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Thiadiazoles. Part I. The Oxidation of Amidinothiourea.

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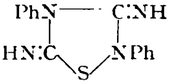
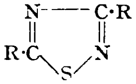
Oxidation, by hydrogen peroxide or iodine, cyclises amidinothiourea to 3 : 5-diamino-1 : 2 : 4-thiadiazole. Some properties of this base are described and reasons for the suggested structure given. Both amidinothiourea and its oxidation product are conveniently characterised as arenesulphonate salts.

Arylthioureas can be oxidised to so-called " Hector bases " for which a thiadiazolidine structure (I) is generally accepted (Hector, *Ber.*, 1889, **22**, 1177; 1890, **23**, 357; Fromm and Heyder, *Ber.*, 1909, **42**, 3804; Lal and Krall, *J. Indian Chem. Soc.*, 1939, **16**, 31); aromatic thioamides similarly yield 3 : 5-diaryl-1 : 2 : 4-thiadiazoles (II) (Hofmann and Gabriel, *Ber.*, 1892, **25**, 1578; Walther, *J. pr. Chem.*, 1904, **69**, 44). The mechanism of these and other syntheses of 1 : 2 : 4-thiadiazoles is generally obscure (cf. Bambas, " The Chemistry of Heterocyclic Compounds," Interscience Publishers Inc., New York, 1952, Vol. IV, p. 35). The work reported in this series of papers aims at the unequivocal synthesis of 1 : 2 : 4-thiadiazoles.

The present paper describes the oxidation of amidinothiourea by hydrogen peroxide and iodine in ionising media. Both reagents yield the same product, which, on the basis of its formation and properties, is regarded as 3 : 5-diamino-1 : 2 : 4-thiadiazole (III). The reaction is thus comparable with the synthesis of 3 : 5-di-*p*-tolyl-1 : 2 : 4-thiadiazole (II; R = *p*-$Me\cdot C_6H_4$) by the iodine oxidation of an *N*-arylimidoylarylthioamide, $R\cdot C(:NH)\cdot NH\cdot CS\cdot R$ (Ishikawa, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1928, **7**, 237).


(I)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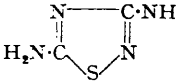
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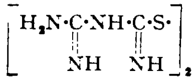
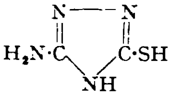

$\left[H_2N\cdot\underset{NH}{\underset{\|}{C}}\cdot NH\cdot\underset{NH}{\underset{\|}{C}}\cdot S\cdot\right]_2$
(IV)


(V)

When treated with an excess of hydrogen peroxide in the presence of mineral acid, amidinothiourea was converted into a monoacid base, which formed arenesulphonate salts and was conveniently isolated in this form in very good yields. The same salts were obtained directly by oxidising amidinothiourea arenesulphonates. In each case, a small proportion (5—6%) of the starting material was desulphurised hydrolytically to amidinourea. In contrast to amidinothiourea, which is instantly desulphurised in the cold by lead salts in alkaline solution, the oxidation product precipitated lead as the sulphide only on heating. This reaction proved a convenient means for testing for completeness of oxidation.

The oxidation of thiourea in ionising media yields the symmetrical " dithioformamidine," $[NH_2\cdot C(:NH)\cdot S\cdot]_2$ (Claus, *Annalen*, 1875, **179**, 139; Werner, *J.*, 1912, **101**, 2177; Fromm and Heyder, *loc. cit.*). A possible analogous disulphide structure (IV) for the present products, almost indistinguishable analytically from (III), was eliminated by molecular-weight determinations, and by the relative stability of the free base. 3 : 5-Diamino-1 : 2 : 4-thiadiazole (III) was unaffected by prolonged treatment with 10% ammonia or pyridine at 100°; although the compound was decomposed by strong alkalis on heating, it was sufficiently stable to be isolated from its salts by cold aqueous sodium hydroxide. Free dithioformamidine, on the other hand, is not known; the base decomposes instantly with elimination of sulphur when attempts are made to liberate it from its salts (McGowan, *J.*, 1886, **49**, 191; Remsen and Turner, *Amer. Chem. J.*, 1901, **25**, 190; Fromm and Heyder, *loc. cit.*).

