

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

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On treatment of 5-amino-1,2,3,4-thiazotriazole with concentrated hydrochloric acid Freund¹ obtained a hydrochloride of sulfur-containing substance which was formulated as $H_2N-CNS \cdot HCl$ and thought to contain the three-membered thiazirine ring. The possibility that it might be a dimer with a 6-membered ring was, however, left open. 5-Alkylamino-1,2,3,4-thiazotriazoles react in the same way as the unsubstituted compound, giving compounds which have also been formulated as hydrochlorides of thiocyanamines, $RNHNCNS$.²

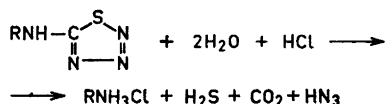
However, according to Sahasrabudhey³ the compound formed from 5-amino-1,2,3,4-thiazotriazole does not have the composition CSN_2H_3Cl but $(CSN_2H_4Cl)_2$, and is in fact the dihydrochloride of "formamidine disulfide", the oxidation product of thiourea.* This conclusion was derived from a comparison of the melting points of 4 salts of Freund'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-thiazotriazole 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-thiazotriazole and formamidine disulfide dihydrochloride being identical. Moreover, it was generally found that the compounds formed from 5-alkylamino-1,2,3,4-thiazotriazoles and hydrochloric acid were identical with alkylsubstituted formamidine disulfides, formed by treatment of monoalkylthioureas with chlorine, as

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

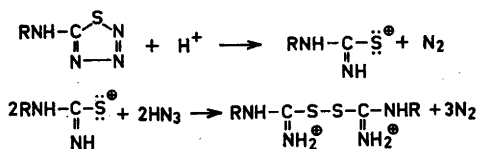
shown by analyses and infrared spectra. 5-*tert*-Butyl-1,2,3,4-thiazotriazole, however, formed formamidine disulfide, the *tert*-butyl group being split off on treatment with hydrochloric acid.

This result is rather surprising since it means that a reduction of the thiazotriazole has taken place. At the same time 50 % of the thiazotriazole 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:

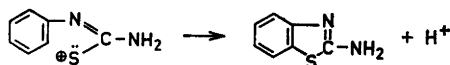


In an experiment with 5-amino-1,2,3,4-thiazotriazole 90 % of the calculated ammoniumchloride was isolated from the filtrate from the formamidine disulfide dihydrochloride.

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 thiazotriazole ring under the influence of the strong acid:



When R = aryl a different reaction takes place, and 2-aminobenzothiazoles are formed.^{3,4} This is readily explained as an electrophilic attack of the initial positive ion on the aromatic nucleus:



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.

Since Sahasrabudhey has advanced the hypothesis that the formula of formamidine disulfide could be bisected,⁵ it should be mentioned that we found formamidine disulfide dihydrochloride to be diamagnetic, which excludes any formula with an odd number of electrons.

The infrared spectrum of formamidine 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.
 2690 m (=NH₂⁺)
 1650 vs (NH₂ deform.)
 1620 m sh
 1515 w ν (N—C—S)
 1410 s ν (N—C=N)
 1100 w NH₂ rock.
 1045 m ν (N—C=N)₂
 770 w, 690 m br. NH₂ wag.

In nujol mull the compound shows practically the same spectrum except that the strong 3000 cm⁻¹ band is absent. Redpath and Smith⁶ 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 formamidine disulfides also show a strong band at 1660 cm⁻¹ due to the NH₂ 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 formamidine 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 thiatriazoles (*cf.* the preceding paper), which were ascribed to the thiatriazole ring, disappear when the thiatriazoles are transformed into formamidine disulfides.

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

(a) *From thioureas.* 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*-butylthiourea, 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 CCl₄ 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 thiatriazoles.* 5-Amino-1,2,3,4-thiatriazole and 5-alkylamino-1,2,3,4-thiatriazoles (alkyl=methyl, propyl or *tert*-butyl) were heated in conc. hydrochloric acid (10 ml to 0.01 mole of the thiatriazole) until the evolution of gas was evident (60—80°C), and then slowly heated to 100°C in the course of 1 h. The formamidine 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 (5 ml).

Formamidinedisulfidedihydrochloride. Found: (a) C 10.41; H 3.88. M.p. 172—74°C. (b) C 10.63; H 3.65. M.p. 173—75°C. Calc. for C₂H₂Cl₂N₄S₂: C 10.76; H 3.61.

Methylformamidine 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 C₄H₁₂Cl₂N₄S₂: C 18.84; H 4.74.

Propylformamidine disulfide dihydrochloride. Found: (a) N 18.32; M.p. 155—56°C. (b) N 18.24. M.p. 154—56°C. Calc. for C₈H₂₀Cl₂N₄S₂: N 18.23.

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

tert-Butylformamidine disulfide dihydrobromide. Found: (a) C 27.62; H 5.70. M.p. 141—42°C. Calc. for C₁₀H₂₄Br₂N₄S₂: C 28.28; H 5.69.

Treatment of 5-*tert*-butyl-1,2,3,4-thiatriazole with hydrochloric acid according to (b) yielded the unsubstituted formamidine disulfide di-

hydrochloride. (Found: C 11.00; H 3.67. M.p. 172–74°C. Calc. for $C_2H_8Cl_2N_4S_2$: C 10.76; H 3.61). The unsubstituted formamidine disulfide dihydrochloride was also obtained when *tert*-butylformamidine disulfide dihydrobromide was heated with conc. hydrochloric acid to 80°C for 1½ 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 (168⁷: 171–72⁸). (Found: C 45.43; H 9.15; N 21.16. Calc. for $C_8H_{12}N_2S$: C 45.44; H 9.15; N 21.20).

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The Structure of (+)- ϵ -Muuro- lene (" ϵ -Cadinene") *,**

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Four sesquiterpenes of the cadalene type yielding (+)-muurolene dihydrochloride¹ (m.p. 87–8°, $[a]_D^{22} + 13.2^\circ$ (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"† ($C_{15}H_{24}$, b.p. 125–7°/10 mm, n_D^{22} 1.5059, $[a]_D^{22} - 1.8^\circ$ (c 2.5); $C_{15}H_{24}$, b.p. 128–30°/10 mm, n_D^{22} 1.5063, $[a]_D^{22} - 85.3^\circ$ (c 2.3), respectively) appear not to have been previously isolated in the pure state (*cf.* Refs.¹⁻³). Spectral data (IR, NMR) indicate a close relationship with the cadinenes 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 (–)-cadinene dihydrochloride (ratio: 1:6), and has been identified as copaene (IR, various physical constants and conversion to the diol⁴ 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 rotation⁵) for which structure (1) has been proposed by Šýkora, 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".

†† I thank Professor G. Büchi for a generous gift of copaene.