*Thiadiazoles. Part II.** 3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole and its 5-Alkyl Homologues.*

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Some properties of 3 : 5-diamino-1 : 2 : 4-thiadiazole, consistent with its suggested structure, are described. The greater reactivity of the 3-amino-group is indicated by the preferential formation of 3-sulphonamido-derivatives. Under suitable conditions the parent compound forms di- and tri-acyl derivatives.

5-Alkylamino-3-amino-1 : 2 : 4-thiadiazoles are obtainable by the oxidative cyclisation of *N*-alkyl-*N'*-amidinothioureas, and yield mono-, di-, and tri-acyl derivatives.

AMIDINOTHIOUREA, when oxidised with iodine or hydrogen peroxide, is cyclised to 3 : 5-diamino-1 : 2 : 4-thiadiazole (II) (cf. Part I*) : the oxidation of suitably substituted amidinothioureas and thiobiurets clearly opens a general route to various types of 1 : 2 : 4-thiadiazoles. Its applicability has now been confirmed, in the first place, by the synthesis 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles (VII). The oxidation of amidinothiourea by iodine is reversible and does not proceed to completion except in very dilute aqueous solution

* Part I, *J.*, 1955, 1.

(Part I): with *N*-alkyl-*N'*-amidinothioureas the position of equilibrium was still less favourable, so that iodine proved unsuitable as oxidising agent; hydrogen peroxide, however, effected the desired cyclisation readily.

N-Alkyl-*N'*-amidinothioureas, prepared by the method of Slotta, Tschesche, and Dressler (*Ber.*, 1930, **63**, 208), were isolated with advantage as highly crystalline arenesulphonates. Direct oxidation of these salts, by 6% hydrogen peroxide in boiling aqueous ethanol, afforded arenesulphonates of 5-alkylamino-3-amino-1 : 2 : 4-thiadiazole (VII) rapidly and in good yields. Small quantities of guanidine, formed as by-product, arose probably by the hydrolysis of the starting materials. In contrast to the parent compound (II) of this series, the 5-alkyl homologues (VII) proved alkali-resistant, so that the liberation of the free bases from their salts presented no difficulty.

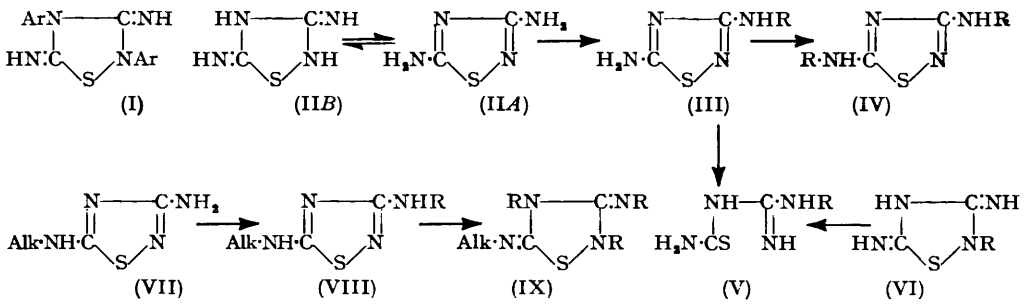
The so-called "Hector bases," obtained by oxidation of arylthioureas, are generally accepted as having 1 : 2 : 4-thiadiazolidine structures (I) (for references see Part I, *loc. cit.*). Alternative structures have been considered, however, in an attempt to account more explicitly for the experimental facts that only one imino-group is replaceable by a ketonic oxygen atom (Dost, *Ber.*, 1906, **39**, 863), or will undergo acylation. The formulæ of such monoacyl derivatives are as yet undecided (Bambas, "The Chemistry of Heterocyclic Compounds," Interscience Pub. Inc., New York, 1952, Vol. IV, p. 76). If the correctness of the structures (I) assigned to "Hector bases" is assumed, 3 : 5-diamino-1 : 2 : 4-thiadiazole (II) may be regarded as the parent compound of this series. It was therefore of interest to examine the behaviour of the simple compounds now synthesised towards acylating agents.

