by condensation of p-toluenesulfonyl chloride with 5-aminotetrazole in pyridine [6]. M.p. 150–151°C after recrystallisation from ethanol. (Found: N 29.31. Calc. for $C_8H_9N_5O_2S$: N 29.27.) The compound is not precipitated by silver nitrate in aqueous solution. By hydrogenation with PtO_2 as catalyst it is transformed into p-toluenesulfonylguanidine. Yiel d0.16 g from 0.20 g of the azide; m.p. 207–208°C after recrystallisation from water, m.p. 206–

208°C on admixture of an authentic sample of *p*-toluenesulfonylguanidine (m.p. 205–206°C). Analysed after drying for 24 h at 100°C over phosphorus pentoxide. (Found: N 19.72; S 14.83. Calc. for $C_8H_{11}N_3O_2S$; N 19.70; S 15.03.) By reduction with hydrogen sulfide, *p*-toluenesulfonylguanidine is similarly formed: 0.5 g of the azide was dissolved in 25 ml of warm ethanol, and hydrogen sulfide was bubled through the solution. After an hour, 10 ml of water was added, and hydrogen sulfide was let in for another hour. The solution was filtered from the free sulfur which had separated and was concentrated somewhat and cooled. A white powder separated. Yield 0.37 g; m.p. 204–206°C, no depression occurring on admixture of *p*-toluenesulfonylguanidine.

The azide is transformed into *p*-toluenesulfonyl chloride by treatment with concentrated hydrochloric acid; 1 g of the azide was shaken with 25 ml of concentrated hydrochloric acid. After three days all the azide had dissolved, and instead colourless, needlelike crystals had separated. Yield 0.72 g with m.p. 63–65°C, no depression on admixture of an authentic sample of *p*-toluenesulfonyl chloride.

5-(p-Toluenesulfonamido)tetrazole (I; R = $p-CH_3C_6H_4$). *p*-Toluenesulfonyl azide (0.20 g) was dissolved in 0.2 N sodium hydroxide (15 ml); the solution was filtered and acidified with hydrochloric acid. A white crystalline product separated. Yield 0.09 g. M.p. 189–191°C after two crystallisations from water. (Found: C 40.11; H 3.99; N 29.22; S 13.29. Calc for $C_8H_9N_5O_2S$: C 40.15; H 3.74; N 29.27; S 13.40.)

The same compound was obtained by treatment of the azide (0.50 g) with a solution of sodium carbonate (4 g) in water (40 ml) for 24 h and heating for a short time at 50°C. Most of the azide had then dissolved. The solution was filtered and acidified with hydrochloric acid. The white precipitate was recrystallised three times from water. M.p. 195–196°C; it was 189–191°C after mixing with the foregoing product. (Found: C 40.16; H 3.75; N 29.27; S 13.40. Calc. for $C_8H_9N_5O_2S$: C 40.15; H 3.79; N 29.27; S 13.40.)

Ring closure also took place when the azide was treated with hydrazine or dissolved in boiling xylene.

The tetrazole was insoluble in concentrated hydrochloric acid and remained unchanged after treatment for three days with this acid. It was not changed by boiling for one hour with 1 N sodium hydroxide. It is neither reduced with hydrogen sulfide nor catalytically. With an aqueous solution of silver nitrate it gives a white precipitate.

5-p-Nitrobenzenesulfonylguanyl azide (III; R = $p-NO_2C_6H_4$). Prepared by condensation of *p*-nitrobenzenesulfonyl chloride with 5-aminotetrazole in pyridine. M.p. 185–186°C after recrystallisation from acetone + water. (Found: C 30.44; H 2.43. Calc. for $C_7H_6N_6O_4S$: C 31.12; H 2.24.) As found by Roblin *et al.*[9], this compound forms sulfanilylguanidine on catalytic hydrogenation and also shows the other properties characteristic of an azide.

