1017. *Heterocyclic Compounds from Urea Derivatives. Part II.* Synthesis and Cyclisation of 4-Substituted 1-Amidino-semicarbazides and -thiosemicarbazides.*

By Leonard E. A. Godfrey and Frederick Kurzer.

The interaction of aminoguanidine and alkyl or aryl iso(thio)cyanates under various conditions affords 4-substituted 1-amidino(thio)semicarbazides in good yield. Members of the sulphur-containing series are cyclised to 3-alkyl(or -aryl)amino-5-amino-1,3,4-thiadiazoles in acidic media. Their *S*-alkyl derivatives are ring-closed to 3-amino-5-arylamino-1,2,4-triazoles by alkali, and to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles by aniline.

In contrast, 4-substituted 1-amidinosemicarbazides are not cyclised under comparable conditions. They are remarkably stable, being merely acetylated by boiling acetic anhydride or sulphonated by hot concentrated sulphuric acid.

The interaction of aminoguanidine (I) with isocyanate or isothiocyanate esters gives rise either to substituted *N*-aminoamidino(thio)ureas (A; X = O or S) or to 4-substituted 1-amidino(thio)semicarbazides (B; X = O or S), in the presence or absence, respectively, of a blocking group on the hydrazine residue. The synthesis and cyclisation of the former class of compounds (A) has already been described;[1] this paper deals with the corresponding reactions of the series (B).[2]

(A) $R{\cdot}NH{\cdot}CX{\cdot}NH{\cdot}C(:NH){\cdot}NH{\cdot}NH_2$ $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}NH{\cdot}CX{\cdot}NHR$ (B)

The action of phenyl isothiocyanate on aminoguanidine hydrogen carbonate in ethanol was originally shown[3] to result directly, with loss of ammonia, in 3-amino-5-mercapto-4-phenyl-1,2,4-triazole (V; R = Ph). Using aminoguanidine hydrochloride, Fry and Lambie[4] recently obtained a series of 4-substituted 1-amidinothiosemicarbazides (B; X = S), which are obviously concerned as intermediates in the above reaction, and demonstrated[5] their ready cyclisation in alkaline media to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles (V). The corresponding reactions of isocyanate esters, however, have apparently not been studied.

In the present work, the condensation under various conditions of aminoguanidine salts and isothiocyanate esters was first re-examined. Fry and Lambie's procedure[4] afforded 4-substituted 1-amidinothiosemicarbazides (II) in satisfactory yields which were however improved, in the aliphatic series, by extending the time of reaction and by use of triethylamine as catalyst. In the preparation of aromatic homologues, nevertheless, prolonged heating was inadmissible, since increasing proportions of triazole (V) were

* Part I, *J.*, 1960, 3437.

[1] Godfrey and Kurzer, *J.*, 1960, 3437.

[2] For a preliminary account of part of this work, see Kurzer and Godfrey, *Chem. and Ind.*, 1961, 107.

[3] Fantl and Silbermann, *Annalen*, 1928, **467**, 274.

[4] Fry and Lambie, B.P. 741,280/1955.

[5] Fry and Lambie, B.P. 741,228/1955.

formed, showing that under suitable conditions, the cyclisation (II ⟶ V) may also proceed in other than alkaline media. In this, as in the other variations of this method, it was advantageous to isolate the products as the sparingly soluble, highly crystalline toluene-*p*-sulphonates.

Condensation of the compounds in aqueous-ethanolic alkali, that has been successful in the synthesis of *N*-substituted *N'*-benzimidoylthioureas [6] R'·NH·CS·NH·CR:NH, gave only moderate yields of the aromatic homologues (II; R = Ph or *p*-C_6H_4Me). The use of ethanolic sodium ethoxide, in the aliphatic series, resulted exclusively in cyclisation to the substituted triazoles (V).

When dimethylformamide was used as solvent reaction of aminoguanidine with isothiocyanate or isocyanate esters was smoother and much faster and there were no side reactions. 1-Amidino-4-phenylthiosemicarbazide (II; R = Ph), for example, was obtained in 82% yield at 100° in 30 min. As expected, the less reactive [7] alkyl isothiocyanates required an extended time of reaction to produce comparable results.

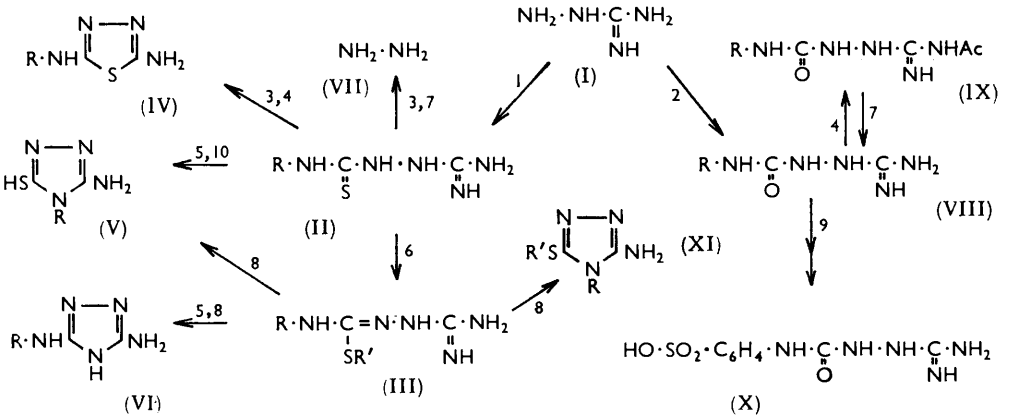
Attempts to condense aminoguanidine salts and isocyanates, for which procedures involving aqueous or alcoholic media are inapplicable, were first made in anhydrous pyridine. Yields were low, however, and much carbanilide was produced. Here, the use of dimethylformamide as solvent proved indispensable, affording the new 4-substituted 1-amidino semicarbazides (VIII) rapidly and in excellent yield. The remarkable power of this solvent of accelerating the present addition reactions may be ascribed, as in numerous other examples,[8] to its high dielectric constant (ε 36·7,[9] compared with ε 12·4 for pyridine, both at 25°) and to the possible formation of highly reactive intermediate addition complexes. The existence of a variety of addition compounds of dimethylformamide is well established; [10] also complexes of aniline or carbanilide with stannous chloride have superior reactivity towards phenyl isocyanate [11] in a comparable synthesis.

4-Substituted 1-amidinothiosemicarbazides (II) are monoacid bases; they were isolated as stable salts only, since cyclisation to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles (V) occurred when attempts were made to liberate the free bases even by dilute ammonia at 0°. They were desulphurised and decomposed, with evolution of isocyanides, by sodium plumbite in the presence of alkali. Their monopicrates were unusually soluble and difficult to crystallise. The 4-substituted 1-amidinothiosemicarbazides (II) were readily converted into their *S*-benzyl-derivatives (as III), which were isolated without difficulty as free bases in the presence of strong alkalis. Since compounds (II) and (III) differ structurally merely in their mercapto- and benzylmercapto-group, neither of which is concerned in the ring-closure to (V) or (XI), it is noteworthy that only the former compounds are rapidly cyclised by cold alkalis; steric hindrance (in III) may contribute to their resistance to cyclisation (to XI) under mild conditions (see also below).