Iodine reacted with amidinothiourea, to yield the same product as hydrogen peroxide. The method offered no advantage from the preparative point of view, but allowed the uptake of the oxidising agent to be observed quantitatively. Although theory required consumption of two equivalents of halogen, reaction in alcohol ceased after absorption of only one equivalent of iodine: 3 : 5-diamino-1 : 2 : 4-thiadiazole hydriodide was isolated in 32—35% yield; the mother-liquors contained much unchanged starting material as the hydriodide, which resists oxidation by iodine as was shown in a separate experiment.

$$2NH_2{\cdot}C({:}NH){\cdot}NH{\cdot}CS{\cdot}NH_2 + I_2 \longrightarrow NH_2{\cdot}C({:}NH){\cdot}NH{\cdot}CS{\cdot}NH_2{,}HI + C_2H_4N_4S{,}HI\text{(as III)} \quad (1)$$

In aqueous solution, the iodine oxidation of amidinothiourea was reversible, and, as with thiourea (cf. Marshall, *Proc. Roy. Soc. Edin.*, 1902, **24**, 233; Reynolds and Werner, *J.*, 1903, **83**, 1; Werner, *ibid.*, 1912, **101**, 2166, 2179), the completeness depended on the concentration of the reactants. In sufficiently great dilution ($<0{\cdot}066$M; cf. Table, p. 5), the halogen consumption was in conformity with the production of the heterocyclic system (equation 1): spontaneous evaporation of suitable reaction mixtures afforded 3 : 5-diamino-1 : 2 : 4-thiadiazole in 65—70% yield.

$$NH_2{\cdot}C({:}NH){\cdot}NH{\cdot}CS{\cdot}NH_2 + I_2 \rightleftharpoons C_2H_4N_4S{,}HI\text{ (as III)} + HI \quad . \quad . \quad . \quad . \quad (2)$$

Zinc and hydrochloric acid reconverted 3 : 5-diamino-1 : 2 : 4-thiadiazole almost quantitatively into amidinothiourea. In this respect, the compound differs from other 1 : 2 : 4-thiadiazoles (*e.g.*, I, II), which on reduction lose sulphur and yield substituted amidines or guanidines as main products (Hector, *Ber.*, 1892, **25**, 799; Ishikawa, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1925, **3**, 147).

The removal of two atoms of hydrogen from amidinothiourea may, theoretically, cause an alternative mode of ring closure, and affect two imino- instead of one thiol and one imino-groups. 3-Amino-5-mercapto-1 : 2 : 4-triazole (V) which would result by this cyclisation, however, has previously been synthesised by other routes (Fromm *et al.*, *Annalen*, 1922, **426**, 313; 1924, **437**, 108; Arndt and Milde, *Ber.*, 1921, **54**, 2089; 1922, **55**, 341), and differs from the base obtained in the present work. The behaviour, on attempted oxidation, of an amidinothiourea structure having its thiol group blocked by a substituent was in agreement with the above observation. *N*-Amidino-*S*-ethylthiourea did not decolorise iodine even in dilute aqueous solution. Diguanide, $NH_2{\cdot}C({:}NH){\cdot}NH{\cdot}C({:}NH){\cdot}NH_2$, containing imino-groups situated exactly as in amidinothiourea, also failed to react with iodine. Finally, hydrogen peroxide did not cyclise *N*-amidino-*S*-ethylthiourea, but gave mixtures of varying proportions of amidinourea and the unchanged reactant. The assumption that oxidation of amidinothiourea involves a thiol group preferentially is therefore confirmed.

Amidinothiourea may conveniently be obtained in 60% yield on a preparative scale by passing hydrogen sulphide through an aqueous solution of dicyandiamide at 70—80°. This is a modification of Bamberger's method (*Ber.*, 1883, **16**, 1461) and permits the free base to be isolated directly. A small amount of dithiobiuret is produced in the reaction, doubtless by interaction between amidinothiourea and excess of hydrogen sulphide.

EXPERIMENTAL

Light petroleum was of boiling range 60—80°.

