1,2,4-Thiadiazolylureas. A Postcript to the Oxidative Cyclisation of Thionoamidines

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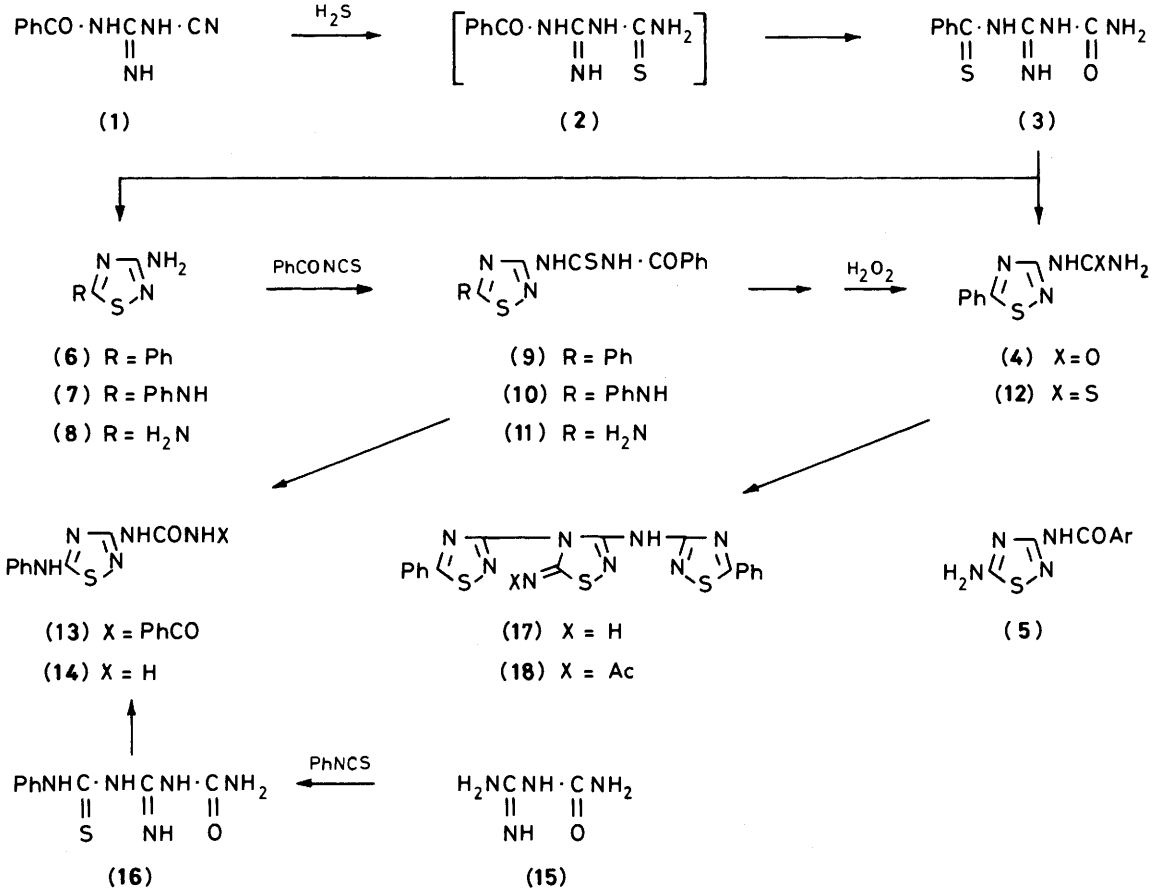
The identity of authentic 5-phenyl-3-ureido-1,2,4-thiadiazole synthesized from the pre-formed heterocycle, and of the product of the oxidative cyclisation of N^1-carbamoyl-N^3-thiobenzoylguanidine, confirms the structure of 5-substituted-3-ureido-1,2,4-thiadiazoles obtained by either route.