Three distinct cyclisations of 4-substituted 1-amidinothiosemicarbazides (II) are theoretically feasible: Two alternative modes of elimination of ammonia, between the amidino- and the alkyl(or aryl)amino- or thiol groups (in II), respectively, give rise to either triazoles (V) or thiadiazoles (IV), while loss of hydrogen sulphide produces 1,2,4-triazoles (VI). The first ring-closure, occurring in basic media, is well established.[3,5] Cyclisations of the second type have recently been observed [12] for the closely related

[6] Pinner, *Ber.*, 1899, **22**, 1600; Kurzer and Tertiuk, *J.*, 1959, 2851.
[7] Orndorff and Richmond, *Amer. Chem. J.*, 1899, **22**, 458; Slotta, Tschesche, and Dressler, *Ber.*, 1930, **63**, 208.
[8] (*a*) Ross and Labes, *J. Amer. Chem. Soc.*, 1957, **79**, 4155; (*b*) Hartman, *Nature*, 1955, **176**, 1024; Blume and Swezey, *TAPPI*, 1954, **37**, 481; (*c*) Kornblum *et al.*, *J. Amer. Chem. Soc.*, 1956, **78**, 1497; Joly, Warnant, and Nominé, *Bull. Soc. chim. France*. 1957, 330; Bunnet and Conner, *J. Org. Chem.*, 1958, **23**, 305; (*d*) Kornblum and Kendall, *J. Amer. Chem. Soc.*, 1952, **74**, 5782.
[9] Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5731.
[10] Haszeldine, *J.*, 1954, 4145; Hall, *J. Amer. Chem. Soc.*, 1956, **78**, 2717; Jaunin, *Helv. Chim. Acta*, 1956, **39**, 111.
[11] Baker and Holdsworth, *J.*, 1945, 724.
[12] Kurzer, *J.*, 1961, 1617.

thiobenzamidoguanidines (D) which are converted by hydrochloric acid or acetic anhydride into 5-substituted 2-amino-1,3,4-thiadiazoles or their acetyl derivatives. In the present work, hydrochloric acid proved unsuitable, degrading the reactants (*e.g.*, II; R = Ph) directly to phenyl isothiocyanate and hydrazine. 3-Amino-5-anilino-1,3,4-thiadiazole



Reagents: 1, PhNCS. 2, PhNCO. 3, H_3PO_4. 4, Ac_2O. 5, NaOH. 6, R'Cl–NaOH. 7, HCl. 8, Ph·NH_2. 9, H_2SO_4. 10, Aq. NH_3.

was not formed intermediately, since its stability in boiling concentrated hydrochloric acid was separately established.

The desired cyclisation occurred in 100% orthophosphoric acid at 120—130°, affording 2-amino-5-alkyl(or -aryl)amino-1,3,4-thiadiazoles (IV) in satisfactory yields. Feeble evolution of hydrogen sulphide indicated the loss of small quantities of reactant in side reactions. The methyl homologue (II; R = Me) reacted anomalously, however, being completely decomposed to hydrazine by this reagent also. The familiar ring-closure of 1-acylthiosemicarbazides to 2-amino-5-alkyl(or -aryl)-1,3,4-thiadiazoles by orthophosphoric acid [13] differs from the present reaction in that water instead of ammonia is eliminated, and illustrates the preferential formation of the 1,3,4-thiadiazole over that of the 1,3,4-oxadiazole ring-system under these conditions.

Acetic anhydride at its boiling point effected the same cyclisation, yielding 1,3,4-thiadiazoles (IV) as the diacetyl derivatives, which were converted into their parent compounds (IV) by acid hydrolysis. The present cyclisation, by phosphoric acid or acetic anhydride, resembles the ring-closures of the comparable oxygen- and sulphur-containing compounds: both types of compound (C; X = O) [14,15] and (C; X = S) [14,16] are cyclised to the appropriate 1,3,4-thiadiazoles in acid media, but the latter reaction differs from the synthesis now described in proceeding with loss (from C; X = S, R = Ph) of both ammonia and hydrogen sulphide simultaneously to yield 2-mercapto- and 2-amino-5-anilino-1,3,4-thiadiazoles side by side.

(C) $NH_2{\cdot}CX{\cdot}NH{\cdot}NH{\cdot}CS{\cdot}NHR$ $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}NH{\cdot}CSR$ (D)

The third type of ring closure (II ⟶ VI), attended by loss of hydrogen sulphide, was achieved indirectly on treatment of the *S*-benzyl derivatives (III) with boiling alkali. 1-Amidino-*S*-benzyl-4-phenylisothiosemicarbazide (III; R = Ph, R' = Ph·CH_2), for example, was converted into 3-amino-5-anilino-1,2,4-triazole (VI; R = Ph) in 78% yield. The free

[13] Hoggarth, *J.*, 1949, 1166.
[14] Guha, *J. Amer. Chem. Soc.*, 1923, **45**, 1041.
[15] Arndt, Milde, and Tschenscher, *Ber.*, 1922, **55**, 341.
[16] Freund, *Ber.*, 1894, **27**, 1774; 1895, **28**, 946; Busch and Schmidt, *Ber.*, 1913, **46**, 2240; Busch and Lotz, *J. prakt. Chem.*, 1914, **90**, 257; for summary cf. Bambas, "The Chemistry of Heterocyclic Compounds," Interscience Publ. Inc., New York, 1952, Vol. IV, p. 124 *et seq.*

thiol group (of II) is presumably stabilised in alkaline media by salt-formation, with consequent preferential elimination of ammonia and production of (V); the *S*-alkylated thiol group (of III), on the other hand, being removed as a whole by alkalis in the familiar manner,[17] provides the conditions for ring-closure to diaminotriazoles (VI).

The replacement of the *S*-alkylthio- by amino-groups (in III) was expected to provide further data concerning cyclisations of compounds of this type. The action of boiling aniline on 1-amidino-*S*-benzyl-4-phenylisothiosemicarbazide (III; R = Ph, R′ = Ph·CH_2) proceeded in two ways depending whether the free base or its toluene-*p*-sulphonate was employed. The base gave approximately equal quantities of 3-amino-5-benzylthio-4-phenyl- (XI; R = Ph, R′ = Ph·CH_2) and 3-amino-5-anilino-1,2,4-triazole (VI; R = Ph), the former arising by direct loss of ammonia, the latter possibly by elimination of aniline from the intermediate substituted aminoguanidine, $(Ph\cdot NH)_2C{:}N\cdot NH\cdot C(:NH)\cdot NH_2$. The toluene-*p*-sulphonate (III; R = Ph or *p*-C_6H_4Me, R′ = Ph·CH_2) afforded 3-amino-4-aryl-5-mercapto-1,2,4-triazoles (V) almost quantitatively: under these conditions, the *S*-alkyl derivative is therefore merely dealkylated, and the resulting parent compound (II) cyclised subsequently in the usual way.

The 4-substituted 1-amidinosemicarbazides (VIII) were monoacid bases that were readily isolated as toluene-*p*-sulphonates and characterised as picrates. They differed completely from the sulphur series (II), however, in their remarkable stability in acid media. Thus, 1-amidino-4-phenylsemicarbazide (VIII; R = Ph), on treatment with acetic anhydride at 120°, gave merely an acetyl derivative (probably IX), which was reconverted into the parent base by acid hydrolysis. Attempts to cyclise 1-amidino-4-phenylsemicarbazide with simultaneous dehydration (*i.e.*, to VI) by concentrated sulphuric acid gave only 1-amino-4-*p*-sulphophenylsemicarbazide (X), the structure of which was established by its degradation to sulphanilic acid.