Amidinothiourea (*and* 2 : 4-*Dithiobiuret*).—A solution of *N*-cyanoguanidine (42·0 g., 0·5 mole) in water (200 ml.) was kept at 75° during 12 hr., and at 65—70° during an additional 24—30 hr., while hydrogen sulphide was passed through it (2—3 bubbles per second). The resulting yellow liquid was cooled to 45°, made strongly alkaline with aqueous sodium hydroxide (40% w/v; 15 ml.), and filtered with suction. The filtrate, on slow cooling to room temperature, and storage at 0° for 24 hr., deposited prismatic leaflets. They were collected (filtrate A) and washed with ice-water (3 × 20 ml.), and consisted of crude amidinothiourea [m. p. 162—164° (decomp.), after sintering at 154—158°; yield, 32·5—35·4 g., 55—60%]. Two crystallisations of the powdered solid from boiling methanol (8 ml. per g.; recovery per crystallisation, 65—70%) gave colourless massive lustrous prisms, m. p. 170—172° (decomp.) (Found: N, 47·2. Calc. for $C_2H_6N_4S$: N, 47·45%). The mother-liquors gave, on partial evaporation under reduced pressure, a crop of satisfactory quality.

Filtrate A was acidified to Congo-red with concentrated hydrochloric acid (25—30 ml.), a powdery precipitate separating and hydrogen sulphide being evolved simultaneously. After storage at 0° for 12 hr., the solid was collected (filtrate B) and washed with ice-water (3 × 30 ml.) (dry weight: 7·5—9 g.). It was stirred in water (120 ml.) at 95° for 2 min., and undissolved material (1—1·5 g., chiefly sulphur) removed by rapid filtration. The yellow filtrate deposited pale yellow needles, which were collected at 0° [m. p. 180—182° (decomp., after sintering at 172—175°); 5·5—7·0 g., 8—10%]. Further crystallisation, with addition of carbon, from water (12 ml. per g.; recovery 80—90%) gave needles of 2 : 4-dithiobiuret, m. p. 181—182° (decomp., after sintering slightly at 178—180°) (Found: C, 18·0; H, 3·8; N, 30·9; S, 46·9; 48·2. Calc. for $C_2H_5N_3S_2$: C, 17·8; H, 3·7; N, 31·1; S, 47·4%). Two additional crystallisations from ethanol–water (10 ml. each, per g.) raised the m. p. to 183—185° (decomp.).

Filtrate B was treated with toluene-*p*-sulphonic acid monohydrate (19·0 g., 0·1 mole) which dissolved rapidly. The separated crystalline amidinothiourea toluene-*p*-sulphonate was collected after 24 hr. at 0°, and washed with ice-water [m. p. 176—178° (decomp., after sintering at 170°); 16·5—18 g., 11—12·5%, calc. on the *N*-cyanoguanidine]. To this salt (14·5 g., 0·05 mole), mixed with water (10 ml.), aqueous sodium hydroxide (20 ml., 12% w/v, 0·06 mole) was added, and the stirred suspension warmed to 35°; dissolution occurred rapidly. Traces of undissolved impurities were quickly filtered off at the pump, and the filtrate was set aside at 0° for 24 hr.; prisms of amidinothiourea (3·8—4·4 g., 65—75%, calc. on the salt) separated.

Extending the time of reaction to 100 hr. increased the yield of dithiobiuret to 15—18%, but reduced that of amidinothiourea to 25%.

In previous syntheses of this compound (Rathke, *Ber.*, 1878, **11**, 963; Bamberger, *loc. cit.*; Slotta and Tschesche, *Ber.*, 1929, **62**, 1398; Thurston and Sperry, U.S.P. 2,364,594; Birtwell, Curd, Hendry, and Rose, *J.*, 1948, 1653), amidinothiourea was collected as a sparingly soluble salt from which the base was isolated by comparatively laborious methods.

The following were prepared from amidinothiourea (0·01 mole) and the appropriate sulphonic acid (0·012 mole) in water solution, and crystallised from aqueous ethanol (yields of uncrystallised salt in parentheses): *Toluene*-p-*sulphonate* (88%), m. p. 177—178° (decomp.) (Found: C, 37·1; H, 4·8; N, 19·9; S, 22·4. $C_9H_{14}O_3N_4S_2$ requires C, 37·2; H, 4·8; N, 19·3; S, 22·0%). m-*Nitrobenzenesulphonate* (95%), m. p. 205—206° (decomp.) (Found: C, 30·2; H, 3·7; N, 22·1. $C_8H_{11}O_5N_5S_2$ requires C, 29·9; H, 3·4; N, 21·8%). *Benzenesulphonate* (30%), m. p. 112—114° (decomp., after sintering at 100—104°) (Found: N, 19·9. $C_8H_{12}O_3N_4S_2$ requires N, 20·3%).