Interaction of equivalent quantities of sulphonyl chlorides and 3 : 5-diamino-1 : 2 : 4-thiadiazole afforded acidic monosubstitution products, which are regarded as 3-sulphonyl derivatives for the following reasons: Reduction, by nascent hydrogen, of the toluene-*p*-sulphonyl derivative to *N*-(toluene-*p*-sulphonylamidino)thiourea (V; R = *p*-$C_6H_4Me{\cdot}SO_2{\cdot}$) limits the site of the substitution (in the absence of rearrangement) to the 2- or the 3-position in the thiadiazole. The pronounced acidic nature of the sulphonyl derivatives favours the 3-sulphonamido-structure (III; R = $Ar{\cdot}SO_2$), since 2-sulphonyl compounds (VI; R = $Ar{\cdot}SO_2$) may be expected to be predominantly basic. The final decision in favour of structure (III) is supported by the analogous reaction of 2-aminothiazole which affords derivatives carrying the substituent on the extranuclear amino-group (2-sulphonamidothiazoles, *e.g.*, sulphathiazole; Fosbinder and Walter, *J. Amer. Chem. Soc.*, 1939, **61**, 2032; Lott and Bergum, *ibid.*, 3593).

Treatment of 3 : 5-diamino-1 : 2 : 4-thiadiazole with two equivalents of benzoyl chloride in pyridine gave an acidic disubstitution product; its formulation as the 3 : 5-dibenzamido-derivative (IV; R = Bz) is based on reasons similar to those given for the sulphonyl derivatives. However large an excess of acid chloride or anhydride was employed, four acyl residues could not be introduced into the molecule. Benzoyl chloride, for example, yielded a tribenzoyl derivative, the structure of which cannot be assigned with certainty at present. Acetic or propionic anhydride, on the other hand, afforded exceptionally sparingly soluble 3 : 5-diacylamino-derivatives (IV; R = Ac or Et·CO) which were instantly precipitated from the pyridine solution. However, their removal from the reacting phase is not likely to be the only reason for their failure to undergo further acylation, since substitution terminated similarly in the case of 3-amino-5-methylamino-1 : 2 : 4-thiadiazole with the formation of a pyridine-soluble monoacetyl derivative (formulated as VIII; Alk = Me, R = Ac).

For comparison, the corresponding acylation reactions of 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles were carried out, the methyl homologue (VII; Alk = Me) being used as the representative example. With one equivalent of benzoyl or sulphonyl halide, the expected monosubstituted derivatives were produced; they were strongly acidic and are regarded, in accordance with previous reasoning, as 3-substitution products (VIII; Alk = Me; R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$). The action of larger proportions of benzoyl chloride produced mixtures of di- and tri-benzoyl derivatives, the latter being the sole products when a large excess of acid chloride was used; di- and tri-arenesulphonyl compounds were similarly obtained. Unlike all the other derivatives described, the triacylated

alkyl-1 : 2 : 4-thiadiazoles were not acidic. In view of the greater difficulty of introducing acyl groups into acylamino- than into unsubstituted amino(or imino)-residues, the absence of diacylamino-groups in all derivatives may reasonably be assumed. The tribenzoyl and



trisulphonyl derivatives of (VII) are therefore formulated as substituted 1 : 2 : 4-thiadiazolidines (IX; Alk = Me; R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$), although a possible 2-acyl-5-acylalkylamino-3-acylimino-2 : 3-dihydro-1 : 2 : 4-thiadiazole structure is not fully excluded. A decision concerning the structure of the diacyl products must be deferred.

The failure of 3 : 5-diamino-1 : 2 : 4-thiadiazole to yield tetra-acyl derivatives under the usual conditions, and the varied behaviour of 1 : 2 : 4-thiadiazoles on acylation in general, suggests that the observed exclusive monoacylation of " Hector bases " is no decisive bar to their having thiadiazolidine structures (I). The greater reactivity of the 3-amino-group in (II) now demonstrated seems to justify the expectation that the acyl derivatives of " Hector bases " are 3-acylated structures.

The presence of substituents in 3 : 5-diamino-1 : 2 : 4-thiadiazole exerts a considerable stabilising influence on the heterocyclic ring system. Thus, sulphur dioxide rapidly opened the nucleus of the parent compound (II) under the mildest conditions with regeneration of amidinothiourea, but did not attack the 3-sulphonyl derivatives (III). Similarly, alkaline hydrolysis quickly converted the 3 : 5-diamino-compound (II) into amidinourea (equation 1) (the eliminated sulphur being simultaneously removed as soluble alkali polysulphide), but failed to bring about the corresponding degradation of the 5-alkyl homologues (VII). Alkaline sodium plumbite desulphurised 3 : 5-diamino-1 : 2 : 4-thiadiazole instantly on warming, or slowly even at room temperature. Its acyl derivatives released sulphur only when boiled with sodium plumbite containing a large excess of alkali, while 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles and their derivatives resisted desulphurisation entirely.