Ollis and his co-workers [1] have recently shown that the addition of hydrogen sulphide to N^1-benzoyl-N^3-cyanoguanidine (**1**) does not yield the expected *N*-(benzoylamidino)thiourea (**2**) as reported in the literature,[2] but results in the isomeric N^1-carbamoyl-N^3-thiobenzoylguanidine (**3**). The assignment of the true structure to this compound has clarified and corrected the interpretation of its oxidative cyclisation to 1,2,4-thiadiazoles which we reported many years ago.[3] The observed formation of 3-amino-5-phenyl-1,2,4-thiadiazole (**6**) from the supposed thiourea (**2**) had been difficult to account for: the role of compound (**3**) [or of ArCSNH·C(:NH)NH_2] as a possible precursor of the thiadiazole (**6**) had indeed been thought probable, but the mechanism of the reaction remained in doubt. The reaction is now seen, as a result of Ollis' work,[1] to involve the usual direct oxidative ring-closure [4a,c] of a thionoamidine (**3**) to yield 3-amino- (**6**) or 3-ureido-5-phenyl-1,2,4-thiadiazole (**4**), or both, depending on the experimental conditions. Because of the mistaken identity of the starting material [as (**2**)], the latter had previously[3] been formulated as (**5**; Ar = Ph).

We have in the past, in another connexion, synthesized a number of (thio)ureido-1,2,4-thiadiazoles, including the 5-phenyl-3-ureido-compound (**4**), from the pre-formed heterocyclic ring-system. In view of their relevance to the foregoing observations, some of these results are now briefly reported.

Benzoyl isothiocyanate[5] reacted additively with 3-amino-1,2,4-thiadiazoles (**6**)—(**8**) to yield the appropriate 3-[*N'*-(benzoyl)thioureido]-5-substituted-1,2,4-thiadiazoles (**9**)—(**11**). Debenzoylation of compound (**9**) by alkaline hydrolysis gave 5-phenyl-3-thioureido-1,2,4-thiadiazole (**12**), which was readily desulphurised to the urea (**4**) by the action of alkaline hydrogen peroxide.[6] 5-Phenyl-3-ureido-1,2,4-thiadiazole (**4**) thus obtained was identical with the ('acidic') oxidation product[3] of N^1-carbamoyl-N^3-thiobenzoylguanidine (**3**); this synthetic evidence supplements the mass-spectral data[1] supporting the formulation of the compound. The accessibility of 5-phenyl-3-ureido(and thioureido)-1,2,4-thiadiazole (**4**) and (**12**) by the present route is of some interest, because neither compound was directly obtainable from the 3-amine (**6**) by the con-



ventional addition of the elements of cyanic[7] or thiocyanic acid[8] to the amino-group [of (**6**)]: the exceptionally low basic strength of 3-amino-1,2,4-thiadiazoles [*e.g.* pK_a of (**6**) is 0.1;[9] that of its 5-ethyl homologue is 0.8[10]] may contribute to their failure to form (thio)cyanate salts capable of isomerising to the desired (thio)ureas [*e.g.* (**4**)].

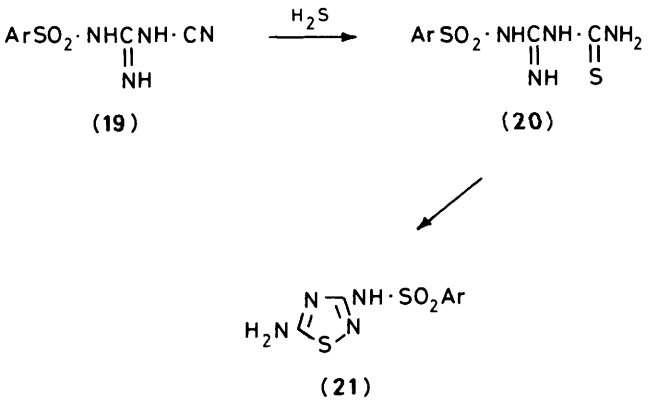
The straightforward desulphurisation of aromatic thioureas to ureas by hydrogen peroxide in alkali [*e.g.* (**12**) ⟶ (**4**)] contrasts with their complex oxidation, by the same reagent in acidic media, to give substituted Δ^2-1,2,4-thiadiazolines ('Hector's bases').[4b,d] 5-Phenyl-3-thioureido-1,2,4-thiadiazole (**12**) underwent the latter reaction readily to yield a product formulated, in accord with current views,[4d] as the substituted Δ^2-1,2,4-thiadiazoline (**17**); it gave a monoacyl derivative (**18**) as expected. The formation of this particular Hector's base is noteworthy in demonstrating the applicability of this reaction to heteroaromatic thioureas, and in leading to a structure consisting of three uncondensed 1,2,4-thiadiazole nuclei linked to one another.

