584. *Thiadiazoles. Part V.*[1] *The Oxidation of* N-(*Arenesulphonamidino*)*thioureas.*

By Frederick Kurzer.

Bromine cyclises *N*-(sulphonamidino)thioureas almost quantitatively to 5-arylamino-3-sulphonamido-1 : 2 : 4-thiadiazoles. Arenesulphonyl chlorides in pyridine are also suitable cyclising agents, which convert *N*-(sulphonamidino)thioureas as well as the parent bases, amidinothiourea and its homologues, into sulphonyl derivatives of 1 : 2 : 4-thiadiazoles directly.

N-(Aroylamidino)thioureas are cyclised by oxidising agents to 5-amino-3-aroyl- or 3-amino-5-aryl-1 : 2 : 4-thiadiazoles or mixtures thereof, depending on the experimental conditions.[1] The present account describes analogous reactions involving *N*-(arenesulphonamidino)thioureas.

Under the usual conditions,[2] bromine cyclised *N*-(toluene-*p*-sulphonamidino)thiourea [3] (I; R = H, R′ = *p*-C_6H_4Me) and its *N*-phenyl-homologue (I; R = Ph) to 5-amino(or anilino)-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole (II; R = H or Ph, R′ = *p*-C_6H_4Me) almost quantitatively. The alternative formulation of the products as (VII) may reasonably be excluded on the basis of the preferential participation of the amino- rather than the sulphonamido-hydrogen in the oxidative ring-closure. Since the cyclisation product from *N*-(toluene-*p*-sulphonamidino)thiourea proved to be identical with the derivative previously obtained [2b] by direct acylation of 3 : 5-diamino-1 : 2 : 4-thiadiazole, the present results indirectly confirm the superior reactivity of the 3-amino- over the 5-amino-group in this heterocyclic system.

Arenesulphonyl chlorides, in pyridine, were next observed to bring about the same cyclisation. *N*-Phenyl-*N*′-(toluene-*p*-sulphonamidino)thiourea (I; R = Ph, R′ = *p*-C_6H_4Me), for example, was converted into 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole (II; R = Ph, R′ = *p*-C_6H_4Me) in 50% yield, a further 25% being isolated as the heterocyclic disulphonyl derivative. The formation of the latter is likely to proceed by acylation of the primarily cyclised product (II) rather than by cyclisation of the appropriate preformed disulphonylamidinothiourea, since sulphonyl chlorides failed to afford sulphonylamidinothioureas (I) from amidinothiourea under a variety of conditions (cf. p. 3001) but are known to acylate 1 : 2 : 4-thiadiazoles readily.[1, 2b, c] It seemed therefore probable, in spite of published data to the contrary,[4] that amidinothiourea itself might undergo an analogous simultaneous ring closure and sulphonylation. This expectation was realised: arenesulphonyl chlorides converted, not only the parent compound (III; R = H) into 5-amino-3-arenesulphonamido-1 : 2 : 4-thiadiazoles in consistent, if moderate yields, but also cyclised and acylated homologues such as *N*-phenyl- (III; R = Ph) and *NN*′-diphenyl-amidinothiourea with equal facility.

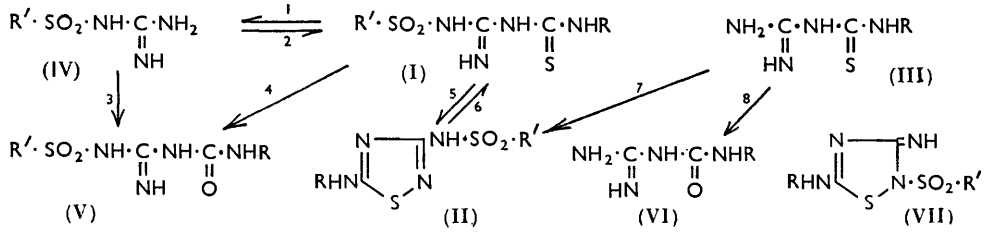
Irrespective of its mechanism, the reaction may be expressed by the overall equation (1); this representation is supported by the observation that approximately one-third of a mole of *p*-tolyl toluene-*p*-thiolsulphonate was isolated for each mole of 1 : 2 : 4-thiadiazole; much of the excess of sulphonyl chloride reappeared, of course, as the sulphonic acid. The patent literature records a claim [4] according to which amidinothiourea and *p*-nitrobenzenesulphonyl chloride react in pyridine, substantially under the conditions of the above cyclisations, to yield the appropriate sulphonylamidinothiourea (I; R = H,