5-(p-Nitrobenzenesulfonylamido)tetrazole (I; R = $p-NO_2C_6H_4$). The azide (1 g) was stirred with 0.2 N NaOH (50 ml) for half an hour; the solution was filtered and acidified with hydrochloric acid. A white precipitate separated (0.35 g). M.p. 204–205°C after recrystallisation from water. (Found: C 30.90; H 2.24. Calc. for $C_7H_6N_6O_4S$: C 31.12; H 2.24.) The compound shows the properties characteristic of a tetrazole. By catalytic hydrogenation it is transformed into 5-sulfanilamidotetrazole, m.p. 202–203°C in accord with Veldstra and Wiardi[4].

5-Acetylaminotetrazole. To an ice-cold solution of anhydrous 5-aminotetrazole (2 g) in pyridine (15 ml), acetyl chloride (2 g) is added dropwise. The solution is then warmed for one hour on a steam bath, and after cooling poured into water (200 ml). After addition of concentrated hydrochloric acid (20 ml) to the cooled solution a white powder separates. Yield 0.8 g with m.p. 271–273°C after recrystallisation from ethanol. (Found: N 55.16. Calc. for $C_3H_5N_5O$:55.12.) The compound is soluble in sodium hydroxide, but is recovered unchanged on acidification. It is not changed by treatment with sodium hydroxide or concentrated hydrochloric acid, and it is not reduced by hydrogen sulfide or catalytically.

5-Benzoylaminotetrazole. Prepared in the same way as the acetyl derivative, but precipitated with 4 N hydrochloric acid. Yield 2.3 g from 2 g of 5-aminotetrazole. M.p. 277–282°C after recrystallisation from ethanol. (Found: C 51.06; H 3.92; N 36.97. Calc. for $C_8H_7N_5O$: C 50.78; H 3.73; N 37.02.) Like the foregoing compound it is recovered unchanged after treatment with sodium hydroxide, hydrochloric acid, or hydrogen sulfide, or by catalytic hydrogenation.

1-Methyl-5-aminotetrazole (VIII). This compound was prepared in two ways:

a) Anhydrous 5-aminotetrazole (1 g) was dissolved in methanol, and a solution of diazomethane in ether was added; the solution attained a yellow colour. The solvent was removed by evaporation, and the residue (0.38 g) was recrystallised from water. M.p. 220–223°C. (Found: C 24.18; H 5.29. Calc. for $C_2H_5N_5$: C 24.25; H 5.08.)

b) An aqueous solution of 2-methyl-1-aminoguanidinium iodide [19] (7.3 g) was shaken with an excess of silver chloride until negative iodine reaction. The filtered solution was cooled in ice, and sodium nitrite (2.3 g) and 1 N hydrochloric acid (34 ml) were added. After 15 min sodium acetate (10 g) was added, and the solution was evaporated to dryness. The residue was extracted repeatedly with boiling acetone. The acetone solution was evaporated and the residue recrystallised from water. Yield 0.77 g. M.p. 223–228°C, no depression on admixture of the foregoing preparation. (Found: N 70.49. Calc. for $C_2H_5N_5$: 70.66.)

By the same method the two following dimethylaminotetrazoles were prepared. They form colourless crystals which are slightly soluble in cold water. The preparation of the necessary dimethylaminoguanidines is described below. After completion of our work these compounds have been described by Finnegan, Henry and Lieber [20].

1-Methyl-5-methylaminotetrazole (IX). Yield 60 %; m.p. 172–174°C (recrystallised from ethanol). (Found: C 31.68; H 6.01; N 61.94. Calc. for $C_3H_7N_5$: C 31.85; H 6.24; N 61.93.)

5-Dimethylaminotetrazole (X). Yield 34 %; m.p. 235–240°C (recrystallised from water). (Found: 32.16; H 6.50; N 61.70. Calc. for $C_3H_7N_5$: C 31.85; H 6.24; N 61.93.)

2,3-Dimethyl-1-aminoguanidinium iodide. *S*-Methyl-4-methylthiosemicarbazidium iodide (7 g) was dissolved in an excess of 30 % aqueous methylamine solution. After standing overnight the solution was evaporated to dryness, and the residue was recrystallised from ethanol. Yield 5.6 g (75 %), m.p. 299–300°C. (Found: C 15.86; H 4.63; I 54.91. Calc for $C_3H_{11}IN_4$: C 15.66; H 4.82; I 55.16.)