The rapid ring-closure of 4-substituted 1-amidinothiosemicarbazides in alkaline media (to V) is also without parallel in the oxygen series: a model compound (VIII; R = Ph) was mostly recovered after brief heating with alkali, but was degraded to aniline on distillation. In their failure to undergo cyclisation, 4-substituted 1-amidinosemicarbazides thus differ, not only from their sulphur analogues, but also from the closely related acylaminoguanidines, $R\cdot CO\cdot NH\cdot NH\cdot C(:NH)\cdot NH_2$, which are converted into 5-substituted 3-amino-1,2,4-triazoles with great ease.[18]

The new ring-closures of 4-substituted 1-amidinothiosemicarbazides now described provide further examples of the usefulness of aminoguanidine as a starting material in heterocyclic syntheses; in general, the observed formation of 1,3,4-thiadiazoles and 1,2,4-triazoles fits into the known pattern of the reactions of substituted thiosemicarbazides under comparable conditions.

Experimental

Light petroleum had b. p. 60—80°. Dimethylformamide used as solvent was redistilled before use, and the water-containing fore-run rejected. Ultraviolet absorption measurements were made with a Unicam S.P. 500 spectrophotometer and 0·00005M-ethanolic solutions.

Aminoguanidine picrate was prepared from the sulphate monohydrate (0·66 g., 0·005 mole) in water (5 ml.) and 0·05M-picric acid (100 ml., 0·005 mole) at room temperature; the yellow precipitate gave deep yellow prisms, m. p. 182—185° (decomp.) (from 90% ethanol) (Found: C, 27·9; H, 3·0. $CH_6N_4,C_6H_3N_3O_7$ requires C, 27·7; H, 3·0%). Thiele [19] prepared this salt but gave no m. p.

Aminoguanidine Toluene-p-*sulphonate*.—Aminoguanidine sulphate monohydrate (1·32 g., 0·01 mole) in water (5 ml.), treated with toluene-*p*-sulphonic acid monohydrate (2·85 g.,

[17] Arndt, *Ber.*, 1921, **54**, 2238.
[18] Thiele and Heidenreich, *Ber.*, 1893, **26**, 2598; Thiele and Manchot, *Annalen*, 1898, **313**, 33; Hoggarth, *J.*, 1950, 612.
[19] Thiele, *Annalen*, 1892, **270**, 1.

0·015 mole) in water (5 ml.), gave crystals (2·0 g., 80%), which gave, on crystallisation from water (5 ml. per g.), prisms of the *toluene*-p-*sulphonate*, m. p. 203—205° (decomp.) (Found: C, 38·9; H, 5·75. $CH_6N_4,C_7H_8O_3S$ requires C, 39·0; H, 5·7%).

Hydrazine Dipicrate.—10% Aqueous hydrazine hydrate (1 ml., 0·002 mole) added to 0·05M-picric acid (100 ml., 0·005 mole) gave a clear solution, which on treatment with ammonium chloride (20 g.) rapidly deposited yellow needles. They were collected at 0°, washed with very little water, and crystallised from ethanol (40 ml. per g.; recovery 60—70%) or water (10 ml. per g.), giving needles of *hydrazine dipicrate*, m. p. 289—292° (decomp., after darkening from 270°), almost quantitatively (Found: C, 29·7; H, 2·3; N, 23·3. $N_2H_4,2C_6H_3N_3O_7$ requires C, 29·4; H, 2·0; N, 22·9%).

Thiosemicarbazide Series

Preparation of 1-*Amidino*-4-*phenylthiosemicarbazide.*—(*a*) A solution of aminoguanidine sulphate monohydrate (5·8 g., 0·044 mole) in water (20 ml.) was treated with phenyl isothiocyanate (5·4 g., 0·04 mole), followed by 3N-aqueous sodium hydroxide (13·3 ml., 0·04 mole) and ethanol (20 ml.), so that a one-phase system was obtained. The orange-brown warm mixture was stirred at room temperature during 2 hr., a little more ethanol being added if necessary to prevent separation into two phases. The solution was set aside overnight, a trace of solid removed, and the orange filtrate treated with toluene-*p*-sulphonic acid monohydrate (11·4 g., 0·06 mole). The resulting solid was collected at 0° (9·5—11 g.) and crystallised from ethanol–water (4 and 1 ml. per g.): prisms (filtrate: F) of solvated 1-*amidino*-4-*phenylthiosemicarbazide toluene*-p-*sulphonate*, m. p. 133—135° (decomp.), were obtained (7·5—8·5 g., 44—50%). A specimen, crystallised twice more from ethanol (25 ml. per g.), had m. p. 134—136° (decomp.) (Found: C, 47·5; H, 5·5; N, 16·3; S, 15·0. $C_8H_{11}N_5S,C_7H_8O_3S,C_2H_5{\cdot}OH$ requires C, 47·8; H, 5·85; N, 16·4; S, 15·0%). It rapidly gave lead sulphide and phenyl isocyanide with hot alkaline sodium plumbite.

The free base was not isolated, since cyclisation to 3-amino-5-mercapto-4-phenyl-1,2,4-triazole occurred on treatment of the toluene-*p*-sulphonate at 0° with such weak bases as ammonia (see below).

Filtrate F, on dilution with an equal volume of ether, gave a white solid which consisted, after crystallisation from 90% ethanol, of aminoguanidine toluene-*p*-sulphonate (0·85 g., 8%), m. p. and mixed m. p. 202—204° (decomp.) (Found: C, 39·2; H, 5·7; N, 23·0; S, 13·35. Calc. for $CH_6N_4,C_7H_8O_3S$: C, 39·0; H, 5·7; N, 22·8; S, 13·0%).

(*b*) Finely powdered aminoguanidine hydrochloride (2·2 g., 0·02 mole) in dimethylformamide (5 ml.) was treated with phenyl isothiocyanate (2·70 g., 0·02 mole) and kept at 100° during 30 min., complete dissolution occurring after 10—15 min. The liquid, stirred into water (40 ml.) and treated with toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) in water (10 ml.), gave solvated 1-amidino-4-phenylthiosemicarbazide toluene-*p*-sulphonate, m. p. and mixed m. p. 134—136° (decomp.) (6·4—6·8 g., 75—82%; from 80% ethanol).

(*c*) The hydrochloride, obtained by Fry and Lambie's procedure [4] in 50—60% yield, formed white crystals, m. p. 172—174° (decomp.) (from ethanol–light petroleum). Fry and Lambie [4] give m. p. 177—180°. More prolonged boiling (10 or 20 hr.) resulted in partial cyclisation to 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see below) 264—266° (decomp.) (15—30%, respectively); this separated directly from the reaction mixture on cooling; the filtrate therefrom, after the usual treatment, gave the above hydrochloride in ~45 and 30% yield, respectively.

A solution of the solvated toluene-*p*-sulphonate (0·002 mole) in warm water (30 ml.), treated with 2N-ammonia (1 ml., 0·002 mole) and 0·05M-picric acid (40 ml., 0·002 mole), slowly deposited a yellow powder at 0°. The product (0·57 g., 65%) formed yellow prisms of the *picrate*, m. p. 180—182° (decomp., somewhat subject to the rate of heating) (from ethanol) (Found: C, 38·0; H, 3·3. $C_8H_{11}N_5S,C_6H_3N_3O_7$ requires C, 38·4; H, 3·2%).