[1] Part IV, Kurzer, *J.*, 1956, 4524.
[2] Parts I—III, Kurzer, (*a*) *J.*, 1955, 1; (*b*) *J.*, 1955, 2288; (*c*) *J.*, 1956, 2345; (*d*) Cf. *Chem. and Ind.*, 1956, 1482.
[3] Kurzer and Powell, *J.*, 1953, 2531.
[4] Winneck, U.S.P. 2,303,972/1942.

R′ = *p*-NO_2·C_6H_4). It seems significant, however, that physical properties were given for neither this compound nor the *p*-amino-analogue prepared therefrom by reduction.

$$5R'\cdot SO_2Cl + 3NH_2\cdot C(:NH)\cdot NH\cdot CS\cdot NH_2 \longrightarrow 3R'\cdot SO_2\cdot C_2H_3N_4S \text{ (cf. II)} + R'\cdot SO_2\cdot SR' + 2H_2O + 5HCl \quad . \quad . \quad (1)$$

Sulphonyl chlorides have previously been found to oxidise compounds incorporating the thioamide structure. In media such as ethanol,[5,6] acetone,[6] and other organic solvents,[6] thiourea yields dithioformamidine, while arylthioureas [7] are oxidised to " Hector's bases " (probably 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines). A comparable reaction is the cyclisation of thiobenzamide to 3 : 5-diphenyl-1 : 2 : 4-thiadiazole under the influence of thionyl chloride.[8] In contrast to these reactions, and the successful cyclisation of amidinothioureas (I; III) in pyridine (to II), arenesulphonyl chlorides in neutral solvents effected merely a partial desulphurisation : in ethanol or acetone, they slowly converted amidinothiourea (III; R = H) into amidinourea (VI; R = H) which separated gradually as the arenesulphonate. The distinctly acidic character of sulphonylthiadiazoles (II) derived from amidinothioureas, contrasting with the basic nature of the oxidation products of thioureas, may necessitate, in the present cyclisation, the use of a basic medium; moreover, this would form the more reactive addition complex with the sulphonyl halide.



Reagents: 1, H_2O_2. 2, R·NCS. 3, R·NCO. 4, H_2O_2. 5, Br_2; R′·SO_2Cl–C_5H_5N; H_2O_2. 6, Zn–HCl. 7, R′·SO_2Cl–C_5H_5N. 8, R′·SO_2Cl–EtOH.

Hydrogen peroxide, so far the most generally applicable cyclising agent for compounds incorporating the CS·NH·C(:NH)· grouping,[1,2] was found to be unsuitable for cyclising sulphonamidinothioureas. Irrespective of the concentration of mineral acid present (cf. ref. 1), its predominating action was fission of such derivatives (I; R = H or Ph; R′ = C_6H_4Me) at the CS–NH bond, giving sulphonylguanidine (IV) as main product (up to 56%). A smaller proportion of the reactant (up to 35%) was desulphurised to sulphonamidinoureas (V), while a minute fraction was occasionally cyclised (to II), particularly in the presence of mineral acid. These observations are significant in connexion with the comparable peroxide oxidation of *N*-benzoylamidinothiourea [1] which affords the expected 5-amino-3-benzamido-1 : 2 : 4-thiadiazole in acid media, but yields 3-amino-5-phenyl-1 : 2 : 4-thiadiazole in neutral solution. Amongst possible mechanisms for this unexpected latter reaction, the intermediate formation of benzoylguanidine has been considered.[1] The course of the analogous oxidation of sulphonamidinothioureas appears to provide some indirect support for this suggestion : while the stability of the sulphonyl group terminates the oxidation at the sulphonylguanidine (IV) stage, analogously formed benzoylguanidine may undergo thiation at its carbonyl group,[9] thus finally yielding the heterocyclic end-product.