5-Anilino-3-[*N'*-(benzoyl)thioureido]-1,2,4-thiadiazole (**10**) resisted debenzoylation by alkali under conditions suitable for hydrolysing its 5-phenyl analogue (**9**). In its reaction with alkaline hydrogen peroxide, it was desulphurised to the urea (**13**) with retention of the benzoyl group, which was again not satisfactorily removed [(**13**) ⟶ (**14**)] by subsequent alkaline hydrolysis. The parent urea (**14**) was accessible, however, by the oxidative cyclisation of 1-[N^1-(anilinothioformyl)amidino]-urea (**16**), itself the product of the addition of phenyl isothiocyanate to the guanidino-moiety of amidinourea (**15**).

3,5-Diamino-1,2,4-thiadiazole (**8**)[11] reacted with only one mole of benzoyl isothiocyanate, even when a large excess of the reagent was employed. The product is regarded as the 1,2,4-thiadiazol-3-ylthiourea (**11**), in accord with the known preferential attack of toluene-*p*-sulphonyl chloride[12] or phosphorochloridic esters [$(RO)_2P(:O)Cl$][13] at the 3-amino-group of (**8**).

The i.r. spectra of the (thio)ureidothiadiazoles are interpreted in accordance with the available information[14–16] concerning the absorption characteristics of the 1,2,4-thiadiazole nucleus between *ca.* 750—1 500 cm^{-1} (see Experimental section). Some of the peaks in the 1 350—1 600 cm^{-1} range assigned to the heterocyclic nucleus are possibly coincident with or broadened by amide[17] or thioamide bands[18] arising from the (thio)ureido-moieties of the present structures. The thiocarbonyl peaks cannot be identified unequivocally: their assignment is not only subject to the usual uncertainties,[18–20] but the problem is compounded, in the present case, by the hetero-ring giving rise to peaks in the thiocarbonyl ranges (for thioamides: D-band:[18] 950—1 300, especially[19] 1 150 ± 70; G-band:[18] 700—850 cm^{-1}). It is tempting to ascribe the intense absorption at 1 255 cm^{-1} in the spectra of the thioureas (**9**) and (**12**), but absent in that of the comparable urea (**4**), to the thiocarbonyl group of (**9**) and (**12**). However, since these correlations are not consistently apparent in other relevant examples, the assignment must be regarded with caution, even though it is in accord with that proposed[21] in respect of adamantylthioureas (ν_{CS} 1 235 cm^{-1}).

The recognition by Ollis *et al.*[1] of the true structure (**3**) of the product of the addition of the elements of hydrogen sulphide to the cyanamide (**1**) accounts for its oxidative cyclisation to 3-amino- (**6**) or 3-ureido-5-phenyl-1,2,4-thiadiazole (**4**) in neutral or acidic media, respectively.[3] The reactions of analogous N^1-carbamoyl-N^3-thioaroylguanidines[3] need to be similarly interpreted. It is significant that the complications arising from the rearrangement of the linear starting materials (**2**) ⟶ (**3**) are without parallel in the oxidative cyclisation of their arylsulphonyl analogues (**20**) which are similarly accessible from compounds (**19**).[22] Being incapable of undergoing a comparable isomeric change, they are ring-closed solely to 5-amino-3-arylsulphonamido-1,2,4-thiadiazoles (**21**) corresponding to (**5**) upon oxidation.[12]



Experimental

Ammonium thiocyanate used for preparing benzoyl isothiocyanate was dried immediately before use by being kept in a mortar at 75—85 °C and occasionally ground during 2—3 h.

I.r. spectra were determined (in KBr) using a Unicam SP 200 instrument. The following abbreviations refer to assignments to the 1,2,4-thiadiazole (td) nucleus of the structures: rs (ring skeletal), ip (CH in-plane deformation), op (CH out-of-plane deformation), rb (ring breathing), sh (shoulder), mt(multiplet).