Reactions of 1-*Amidino*-4-*phenylthiosemicarbazide.*—(a) *With phosphoric acid.* A solution of the solvated toluene-*p*-sulphonate (4·27 g., 0·01 mole) in 100% orthophosphoric acid (30 ml.) was kept at 120° during 1 hr. The pale pink liquid was stirred into concentrated aqueous ammonia (60 ml.)–ice (100 g.), and the crystalline precipitate collected after 12 hr. at 0° (1·5 g.). The product gave prisms from ethanol (20 ml.)–light petroleum (40 ml.) or platelets from water (100 ml. per g.) of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. 204—206° (1·06—1·30 g., 56—68%)

(lit., m. p. 205° [20] or 215° [14]) (Found: C, 50·1; H, 4·3; N, 29·9. Calc. for $C_8H_8N_4S$: C, 50·0; H, 4·2; N, 29·2%).

1-Amidino-4-phenylthiosemicarbazide hydrochloride [4] was cyclised under the same conditions (with evolution of hydrogen chloride) to 2-amino-5-anilino-1,3,4-thiadiazole in 60% yield.

The picrate formed yellow needles, m. p. 225—228° (decomp.) (Guha [14] gives m. p. 226°) (Found: C, 41·65; H, 3·2. Calc. for $C_8H_8N_4S,C_6H_3N_3O_7,C_2H_5{\cdot}OH$: C, 41·1; H, 3·6%). The *toluene*-p-*sulphonate*, obtained nearly quantitatively from the thiadiazole and toluene-*p*-sulphonic acid (100% excess) in the minimum volume of boiling water, consisted of needles, m. p. 268—269° (decomp. after sintering at 262°) (from ethanol, 100 ml. per g.) (Found: C, 49·6; H, 4·4; N, 14·1; S, 16·0. $C_8H_8N_4S,C_7H_8O_3S,C_2H_5{\cdot}OH$ requres C, 49·8; H, 5·4; N, 13·7; S, 15·6%). The diacetyl derivative, obtained on boiling the thiadiazole (0·001 mole) in acetic anhydride (4 ml.) during 30 min., formed prisms (65%), m. p. 274—276° (decomp., after shrinking at 270°) (from ethanol). Fromm and Jokl [20] give m. p. 264°.

(b) *With acetic anhydride.* The solvated toluene-*p*-sulphonate (2·14 g., 0·005 mole) in acetic anhydride (20 ml.) was refluxed during 20 min., then added to water (80 ml.). The separated solid (0·76 g., 55%) gave, on crystallisation from ethanol (carbon), needles of the diacetyl derivative of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. [and mixed m. p. with the derivative obtaind in (a), above] 274—276° (after shrinking at 270°) (Found: C, 51·9; H, 4·4; N, 20·7; S, 11·8. Calc. for $C_{12}H_{12}N_4O_2S$: C, 52·2; H, 4·35; N, 20·3; S, 11·6%).

(c) *With hydrochloric acid.* The thiosemicarbazide (2·14 g., 0·005 mole) in concentrated hydrochloric acid (10 ml.) was refluxed during 30 min. There was slight evolution of hydrogen sulphide, and oily drops in the refluxing liquid smelled of phenyl isothiocyanate. The clear solution, set aside in an evaporation basin overnight, deposited crystals (0·86 g., 40%) of recovered reactant (m. p. and mixed m. p. 131—135°, from ethanol). The acidic filtrate therefrom, nearly neutralised by concentrated aqueous ammonia and treated with picric acid, slowly deposited a yellow precipitate (1·22—1·45 g., 50—60%) of hydrazine dipicrate, m. p. and mixed m. p. 288—292° (decomp., after darkening from 270°) (from 95% ethanol) (Found: C, 29·4; H, 2·7; N, 23·0%). The use of 3N-hydrochloric acid resulted in 65% recovery of the reactant, and 20—30% yields of hydrazine dipicrate. 2-Amino-5-anilino-1,3,4-thiadiazole (0·005 mole) was substantially recovered after its solution in concentrated hydrochloric acid (10 ml.) had been boiled during 30 min.

(d) *With alkali.* The reactant (0·005 mole), on being refluxed with 3N-sodium hydroxide (10 ml., 0·03 mole) during 30 min., gave an intensely yellow and later colourless solution, while ammonia was evolved. Acidification with 3N-hydrochloric acid gave crystals (0·86 g., 90%) of 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. 264—266° (decomp.) (from water). (Found: C, 45·95; H, 4·8. Calc. for $C_8H_8N_4S,H_2O$: C, 45·7; H, 4·8%). $\lambda_{min.}$ 237 (log ε 3·75); $\lambda_{max.}$ 265 mμ (log ε 3·93). The m. p. is variously given between 260° and 268° in the literature.[3,5,15,20–22]

(e) *With ammonia.* A solution of the toluene-*p*-sulphonate (0·005 mole) in 6N-ammonia (15 ml.) at 0° during 2 days deposited crystals (0·74 g., 77%) of the same triazole, m. p. and mixed m. p. 264—266° (decomp.) (from ethanol). The ammoniacal filtrate, on being boiled during 5 min., gave a further crop (12%) of the triazole on subsequent storage at 0°.

1-*Amidino*-4-p-*tolylthiosemicarbazide.*—(*a*) To a solution of aminoguanidine sulphate monohydrate (2·90 g., 0·022 mole) in water (10 ml.) were added successively *p*-tolyl isothiocyanate (3·0 g., 0·02 mole), 3N-sodium hydroxide (6·7 ml., 0·02 mole), and ethanol (30 ml.). The resulting suspension was stirred at room temperature during 6 hr., further ethanol (10 ml.) being added after 1 hr.; after a further 72 hr., water (20 ml.) was added, inorganic material (1·5—2 g.) removed, and the filtrate treated with toluene-*p*-sulphonic acid monohydrate (7·60 g., 0·04 mole). The separated crystals (4—4·5 g.), when recrystallised from ethanol (15 ml. per g., recovery 80%), then water (20 ml. per g., recovery 60%), formed granules of the *toluene*-p-*sulphonate*, m. p. 160—162° (decomp., dependent on the rate of heating) (2·2—2·8 g., 28—

[20] Fromm and Jokl, *Monatsh.*, 1923, **44**, 303.

[21] Mazurewich, (*a*) *Bull. Soc. chim. France*, 1927, **41**, 644, 648; 1930, **47**, 1163, 1176; *J. Russ. Phys. Chem. Soc.*, 1927, **59**, 34; 1930, **62**, 1141, 1155; (*b*) *Bull. Soc. chim. France*, 1927, **41**, 659; *J. Russ. Phys. Chem. Soc.*, 1927, **59**, 61; see also *Univ. État Kiev, Bull. sci. Rec. chim.*, 1935, **1**, No. 4, 9 (*Chem. Abs.*, 1936, **30**, 7574).

[22] Guha and Mehta, *J. Indian Inst. Sci.*, 1938, **21**, *A*, 41, 53.

36%) (Found: C, 49·1; H, 5·0; N, 17·25. $C_9H_{13}N_5S,C_7H_8O_3S$ requires C, 48·6; H, 5·3; N, 17·7%). It gave lead sulphide, and a strong smell of isocyanide, with boiling alkaline sodium plumbite.