[5] McGowan, *J.*, 1886, **49**, 191; 1887, **51**, 666; *J. prakt. Chem.*, 1886, **33**, 188; Remsen and Turner, *Amer. Chem., J.*, 1901, **25**, 190.
[6] Leitch, Baker, and Brickman, *Canad. J. Res.*, 1945, **23**, *B*, 139.
[7] Fromm and Heyder, *Ber.*, 1909, **42**, 3804.
[8] Ishikawa, *Sci. Papers Inst. Phys. Chem. Res.* (*Tokyo*), 1928, **7**, 237.
[9] Kindler and Finndorf, *Ber.*, 1921, **54**, 1079; Kindler, *Annalen*, 1923, **431**, 209; Gatewood and Johnson, *J. Amer. Chem. Soc.*, 1926, **48**, 2904.

N-Phenyl-*N'*-toluene-*p*-sulphonamidino-urea and -thiourea (V and I; R = Ph, R' = *p*-C_6H_4Me), required in these experiments, were readily accessible by condensation of toluene-*p*-sulphonylguanidine (IV) with phenyl *iso*cyanate or *iso*thiocyanate in the presence of sodium, by the procedure generally applicable for synthesising amidinothioureas.[2,10] In the former case, a product formulated as *NN'*-di(phenylcarbamoyl)-*N''*-(toluene-*p*-sulphonimido)guanidine, $R'\cdot SO_2\cdot N{:}C(NH\cdot CO\cdot NHPh)_2$, arising by the addition of two molecules of phenyl *iso*cyanate to the guanidine, was obtained in addition to the expected urea (V). In this respect, the behaviour of the sulphonylguanidine resembles that of *O*-methyl*iso*urea,[11] which is capable of condensing with two molecules of phenyl *iso*cyanate, but reacts with one molecule of *iso*thiocyanate only.

Experimental

The pyridine used was the commercially available anhydrous grade. Light petroleum was of boiling range 60—80°.

Toluene-*p*-sulphonamidinothiourea was prepared by addition of hydrogen sulphide to *N*-cyano-*N'*-toluene-*p*-sulphonylguanidine.[3] It was not obtainable from amidinothiourea and toluene-*p*-sulphonyl chloride in the presence of ethanolic sodium ethoxide, or of aqueous sodium hydroxide and acetone, by variations of Kaiser and Thurston's general procedure.[12]

N-*Phenyl*-N'-(*toluene*-p-*sulphonamidino*)*thiourea* (I; R = Ph, R' = *p*-C_6H_4Me).—(*a*) The suspension obtained by adding sodium (0·92 g., 0·04 g.-atom) to acetone (50 ml.) was treated with a solution of toluene-*p*-sulphonylguanidine monohydrate (9·24 g., 0·04 mole) in boiling acetone (200 ml.). To the resulting white suspension at 40°, phenyl *iso*thiocyanate (6·75 g., 0·05 mole) was added: all the material rapidly passed into solution, the temperature of which rose spontaneously. After the removal of the solvent in a vacuum during 15 min., the residue was treated with water (300 ml.), the alkaline suspension set aside at 0° overnight, and the separated crude sodium salt collected (filtrate A). It was dissolved in water (250 ml.) at 80° and filtered hot (carbon), and the filtrate slowly acidified, with addition of ice, with concentrated hydrochloric acid (to Congo-red). The precipitated white granular solid gave, on crystallisation from ethanol (10 ml. per g.), prisms of N-*phenyl*-N'-(*toluene*-p-*sulphonamidino*)*thiourea*, m. p. 180—182° (7·8—8·9 g., 56—64%) (Found: C, 51·95; H, 4·5; N, 16·8; S, 18·2. $C_{15}H_{16}O_2N_4S_2$ requires C, 51·7; H, 4·6; N, 16·1; S, 18·4%). Acidification of filtrate A (to Congo-red) precipitated a viscous oil, from which only small quantities of inferior product (m. p. 175—180°) were isolated by crystallisation from ethanol. The product gave a precipitate of lead sulphide on being boiled in 12% aqueous sodium hydroxide containing lead acetate.