3-[N'-(*Benzoyl*)*thioureido*]-5-*phenyl*-1,2,4-*thiadiazole* (**9**).—Benzoyl chloride (5.6 g, 0.04 mol) was added dropwise to a stirred solution of ammonium thiocyanate (3.8 g, 0.05 mol) in anhydrous acetone (50 ml) and the suspension was refluxed for 5 min. A solution of 3-amino-5-phenyl-1,2,4-thiadiazole (**6**)[3] (2.66 g, 0.015 mol) in anhydrous acetone (40 ml) was run in, the resulting suspension was stirred and refluxed for 1 h, then distilled to a third of its volume under reduced pressure, and the deep-yellow suspension was stirred into ice–water (200 ml). The precipitated pale-yellow needles were filtered off and rinsed with water, then with cold acetone (acetone filtrates: F). The product, m.p. 166—172 °C (decomp.) (3.55—4.2 g, 70—82%) gave bright-yellow needles of the *substituted* 1,2,4-*thiadiazole* (**9**), m.p. 172—174 °C (decomp.) (from acetone) (Found: C, 56.4; H, 3.4; N, 16.0; S, 19.2. $C_{16}H_{12}N_4OS_2$ requires C, 56.5; H, 3.5; N, 16.5; S, 18.8%); $\nu_{max.}$ 3 470ms, 3 210s, and 3 090s (NH), 1 725ms (CO), 1 580vs br, 1 475s, 1 440vs, and 1 365vs (td rs), 1 255 and 1 240vs d br (? NCS/td ip), 875m, 735m (td op), 770ms, 705, and 685ms br (2 Ph), and 1 200s, and 915 mw cm^{-1}. Compound (**9**) gave a strongly positive sodium plumbite test on being briefly boiled, and has an exceedingly bitter taste.

The filtrates F deposited more (impure) product (m.p. 160—170 °C; 8—10%), suitable for hydrolysis to the thiourea, see below; the final crops were *N*-benzoylthiourea (0.6—1.1 g, 8—15% calc. on the benzoyl chloride used), m.p. and mixed m.p.[23] 169—170 °C (from ethanol–benzene) (Found: C, 53.1; H, 4.5. Calc. for $C_8H_8N_2OS$: C, 53.3; H, 4.4%).

5-*Phenyl*-3-*thioureido*-1,2,4-*thiadiazole* (**12**).—A solution of the foregoing (crude) benzoyl derivative (10.2 g, 0.03 mol) in 3M-sodium hydroxide (90 ml) was boiled for 6—8 min. The colourless liquid was acidified with conc. hydrochloric acid, then just basified with ammonia. The white precipitate, collected at 0 °C, m.p. 244—248 °C (decomp.) (6.0 g, 85%) (filtrate: M) gave, on crystallisation from acetone–ethanol (1:1; 300 ml per g, followed by partial evaporation), or from nitro-

benzene (5 ml per g; recovery >90%), prisms of 5-*phenyl*-3-*thioureido*-1,2,4-*thiadiazole* (**12**), m.p. 248—250 °C (decomp.) (Found: C, 46.2; H, 3.2; N, 23.45. $C_9H_8N_4S_2$ requires C, 45.8; H, 3.4; N, 23.7%); $\nu_{max.}$ 3 375vs (NH_2), 3 190vs and 3 050s (NH), 1 625vs (NH/CN), 1 560vs, 1 525, 1 505vs br, 1 455, 1 440vs br, and 1 365ms (td rs), 1 255vs—1 220s vbr (? NCS/td ip), 1 030vs (td rb), 965s, 830ms, and 735s (td op), and 765s and 685s (Ph) cm^{-1}. The compound gave a strongly positive sodium plumbite test on being heated, and has an exceedingly bitter taste. Filtrate M gave benzoic acid (65%) on acidification.