Amidinothiourea hydriodide was prepared (84%) by adding hydriodic acid (*d* 1·7; 13 g., 0·06 mole) to a suspension of powdered amidinothiourea (5·90 g., 0·05 mole) in boiling methanol (8 ml.). The *hydriodide* formed prisms, m. p. 186—187° (decomp.) [Found: I (Volhard), 52·3, 52·6. $C_2H_6N_4S,HI$ requires I, 51·6%].

Oxidation of Amidinothiourea by Hydrogen Peroxide.—(*a*) To a boiling solution of amidinothiourea (11·8 g., 0·1 mole) in ethanol (96%, 250 ml.), concentrated hydrochloric acid (10 ml., 0·1 mole) was added, followed by aqueous hydrogen peroxide (6% w/v; 170 ml., 0·3 mole) during 20—25 min. Most of the ethanol was removed under reduced pressure during 20—25 min. and the warm residual colourless liquid (180—200 ml.) treated with toluene-*p*-sulphonic acid monohydrate (23·75 g., 0·125 mole), which dissolved instantly. After 12 hr. at 0°, the product was collected and washed with the minimum of ice-water [m. p. 230—234° (decomp.), after sintering at 226—228°; 18·7—21·9 g., 65—76%] (aqueous filtrates A). Two crystallisations from 96% ethanol–light petroleum (20 and 8 ml., respectively, per g.; recovery per crystallisation, 80%) gave platelets of 3 : 5-*diamino*-1 : 2 : 4-*thiadiazole toluene*-p-*sulphonate*, m. p. 238—240° (decomp.) (Found: C, 37·3; H, 3·9; N, 19·4; S, 21·9. $C_9H_{12}O_3N_4S_2$ requires C, 37·5; H, 4·2; N, 19·4; S, 22·2%), very sparingly soluble in boiling absolute ethanol, soluble in boiling ethanol containing small percentages of water. A solution of the salt in cold 12% aqueous sodium hydroxide remained clear on dropwise addition of aqueous lead acetate; lead sulphide was only precipitated on heating.

The aqueous filtrate A was allowed to evaporate spontaneously at room temperature to small volume (50—60 ml.). Two crystallisations of the collected solid (3·4—4 g.) from 95% ethanol gave platelets (1·35—1·65 g., 5—6%) of amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. (Haag, *Annalen*, 1862, **122**, 25) 238—242° (decomp.) (Found : C, 39·9; H, 5·1. Calc. for $C_9H_{14}O_4N_4S$: C, 39·4; H, 5·1%). The material gave the characteristic yellow nickel salt on addition of nickel chloride (Grossmann and Schück, *Ber.*, 1906, **39**, 3357).

(*b*) The *m*-nitrobenzenesulphonate was similarly obtained as a pale buff solid, m. p. 228—230° (decomp.), after sintering at 222—226° (91%). Two crystallisations from 96% ethanol–light petroleum (70 and 40 ml. per g., respectively; recovery per crystallisation, 80%) gave the m-*nitrobenzenesulphonate* as a buff crystalline powder, m. p. 226—228° (decomp., after sintering at 224—226°) (Found : N, 21·3; S, 20·2. $C_8H_9O_5N_5S_2$ requires N, 21·9; S, 20·1%).

(*c*) Similarly, there was obtained (35%) 3 : 5-*diamino*-1 : 2 : 4-*thiadiazole benzenesulphonate*, forming platelets, m. p. 229—231° (decomp., after sintering at 226°), from ethanol (Found : C, 34·7; H, 3·5. $C_8H_{10}O_3N_4S_2$ requires C, 35·0; H, 3·65%).