$$C_2H_4N_4S\ (II) + H_2O \longrightarrow NH_2{\cdot}C(:NH){\cdot}NH{\cdot}CO{\cdot}NH_2 + S \quad . \quad . \quad . \quad (1)$$

The synthesis of 3 : 5-diamino-1 : 2 : 4-thiadiazole has been simplified by oxidising amidinothiourea, in dilute mineral acid at moderate temperatures, with " Perhydrol." A similar procedure had been successfully used in the oxidative cyclisation of dithiobiuret (Preisler and Bateman, *J. Amer. Chem. Soc.*, 1947, **69**, 2632). In a slightly higher temperature range, however, " Perhydrol " converted amidinothiourea into amidinourea; this desulphurisation proceeds probably by way of primarily formed thiadiazole (II), since this base is also rapidly converted into amidinourea under identical conditions.

Both amidinothioureas and 1 : 2 : 4-thiadiazoles derived therefrom formed sparingly soluble monopicrates which were suitable for recovering small quantities of the bases from dilute solution; those prepared from thiadiazoles had m. p.s ranging sufficiently widely to allow their use for identification purposes.

Experimental

Light petroleum was of boiling range 60—80°. The 5-alkylamino-3-amino-1 : 2 : 4-thiadiazole sulphonates were, in general, considerably more soluble in 96% than in absolute ethanol; unless otherwise specified, the former grade was used.

3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole*.—A solution of amidinothiourea (11·8 g., 0·1 mole) in

2N-hydrochloric acid (50 ml., 0·1 mole) at 20° was treated with hydrogen peroxide (30% w/v; 34 ml., 0·3 mole) in three portions at 3-min. intervals. The resulting clear colourless solution was kept at 35° during 30 min. (external cooling). Toluene-*p*-sulphonic acid monohydrate (23·75 g., 0·125 mole) was then added to the stirred liquid and dissolved instantly, while a copious crystalline precipitate of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate appeared. The suspension was immediately cooled to 0° in a freezing mixture, to avoid a possible rapid spontaneous rise in temperature, resulting in the conversion of the material into amidinourea. The salt was collected at 0° [m. p. 236—238° (decomp.); 21—23 g., 73—80%] and purified as before (cf. Part I, *loc. cit.*).

Interaction of the above reactants at 60—70° yielded only amidinourea toluene-*p*-sulphonate (10—15 g., 36—55%).

3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole.*—*Reduction.* A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·44 g., 0·005 mole) in water (10 ml.) at 65° was treated with a slow stream of sulphur dioxide during 20 min., followed by toluene-*p*-sulphonic acid monohydrate (0·95 g., 0·005 mole). The large prisms which separated on cooling to 0° (1·32 g., 91%) were amidinothiourea toluene-*p*-sulphonate, m. p. (after crystallisation from ethanol) and mixed m. p. 177—178° (decomp.).

Alkaline hydrolysis. A solution of the toluene-*p*-sulphonate (2·88 g., 0·01 mole) in aqueous sodium hydroxide (12%; 7 ml., 0·02 mole) was boiled during 3 min. The cooled orange liquid, on acidification with concentrated hydrochloric acid (2·5 ml., 0·025 mole), evolved hydrogen sulphide, and gave a granular precipitate of sulphur (0·19 g., 60%). The decanted liquid was filtered (carbon) while hot, and the clear filtrate treated with toluene-*p*-sulphonic acid monohydrate (0·95 g., 0·005 mole). On partial spontaneous evaporation, lustrous prisms [m. p. 226—232° (decomp.); 1·95 g., 72%] of amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. 238—240° (decomp.) (from 90% aqueous ethanol) were deposited.

Further interaction with hydrogen peroxide. A suspension of the powdered toluene-*p*-sulphonate (4·3 g., 0·015 mole) in N-hydrochloric acid (15 ml., 0·015 mole) was treated with hydrogen peroxide (30%; 5 ml., 0·045 mole) and warmed to 50°. The temperature of the resulting solution was thereupon maintained at 60—65° by external cooling. When no further spontaneous temperature rise occurred (20—30 min.), the solution was set aside at 0° overnight. The separated prisms (2·15—2·5 g., 52—61%) were amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. 238—240° (decomp.) (from 90% ethanol).