Attempts to convert 3-amino- into 5-phenyl-3-thioureido-1,2,4-thiadiazole directly, by the addition of the elements of thiocyanic acid (heating or boiling, then evaporation of solutions of the reactant with 2—6 moles of ammonium thiocyanate in 3M-hydrochloric acid during 1—2.5 h) were unsuccessful. Deep yellow to orange granular non-homogeneous substances (with indistinct m.p.s, subliming on pyrolysis, and giving very strongly positive plumbite tests) were the only water-insoluble products isolated. In experiments employing conditions successfully used with arylamines,[8] the aminothiadiazole was recovered almost quantitatively.

5-*Imino*-4-(5′-*phenyl*-1′,2′,4′-*thiadiazol*-3′-*yl*)-3-(5′-*phenyl*-1′,2′,4′-*thiadiazol*-3′-*ylamino*)-4,5-*dihydro*-1,2,4-*thiadiazole* (**17**).—A solution of 5-phenyl-3-thioureido-1,2,4-thiadiazole (**12**) (2.36 g, 0.01 mol) in dioxane (75 ml) was treated at 75—80 °C with a mixture of 6% hydrogen peroxide (11.3 ml, 0.02 mol) and conc. hydrochloric acid (1 ml, 0.01 mol) during 5 min. A white crystalline solid first appeared, but redissolved as the addition proceeded. The mixture was set aside (*ca.* 12 min), and was then added to ice–water (150 ml); the finely divided yellow precipitate (1.7 g) was crystallised from nitrobenzene (30 ml), to give ivory felted needles of the *substituted* Δ^2-1,2,4-*thiadiazoline* (**17**), m.p. 328—330 °C (decomp.) (1.0 g, 46%) (Found: C, 49.5; H, 2.8; N, 26.5; S, 21.7. $C_{18}H_{12}N_8S_3$ requires C, 49.5; H, 2.75; N, 25.7; S, 22.0%); $\nu_{max.}$ 3 530—3 450s mt, 3 300s, 3 070, and 3 030s d br (NH), 1 600vs and 1 640ms sh br (? NH/CN), 1 525vs, 1 510s sh, 1 435vs, and 1 355s (td rs), 1 250ms br, 1 175m, and 1 100mw (td ip), 830mw, and 725ms (td op), 765ms and 685ms (Ph), and 970w cm^{-1}. The use of 3 molar proportions of hydrogen peroxide reduced the yield to 35%.

Acetyl Derivative (**18**).—A suspension of the foregoing base (0.44 g, 0.001 mol) in pyridine (12 ml)–acetic anhydride (25 ml) was heated at 100 °C during 1.5 h, complete dissolution occurring within 30 min; addition of the deep-red liquid to ice–water gave a brown granular solid. Its solution in benzene (8 ml) deposited crystals, which yielded platelets of the *monoacetyl derivative* (**18**), m.p. 190—192 °C (decomp.) (from a little ethanol) (total 0.28 g, 50%) (Found: C, 50.7; H, 3.4; N, 22.7. $C_{20}H_{14}N_8OS_3$ requires C, 50.2; H, 2.9; N, 23.4%); $\nu_{max.}$ 3 480—3 430s mt, 3 260s, 3 100, and 3 000s (NH), 1 690s (CO of Ac), 1 610s (? NH/CN), 1 555vs br, 1 475vs, 1 450vs, 1 360—1 340vs br (td rs), 1 260vs br, and 1 100mw (td ip), 1 065mw and 1 010m (td rb), 860ms and 735m (td op), 770ms and 690s (Ph), and 1 295s br and 985m cm^{-1}. Crystallisation of the derivative from benzene gave solvated platelets, m.p. 128—130 °C (which resolidified and remelted at 188—190 °C) (Found: C, 55.5; H, 3.3. $C_{20}H_{14}N_8OS_3 \cdot C_6H_6$ requires C, 56.1; H, 3.6%).