(*d*) *Direct oxidation of amidinothiourea arenesulphonates by hydrogen peroxide.* A boiling solution of amidinothiourea *m*-nitrobenzenesulphonate (3·21 g., 0·01 mole) in aqueous ethanol (75%; 20 ml.) containing hydrochloric acid (1 ml., 0·01 mole) was treated with hydrogen peroxide (6%; 17 ml., 0·03 mole). The resulting liquid, when diluted with ethanol (10 ml.) and cooled to 0°, deposited a crystalline solid (2·40 g., 75%) which gave, on crystallisation (cf. example *b*), 3 : 5-diamino-1 : 2 : 4-thiadiazole *m*-nitrobenzenesulphonate, m. p. and mixed m. p. (specimen *b*) 226—228° (decomp. after sintering at 224°). Other amidinothiourea arenesulphonates were similarly oxidised.

Oxidation of Amidinothiourea by Methanolic Iodine.—Amidinothiourea (5·90 g., 0·05 mole), dissolved in hot methanol (150 ml.), was treated, at 30°, with a solution of iodine (6·35 g., 0·05 g.-atom) in methanol (40 ml.) during 1—2 min. All but the last 1—2 ml. of the iodine solution were instantly decolorised. The liquid was rapidly evaporated in a vacuum (bath-temp., 40—45°; 15—20 min.; severe frothing) to small volume (70—80 ml.). The residual orange-brown liquid was gently agitated and slowly diluted with ether (300—350 ml.); crystallisation was completed by storage at 0° during 24 hr. The collected material (filtrate A) was washed with ether, and formed a white crystalline powder (3·90—4·25 g., 32—35%) of 3 : 5-*diamino*-1 : 2 : 4-*thiadiazole hydriodide*, m. p. 174—178° (decomp.) [Found : I (Volhard), 52·3, 51·6. $C_2H_4N_4S,HI$ requires I, 52·0%].

The methanol-ethereal filtrates A, on gradual dilution with light petroleum (3 × 100 ml., at 1-hr. intervals), and storage at 0°, deposited more crystalline material (3·0—3·3 g.), consisting of impure amidinothiourea hydriodide. This was identified by conversion into the toluene-*p*-sulphonate, m. p. and mixed m. p. 175—178° (decomp.) [2·9 g., corresponding to 20% unchanged starting material].

Conversion of hydriodide into arenesulphonates. The above hydriodide (2·45 g., 0·01 mole), dissolved in cold water (20 ml.), was treated with a saturated aqueous solution of the appropriate sulphonic acid (0·012 mole); the following salts (yields of uncrystallised product in parentheses) were prepared : Toluene-*p*-sulphonate (80%), m. p. and mixed m. p. 236—240° (decomp.) (Found : C, 37·6; H, 4·2; N, 19·6%). *m*-Nitrobenzenesulphonate (82%), m. p. and mixed m. p. 226—229° (decomp., after sintering at 223—226°) (Found : C, 30·0; H, 2·9. Calc. for $C_8H_9O_5N_5S_2$: C, 30·1; H, 2·8%). Benzenesulphonate (54%), m. p. and mixed m. p. 228—231° (decomp., after sintering at 225°) (Found : N, 20·8; S, 23·6. Calc. for $C_8H_{10}O_3N_4S_2$: N, 20·4; S, 23·4%).

Treatment of Amidinothiourea Hydriodide with Methanolic Iodine.—A solution of the reactant (0·01 mole) in warm methanol (8 ml.) was treated with iodine (0·01 mole) in methanol (15 ml.); no decolorisation occurred and amidinothiourea was recovered as the toluene-*p*-sulphonate, m. p. and mixed m. p. 175—177° (decomp.) (total yield, 1·95 g., 68%). In dilute aqueous solution (2·5% w/v), however, amidinothiourea hydriodide decolorised an equimolecular quantity of iodine.

Oxidation of Amidinothiourea by Aqueous Iodine.—A solution of amidinothiourea (1·18 g., 0·01 mole) in water (80 ml.) was treated, at room temperature, with N-iodine (20 ml.). Almost all the iodine was decolorised; the pale yellow liquid was treated with toluene-*p*-sulphonic acid monohydrate (2·85 g., 0·015 mole), and set aside for spontaneous evaporation nearly to dryness. The crystalline pink to violet solid was collected, washed with water (3 × 4 ml.), and fractionated by crystallisation from 96% ethanol. The less soluble product was the toluene-*p*-sulphonate of 3 : 5-diamino-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. 236—238° (decomp.) (total, 1·85 g., 65%), the more soluble material that of amidinothiourea, m. p. and mixed m. p. 176—178° (decomp.) (0·35 g., 12%).