2,2-Dimethyl-1-aminoguanidinium iodide. Prepared in the same way as the foregoing compound from *S*-methylthiosemicarbazidium iodide (20 g) and dimethylamine (yield 16.6 g, 84 %). Recrystallised from abs. ethanol; m.p. 185–187°C. (Found: C 15.59; H 4.90; I 55.12. Calc. for $C_3H_{11}IN_4$: C 15.66; H 4.82; I 55.16.)

3-(p-Toluenesulfonyl)-1-aminoguanidine (IV). A suspension of *p*-toluenesulfonyl-*S*-methylisothiourea [21] (10 g) in water (100 ml) to which had been added an excess of hydrazine hydrate (5 ml) was kept for 3–4 h with shaking and warming now and then, until the evolution of methanethiol had ceased and the solid had dissolved. The solution was evaporated to dryness and the residue crystallised from water. Yield 3.9 g (41 %) with m.p. *ca.* 160°C. After four more recrystallisations from water the product showed a constant m.p. of 185–186°C. (Found: N 24.63; S 14.12. Calc. for $C_8H_{12}N_4O_2S$: N 24.55; S 14.04.)

This compound reacts with nitrous acid with the formation of *p*-toluenesulfonylguanyl azide: 0.59 g of IV was dissolved in 15 ml of 4 N sulfuric acid, and a solution of sodium nitrite (0.3 g) in water (2 ml) was slowly added. The solution was heated to 80°C for a moment and then cooled in ice. The crystals which separated were recrystallised from ethanol. Yield 0.25 g. M.p. 150–151°C, not depressed on admixture of III. (Found: S 13.33. Calc. for $C_8H_9N_5O_2S$: S 13.40.)

1-(p-Toluenesulfonyl)-1-nitroguanidine. (VII). Nitroguanidine (10.4 g) was suspended in acetone (150 ml), and a solution of potassium hydroxide (12.3 g) in water (25 ml) was added. When the nitroguanidine had dissolved, 20 g of *p*-toluenesulfonyl chloride were added in small portions to the stirred solution while the temperature was kept at 18°C. When all the sulfonyl chloride had been added a white precipitate separated; 50 ml of water was added, and the stirring was continued for 3 h. Then the suspension was neutralised with acetic acid and filtered. The isolated product was the potassium salt of VII. Yield 19.5 g (66 %). It is easily soluble in hot water, slightly soluble in cold water and in ethanol. After three recrystallisations from water the m.p. was 230–231°C. (Found: C 32.32; H 3.00. Calc. for $C_8H_9KN_4O_4S$: C 32.43; H 3.06.) On addition of dilute hydrochloric acid to an aqueous solution of the potassium salt, 1-(*p*-toluenesulfonyl)-1-nitroguanidine separated as a white solid, which was recrystallised from water. M.p. 181–183°C. (Found: N 21.60; S 12.73. Calc. for $C_8H_{10}N_4O_4S$: N 21.69; S 12.40.)

1-(p-Toluenesulfonyl)-1-aminoguanidine (V). A solution of the nitro compound (VII) in ethanol was hydrogenated (catalyst PtO_2); the solution was filtered and evaporated to dryness and the residue recrystallised from water. Yield almost quantitative.

M.p. 159—161°C, strongly depressed on admixture of the isomer (IV). (Found: C 41.95; H 5.56; S 14.06. Calc. for $C_8H_{12}N_4O_2S$: C 42.09; H 5.30; S 14.04.)

Treatment of this compound with sodium nitrite as described for IV yielded *p*-toluenesulfonylguanidine, m.p. 206—207°C, not depressed on admixture of an authentic sample.

p-*Toluenesulfonylamidoguanidine (VI).* *p*-Toluenesulfonyl chloride (3.8 g) was added to a solution of aminoguanidinium sulfate (3.4 g) and sodium acetate (6 g) in 15 ml of water. The mixture was boiled until the sulfonyl chloride had dissolved completely. On cooling, a white crystalline solid separated. Yield 4.0 g (75 %). It was recrystallised three times from ethanol. M.p. 204—205°C. (Found: C 39.15; H 5.66; N 22.63. Calc. for $C_8H_{12}N_4O_2S.H_2O$: C 39.02; H 5.73; N 22.76).