(*b*) Interaction of aminoguanidine hydrochloride and *p*-tolyl isothiocyanate (0·02 mole each) in dimethylformamide (5 ml.) at 100° during 1 hr., followed by addition of the liquid to water (40 ml.), gave a white solid which was collected at 0° (4·25 g., 77%) (filtrate: T). Crystallisation from 90% ethanol (10 ml. per g.) gave needles of the *hydrochloride monohydrate*, m. p. 195—197° (decomp.) (Found: C, 38·2; H, 5·5; N, 25·0; Cl, 12·3. $C_9H_{13}N_5S,HCl,H_2O$ requires C, 38·9; H, 5·8; N, 25·2; Cl, 12·8%). A further quantity (up to 20%) of the compound was isolated from filtrate T as the toluene-*p*-sulphonate.

(*c*) Interaction of the same reactants (0·02 mole each) in boiling ethanol (20 ml.) during 4 hr. gave, after several days' storage, the hydrochloride (3·60 g., 65%), m. p. and mixed m. p. (see *b*, above) 194—196° (decomp.). A litte more material was isolated from the filtrates as the toluene-*p*-sulphonate (5%). More prolonged refluxing resulted solely in partial cyclisation (15%) to 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole (cf. below).

Addition of picric acid (0·115 g., 0·0005 mole) in ethanol (3 ml.) to a solution of the hydrated hydrochloride (0·14 g., 0·0005 mole) in boiling ethanol (12 ml.), followed by dilution with ether (20 ml.), gave a liquid which slowly deposited yellow prisms (0·06 g., 25%) and a white powder. Slow crystallisation of the former (hand-picked) from ethanol (5 ml.) gave the *picrate*, m. p. 175—177° (decomp.) (Found: C, 41·1; H, 4·3. $C_9H_{13}N_5S,C_6H_3N_3O_7,C_2H_5{\cdot}OH$ requires C, 41·0; H, 4·4%). Attempts to convert the toluene-*p*-sulphonate into this picrate, in the presence or absence of ammonia, failed, because of its unusually high solubility, the reactant being largely recovered.

(*d*) Treatment of the toluene-*p*-sulphonate (1·0 g., 0·0025 mole) with orthophosphoric acid and isolation of the product as described above for the phenyl homologue gave plates (0·23 g., 45%) of 2-amino-5-*p*-toluidino-1,3,4-thiadiazole, m. p. 205—206° (once from water, once from ethanol–light petroleum [carbon]) (Guha and Mehta [22] give m. p. 203°) (Found: C, 53·0; H, 4·9; N, 27·3; S, 15·35. Calc. for $C_9H_{10}N_4S$: C, 52·4; H, 4·85; N, 27·2; S, 15·5%).

(*e*) Treatment of the toluene-*p*-sulphonate (0·005 mole) with alkali as described for the phenyl homologue gave (0·77 g., 75%) 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole, m. p. 278—280° (prisms from ethanol) (Found: C, 52·2; H, 4·7. Calc. for $C_9H_{10}N_4S$: C, 52·4; H, 4·85%). It had $\lambda_{min.}$ 241 (log ε 3·78), $\lambda_{max.}$ 268 mμ (log ε 3·96). The m. p. is variously given between 272° and 277° in the literature.[21b,22]

Preparation of 1-*Amidino*-4-*methylthiosemicarbazide*.—(*a*) Interaction of aminoguanidine hydrochloride and methyl isothiocyanate (0·02 mole each) in dimethylformamide (6 ml.) at 100° during 3 hr., followed by dilution with water (25 ml.) and treatment with toluene-*p*-sulphonic acid (0·024 mole), gave, on storage at 0° and subsequent spontaneous evaporation of the filtrates, two successive crops of the *toluene*-p-*sulphonate*, (4·1 g., 64%), forming prisms, m. p. 205—207° (decomp.) (from ethanol; 30 ml. per g.) (Found: C, 37·6; H, 5·3. $C_3H_9N_5S,C_7H_8O_3S$ requires C, 37·6; H, 5·3%). The same salt (80%), m. p. and mixed m. p. 205—207° (decomp.), resulted from equimolecular quantities (0·002 mole) of the hydrochloride (see *b*, below) and toluene-*p*-sulphonic acid in water (8 ml.).

(*b*) The hydrochloride was prepared by Fry and Lambie's procedure,[4] but with addition of a little triethylamine as catalyst, in 50—72% yield, after 20—50 hours' refluxing. Crystallised from 85% ethanol (25 ml. per g., recovery 50%), it formed prisms, m. p. 220—222°, (decomp.) (Found: C, 19·9; H, 5·4. Calc. for $C_3H_9N_5S,HCl$: C, 19·6; H, 5·45%). Fry and Lambie [4] give m. p. 209—210° (from water). Solutions of the product slowly gave a black precipitate with boiling alkaline sodium plumbite.

The *picrate*, prepared from the hydrochloride in 80% ethanol, formed yellow needles (70%), m. p. 212—214° (decomp.) (from 90% ethanol) (Found: C, 28·85; H, 3·1. $C_3H_9N_5S,C_6H_3N_3O_7$ requires C, 28·7; H, 3·2%).

(*c*) A suspension of aminoguanidine sulphate monohydrate (7·25 g., 0·055 mole) in a solution from sodium (1·15 g., 0·05 g.-atom) in ethanol (80 ml.) was stirred during 30 min. After addition of methyl isothiocyanate (3·65 g., 0·05 mole), the stirred mixture was kept at room temperature during 15 min. and refluxed during 1 hr. Most of the ethanol was removed in a vacuum, the residual liquid stirred into water (50 ml.), and the acidity adjusted to pH 6·5 with concentrated hydrochloric acid. The product, collected at 0° (3·3 g., 51%) and crystallised from water (25 ml. per g., recovery 75%), consisted of needles of 3-amino-5-mercapto-4-methyl-1,2,4-triazole,

m. p. 267—269° (Fry and Lambie [5] give m. p. 269—272°) (Found: C, 28·0; H, 4·6; N, 43·2; S, 24·95. Calc. for $C_3H_6N_4S$: C, 27·7; H, 4·6; N, 43·1; S, 24·6%), $\lambda_{min.}$ 228 (log ε 3·52), $\lambda_{max.}$ 260 mμ (log ε 4·14).

Aminoguanidine sulphate monohydrate, suspended in pyridine, failed to react with methyl isothiocyanate at 100° during 4 hr.

3-*Amino*-5-p-*chlorobenzylthio*-4-*methyl*-1,2,4-*triazole*.—A solution of the foregoing triazole (0·65 g., 0·005 mole) and 4-chlorobenzyl chloride (0·97 g., 0·006 mole) in ethanol (10 ml.), treated with N-sodium hydroxide (5 ml., 0·005 mole), was kept at 100° during 15 min., then diluted with water (20 ml.). The solid (1·2 g.), collected at 0°, crystallised from benzene–ethanol (3 : 1) as plates of the p-*chlorobenzylthio-derivative*, m. p. 165—167° (Found: C, 47·4; H, 4·3. $C_{10}H_{11}ClN_4S$ requires C, 47·2; H, 4·3%).

Reactions of 1-*Amidino*-4-*methylthiosemicarbazide*.—(a) *Action of phosphoric acid*. A solution of the hydrochloride (0·92 g., 0·005 mole) in 100% orthophosphoric acid (10 ml.) was kept at 120° during 30 min. (slight evolution of hydrogen chloride), added to ice (40 g.) and ammonia (*d* 0·88; 20 ml.), and acidified (to pH 6) with 3N-acetic acid (slight odour of hydrogen sulphide). Addition of 0·075M-picric acid (100 ml., 0·0075 mole) slowly gave hydrazine dipicrate (1·57 g., 64%), m. p. and mixed m. p. 288—290° (decomp., after darkening from 260—270°) (Found: C, 30·0; H, 2·4; N, 22·8%).