Effect of the Concentration of Amidinothiourea on the Completeness of Oxidation (*by Aqueous Iodine*).—(i) Portions of amidinothiourea (0·59 g., 0·005 mole), dissolved in the appropriate volume of water (Table, line 2), were titrated with N-iodine, completeness of reaction being tested for by starch solution. The " end-point " was taken when the blue colour produced by starch and successive drops withdrawn ½, 1, and 1½ min. after the addition of iodine was of reasonably undiminished intensity. However, this point could not be determined with accuracy, particularly in the more concentrated solutions.

(ii) Portions of amidinothiourea (0·59 g., 0·005 mole), dissolved in the appropriate volume of water (Table, line 2), were treated with aqueous N-iodine (10 ml., 0·005 mole) at room temperature. After 2 min., the unused iodine was titrated with 0·1N-sodium thiosulphate, starch being used as external indicator. In experiments 5—7, the " end-point " was ill-defined. The results of experiments (i) and (ii) are summarised in the Table.

Experiment (i)

Run	1	2	3	4	5	6	7	8
Water (ml.)	140	90	65	40	30	20	10	5
N-Iodine absorbed (ml.)	9·8	9·6	9·3	8·9	8·2	7·8	6·8	6·0
Molarity of amidinothiourea at "end-point"	0·033	0·050	0·066	0·102	0·13	0·18	0·29	0·45
Mols. of iodine absorbed •	0·98	0·96	0·93	0·89	0·82	0·78	0·68	0·60

Experiment (ii)

Molarity of amidinothiourea	0·033	0·050	0·066	0·100	0·125	0·166	0·250
Mols. of iodine absorbed •	0·99	0·99	0·95	0·88	0·84	0·75	0·65

• Per mol. of amidinothiourea.

3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole*.—A cooled suspension of the toluene-*p*-sulphonate (5·75 g., 0·02 mole) or the hydriodide (4·9 g., 0·02 mole) of this base in water (8 ml.) was slowly treated with aqueous sodium hydroxide (50% w/v; 2·4 ml., 0·03 mole). The warm (30—35°) solution was quickly filtered to remove traces of insoluble impurities and set aside at 0° for 48 hr. The separated prisms (m. p. 163—167°; 1·48—1·75 g., 64—76%) were collected, and gave, after two crystallisations from ethanol–light petroleum (10 and 3 ml., respectively, per g.; recovery per crystallisation, 80—90%), prisms of 3 : 5-*diamino*-1 : 2 : 4-*thiadiazole*, m. p. 169—171° [Found: C, 21·2, 20·6; H, 3·3, 3·4; N, 49·2; S, 28·0; *M* (cryoscopic) in thymol, 110, 115; in camphor, 130, 140. $C_2H_4N_4S$ requires C, 20·7; H, 3·45; N, 48·3; S, 27·6%; *M*, 116], highly soluble in warm ethanol, acetone, and water, sparingly soluble in light petroleum.

A solution of the base in cold 12% alkali, when treated with aqueous lead acetate, only precipitated lead sulphide on subsequent heating. The compound was unaffected when its 5% solution in aqueous ammonia (10%), or in pyridine, was kept at 100° during 30 min. The identity of the base was confirmed by its reconversion into the toluene-*p*-sulphonate, m. p. and mixed m. p. 236—238° (decomp.), and the *m*-nitrobenzenesulphonate, m. p. and mixed m. p. 227—228° (decomp., after sintering at 225°).

Reduction of 3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole*.—A suspension of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (2·30 g. 0·008 mole) in boiling absolute ethanol (30 ml.) was treated with zinc foil (4 g.), followed by concentrated hydrochloric acid (3 ml.), and the suspension was gently refluxed during 15 min. The liquid was decanted from the zinc (which was once again extracted with a little boiling ethanol), and the combined solution rapidly evaporated in a vacuum to small volume (6—8 ml.). Dilution of the clear colourless residual liquid with water (12 ml.) and addition of toluene-*p*-sulphonic acid monohydrate (0·95 g., 0·005 mole) gave, on storage at 0°, lustrous prisms [m. p. (174°) 176—178° (decomp.); 2·12 g., 91%] which, on crystallisation from ethanol, gave amidinothiourea toluene-*p*-sulphonate, m. p. and mixed m. p. 177—178° (decomp.).