3 : 5-*Di*(*acetamido*)-1 : 2 : 4-*thiadiazole.*— A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (2·88 g., 0·01 mole) in anhydrous pyridine (15 ml.) was treated with acetic anhydride (6·12 g., 0·06 mole), and the resulting hot (50°) solution heated on the steam-bath. Already after 2—3 min., a white crystalline solid separated. Heating was continued for 30 min., the suspension stirred into N-hydrochloric acid (150 ml.), and the white product collected and washed with water [m. p. 310—315° (decomp.); 1·77—1·90 g., 88—95%]. Two crystallisations from glacial acetic acid (100 ml. per g., recovery 90%) gave lustrous needles of 3 : 5-*di*(*acetamido*)-1 : 2 : 4-*thiadiazole*, m. p. 314—316° (decomp., after sintering slightly at 305°) (Found: C, 36·1; H, 4·0; N, 28·5; S, 16·5. $C_6H_8O_2N_4S$ requires C, 36·0; H, 4·0; N, 28·0; S, 16·0%), insoluble in boiling ethanol, benzene, chloroform, or dioxan, soluble in boiling glacial acetic acid, nitrobenzene, or in cold alkalis, and reprecipitated therefrom by acids.

3 : 5-*Di*(*propionamido*)-1 : 2 : 4-*thiadiazole*, similarly prepared, separated from the hot pyridine solution as above [m. p. 288—290° (decomp., previously sintering at 270°); 85%]. Two crystallisations from boiling ethanol (200 ml. per g., recovery 80%) gave needles, m. p. 292—293° (decomp., becoming brown at 280—285°) (Found: C, 42·1; H, 5·6; N, 25·1. $C_8H_{12}O_2N_4S$ requires C, 42·1; H, 5·3; N, 24·6%), very sparingly soluble in boiling water and ethanol.

3 : 5-*Di*(*benzamido*)-1 : 2 : 4-*thiadiazole.*—A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (2·88 g., 0·01 mole) in pyridine (20 ml.), treated with benzoyl chloride (3·1 g., 0·022 mole), was kept at 100° during 30 min. The crystalline precipitate obtained on pouring the liquid into 2N-hydrochloric acid (120 ml.) at 0° was collected, heated with water (50 ml.) to 100° (to remove benzoic acid), and filtered (m. p. 256—260°; 2·60 g., 80%), and the solid twice crystallised from ethanol (100 ml. per g.; recovery per crystallisation, 85%), yielding 3 : 5-*di*(*benzamido*)-1 : 2 : 4-*thiadiazole*, as needles, m. p. 263—265° (Found: C, 58·6; H, 4·1; N, 16·9; S, 9·4. $C_{16}H_{12}O_2N_4S$ requires C, 59·3; H, 3·7; N, 17·3; S, 9·9%), soluble in warm alkalis and reprecipitated by acids.

Tribenzoyl Derivative of 3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole.*—Treatment of 3 : 5-diamino-1 : 2 : 4-thiadiazole (0·01 mole) with an excess of benzoyl chloride (7·05 g., 0·05 mole) gave,

by the above procedure, a granular solid (4·6 g.). Three crystallisations from ethanol (30 ml. per g.) gave prisms of the *tribenzoyl derivative*, m. p. 219—221° (yield, including material from the mother-liquors, 2·9—3·5 g., 68—81%) [Found: C, 64·1; H, 4·1; N, 13·4; S, 7·25%; *M* (cryoscopically, in naphthalene), 380. $C_{23}H_{16}O_3N_4S$ requires C, 64·5; H, 3·7; N, 13·1; S, 7·5%; *M*, 428], soluble in warm alkalis and reprecipitated by acids.

Small quantities (up to 8%) of the dibenzoyl derivative, m. p. 263—265°, formed as by-product in some experiments, were removed by fractional crystallisation.

The use of a large excess (8 equiv.) of benzoyl chloride did not introduce a fourth benzoyl residue, but afforded the tribenzoyl derivative exclusively in 85—90% yield.

5-Amino-3-toluene-p-*sulphonamido*-1 : 2 : 4-*thiadiazole*.—A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (8·64 g., 0·03 mole) in pyridine (30 ml.), treated with toluene-*p*-sulphonyl chloride (6·3 g., 0·033 mole), was heated on the steam-bath during 30 min. The white semicrystalline precipitate obtained on addition of the pyridine solution to N-hydrochloric acid (120 ml.) at 0° was collected, air-dried (m. p. 228—232°, after sintering at 220°; 6·9 g., 85%), and crystallised by dissolution in ethanol (20 ml.)–acetone (60 ml.), followed by addition of light petroleum (120 ml.); prisms of *5-amino-3-toluene*-p-*sulphonamido*-1 : 2 : 4-*thiadiazole*, m. p. 231—233° (decomp., after sintering at 228°), were deposited (Found: C, 40·3; H, 3·9; N, 20·5; S, 23·5. $C_9H_{10}O_2N_4S_2$ requires C, 40·0; H, 3·7; N, 20·7; S, 23·7%). The material dissolved in dilute alkalis and was reprecipitated by acids.

