On the Reaction Between 5-Amino-1,2,3,4-thiatriazole and Hydrochloric Acid

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On treatment of 5-amino-1,2,3,4-thiatriazole with concentrated hydrochloric acid Freud obtained a hydrochloride of sulfur-containing substance which was formulated as $\text{H}_2\text{N-CNS-Cl}_2$ and thought to contain the three-membered thiazine ring. The possibility that it might be a dimer with a 6-membered ring was, however, left open. 5-Alkylamino-1,2,3,4-thiatriazoles react in the same way as the unsubstituted compound, giving compounds which have also been formulated as hydrochlorides of thiocyanocamines, RNHNCS.$^4$

However, according to Sahasrabudhey, the compound formed from 5-amino-1,2,3,4-thiatriazole does not have the composition CSN$_2$HCl, but (CSN$_2$H$_2$Cl)$_2$, and is in fact the dihydrochloride of "formamidine disulfide", the oxidation product of thiourea.$^*$ This conclusion was derived from a comparison of the melting points of 4 salts of Freud's compound with the melting points of the corresponding salts of formamidine disulfide.

Since the melting points are rather ill defined decomposition points we have not considered this evidence as convincing. Therefore the reaction product from 5-amino-1,2,3,4-thiatriazole and hydrochloric acid was studied more closely and it was found that the formulation by Sahasrabudhey is actually correct, the infrared spectra of the degradation product of 5-amino-1,2,3,4-thiatriazole and formamidine disulfide dihydrochloride being identical. Moreover, it was generally found that the compounds formed from 5-alkylamino-1,2,3,4-thiatriazoles and hydrochloric acid were identical with alkylsubstituted formamidine disulfides, formed by treatment of monoalkylthioureas with chlorine, as shown by analyses and infrared spectra.

5-tert-Butyl-1,2,3,4-thiatriazole, however, formed formamidine disulfide, the tert-butyl group being split off on treatment with hydrochloric acid.

This result is rather surprising since it means that a reduction of the thiazone has taken place. At the same time 50% of the thiazone is hydrolysed with the formation of hydrogen sulfide, hydrazoic acid and carbon dioxide. No sulfur or thiocyanic acid is formed in this reaction, which therefore takes place according to the scheme:

$$\text{RNH-} \begin{array}{c} \text{C} \\ \text{S} \\ \text{N} \\ \text{N}\ \text{N} \end{array} + 2\text{H}_2\text{O} + \text{HCl} \rightarrow$$

$$\rightarrow \text{RNHCl} + \text{H}_2\text{S} + \text{CO}_2 + \text{HN}_3$$

In an experiment with 5-amino-1,2,3,4-thiatriazole 90% of the calculated ammoniumchloride was isolated from the filtrate from the formamidine disulfide dihydrochloride.

Therefore a plausible explanation for the formation of the formamidine disulfide is that hydrazoic acid functions as a reducing agent (as it does in the iodine-azide reaction) and reduces the positive ion formed by opening of the thiazone ring under the influence of the strong acid:

$$\text{RNH-} \begin{array}{c} \text{C} \\ \text{S} \\ \text{N} \\ \text{N}\ \text{N} \end{array} + \text{H}^+ \rightarrow \text{RNH-} \begin{array}{c} \text{C} \\ \text{S} \\ \text{N} \\ \text{N}\ \text{N} \end{array} + \text{N}_2$$

$$2\text{RNH-} \begin{array}{c} \text{C} \\ \text{S} \\ \text{N} \\ \text{N}\ \text{N} \end{array} + 2\text{HN}_3 \rightarrow \text{RNH-} \begin{array}{c} \text{C} \\ \text{S} \\ \text{S} \\ \text{S} \\ \text{C-NHR} \end{array} + 3\text{N}_2$$

When R = aryl a different reaction takes place, and 2-aminobenzothiazoles are formed.$^4$ This is readily explained as an electrophilic attack of the initial positive ion on the aromatic nucleus:

$$\text{C-NH}_2 \rightarrow \text{C-NH}_2 + \text{H}^+$$

Hydrazoic acid may also function as an oxidising agent and it was found that thiourea dissolved in hydrochloric acid was converted into formamidine disulfide dihydrochloride on treatment with hydrazoic acid.