Toluene-*p*-sulphonylguanidine and phenyl *iso*thiocyanate failed to interact in boiling acetone, or in pyridine–triethylamine at 100° during 2 hr.

(*b*) A boiling suspension of 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole (1·73 g., 0·005 mole) in ethanol (50 ml.) containing zinc foil (4 g.) was treated with concentrated hydrochloric acid (5 ml.) during 2 min., and refluxed during 8 min. The clear solution, decanted from the zinc, was distilled in a vacuum to 10 ml. and stirred into water. The precipitated granular solid, crystallised as above, was *N*-phenyl-*N'*-(toluene-*p*-sulphonamidino)thiourea, m. p. and mixed m. p. 180—182° (yield, 65%).

N-*Phenyl*-N'-(*toluene*-p-*sulphonamidino*)*urea* (V; R = Ph, R' = *p*-C_6H_4Me).—Interaction of the reactants [quantities and conditions as described immediately above, method (*a*), except for the use of phenyl *iso*cyanate (6·0 g., 0·05 mole) instead of *iso*thiocyanate] gave, after the removal of the acetone, a treacly residue, which was immediately dissolved by the addition of hot 0·25N-sodium hydroxide (300—350 ml.). The orange liquid was then quickly acidified (to Congo-red) with concentrated hydrochloric acid (before separation of sodium salt set in), and the precipitated semisolid orange product separated from the aqueous phase by decantation. When suspended in ice-water, the product solidified rapidly and was collected. It was dissolved by being added to boiling acetone–ethanol (2 : 1; 300 ml.); the solution was refluxed with carbon and filtered at the pump. On storage, the yellow filtrate deposited successive crops of

[10] Slotta, Tschesche, and Dressler, *Ber.*, 1930, **63**, 208.
[11] Bruce, *J. Amer. Chem. Soc.*, 1904, **26**, 449.
[12] Cf. Adams, Kaiser, Nagy, Peters, Sperry, and Thurston, *J. Org. Chem.*, 1952, **17**, 1162.

massive prisms (A), and finally more soluble fractions of felted needles (B). The combined fractions A, crystallised from acetone–ethanol–benzene (2 : 1 : 1) (followed by partial evaporation), gave platelets (7·45 g., 56%) of N-*phenyl*-N′-(*toluene*-p-*sulphonamidino*)*urea*, m. p. 209—211° (after sintering at 207°; somewhat subject to the rate of heating) (Found: C, 54·1; H, 4·8; N, 16·2; S, 9·2. $C_{15}H_{16}O_3N_4S$ requires C, 54·2; H, 4·8; N, 16·9; S, 9·6%).

Fractions B were crystallised by being dissolved in acetone–ethanol (1 : 1, 10 ml. per g.), and the filtered solution evaporated to remove most of the acetone. The product was NN′-*di*-(*phenylcarbamoyl*)-N″-(*toluene*-p-*sulphonimido*)*guanidine*, m. p. 178—179°, crystallising as prisms from ethanol, or as needles from ethanol containing little acetone (yield, 1·95 g., 11%) (Found: C, 58·7; H, 4·7; N, 15·9; S, 7·0. $C_{22}H_{21}O_4N_5S$ requires C, 58·5; H, 4·7; N, 15·5; S, 7·1%). The use of a larger excess of phenyl *iso*cyanate (0·1 mole) and of sodium (0·08 g.-atom) increased the yields of the two products to 70 and 18% respectively.

