696. *Heterocyclic Compounds from Urea Derivatives. Part IV.* Addition Products of Diphenylcarbodi-imide and Aminoguanidine, Thiosemicarbazide, or Semicarbazide, and their Cyclisation.*

By Leonard E. A. Godfrey and Frederick Kurzer.

The addition of diphenylcarbodi-imide to aminoguanidine yields successively 1,2-diphenylbiguanidine and 1-amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine. Cyclisation of the biguanidine derivative under various conditions yields substituted 3,5-diamino-1,2,4-triazoles.

Similarly, diphenylcarbodi-imide is readily added at the hydrazino-group of thiosemicarbazide or semicarbazide, forming the appropriate 1-(*NN'*-diphenylamidino)-derivatives. Their ring closure to 1,2,4-triazoles and 1,3,4-thiadiazoles is described.

The action of an excess of diphenylcarbodi-imide on aminoguanidine, thiosemicarbazide, or semicarbazide yields, in each case, 3,5-dianilino-4-phenyl-1,2,4-triazole. The mechanism of the above reactions is discussed.

Previous Parts of this series described the addition of isocyanate and isothiocyanate esters to aminoguanidine at the guanidino-[1] or hydrazino-group,[2] and also a number of ring-closures of the resulting products. In view of the broad similarities in the chemical

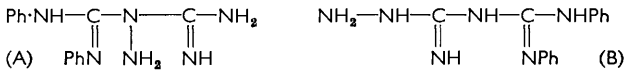
* Part III, *J.*, 1962, 230.

[1] Godfrey and Kurzer, *J.*, 1960, 3437.
[2] Godfrey and Kurzer, *J.*, 1961, 5137.

behaviour of structures featuring twinned double bonds,[3] comparable addition reactions of carbodi-imides to aminoguanidine and analogous compounds have now been examined.

The interaction, in dimethylformamide, of diphenylcarbodi-imide and an excess of aminoguanidine hydrochloride gave 1,2-diphenylbiguanidine (I) and 1-amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine (III) as main products, each in approximately 35—40% yield; they were separated without difficulty by fractional precipitation of their toluene-*p*-sulphonates. They are thought to arise by successive addition of two mol. of carbodi-imide to aminoguanidine, one to each of the nitrogen atoms of the hydrazino-group, followed by elimination of aniline (I ⟶ II ⟶ III).

The 1,2-diphenylbiguanidine structure (I) for the initial monoaddition product was likely because of the established superior reactivity of the hydrazino-group in amino-guanidine.[4] The two alternative formulations (A and B, involving addition at the imino-



or amino-moiety of the guanidino-group) were inadmissible, being incompatible with the results of the cyclisation of the compound to 1,2,4-triazoles and with its inability to yield derivatives with ketones. 1,2-Diphenylbiguanidine (I) was a diacid base which was unexpectedly stable towards acids and alkalis (compare compounds X, below), but was pyrolysed at 160°, with loss of ammonia or aniline, to 3-amino-5-anilino-4-phenyl- (VII) and 3-amino-5-anilino-1,2,4-triazole (IX). The same ring-closures also occurred in boiling aniline, but may have been merely due to a thermal effect. Whatever the mechanism, this observation supports the previous suggestion [2] that 1,2-diphenylbiguanidine is formed intermediately in the conversion of 1-amidino-*S*-benzyl-4-phenylisothiosemicarbazide into 3-amino-5-anilino-1,2,4-triazole by boiling aniline.

Acetylation of 1,2-diphenylbiguanidine and subsequent treatment with alkali gave 3-anilino-5-methyl-4-phenyl-1,2,4-triazole (XIII); this is believed to arise from the intermediate acyl derivative (XII; X = :NH) by the well-known [4,5] dehydrative cyclisation, with hydrolytic removal of the side chain from N-1 of the ring. Participation of the acetanilido-compound (XIIa; X = :NH) as the possible alternative intermediate in this reaction, yielding the same final product (XIII) on dehydration, is considered unlikely (see below).