5-*Phenyl*-3-*ureido*-1,2,4-*thiadiazole* (**4**).—A (filtered) solution of 5-phenyl-3-thioureido-1,2,4-thiadiazole (**12**) (0.47 g, 0.002 mol) in 1.5M-sodium hydroxide (10 ml) at 90 °C was treated during 2 min with 6% hydrogen peroxide (5.1 ml, 0.009 mol). The liquid was kept at 75—80 °C during 8 min, then acidified with conc. hydrochloric acid. The pale-yellow granular solid (0.35 g), collected at 0 °C gave, on crystallisation from nitrobenzene (10 ml per g), ivory platelets of 5-phenyl-3-ureido-1,2,4-thiadiazole (**4**), m.p. 212—214 °C (decomp.) (0.3 g, 68%) (Found: C, 49.3; H, 3.9; N, 24.8. Calc. for $C_9H_8N_4OS$: C, 49.1; H, 3.6; N, 25.45%); $\nu_{max.}$ 3 420vs, 3 285s, 3 180s, 3 080—2 920s mt (NH), 1 690vs br, and 1 600s br (CO), 1 560s br, 1 440s, and 1 330s (td rs), 845m (td ip), 815m and 735 s (td op), 770ms and 680s (Ph) and 1 400vs cm^{-1}. The compound was identical (mixed m.p., i.r.) with the product of the oxidative cyclisation of N^1-carbamoyl-N^3-thiobenzoylguanidine.[1,3]

This urea was not obtainable by the interaction of sodium cyanate and 3-amino-5-phenyl-1,2,4-thiadiazole (**6**) in acid solution under the usual conditions,[7] the thiadiazole being recovered almost quantitatively.

5-*Anilino*-3-[N′-(*benzoyl*)*thioureido*]-1,2,4-*thiadiazole* (**10**).—To benzoyl isothiocyanate (prepared as described above from benzoyl chloride, 0.04 mol) was added a solution of 3-amino-5-anilino-1,2,4-thiadiazole (**7**)[24] (solvate; 2.38 g, 0.01 mol) in hot ethanol–acetone (1:5; 36 ml). The stirred suspension was boiled under reflux for 1 h, and the product was isolated as described for the 5-phenyl analogue (**9**). Crystallisation from nitrobenzene gave pale-yellow minute prisms (1.14 g, 32%) of the *substituted* 1,2,4-*thiadiazole* (**10**), m.p. 256—258 °C (deccomp.) (Found: C, 54.4; H, 3.6; N, 19.3. $C_{16}H_{13}N_5OS_2$ requires C, 54.1; H, 3.7; N, 19.7%); $\nu_{max.}$ 3 260vs and 3 100vs br (NH), 1 670vs br (CO of Bz), 1 600s (NH/CN), 1 570—1 500vs br mt and 1 460s (td rs), 1 290vs br and 1 230s (? NCS, td rs), 1 195vs br (td ip), 1 040, 1 025s d (td rb), 865s, 725, 710vs d (td op), 750s and 690vs (Ph), and 2 860vs br and 1 390vs br cm^{-1}. Yields were not improved when the 3-amino-compound was added (a) as finely powdered solid, (b) in pyridine (20 ml), (c) in ethoxyethanol–acetone (1:5; 60 ml).

The compound was recovered (80%) when its solution in 3M-sodium hydroxide (0.005 mol in 20 ml) was boiled for 8 min, then acidified (*i.e.* under conditions that debenzoylate the 5-phenyl analogue, see above).

5-*Anilino*-3-(N′-*benzoylureido*)-1,2,4-*thiadiazole* (**13**).—A solution of the foregoing benzoylthiourea (1.78 g, 0.005 mol) in 1.5M-aqueous sodium hydroxide (50 ml) at 70 °C was treated with 6% hydrogen peroxide (8.5 ml, 0.015 mol); the yellow colour of the solution was discharged and a white granular solid separated rapidly. The mixture was kept at 70 °C during 15 min, cooled, and the solid was collected at 0 °C. The product (1.5 g) gave, on crystallisation from nitrobenzene (200 ml per g), felted needles of the *substituted* 1,2,4-*thiadiazole* (**13**), m.p. 332—335 °C (decomp.) (0.95 g, 55%) (Found: C, 56.8; H, 4.0; N, 20.6; S, 9.3. $C_{16}H_{13}N_5O_2S$ requires C, 56.6; H, 3.8; N, 20.65; S, 9.4%); $\nu_{max.}$ 3 280—2 940vs vbr with peaks at 3 220, 3 140, and 2 980 (NH), 1 695vs, 1 675vs, and 1 605vs (CO of Bz and urea), 1 580—1 500vs vbr (with peaks at 1 575, 1 545, and 1 510), 1 455vs and 1 340vs (td rs), 1 255vs (td ip), 1 030 and 1 010m (td rb), 895s, 845mw, 800ms, and 725vs (td op), 755s, 700vs, and 690vs (2 Ph) and 1 315—1 300vs, 1 075ms cm^{-1}. The compound (0.001 mol) was recovered (75%) after its solution in 3M-sodium hydroxide–ethanol (1:2; 12 ml) had been boiled under reflux for 1 h (2:1; 15 ml; 4 h; recovery 35%).