* In lack of officially accepted names for this type of compounds the common, but misleading name "formamidine disulfide" will be used.

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Since Sahasrabudhey has advanced the hypothesis that the formula of formamide disulfide could be bisected, it should be mentioned that we found formamidin disulfide dihydrochloride to be diamagnetic, which excludes any formula with an odd number of electrons.

The infrared spectrum of formamidin disulfide dihydrochloride in KBr shows the following bands (Perkin Elmer model 21 double beam spectrophotometer with NaCl optics):

3200 vs (N-H stretch)
3000 vs br.
2990 m (=NH$_2$)
1650 vs (NH$_2$ deform.)
1620 m sh
1515 w v (N-C-S)
1410 s v (N-C=N)
1100 w NH$_2$ rock.
1045 m v (N-C=N$_2$)
770 w, 690 m br. NH$_2$ wag.

In nujol mull the compound shows practically the same spectrum except that the strong 3000 cm$^{-1}$ band is absent. Redpath and Smith list a number of other weak bands which are completely absent in the spectra of our preparations and probably are due to impurities.

On deuteration the bands at 690, 770, 1045 and 1100 cm$^{-1}$ disappear completely and are replaced by bands of much smaller intensity at 825, 920, 1130 and 1170 cm$^{-1}$. The strong bands at 1650 cm$^{-1}$ and 1410 cm$^{-1}$, however, are only weakened somewhat and shifted to 1625 cm$^{-1}$ and 1380 cm$^{-1}$, which shows that these bands are only to a minor degree due to N-H deformation.

The alkylsubstituted formamidin disulfides also show a strong band at 1660 cm$^{-1}$ due to the NH$_2$ group and in addition a medium to strong band at 1610-1615 cm$^{-1}$ which undoubtedly is due to the -NHR group and is comparable with the amide II band of secondary amides. Most of the other bands in these spectra can be assigned to the alkyl groups. No bands comparable to the strong bands at 1410 and 1045 cm$^{-1}$ in the spectrum of formamidin disulfide were found in the spectra of the alkyl derivatives. The bands at 930-960 cm$^{-1}$ and 1060-1115 cm$^{-1}$ in the spectra of the thiatiazoles (cf. the preceding paper), which were ascribed to the thiatiazole ring, disappear when the thiatiazoles are transformed into formamidin disulfides.

**Experimental.** The hydrochlorides of the formamidin disulfides were prepared by the following methods:

(a) From thiourea. A stream of chlorine was passed into a cooled saturated solution of the thiourea in abs. ethanol until the solution attained a slightly yellow colour. The precipitates were filtered, washed with ethanol and dissolved in water; on filtering the solutions into concentrated hydrochloric acid the hydrochlorides separated as colourless crystals. This method failed in the case of tert-butyl-thiourea, and instead the dihydrobromide was prepared by the following method: A solution of bromine in carbon tetrachloride was added to a cooled solution of tert-butylthiourea (0.264 g) in acetic acid (6 ml) until the solution was slightly coloured by excess bromine and an orange-yellow oil had separated. The supernatant liquid was decanted off and the oil washed with a little CCl$_4$ and dissolved in 2 ml of 96 % ethanol to form a colourless solution. On subsequent addition of 20 ml of abs. ethanol the dihydrobromide separated as a white crystalline substance, which was filtered and washed with ether. Yield 0.210 g (50%).

(b) From the thiatiazoles. 5-Amino-1,2,3,4-thiatiazole and 5-alkylamino-1,2,3,4-thiatiazoles (alkyl = methyl, propyl or tert-butyl) were heated in conc. hydrochloric acid (10 ml to 0.01 mole of the thiatiazole) until the evolution of gas was evident (60-80°C), and then slowly heated to 100°C in the course of 1 h. The formamidin hydrochlorides separated out on cooling, or on concentrating the solutions in vacuo, and were purified by dissolving in water (2 ml) and filtering into conc. hydrochloric acid (6 ml).