(b) *Action of acetic anhydride*. The hydrochloride (1·83 g., 0·01 mole) was refluxed in acetic anhydride (20 ml.) during 1 hr., but complete solution did not occur. The resulting needles were collected at 0°; addition of the filtrate to water gave a little more product (total, 1·18 g., 55%). Crystallised from methanol (120 ml. per g.), it consisted of the *diacetyl derivative* of 2-amino-5-methylamino-1,3,4-thiadiazole, m. p. 319—320° (Found: C, 40·1; H, 5·2; N, 25·6; S, 14·6. $C_7H_{10}N_4O_2S$ requires C, 39·25; H, 4·7; N, 26·2; S, 14·95%).

The diacetyl derivative (1·07 g., 0·005 mole) was refluxed with 3N-hydrochloric acid (5 ml.) during 30 min., the solution neutralised with 3N-ammonia, and the filtered liquid treated with 0·05M-aqueous picric acid (100 ml., 0·005 mole). The yellow precipitate (1·53 g., 85%) was 2-*amino*-5-*methylamino*-1,3,4-*thiadiazole picrate*, m. p. 218—221° (decomp., darkening from 210°) (from 80% ethanol) (Found: C, 30·9; H, 2·7. $C_3H_6N_4S,C_6H_3N_3O_7$ requires C, 30·1; H, 2·5%).

Attempts to isolate the thiadiazole as the base or the toluene-*p*-sulphonate from the hydrolysate were unsuccessful, because of the high solubility of these compounds in water.

1-*Amidino*-4-*n*-*butylthiosemicarbazide*.—(*a*) Interaction of aminoguanidine hydrochloride and butyl isothiocyanate (0·03 mole each) in dimethylformamide (8 ml.) at 100° during 3 hr., dilution with water (40 ml.), and addition of toluene-*p*-sulphonic acid (0·035 mole) gave the toluene-*p*-sulphonate monohydrate (9·1 g., 80%), m. p. and mixed m. p. (see below) 160—163° (decomp.) (from water). It gave lead sulphide and isocyanide with boiling basified sodium plumbite.

(*b*) A solution of powdered aminoguanidine hydrochloride (5·53 g., 0·05 mole), butyl isothiocyanate (5·75 g., 0·05 mole), and triethylamine (0·1 ml.) in ethanol (100 ml.) was refluxed during 48 hr., then distilled to small volume (20 ml.). The separated product (1·5—2 g.), collected at room temperature, was recovered aminoguanidine hydrochloride (m. p. 161—162°; from ethanol). Dilution of the filtrate with ether (3 volumes) gave a white powder (filtrate F) (5·5—6·5 g., 49—58%), which consisted after crystallisation from ethanol–ether (1 : 3) of needles of the *hydrochloride*, m. p. 171—173° (decomp.) (Found: C, 31·8; H, 7·0; Cl, 15·1. $C_6H_{15}N_5S,HCl$ requires C, 31·9; H, 7·1; Cl, 15·7%). Filtrate F, on evaporation and dilution with ether, afforded more of the salt (8—12%).

Alternatively, the solution, after refluxing, was evaporated in a vacuum to remove most of the solvent, and the residual viscous liquid was dissolved in warm water (40 ml.) and treated with toluene-*p*-sulphonic acid monohydrate (10·5 g., 0·055 mole) in water (10 ml.). The white solid, collected at 0° and recrystallised from water (8 ml. per g., recovery 90%), consisted of needles (11·4 g., 60%) of the *toluene*-p-*sulphonate monohydrate*, m. p. 161—163° (decomp.) (Found: C, 41·9; H, 6·4; N, 18·85; S, 17·0. $C_6H_{15}N_5S,C_7H_8O_3S,H_2O$ requires C, 41·2; H, 6·6; N, 18·5; S, 16·9%). Boiling alkaline sodium plumbite slowly gave a small black precipitate and a strong smell of isocyanide.

The last-mentioned salt (0·38 g., 0·001 mole) dissolved on being stirred with water (5 ml.) and 3N-ammonia (0·5 ml., 0·0015 mole). Addition of 0·05M-picric acid (20 ml., 0·001 mole) gave the *picrate hydrate* (55%) as plates, m. p. 174—177° (decomp.) (from ethanol–light petroleum)

(Found: C, 33·4; H, 4·4; N, 25·0. $C_6H_{15}N_5S,C_6H_3N_3O_7,H_2O$ requires C, 33·0; H, 4·6; N, 25·7%).

(*c*) Interaction of aminoguanidine sulphate and butyl isothiocyanate in the presence of sodium (conditions and quantities as described for the methyl homologue, *c* above, except for time of refluxing, 2 hr.) gave, on acidification, crystals which were collected at 0° (5·7—6·5 g.). Recrystallisation from very little ethanol–light petroleum or preferably water (20 ml. per g., recovery 70—80%) gave needles (4·3—5·2 g., 50—60%) of *3-amino-4-butyl-5-mercapto-1,2,4-triazole*, m. p. 151—153° (Found: C, 41·9; H, 6·8. $C_6H_{12}N_4S$ requires C, 41·9; H, 7·0%). It had a wide unsymmetrical absorption maximum defined by λ 230, 240, 250, 260 mμ (log ε 4·30, 4·36, 4·35, 4·30), followed by a steep drop in absorption towards the longer wavelengths.

(*d*) A solution of the toluene-*p*-sulphonate monohydrate (1·9 g., 0·005 mole) in 100% orthophosphoric acid (10 ml.) was heated at 130° during 1 hr., and the cooled liquid diluted with water (40 ml.) (slight evolution of hydrogen sulphide), kept at 0° during 1 hr., filtered, and treated with 0·05M-aqueous pricric acid (100 ml., 0·005 mole). The precipitate (1·6 g., 80%) gave, on crystallisation from 90% ethanol (20 ml. per g.) and finally ethanol (100 ml. per g.), *2-amino-5-butylamino-1,3,4-thiadiazole picrate*, m. p. 218—221° (decomp.) (Found: C, 36·0; H, 3·6; N, 25·1. $C_6H_{12}N_4S,C_6H_3N_3O_7$ requires C, 35·9; H, 3·7; N, 24·4%). Interaction at 120° during 30 min. gave the same product in 55% yield.

(*e*) A solution of the same reactant (0·005 mole) in acetic anhydride (12 ml.) was refluxed during 20 min. Addition of the brown liquid to warm water (40 ml.) gave a white solid (0·72 g., 56%) which crystallised from ethanol (25 ml. per g.) as needles of the *diacetyl derivative*, m. p. 206—209°, of 2-amino-5-*n*-butylamino-1,3,4-thiadiazole (Found: C, 47·3; H, 6·2; N, 21·9. $C_{10}H_{16}N_4O_2S$ requires C, 46·9; H, 6·25; N, 21·9%).

The diacetyl derivative (0·51 g., 0·002 mole) dissolved on being boiled with 3N-hydrochloric acid (6 ml.). After 30 min. the solution was basified with 3N-ammonia and the crystals collected after storage at 0° (0·3 g.). Recrystallisation from ethanol–light petroleum (b. p. 40—60°) (1 : 2) gave *2-amino-5-n-butylamino-1,3,4-thiadiazole*, m. p. 147—149° (0·22 g., 64%) (Found: C, 41·7; H, 7·0; N, 32·55. $C_6H_{12}N_4S$ requires C, 41·9; H, 7·0; N, 32·6%). The picrate had m. p. and mixed m. p. with material obtained as in (*d*) 218—220° (decomp.).