5-Amino-3-m-*nitrobenzenesulphonamido*-1 : 2 : 4-*thiadiazole* was similarly prepared. The precipitated crude powder dissolved readily in boiling acetone, and was deposited therefrom, on cooling and partial evaporation, as a pale yellow powder [m. p. 258—264° (decomp., after sintering at 240°); 62%], now almost insoluble in the usual solvents. Two crystallisations from boiling nitrobenzene afforded pale yellow prisms of the solvated derivative, m. p. 274—276° (decomp., after sintering at 260°). Removal of the nitrobenzene of crystallisation, by keeping the solvate at 210—230° during 30 min., gave the microcrystalline derivative, m. p. 274—276° (decomp., after sintering at 270°) (Found: C, 32·1; H, 2·25; N, 23·2; S, 20·8. $C_8H_7O_4N_5S_2$ requires C, 31·9; H, 2·3; N, 23·25; S, 21·3%).

5-Amino-3-toluene-p-*sulphonamido*-1 : 2 : 4-*thiadiazole*.—*Reduction*. A boiling solution of the reactant (2·70 g., 0·01 mole) in ethanol (40 ml.) containing zinc foil (4 g.) was treated dropwise with concentrated hydrochloric acid (4 ml.) during 1 min.; after the initial vigorous reaction, the suspension was gently refluxed during 15 min. The liquid was decanted from the zinc (which was again extracted with a little boiling ethanol), and the combined clear solution evaporated in a vacuum to small volume (10 ml.). After storage at 0° during 24 hr., the white crystalline solid was collected, twice stirred with N-hydrochloric acid (2 × 5 ml.) [to remove zinc salt], filtered off, and washed with cold water. The air-dried product (m. p. 198—202°, after sintering at 185°; 2·25 g., 82%) gave, on crystallisation from ethanol (10 ml. per g.), prisms of *N*-(toluene-*p*-sulphonylamidino)thiourea, m. p. and mixed m. p. (cf. Kurzer and Powell, *J.*, 1953, 2531) 201—202° (decomp.) (Found: C, 40·0; H, 4·6; N, 20·8. Calc. for $C_9H_{12}O_2N_4S_2$: C, 39·7; H, 4·4; N, 20·6%).

5-Amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, dissolved in boiling ethanol–acetone, was recovered unchanged after treatment with sulphur dioxide during 1 hr.

5-Alkylamino-3-amino-1 : 2 : 4-*thiadiazoles*.

N-*Alkyl*-N′-*amidinothiourea Toluene*-p-*sulphonates*.—*N*-Alkyl-*N*′-amidinothioureas, prepared by the method of Slotta, Tschesche, and Dressler (*Ber.*, 1930, **63**, 208), were conveniently isolated as toluene-*p*-sulphonates as follows: The solution obtained after refluxing guanidine thiocyanate and methyl *iso*thiocyanate (0·15 mole each) in ethanolic sodium ethoxide (90 ml., containing 0·15 g.-atom of sodium) for 1 hr., was quickly evaporated to approx. half its bulk under reduced pressure. Dilution with hot water (25 ml.) redissolved the separated crystalline solid; the warm solution was filtered to remove flocculent impurities, and the filtrate treated with toluene-*p*-sulphonic acid monohydrate (38·1 g., 0·2 mole) and set aside at 0°. The separated crystals were collected at 0°, and successively washed with ice-water (2 × 10 ml.) and ethanol (15 ml.). The dry product (32—35 g.) was refluxed with ethanol (40 ml.), and a small quantity of insoluble material (3—4 g.) filtered off at the pump while hot. The product which separated from the filtrate on cooling to 0° was twice recrystallised from ethanol (1·5 ml. per g.) and formed white opaque prisms of N-*amidino*-N′-*methylthiourea toluene*-p-*sulphonate*, m. p. 160—162° (decomp.) (total yield, including material from the mother-liquors, 25—29·5 g., 55—65%) (Found: C, 39·2; H, 5·3; N, 17·9. $C_{10}H_{16}O_3N_4S_2$ requires C, 39·5; H, 5·3; N, 18·4%).

By the same method, N-*amidino*-N′-*ethylthiourea toluene*-p-*sulphonate* was obtained (45—55%) as opaque prisms (from ethanol; 3 ml. per g.), m. p. 139—141° (decomp.) (Found: C, 41·7; H, 5·85; N, 16·8. $C_{11}H_{18}O_3N_4S_2$ requires C, 41·5; H, 5·7; N, 17·6%).