**Formamidin(1,2,3,4-thiatiazole)dihydrochloride.** Found: (a) C 10.41; H 3.88. M.p. 172-74°C. (b) C 10.63; H 3.65. M.p. 175-75°C. Calc. for C$_7$H$_8$Cl$_2$N$_2$S$_2$: C 10.76; H 3.61.

**Methylformamidin disulfide dihydrochloride.** Found: (a) C 18.69; H 4.75. M.p. 163-65°C. (b) C 18.87; H 4.75. M.p. 162-64°C. Calc. for C$_7$H$_8$Cl$_2$N$_2$S$_2$: C 18.84; H 4.74.


Infrared spectra of products (a) and (b) were identical in all details.


Treatment of 5-tert-butyl-1,2,3,4-thiatiazole with hydrochloric acid according to (b) yielded the unsubstituted formamidin disulfide di-
hydrochloride. (Found: C 11.00; H 3.67. M.p. 172–74°C. Calc. for C₉H₈ClN₄S₂: C 10.76; H 3.61). The unsubstituted formamidine dicyl fluoride dihydrochloride was also obtained when tert-butylformamidine disulfide dihydrobromide was heated with conc. hydrochloric acid to 80°C for 1 ½ h and then to 100°C for 5 min. The infrared spectra of these two samples were identical with the spectrum of an authentic sample of formamidine disulfide dihydrochloride.

The melting points were determined in capillary tubes with a heating rate of 2–3°C/min.

In conclusion it should be mentioned that the melting point of tert-butylthiourea was found to be 181–181.5°C, i.e. considerably higher than the values given in the literature (185°; 171–72°). (Found: C 45.43; H 9.15; N 21.16. Calc. for C₉H₁₂N₂S: C 45.44; H 9.15; N 21.20).

The Structure of (+)-ε-Muurolene ("ε-Cadinene")

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Four sesquiterpenes of the cadalene type yielding (+)-muurolene dihydrochloride¹ (m.p. 87–89°, [α]D<sup>20</sup> +13.2° (c 1.5) *** have been isolated from the wood of Pinus silvestris L. as well as from the fraction b.p. 100–140°/10 mm of Swedish sulphate turpentine. Two of them, "muurolene-I" and "muurolene-II"⁴⁺⁺ (C₇H₉<sub>12</sub> b.p. 125–7°/10 mm. m<sub>p</sub>11 1.5059, [α]D<sup>20</sup> +1.8° (c 2.5); C₇H₉<sub>12</sub> b.p. 128–30°/10 mm. m<sub>p</sub>11 1.5063, [α]D<sup>20</sup> –85.3° (c 2.3), respectively) appear not to have been previously isolated in the pure state (cf. Refs.¹⁻²). Spectral data (IR, NMR) indicate a close relationship with the cadinones and also that "muurolene-I" possesses one trisubstituted and one exocyclic double bond and that "muurolene-II" has two trisubstituted double bonds. Attempts to determine the positions of the double bonds in these compounds are being made.

A third component yielded (+)-muurolene dihydrochloride and (−)-cadene dihydrochloride (ratio: 1:6) and has been identified as copeane (IR, various physical constants and conversion to the diol prepared by Büchi et al.††). A mixture of the same dihydrochlorides (ratio 3:1) was also formed from the fourth hydrocarbon, which was shown to be identical with the so-called "ε-cadinene" (IR, refractive index, optical rotation)⁴ for which structure (1) has been proposed by Sýkora, Herout and Šorm.⁶

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*** Rotations were taken in chloroform.
† Provisional names. Aschan¹ isolated a sesquiterpene fraction from an industrial extract of resinous pine stumps (Pinus silvestris) produced in Muurola, Finland, which he called "muurolene".
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