The S-Benzyl Derivative (III; R = Ph, R′ = CH_2Ph).—A solution of 1-amidino-4-phenylthiosemicarbazide toluene-*p*-sulphonate solvate (6·41 g., 0·015 mole) in boiling ethanol (25 ml.) and water (10 ml.) was cooled to 40°, and benzyl chloride (1·9 g., 0·015 mole) was added. The stirred liquid was treated with 3N-sodium hydroxide (10 ml., 0·03 mole) during 10 min., and stirring at room temperature continued during 1·5 hr. Neutralisation to pH 6·5 with glacial acetic acid (5—6 ml.) converted the purple cloudy liquid into a colourless clear solution, which began to deposit crystals immediately. These (5·1 g., 72%) were collected after 3 hr. at 0°, rinsed with a little water and crystallised from 95% ethanol (15 ml. per g., recovery 80%) or ethanol (40 ml. per g.), affording plates of the *toluene-p-sulphonate*, m. p. 181—183°, of the *S*-benzyl derivative (Found: C, 56·1; H, 5·0; N, 14·9; S, 13·95. $C_{15}H_{17}N_5S,C_7H_8O_3S$ requires C, 56·05; H, 5·3; N, 14·9; S, 13·6%). The product dissolved readily in 3N-sodium hydroxide; on boiling, the resulting purple solution evolved toluene-α-thiol.

A suspension of this salt (0·94 g., 0·002 mole) in cold ethanol (10 ml.) was treated with 3N-sodium hydroxide (2 ml., 0·006 mole), added to water (50 ml.), and extracted with ether. On evaporation at room temperature, the washed dried extracts gave a white solid, which was covered with light petroleum and collected (0·54 g., 90%). Crystallisation from 1 : 3 ethanol–light petroleum (20 ml., b. p. 40—80°) gave needles of *1-amidino-S-benzyl-4-phenylisothiosemicarbazide*, m. p. 88—90° (sintering at 82°) (Found: C, 59·6; H, 5·5; N, 23·5; S, 10·8. $C_{15}H_{17}N_5S$ requires C, 60·2; H, 5·7; N, 23·4; S, 10·7%).

(*a*) The above salt (0·94 g., 0·002 mole) in 3N-sodium hydroxide (4 ml.) was refluxed during 20 min., diluted with water (20 ml.), and *just* acidified with 3N-acetic acid. The precipitate, collected after storage at 0°, was dibenzyl disulphide, m. p. 68—70° (0·17 g., 70%). The filtrate, treated with 0·05M-picric acid (50 ml., 0·0025 mole), gave an immediate precipitate (0·63 g., 78%) of 3-amino-5-anilino-1,2,4-triazole picrate, m. p. and mixed m. p.[1] 228—231° (decomp.) (from 90% ethanol) (Found: C, 41·6; H, 2·8. Calc. for $C_8H_9N_5,C_6H_3O_7N_3$: C, 41·6; H, 3·0%).

(*b*) The toluene-*p*-sulphonate (0·94 g., 0·002 mole) of the benzyl derivative in aniline (5 ml.) was refluxed during 1 hr., treated with water (20 ml.), and steam-distilled. The residual liquid

deposited crystals which were collected at 0° (0·345 g., 90%); they consisted of 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 264—266° (decomp.) (from ethanol) (Found: C, 49·9; H, 4·3; N, 28·9; S, 16·55. Calc. for $C_8H_8N_4S$: C, 50·0; H, 4·2; N, 29·2; S, 16·7%).

(*c*) The free benzyl derivative, freshly liberated and extracted with ether from the toluene-*p*-sulphonate (2·35 g., 0·005 mole), was treated with aniline (10 ml.), the ether distilled off, and the residual liquid refluxed during 30 min., and steam-distilled to remove the aniline. The residual oily (O) and aqueous (A) phase were separated by decantation. The oil (O), dissolved in ethanol (5 ml.) and treated with picric acid (1·15 g., 0·005 mole) in hot ethanol (8 ml.) gave yellow needles (0·82 g., 32%) of 3-amino-5-benzylthio-4-phenyl-1,2,4-triazole picrate, m. p. and mixed m. p. (see below) 222—228° (decomp.) (Found: C, 49·3; H, 3·3%). The aqueous phase (A), treated with 0·05M-picric acid (50 ml., 0·0025 mole) gave 3-amino-5-anilino-1,2,4-triazole picrate (0·70 g., 35%), m. p. and mixed m. p.[1] 228—232° (decomp.) (Found: C, 41·4; H, 2·8. Calc. for $C_8H_9N_5,C_6H_3N_3O_7$: C, 41·6; H, 3·0%).

3-*Amino*-5-*benzylthio*-4-*phenyl*-1,2,4-*triazole picrate*, obtained from the authentic components [3] in ethanol, formed yellow needles, m. p. 226—228° (decomp.) (from 75% ethanol) (Found: C, 48·85; H, 3·4; N, 19·8. $C_{15}H_{14}N_4S,C_6H_3N_3O_7$ requires C, 49·3; H, 3·3; N, 19·2%).

1-*Amidino*-S-*benzyl*-4-p-*tolylisothiosemicarbazide*.—The thiosemicarbazide toluene-*p*-sulphonate (3·95 g., 0·01 mole) dissolved, when to its stirred suspension in ethanol (20 ml.), water (10 ml.), and benzyl chloride (1·27 g., 0·01 mole) there was added 3N-sodium hydroxide (6·7 ml., 0·02 mole) dropwise during 10 min. at room temperature. Stirring was continued during 3 hr., the liquid acidified with 3N-acetic acid, and the solid collected after 24 hr. at 0°. Crystallisation from ethanol–ether (3 ml. each, per g.) and then from ethanol alone gave prisms (3·4 g., 70%) of the *toluene*-p-*sulphonate*, m. p. 145—147° (Found: C, 56·7; H, 5·7; N, 15·0. $C_{16}H_{19}N_5S,C_7H_8O_3S$ requires C, 56·9; H, 5·6; N, 14·4%), of the derivative.

This salt with sodium hydroxide or aniline gave, as above, 3-amino-5-*p*-toluidino-1,2,4-triazole picrate (60%), m. p. and mixed m. p. 235—238° (decomp.), or 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole, m. p. and mixed m. p. 278—280° (decomp.), respectively.

In the presence of an excess of toluene-*p*-sulphonic acid, the product was isolated as the *ditoluene*-p-*sulphonate*, m. p. 186—188° (white powder from ethanol), also formed from equimolar proportions of the monotoluene-*p*-sulphonate and toluene-*p*-sulphonic acid in 50% ethanol (Found: C, 54·4; H, 5·5; N, 10·7; S, 14·35. $C_{16}H_{19}N_5S,2C_7H_8O_3S$ requires C, 54·8; H, 5·3; N, 10·65; S, 14·6%).

3-*Amino*-5-p-*toluidino*-1,2,4-*triazole picrate*, obtained nearly quantitatively from the authentic components in ethanol, had m. p. 235—238° (decomp.) (from 90% ethanol) (Found: C, 42·9; H, 3·2. $C_9H_{11}N_5,C_6H_3N_3O_7$ requires C, 43·1; H, 3·35%). (Erratum: Part I, *J.*, 1960, 3437. On p. 3442, line 25: *For* 3-amino-5-anilino-1,2,4-triazole picrate, *read* 3-amino-5-*p*-toluidino-1,2,4-triazole picrate.)