The same procedure gave N-*amidino*-N′-n-*propylthiourea toluene*-p-*sulphonate* (45%) as prisms, m. p. 137—139° (decomp.) (Found: C, 43·6; H, 5·8; N, 16·2. $C_{12}H_{20}O_3N_4S_2$ requires C, 43·4; H, 6·0; N, 16·9%).

3-*Amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole*.—A solution of *N*-amidino-*N*′-methylthiourea toluene-*p*-sulphonate (6·08 g., 0·02 mole) in boiling ethanol (35 ml.) was treated with hydrogen peroxide (6%; 34·5 ml., 0·06 mole) in three equal portions at 3-min. intervals. The resulting solution was rapidly evaporated to approximately half its volume in a vacuum, and the residual clear liquid treated with toluene-*p*-sulphonic acid monohydrate (1·90 g., 0·01 mole). The crystals separating on storage at 0° were collected (m. p. 174—177°; 3·75 g., 62%) [aqueous filtrate, A] and crystallised from boiling ethanol (8 ml. per g.; recovery, 75%), affording prisms of 3-*amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole toluene*-p-*sulphonate*, m. p. 177—179° (decomp.) (Found: C, 39·9; H, 4·8; N, 18·2; S, 20·75. $C_{10}H_{14}O_3N_4S_2$ requires C, 39·7; H, 4·6; N, 18·5; S, 21·2%).

The aqueous filtrates A, on spontaneous evaporation to small volume (10 ml.), gave large lustrous prisms (m. p. 222—224°; 0·4—0·6 g., 8—13%), which consisted of guanidine toluene-*p*-sulphonate, m. p. and mixed m. p. 225—228° (from ethanol).

The (crude) toluene-*p*-sulphonate (3·02 g., 0·01 mole) was warmed with aqueous sodium hydroxide (12%; 6·7 ml., 0·02 mole) to about 40°; on cooling, the clear liquid rapidly deposited minute needles, which were collected at 0°, washed with a few drops of water [m. p. 156—162°; 0·98 g., 75%], and twice crystallised from ethanol–light petroleum (10 and 4 ml. respectively, per g.; recovery per crystallisation, 70—80%). The 3-*amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole* formed needles, m. p. 158—159° [Found: C, 28·1; H, 4·55; N, 43·0; S, 24·4%; *M* (Rast), 135, 145; (cryoscopically, in thymol) 130, 135. $C_3H_6N_4S$ requires C, 27·7; H, 4·6; N, 43·1; S, 24·6%; *M*, 130].

3-*Amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole*.—Oxidation of *N*-amidino-*N*′-ethylthiourea toluene-*p*-sulphonate (6·35 g., 0·02 mole) by the above procedure gave a product [m. p. 138—140° (decomp.); 4·1—4·75 g., 65—75%], which on crystallisation from ethanol–light petroleum (5 and 2 ml. per g., respectively; recovery 60%) formed prisms of 3-*amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole toluene*-p-*sulphonate*, m. p. 140—142° (decomp.) (Found: C, 41·6; H, 5·0; N, 17·8; S, 19·9. $C_{11}H_{16}O_3N_4S_2$ requires C, 41·8; H, 5·1; N, 17·7; S, 20·25%). Small yields of guanidine toluene-*p*-sulphonate were again isolated from the appropriate aqueous filtrates (see above).

The crude salt (3·16 g., 0·01 mole) was dissolved in aqueous sodium hydroxide (4%; 20 ml., 0·02 mole) at 80°. The filtered clear solution deposited prisms, which were collected at 0° (m. p. 174—176; 1·15 g., 80%). Crystallisation from ethanol (10 ml. per g., recovery 60%) gave 3-*amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole*, m. p. 177—179° (Found: C, 33·4; H, 5·4; N, 37·9; S, 22·0. $C_4H_8N_4S$ requires C, 33·3; H, 5·6; N, 38·9; S, 22·2%).

3-*Amino*-5-n-*propylamino*-1 : 2 : 4-*thiadiazole*.—Oxidation of *N*-amidino-*N*′-*n*-propylthiourea toluene-*p*-sulphonate (0·015 mole) in boiling ethanol (30 ml.) with hydrogen peroxide (6%; 0·045 mole) during 15 min., followed by rapid vacuum evaporation to 30 ml., gave a colourless liquid, which was made strongly alkaline (at 0—5°) with sodium hydroxide (20% w/v; 6 ml., 0·03 mole). Separation of the product was completed by spontaneous evaporation, at room temperature, to 15—20 ml. The collected (0°) crude product (1·23 g., 52%) gave, after two crystallisations from water (6 ml. per g.), prismatic needles of 3-*amino*-5-n-*propylamino*-1 : 2 : 4-*thiadiazole*, m. p. 146—148° (Found: C, 38·15; H, 6·15; N, 34·7; S, 19·9. $C_5H_{10}N_4S$ requires C, 38·0; H, 6·3; N, 35·4; S, 20·25%).