The compound is easily soluble in hot water and quite soluble also in cold water, but slightly soluble in cold ethanol and insoluble in benzene.

p-*Toluenesulfonylthiosemicarbazide* was prepared in two ways:

a) 2.9 g of $Ba(SCN)_2 \cdot 2H_2O$ was dissolved in 10 ml water, and 5 ml of 4 N sulfuric acid was added. The barium sulfate was filtered off, 1.9 g of *p*-toluenesulfonic hydrazide was added, and the solution was heated on a steam bath for one hour. After cooling, the white solid which had formed was filtered off, washed with water, and recrystallised from ethanol. Yield 1.3 g (60 %). M.p. 214—215°C. (Found: N 17.10; Calc. for $C_8H_{11}N_3O_2S_2$: N 17.13.)

b) The same compound was obtained from *p*-toluenesulfonyl chloride and thiosemicarbazide under the conditions described for VI, but only in slight yield (6—16 %). From the reaction between *p*-toluenesulfonyl chloride and thiosemicarbazide in pyridine solution no pure compound could be obtained, but the product seemed mainly to consist of di-*p*-toluenesulfonylthiosemicarbazide.

p-*Toluenesulfonyl*-S-*methyl-isothiosemicarbazide (XI).*

a) A solution of *p*-toluenesulfonylthiosemicarbazide (210 mg) and methyl iodide (150 mg) in ethanol (10 ml) was refluxed for one hour. The ethanol was removed *in vacuo* and the residue dissolved in water; on addition of sodium carbonate, XI separated. Yield 175 mg (80 %). When recrystallised from water it formed colourless needles with m.p. 175—177°C. (Found: N 16.24. Calc. for $C_9H_{13}N_3O_2S_2$: N 16.21.)

b) *S*-Methyl*iso*thiosemicarbazidium iodide (2.3 g) was dissolved in pyridine (8 ml), *p*-toluenesulfonyl chloride (1.9 g) was added, and the solution was heated to boiling and cooled in ice. On addition of water an oil separated; it soon crystallised. Yield 0.7 g (27 %). After recrystallisation from water it had m.p. 175—176°C. (Found: S 24.89; Calc. for $C_9H_{13}N_3O_2S_2$: S 24.73.)

The molten substance gives off methanethiol and soon solidifies to a substance melting at about 250°C. On boiling a solution of XI in aqueous ammonia, methanethiol is similarly formed; on acidification of the cooled solution, *p*-toluenesulfinic acid separates; m.p. 84—86°C (litt. 87°C).

Infrared spectra. Characteristic of the infrared spectra of the sulfonylguanyl azides (III) is a relatively strong band at 4.66 μ, which was also found in the spectra of benzazide and guanyl azide. The spectra of the sulfonylguanyl azides exhibit most of the bands of acetylsulfanilamide and *p*-toluenesulfonamide except a strong band in the 11 μ range; the azides have a band at 12.7 μ not found in the spectra of the sulfonamides or of aminotetrazole and tetrazole. Samples of *p*-acetaminobenzenesulfonamidotetrazole, prepared in pyridine solution and in aqueous solution containing sodium carbonate, yielded identical spectra.

The infrared spectra of the 5-sulfonamidotetrazoles lack the band at 4.66 μ. Bands which could be atributed to the tetrazole ring could not be identified with certainty, because acetylsulfanilamide and *p*-toluenesulfonamide have strong bands overlapping the bands of tetrazole and 5-aminotetrazole. 5-(*p*-Acetamidobenzenesulfonamido)tetrazole has a band at 9.5 μ, at the same place where 5-aminotetrazole has a strong band, but this band is lacking in the spectrum of 5-(*p*-toluenesulfonamido)tetrazole; more likely it corresponds to a band at 9.6 μ in the spectrum of acetylsulfanilamide. The products obtained from *p*-toluenesulfonylguanyl azide by treatment with sodium hydroxide and by heating in xylene, respectively, yielded identical spectra.

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