Semicarbazide Series

1-*Amidino*-4-*phenylsemicarbazide*.—A suspension of aminoguanidine hydrochloride (2·21 g., 0·02 mole) in dimethylformamide (8 ml.) was treated with phenyl isocyanate (2·4 g., 0·02 mole) (slightly exothermic reaction). The mixture was kept at 100° during 15 min., and the resulting liquid stirred into water (75 ml.). The precipitate, collected and crystallised from ethanol, was *s*-diphenylurea (0·2 g.), m. p. and mixed m. p. 237—239°. Addition of toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) to the filtrate gave a precipitate (5·25—6·2 g., 72—85%), which was collected at 0°, rinsed with a little ice-water, and recrystallised from water and then from 1 : 2 ethanol–light petroleum (b. p. 40—80°), affording prisms of 1-*amidino*-4-*phenylsemicarbazide toluene*-p-*sulphonate*, m. p. 182—185° (decomp.) (Found: C, 48·75; H, 5·5; N, 19·1. $C_8H_{11}N_5O,C_7H_8O_3S$ requires C, 49·3; H, 5·2; N, 19·2%).

Interaction in anhydrous pyridine (10 ml.) at 100° during 1 hr. or at its b. p. during 30 min. gave the above product in 24 and 34% yield, respectively, the formation of carbanilide being correspondingly increased (0·8—1·6 g.).

The toluene-*p*-sulphonate (0·003 mole) dissolved instantly in 3N-sodium hydroxide (3 ml.) at room temperature, giving a red solution. Because of its very high solubility, the base was not isolated in the pure state.

The *picrate*, prepared from equimolar quantities of the toluene-*p*-sulphonate and picric acid

(0·0025 mole) in ethanol (10 ml.), formed needles, m. p. 236—239° (decomp.) (from 80% ethanol) (Found: C, 40·1; H, 3·35. $C_8H_{11}N_5O,C_6H_3N_3O_7$ requires C, 39·8; H, 3·3%.).

Reactions of 1-*Amidino-4-phenylsemicarbazide Toluene*-p-*sulphonate*.—(a) *With acetic anhydride*. A solution of the reactant (0·91 g., 0·0025 mole) in acetic anhydride (10 ml.) was kept at 120—125° during 20 min., then stirred into water (50 ml.); after the anhydride had dissolved, 0·05M-picric acid (50 ml., 0·0025 mole) was added. The resulting precipitate was crystallised from 90% ethanol (30 ml. per g.), giving needles of 1-N-*acetylamidino-4-phenylsemicarbazide picrate*, m. p. 194—198° (decomp., subject to the rate of heating) (0·70 g., 60%) (Found: C, 41·4, 41·3; H, 3·55, 3·4; N, 24·45. $C_{10}H_{13}N_5O_2,C_6H_3N_3O_7$ requires C, 41·4; H, 3·45; N, 24·1%).

This picrate (0·23 g., 0·0005 mole) in 3N-hydrochloric acid (8 ml.) was boiled during 15 min. The hot filtered liquid deposited yellow needles (0·12 g., 55%) of 1-amidino-4-phenylthiosemicarbazide picrate, m. p. and mixed m. p. 235—238° (decomp.) (from 80% ethanol) (Found: C, 39·9; H, 3·3%).

The *diacetyl derivative* of 3-amino-5-anilino-1,2,4-triazole, prepared by boiling the triazole (0·35 g., 0·002 mole) in acetic anhydride (3 ml.) during 15 min., formed needles (50%), m. p. 159—161° (from ethanol) (Found: C, 55·5; H, 5·05; N, 28·0. $C_{12}H_{13}N_5O_2$ requires C, 55·6; H, 5·0; N, 27·0%).

(b) *With concentrated sulphuric acid*. The reactant (1·825 g., 0·005 mole) dissolved readily in concentrated sulphuric acid (5 ml.) at room temperature. After 30 min. at 100° the pale brown liquid was added to ice (60 g.); the white powder which slowly separated was collected after 2 hr. at 0° (1·10 g., 80%). Two crystallisations from boiling water gave 1-*amidino*-4-p-*sulphophenylsemicarbazide*, m. p. 276—279° (decomp.) (Found: C, 35·1; H, 3·6; N, 25·8; S, 11·8. $C_8H_{11}N_5O_4S$ requires C, 35·2; H, 4·0; N, 25·6; S, 11·7%). This (2·73 g.) in 3N-sodium hydroxide (25 ml.) was refluxed during 2 hr. The crystalline deposit which separated on 12 hours' storage at 0° was collected and redissolved in boiling water (6 ml.) and the filtered liquid was acidified with 3N-hydrochloric acid (1 ml.), giving sulphanilic acid (0·45 g., 26%), decomp. above 300° (orange dye on diazotisation and coupling with β-naphthol) (Found: C, 41·7; H, 3·7; N, 8·0; S, 17·8. Calc. for $C_6H_7NO_3S$: C, 41·6; H, 4·05; N, 8·1; S, 18·5%); its ultraviolet absorption was identical with that of an authentic specimen.

(c) *With sodium hydroxide*. The toluene-*p*-sulphonate (0·005 mole) was recovered (60%) after being boiled in 3N-sodium hydroxide (10 ml.) (followed by acidification). When the salt was distilled with this reagent during 20 min., the distillate contained aniline (isolated as benzanilide, 65%).

1-*Amidino*-4-p-*tolylsemicarbazide*.—Interaction of aminoguanidine hydrochloride and *p*-tolyl isocyanate (0·02 mole) in dimethylformamide gave, by the above procedure, plates (5·46 g., 72%) of the *semicarbazide toluene*-p-*sulphonate*, m. p. 225—228° (decomp.) (Found: C, 50·8; H, 5·65. $C_9H_{13}N_5O,C_7H_8O_3S$ requires C, 50·7; H, 5·5%).

This salt (0·0025 mole) in 85% ethanol (15 ml.), treated with saturated ethanolic picric acid (0·0025 mole), deposited the *picrate* (80%) as needles, m. p. 236—239° (decomp.) (from 75% ethanol) (Found: C, 41·8; H, 3·7. $C_9H_{13}N_5O,C_6H_3N_3O_7$ requires C, 41·3; H, 3·7%).

1-*Amidino*-4-*butylsemicarbazide*.—Interaction of aminoguanidine hydrochloride and butyl isocyanate (0·02 mole each) in dimethylformamide (5 ml.) at 100° during 45 min., addition of the liquid to ice-water (20 ml.), and treatment of the clear solution with toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) gave crystals (5 g.) at 0° during 24 hr. Crystallisation from ethanol–ether (3 and 5 ml. per g.) gave the solvated *toluene*-p-*sulphonate*, m. p. 132—134° (decomp.) (4·35 g., 56%) (Found: C, 46·6; H, 7·3; N, 17·4. $C_6H_{15}N_5O,C_7H_8O_3S,C_2H_5{\cdot}OH$ requires C, 46·0; H, 7·4; N, 17·9%).

The *picrate* formed needles, m. p. 218—221° (decomp.) (from ethanol) (Found: C, 35·75; H, 4·5. $C_6H_{15}N_5O,C_6H_3N_3O_7$ requires C, 35·8; H, 4·5%).

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