The *toluene*-p-*sulphonate*, prepared from equivalent proportions of the above base and toluene-*p*-sulphonic acid in hot saturated aqueous solution, formed prisms, m. p. 110—112° (decomp.) (from ethanol–light petroleum) (Found: C, 43·6; H, 5·5. $C_{12}H_{18}O_3N_4S_2$ requires C, 43·6; H, 5·45%).

Picrates.—Amidinothiourea and 1 : 2 : 4-thiadiazole picrates were prepared in 70—95% yield from equivalent quantities of picric acid and the requisite toluene-*p*-sulphonate (except in the case of amidinothiourea, where the free base was used) in saturated aqueous or ethanolic solution. The results are summarised in the Table.

3-*Acetamido*-5-*methylamino*-1 : 2 : 4-*thiadiazole*.—3-Amino-5-methylamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·50 g., 0·005 mole), dissolved in pyridine (6 ml.), was heated with acetic anhydride (6·1 g., 0·06 mole) on the steam-bath during 1 hr., and the yellow liquid diluted with water (40 ml.) and acidified to Congo-red with concentrated hydrochloric acid (10 ml.).

On partial evaporation at room temperature, the solution deposited massive needles [m. p. 245—248° (decomp., after sintering at 240°); 0·72 g., 84%]. Crystallisation from boiling water–ethanol (4 : 1, 100 ml. per g.) gave needles of *3-acetamido-5-methylamino-1 : 2 : 4-thiadiazole*,

Amidinothiourea picrates R·NH·CS·NH·C(:NH)·NH_2,$C_6H_3O_7N_3$.

R	Medium[a]	Crystn.[b]	M. p.[c]	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
H	i	A	208—209°	$C_8H_9O_7N_7S$	28·2	2·6	27·7	2·6
Me	ii	A	224—226	$C_9H_{11}O_7N_7S$	30·3	3·0	29·9	3·0
Et	ii	A	223—225	$C_{10}H_{13}O_7N_7S$	32·0	3·7	32·0	3·5
Pr^n	ii	A	218—219	$C_{11}H_{15}O_7N_7S$	34·2	3·9	33·9	3·85

3 : 5-*Disubstituted* 1 : 2 : 4-*thiadiazole picrates* 5-R·NH·$C_2H_2N_3S$,$C_6H_3O_7N_3$ [cf. (VII)].

H	i	A	230—232	$C_8H_7O_7N_7S$	28·0	2·3	27·8	2·0
Me	i	B	227—228	$C_9H_9O_7N_7S$	30·3	2·5	30·1	2·5
Et	i	C	169—171	$C_{10}H_{11}O_7N_7S$	32·6	2·85	32·2	2·95
Pr^n	i	A	171—173	$C_{11}H_{13}O_7N_7S$	33·9	3·3	34·1	3·4

[a] Prepared (i) in saturated boiling H_2O, (ii) in saturated boiling 96% EtOH. [b] Crystallised (A) from 60% EtOH, (B) from EtOH–acetone, (C) from EtOH–light petroleum. [c] All picrates decomposed on melting.

m. p. 248—251° (decomp., after sintering at 240—245°) (Found: C, 34·9; H, 4·5; N, 31·8; S, 17·9. $C_5H_8ON_4S$ requires C, 34·9; H, 4·65; N, 32·6; S, 18·6%).

3-Benzamido-5-methylamino-1 : 2 : 4-thiadiazole was similarly prepared from equimolar proportions of the thiadiazole toluene-*p*-sulphonate and benzoyl chloride in pyridine (40%), and after crystallisation from ethanol, consisted of prisms, m. p. 201—203° (Found: C, 51·7; H, 3·9. $C_{10}H_{10}ON_4S$ requires C, 51·3; H, 4·3%).