1-[N^1-(*Anilinothioformyl*)*amidino*]*urea* {1-*Carbamoyl*-3-[N-(*phenyl*)*thiocarbamoyl*]*guanidine*} (**16**).—A stirred suspension, obtained on addition of sodium (2.3 g, 0.1 g-atom) to dry acetone (250 ml), was treated while nearly boiling with finely powdered, dried (80 °C) amidinourea (**15**) sulphate monohydrate (16.9 g, 0.1 mol). The stirred mixture, containing initially a soft suspended material, was refluxed for 10 min; the deep-yellow, now granular suspension was then treated with phenyl isothiocyanate (13.5 g, 0.1 mol), refluxed for 20 min, reduced to small bulk (60—80 ml) under reduced pressure, and added to stirred ice–water (200 ml). The resulting precipitated

orange-yellow oil (forming an upper layer) changed, on addition of conc. hydrochloric acid (12 ml), instantly to a crystalline suspended solid. It was collected, twice warmed with ethanol (2 × 50 ml), each time collected at the pump, then washed successively with cold water and ethanol. The white flaky crystalline powder was 1-[N^1-(*anilinothioformyl*)-*amidino*]*urea dihydrate* (**16**)·$2H_2O$, which sintered at 175—180 °C and decomposed above 300 °C (13.1—14.7 g, 48—54%). Crystallisation from ethanol (100 ml per g, recovery 40%) gave white microprisms which sintered and decomposed at 185—190 °C (Found: C, 39.6; H, 4.8; N, 26.0. $C_9H_{11}N_5OS·2H_2O$ requires C, 39.6; H, 5.5; N, 25.6%); $\nu_{max.}$ 3 480—2 900 s mt, with peaks at 3 440s, 3 310s, and 3 100s (NH), 1 725vs, 1 645, 1 640vs d, and 1 595vs (CO/C=N), 765m and 690m (Ph), and 1 565s, 1 125s, and 1 095s cm^{-1}. The compound dissolved in dil. sodium hydroxide but was very sparingly soluble in the usual organic solvents. It gave a positive plumbite test on being boiled.

The *picrate*, produced from the base (0.001 mol) in aqueous ethanol (1:1; 12 ml) and 0.05M-picric acid (0.001 mol), separated gradually, and formed yellow granules (0.33 g, 70%), m.p. 228—232 °C (decomp., after sintering at 190 °C) (Found: C, 39.2; H, 3.1. $C_9H_{11}N_5OS·C_6H_3N_3O_7$ requires C, 38.6; H, 3.0%).