5-*Amino*-3-*toluene*-p-*sulphonamido*-1 : 2 : 4-*thiadiazole* (II; R = H, R′ = *p*-C_6H_4Me).—(*a*) A solution of amidinothiourea (2·36 g., 0·02 mole) in pyridine (40 ml.) was treated with toluene-*p*-sulphonyl chloride (7·6 g., 0·04 mole). To the resulting hot liquid, kept at 100° during 45 min., more sulphonyl chloride was added at ¼-hour intervals (2 × 0·01 mole). The soft brown material obtained by adding the mixture to ice (300 g.) and concentrated hydrochloric acid (45 ml.) was collected, rinsed with water, and dissolved in boiling ethanol (30 ml.). The resulting brown solution deposited successive crops of crystals: (*A*) The powdery least soluble high-melting fractions gave, after crystallisation from ethanol–acetone–light petroleum, prisms of 5-amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. [with authentic material prepared by method (*b*)] 231—233° (decomp., after sintering at 226°). Yield 1·51 g., 28%. (*B*) The most soluble crop, consisting of glass-like prisms, was *p*-tolyl toluene-*p*-thiolsulphonate, m. p. and mixed m. p. 77—78° (from ethanol) (0·59 g., 32%, calc. according to eqn. 1).

(*b*) A solution of *N*-(toluene-*p*-sulphonamidino)thiourea [3] (2·72 g., 0·01 mole) in boiling ethanol (40 ml.) was allowed to cool to 40°, and treated with bromine (1·60 g., 0·01 mole) in chloroform (10 ml.); the resulting colourless liquid was immediately stirred into ice-water (250 ml.). The aqueous layer was decanted; to it was later added the granular white solid obtained on spontaneous evaporation of the solvent from the small chloroform layer. The collected combined product (m. p. 230—236°; 2·48 g., 92%) gave, after crystallisation as above, prisms of 5-amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. with material prepared by method (*a*) above, or from 3 : 5-diamino-1 : 2 : 4-thiadiazole [2b], 232—234° (decomp., after sintering at 228°).

5-*Amino*-3-m-*nitrobenzenesulphonamido*-1 : 2 : 4-*thiadiazole*.—Interaction of amidinothiourea (2·36 g., 0·02 mole) and *m*-nitrobenzenesulphonyl chloride (0·06 mole) in pyridine (45 ml.) [according to method (*a*) immediately above] gave a crude product which was boiled with ethanol (25 ml.). The separated solid, collected at 0° (filtrate A), and crystallised from nitrobenzene–ethanol,[2b] was 5-amino-3-*m*-nitrobenzenesulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p.[2b] 272—275° (decomp., after sintering at 270°) (yield, 1·56 g., 26%). From the ethanol filtrates A, small quantities of *m*-nitrophenyl *m*-nitrobenzenethiolsulphonate, m. p. and mixed m. p.[13] 122—123°, were isolated.

5-*Anilino*-3-*toluene*-p-*sulphonamido*-1 : 2 : 4-*thiadiazole* (II; R = Ph, R′ = *p*-C_6H_4Me).—(*a*) Interaction of *N*-phenyl-*N*′-(toluene-*p*-sulphonamidino)thiourea (1·05 g., 0·003 mole) and toluene-*p*-sulphonyl chloride (1·72 g., 0·009 mole) in pyridine (12 ml.) at 100° during 45 min. followed by addition of the liquid to N-hydrochloric acid (100 ml.) at 0° gave an orange viscous product. This was boiled with ethanol (20 ml.): the separated granular solid (m. p. 245—250°; 0·55 g., 53%) consisted, after crystallisation,[2c] of prisms of 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. with authentic material,[2c] 256—258° (after sintering at 250°). The ethanol filtrates deposited crystals, which gave, on fractionation from acetone–ethanol, platelets (0·35 g., 23%) of the ditoluene-*p*-sulphonyl derivative of 3-amino-5-anilino-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. with authentic material [2c] 203—205° (Found: C, 52·8; H, 3·8; N, 11·3; S, 19·35. Calc. for $C_{22}H_{20}O_4N_4S_3$: C, 52·8; H, 4·0; N, 11·2; S, 19·2%).

(*b*) A solution of *N*-phenyl-*N*′-(toluene-*p*-sulphonamidino)thiourea (3·48 g., 0·01 mole) in ethanol (100 ml.) at 40° was treated with bromine (1·60 g., 0·01 mole) in chloroform. The

[13] Limpricht, *Annalen*, 1894, **278**, 253.

product, isolated and crystallised in the usual manner, was 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. (with material prepared from 3-amino-5-anilino-1 : 2 : 4-thiadiazole [2c]) 256—257° (yield, 85%).