Di- and Tri-benzoyl Derivatives.—Treatment, as above, of the thiadiazole toluene-*p*-sulphonate (0·005 mole) with three equiv. of benzoyl chloride gave a crude product (1·75 g.), which was boiled with ethanol (25 ml.). The ethanol-insoluble fraction (0·62 g., 28%) (filtrate A) was twice crystallised from ethanol–benzene (1 : 1; 40 ml. per g.) and gave prisms of *2 : 4-dibenzoyl-3-benzoylimino-5-methylimino-1 : 2 : 4-thiadiazolidine*, m. p. 199—200° (Found: C, 65·5; H, 3·9; N, 12·4; S, 7·4. $C_{24}H_{18}O_3N_4S$ requires C, 65·2; H, 4·1; N, 12·7; S, 7·2%). The ethanolic filtrates A contained a product, which consisted, after recrystallisation from ethanol–light petroleum, of prisms (0·85 g., 50%) of the *dibenzoyl derivative*, m. p. 182—185° (Found: C, 61·1; H, 4·05. $C_{17}H_{14}O_2N_4S$ requires C, 60·35; H, 4·1%). The use of 8 molar proportions of benzoyl chloride gave the tribenzoyl derivative, m. p. 199—200°, exclusively in 85% yields.

*5-Methylamino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole* was prepared from equimolecular proportions of the reactants in pyridine in the usual manner (see above). The crude product was twice crystallised from acetone–ethanol (1 : 1; approx. 100 ml. per g.) and gave prisms, m. p. 254—256° (yield, including material from the mother-liquors, 80%) (Found: C, 42·15; H, 4·2; N, 19·2; S, 22·3. $C_{10}H_{12}O_2N_4S_2$ requires C, 42·25; H, 4·2; N, 19·7; S, 22·5%). The material dissolved in dilute alkalis and was reprecipitated by acids.

Di- and Tri-arenesulphonyl Derivatives.—Treatment of 3-amino-5-methylamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·50 g., 0·005 mole) with toluene-*p*-sulphonyl chloride (3·80 g., 0·02 mole) in anhydrous pyridine (10 ml.) at 100° during 30 min., followed by addition of the orange liquid to ice–hydrochloric acid, gave a crude product which was briefly boiled with ethanol (30 ml.). The undissolved white solid was quickly collected (ethanolic filtrate A) [m. p. 200—208°; 0·45 g., 15%] and afforded, after two crystallisations from acetone–ethanol (25 ml. each per g.), prisms of *5-methylimino-3-toluene-*p*-sulphonylimino-2 : 4-ditoluene-*p*-sulphonyl-1 : 2 : 4-thiadiazolidine*, m. p. 210—212° (Found: C, 48·2; H, 4·05; N, 9·8; S, 22·2. $C_{24}H_{24}O_6N_4S_4$ requires C, 48·65; H, 4·05; N, 9·5; S, 21·6%), insoluble in caustic alkalis.

The ethanol filtrates A deposited a crystalline solid on storage at 0°. Two crystallisations from boiling ethanol (15 ml. per g.) [a trace of insoluble material being quickly filtered off in each crystallisation] gave platelets of the *ditoluene-*p*-sulphonyl derivative*, m. p. 171—173° (yield, including material from the mother-liquors, 1·15 g., 52%) (Found: C, 46·3; H, 3·9; N, 12·8; S, 21·8. $C_{17}H_{18}O_4N_4S_3$ requires C, 46·6; H, 4·1; N, 12·8; S, 21·9%), sparingly soluble in very dilute alkalis and reprecipitated by mineral acids.

The use of 8 molar proportions of sulphonyl chloride did not substantially alter the relative amounts of tri- and di-sulphonyl derivatives isolated.

Sodium Plumbite Tests.—Solutions or suspensions of the appropriate product (0·1 g.) in 6, 12, or 20% aqueous sodium hydroxide (3 ml.) containing 3 drops of 10% lead acetate were

boiled during 2 min. The following compounds gave immediate copious precipitates of lead sulphide in 6% sodium hydroxide: *N*-alkyl-*N'*-amidinothioureas (alkyl = Me, Et, Pr^i); (toluene-*p*-sulphonylamidino)thiourea (V; R = *p*-$C_6H_4Me{\cdot}SO_2$). The following gave small precipitates slowly on boiling: In 6% sodium hydroxide: (IV; R = Ac or Et·CO). In 12% sodium hydroxide: (IV; R = Bz); tribenzoyl derivative of (II). In 20% sodium hydroxide: (VII; Alk = Me). The following compounds did not give any lead sulphide in boiling 20% sodium hydroxide during 3 min.: (VII; Alk = Et or Pr^n); (VIII; Alk = Me, R = Ac or *p*-$C_6H_4Me{\cdot}SO_2$); (IX; Alk = Me, R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$); dibenzoyl and ditoluene-*p*-sulphonyl derivatives of (VII; Alk = Me).

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