N-*Amidino*-S-*ethylthiourea Salts*.—Amidinothiourea (11·8 g., 0·1 mole) in methanol (80 ml.) was refluxed with ethyl bromide (55 g., 0·5 mole) during 4 hr. After removal of the excess of the ethyl bromide and most of the solvent under reduced pressure, the residual colourless liquid (30 ml.) was diluted with acetone (25 ml.) and cooled; crystals appeared slowly. Separation of the product was completed by very gradual dilution of the crystallising mixture with ether (150—180 ml.; avoiding precipitation of the hydrobromide as an oil), followed by storage at 0°. The collected material was washed with ether, and formed prisms of *N*-amidino-*S*-ethylthiourea hydrobromide, m. p. 125—128° (decomp., after sintering at 115—120°) (17·0—19·3 g., 75—85%) (Found: C, 21·6; H, 4·6%). Two crystallisations from ethanol–ether raised the m. p. to 128—134° (decomp.) (Found: C, 21·8; H, 4·9; Br, 34·6. Calc. for $C_4H_{10}N_4S$,HBr: C, 21·2; H, 4·85; Br, 35·2%). [Slotta and Tschesche (*Ber.*, 1929, **62**, 1398) obtained this salt from amidinothiourea carbonate, and give m. p. 166° (decomp.).] Amidinothiourea, being insoluble in boiling ethyl bromide, was recovered unchanged after prolonged refluxing with a large excess of this reagent.

Treatment of a solution of *N*-amidino-*S*-ethylthiourea hydrobromide (0·01 mole) in cold water (8 ml.) with toluene-*p*-sulphonic acid monohydrate (0·02 mole) afforded, after two crystallisations from ethanol (4 ml. per g.), prisms (91%) of N-*amidino*-S-*ethylthiourea toluene*-p-*sulphonate,* m. p. 151—153° (decomp.) (Found : C, 41·3; H, 5·6; N, 17·3; S, 19·7. $C_{11}H_{18}O_3N_4S_2$ requires C, 41·5; H, 5·7; N, 17·6; S, 20·1%). The m-*nitrobenzenesulphonate,* similarly prepared (92%), consisted of pale yellow prisms, m. p. 161—163° (decomp.) (from ethanol) (Found : C, 34·1; H, 4·3. $C_{10}H_{15}O_5N_5S_2$ requires C, 34·4; H, 4·3%).

Action of Iodine and Hydrogen Peroxide on N-*Amidino*-S-*ethylthiourea.*—(i) Aqueous or ethanolic N-iodine was not decolorised when added to 0·5M-aqueous or -ethanolic *N*-amidino-*S*-ethylthiourea hydrobromide at room temperature. (ii) A boiling solution of *N*-amidino-*S*-ethylthiourea hydrobromide (2·27 g., 0·01 mole) in absolute ethanol (15 ml.) was treated with hydrogen peroxide (6% w/v; 17 ml., 0·03 mole) during 15 min. The solution was distilled (to 20 ml.), and treated with toluene-*p*-sulphonic acid (3·44 g., 0·02 mole). The clear liquid was allowed to evaporate spontaneously at room temperature (to approx. 12 ml.). The crystals were collected (2·5 g.), powdered, and heated with absolute ethanol (6 and 2 ml.), and the mixture was filtered hot (filtrate A). The residual solid (1·45 g.) gave, after two or three crystallisations from 95% ethanol, prisms (1·15 g., 42%) of amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. 238—240° (Found : C, 39·1; H, 4·9; N, 19·9. Calc. for $C_9H_{14}O_4N_4S$: C, 39·4; H, 5·1; N, 20·4%). The hot ethanolic filtrate A was diluted with light petroleum (6 ml.) and deposited a product which consisted, after crystallisation from ethanol–light petroleum, of *N*-amidino-*S*-ethylthiourea toluene-*p*-sulphonate (0·55 g., 17%), m. p. and mixed m. p. 150—153° (decomp.). (iii) Aqueous solutions of diguanide sulphate (Ostrogovich, *Chem. Zentr.*, 1910, II, 1890; Rackmann, *Annalen*, 1910, **376**, 170) did not decolorise aqueous iodine.

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