5-*Anilino*-3-*ureido*-1,2,4-*thiadiazole* (**14**).—(a) *By hydrogen peroxide oxidation.* A boiling solution of 1-[N^1-(anilinothioformyl)amidino]urea (**16**) dihydrate (2.73 g, 0.01 mol) in 50% aqueous ethanol (60—70 ml) was treated with 3M-hydrochloric acid (3.33 ml, 0.01 mol), followed by 6% hydrogen peroxide (17 ml, 0.03 mol; the first half in one portion, and the remainder during 3 min), and the mixture was boiled for a further 3—5 min. The separated silky needles, collected at 0 °C and washed with ethanol [m.p. 296—298 °C (decomp.); 1.88 g, 80%] gave, on crystallisation from nitrobenzene (150 ml per g), lustrous platelets of 5-*anilino*-3-*ureido*-1,2,4-*thiadiazole* (**14**), m.p. 294—296 °C (decomp.; the compound melts and decomposes vigorously when heated rapidly, but merely shrinks and sinters when heated slowly) (Found: C, 46.3; H, 3.75; N, 30.5; S, 14.0. $C_9H_9N_5OS$ requires C, 45.95; H, 3.8; N, 29.8; S, 13.6%); $\nu_{max.}$ 3 420s (NH_2), 3 210vs and 3 060vs (NH), 1 725vs and 1 605vs (CO), 1 585vs, 1 540s br, 1 510vs, 1 475vs, 1 335s, and 1 310vs (? td rs), 1 220ms (td ip), 790ms and 740s (td op), 765m and 675ms (Ph), and 1 425vs and 700ms cm^{-1}. The product was almost insoluble in ethanol, acetone and dioxane, and very sparingly so in 2-ethoxyethanol.

(b) *By bromine oxidation.* A suspension of the finely powdered reactant (**16**) (1.36 g, 0.005 mol) in chloroform (50 ml) rapidly decolourised a 1M-bromine solution in chloroform (5 ml, 0.005 mol). After the removal of the solvent under reduced pressure, the white residue was successively washed with water and hot ethanol (yield 0.68 g, 58%) and recrystallised as above, to give the 3-ureido derivative, identical with material obtained in method (a).

5-*Amino*-3-[N′-(*benzoyl*)*thioureido*]-1,2,4-*thiadiazole* (**11**).—To benzoyl isothiocyanate [prepared from benzoyl chloride (0.15 mol) as described above] was added finely powdered 3,5-diamino-1,2,4-thiadiazole toluene-*p*-sulphonate[11,12] (11.52 g, 0.04 mol), and the yellow suspension was stirred for 15—20 min, during which time its temperature dropped to 35—30 °C. Sodium (0.69 g, 0.03 g-atom) was added to acetone (40 ml), the resulting suspension was added to the reaction mixture, and the entire mixture was stirred at room temperature for 2.5 h. The mixture was next heated to boiling, allowed to cool somewhat, treated with more sodium (0.23 g, 0.01 g-atom) in acetone (20 ml), and stirred at room temperature for another 1 h. It was evaporated under reduced pressure to *ca.* one-third its original bulk, and the residual deep-yellow suspension was diluted with water (500 ml). The aqueous phase was decanted from the resulting soft deep-orange product, which was rinsed with more water and then stirred with successive quantities of cold acetone (5 × 20 ml). The remaining finely divided yellow solid was collected, suspended in boiling ethanol (50 ml; 1—2 min), and again collected by filtration. The crude product, m.p. 270—276 °C (decomp.) (5.8—6.7 g, 52—60%) was crystallised from 2-ethoxyethanol (500 ml per g) or nitrobenzene (100 ml per g) to give pale-yellow microcrystalline 5-*amino*-3-[N′-(*benzoyl*)-*thioureido*]-1,2,4-*thiadiazole* (**11**), m.p. 284—285 °C (decomp.) (Found: C, 43.3; H, 3.2; N, 25.2; S, 22.2. $C_{10}H_9N_5OS_2$ requires C, 43.0; H, 3.2; N, 25.1; S, 22.9%); $\nu_{max.}$ 3 270vs and 3 110s (NH), 1 675s (CO, Bz), 1 625s (? NH/CN), 1 555—1 540vs br mt and 1 455ms br (td rs), 1 295vs and 1 240ms (? NCS/td ip), 1 025ms (td rb), 885mw, 835mw, and 720m (td op), 700ms (Ph), and 2 910s, and 2 870s d cm^{-1}.

The acetone–ethanol filtrates gave, on spontaneous evaporation, deep-orange crystalline unidentified fractions (2—2.5 g), and a final crop (1—1.5 g) of *N*-benzoylthiourea, m.p. and mixed m.p.[23] 170—172 °C. Experiments employing a larger excess of benzoyl isothiocyanate [from benzoyl chloride (0.3 mol)] gave the same product in comparable yields, but the final fractions (4—6 g) were benzamide.

References

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