(*c*) Interaction of *N*-phenyl-*N'*-amidinothiourea [10] (1·94 g., 0·01 mole) and toluene-*p*-sulphonyl chloride (5·72 g., 0·03 mole) in pyridine (30 ml.) at 100° during 45 min., followed by the usual working-up, gave a crude product which was boiled with ethanol (10 ml.). The undissolved granular product was collected at 0° and consisted, after crystallisation, of 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. 256—257° (25—35%) (Found : C, 52·1; H, 3·8. Calc. for $C_{15}H_{14}O_2N_4S_2$: C, 52·0; H, 4·05%).

5-*Anilino*-3-m-*nitrobenzenesulphonamido*-1 : 2 : 4-*thiadiazole*.—(*a*) Reaction between *N*-phenyl-*N'*-amidinothiourea and *m*-nitrobenzenesulphonyl chloride in pyridine (as detailed immediately above) gave the *thiadiazole* (28%), m. p. and mixed m. p. (with the authentic specimen prepared by method *b*) 258—259°.

(*b*) Interaction of 3-amino-5-anilino-1 : 2 : 4-thiadiazole (1·92 g., 0·01 mole) and *m*-nitrobenzenesulphonyl chloride (2·66 g., 0·012 mole) in pyridine by the general procedure [2c] gave a product which was crystallised by dissolution in acetone–ethanol–benzene (2 : 1 : 1, 100 ml. per g.), followed by distillation of the filtered solution to incipient crystallisation. The derivative (2·55 g., 68%) formed a pale-yellow microcrystalline powder, m. p. 257—259° (after sintering at 254°) (Found : C, 44·9; H, 2·7; N, 18·2; S, 16·5. $C_{14}H_{11}O_4N_5S_2$ requires C, 44·6; H, 2·9; N, 18·6; S, 17·0%).

3 : 5-*Dianilino*-2 : 4-*ditoluene*-p-*sulphonyl*-1 : 2 : 4-*thiadiazolidine*.—Interaction of *N*-phenyl-*N'*-phenylamidinothiourea (2·70 g., 0·01 mole) and toluene-*p*-sulphonyl chloride (0·03 + 3 × 0·01 mole) in pyridine (45 ml.) gave a crude product, which after crystallisation from acetone–ethanol, consisted of the derivative, m. p. and mixed m. p.[2c] 240—242° (1·15 g., 20%).

Interaction of Amidinothiourea and Toluene-p-*sulphonyl Chloride in Organic Solvents*.—Amidinothiourea (3·54 g., 0·03 mole), dissolved in boiling ethanol (125 ml.), was treated at 50° with toluene-*p*-sulphonyl chloride (12·54 g., 0·066 mole). The clear liquid, diluted with ether (50 ml.), was set aside at room temperature in an open beaker. The yellow droplets of oil which were deposited within the first 2—3 days redissolved, while crystals were slowly deposited. These were collected (after 10—14 days), and rinsed with a little acetone (product A). Continued spontaneous evaporation of the filtrate at room temperature to small volume similarly afforded successive crops, B and C. Product A (3—3·8 g.) was dissolved by being boiled with successive portions of 90% ethanol (6 × 10 ml.). A small undissolved residue consisted of sulphur (0·35—0·45 g.). The combined decanted liquid deposited platelets (2·85—3·3 g., 35—40%) of amidinourea toluene-*p*-sulphonate, m. p. and mixed [14] m. p. 242—244° (decomp., resolidifying after melting instantly to a white wax-like solid) (Found : C, 39·6; H, 4·8. Calc. for $C_9H_{14}O_4N_4S$: C, 39·4; H, 5·1%). The material gave the characteristic yellow nickel salt.[15] Products B and C consisted chiefly of recovered impure amidinothiourea toluene-*p*-sulphonate (3·5 g., 40%), forming platelets, m. p. and mixed m. p. [2a] 176—178° (from aqueous ethanol). The filtrates therefrom contained unidentified non-homogeneous material.

In experiments employing benzenesulphonyl chloride, amidinourea and amidinothiourea benzenesulphonates [m. p. 234—236° (decomp.) and 111—114° (decomp.) respectively] were isolated in 25 and 34% yields respectively.

Oxidation of N-*Phenyl*-N'-(*toluene*-p-*sulphonamidino*)*thiourea with Hydrogen Peroxide*.—(*a*) A boiling solution of the reactant (3·50 g., 0·01 mole) in ethanol (60 ml.), acidified with 1 drop of 3N-hydrochloric acid, was treated with 6% hydrogen peroxide (3 × 5·7 ml., at 3 min. intervals; 0·03 mole), and the resulting liquid stirred into ice-water (300 ml.). The precipitated solid was collected after 2 days' storage at 0° (filtrate A), successively extracted with 4N-hydrochloric acid (40, 30, 20, and 10 ml.) at 40—50° (combined filtered-off extracts : B), washed with water, and dried. The residue (1·85 g.) was dissolved in boiling ethanol–acetone–benzene (20, 50, and 10 ml. respectively), and the filtered liquid boiled to half volume. The product which separated on cooling consisted of prisms of 5-anilino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. 255—256° (0·14 g., 4%). Spontaneous evaporation of the filtrate therefrom gave prisms (m. p. 206—208°; 1·18 g., 35%), which consisted, after crystallisation from ethanol–acetone, of *N*-phenyl-*N'*-(toluene-*p*-sulphonamidino)urea, m. p. and mixed m. p. 212—214° (Found : C, 54·2; H, 4·9%). Filtrate A, after vacuum-evaporation to small volume,

[14] Haag, *Annalen*, 1862, **122**, 25.
[15] Grossmann and Schück, *Ber.*, 1906, **39**, 3357.

basification and ether-extraction, afforded aniline, which was isolated as the benzoyl derivative, m. p. and mixed m. p. 161—162° (0·55 g., 28%). Slow basification of the combined extracts B with sodium hydroxide pellets gave a crystalline precipitate (0·97 g., 42%) of toluene-*p*-sulphonylguanidine hydrate, m. p. and mixed m. p. 203—205° (from ethanol).

(*b*) Oxidation of the reactant as above, but in the presence of an equivalent of hydrochloric acid (0·01 mole), gave the same products in roughly comparable proportions, except that the yield of the thiadiazole fraction was raised to 18%.

Oxidation of N-(*Toluene*-p-*sulphonamidino*)*thiourea with Hydrogen Peroxide.*—(*a*) The reactant (0·01 mole) was oxidised as described in the foregoing paragraphs (method *a*). Exhaustive extraction of the crude product (2·2 g.) with warm 4N-hydrochloric acid gave toluene-*p*-sulphonylguanidine (crystallised hydrate, isolated as before; 1·29 g., 56%) (Found: C, 41·6; H, 5·8; N, 18·3. Calc. for $C_8H_{11}O_2N_3S,H_2O$: 41·6; H, 5·6; N, 18·2%). The acid-insoluble residue was dissolved in warm 2N-sodium hydroxide, and a small insoluble residue (0·12 g.) removed by filtration. The product (0·65 g.), reprecipitated by mineral acid, was next extracted with boiling ethanol–acetone (1 : 1, 10 ml.); the solution contained 5-amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole (0·16 g., 6%), m. p. 227°. The residue (0·41 g., 16%) was *N*-(toluene-*p*-sulphonamidino)urea, m. p. and mixed m. p.[3] 238—241° (from ethanol) (Found: C, 42·4; H, 4·5. Calc. for $C_9H_{12}O_3N_4S$: C, 42·2; H, 4·7%).

(*b*) Oxidation of the reactant (0·01 mole) as above, but in the presence of concentrated hydrochloric acid (1 ml., 0·01 mole), gave, by the same procedure: toluene-*p*-sulphonylguanidine hydrate (0·80 g., 35%); toluene-*p*-sulphonamidinourea (0·52 g., 20%), and 5-amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole (0·32 g., 12%). Only traces of carbon dioxide were evolved during these oxidations (cf. ref. 1).

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