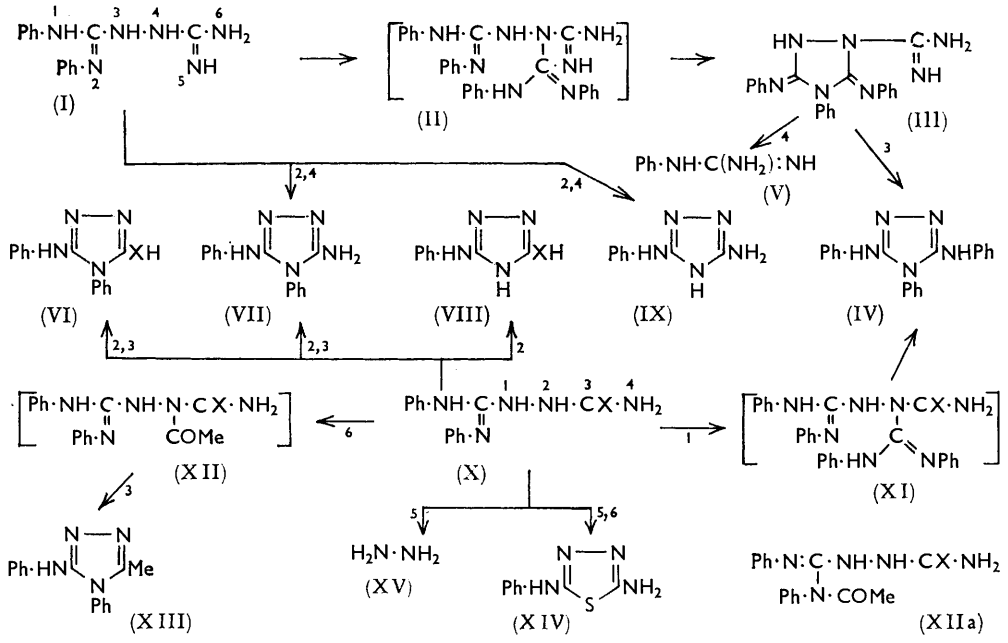
1-Amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine (III), the second product of the addition, was prepared more advantageously by the action of a further mol. of carbodi-imide on 1,2-diphenylbiguanidine (I). It thus arises almost certainly, in both reactions, by addition of the carbodi-imide to the 4-imino-group of the biguanidine (I), followed by cyclisation of the resulting intermediate (II) with loss of aniline. The 4-NH-group (in I) appears to act as a particularly reactive centre, competing strongly for the available carbodi-imide, since compounds (I) and (III) are formed side by side in approximately equal proportions, in spite of the presence of a 100% excess of aminoguanidine. Addition of di-imide may occur theoretically in three other positions in 1,2-diphenylbiguanidine (at N-1, N-3, or N-5), but only the first of the resulting intermediate products can conceivably yield the triazole (III) by loss of aniline. This mechanism is considered unlikely, however, because of the probable greater reactivity of an –NH– over an anilino-group in additions of this type.

The formulation of 1-amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine (III) is based on its rapid and almost quantitative conversion, by alkaline hydrolysis, into 3,5-dianilino-4-phenyl-1,2,4-triazole (IV) of established structure.[6,7] The presence of the

[3] Khorana, *Chem. Rev.*, 1953, **53**, 145, 162.
[4] Lieber and Smith, *Chem. Rev.*, 1939, **25**, 213.
[5] Thiele *et al.*, *Ber.*, 1893, **26**, 2598; *Annalen*, 1898, **303**, 33; Franklin and Bergström, *Chem. Rev.*, 1935, **16**, 305; Reilly *et al.*, *J.*, 1926, 1729; 1929, 815.
[6] Busch and Bauer, *Ber.*, 1900, **33**, 1058.
[7] Busch and Ulmer, *Ber.*, 1902, **35**, 1710, 1716.

amidino-group was confirmed by the production (from III) of phenylguanidine (V) by aminolysis in boiling aniline. The removal of *N*-amidino-groups from heterocyclic nuclei (*e.g.*, amidino-pyrazoles [8] or -pyrazolones [9]) as substituted guanidines by aminolysis or hydrazinolysis is well authenticated. The product (III) is thus formally related to the parent 1-amidino-3,5-di-imino-1,2,4-triazolidine, which has been synthesised directly from aminoguanidine and dicyandiamide.[10]

The interaction of diphenylcarbodi-imide and an excess of thiosemicarbazide differed from the corresponding reaction of aminoguanidine in that monoaddition occurred almost exclusively, 1-(*NN'*-diphenylamidino)thiosemicarbazide (X; X = S) being obtained in



60—72% yield, together with small quantities (6—9%) of 3-anilino-5-mercapto-1,2,4-triazole (VIII; X = S) formed by cyclisation. Evidence for limited diaddition was provided by the isolation of small yields (5—7%) of 3,5-dianilino-4-phenyl-1,2,4-triazole (X ⟶ XI ⟶ IV). The formulation of 1-(*NN'*-diphenylamidino)thiosemicarbazide (X; X = S) and of its semicarbazide analogue (X; X = O, see below) is based, as in the case of the corresponding biguanidine (I), on their failure to yield derivatives with ketones and their behaviour on cyclisation.

The analogous reaction between diphenylcarbodi-imide and 4-phenylthiosemicarbazide did not terminate with the formation of the expected 1-(*NN'*-diphenylamidino)-4-phenyl-thiosemicarbazide.[6] This monoaddition product was evidently cyclised, with loss of hydrogen sulphide or aniline, either immediately under the usual experimental conditions or during the isolation process, producing a mixture of 3,5-dianilino-4-phenyl- (IV) and (mainly) 3-anilino-5-mercapto-4-phenyl-1,2,4-triazoles (VI; X = S).

In contrast to its imino-analogue (I), 1-(*NN'*-diphenylamidino)thiosemicarbazide

[8] Scott, Murphy, and Reilly, *Nature*, 1951, **167**, 1037; Scott, Kennedy, and Reilly, *Nature*, 1952, **169**, 72; *J. Amer. Chem. Soc.*, 1953, **75**, 1294; Scott, O'Donovan, and Reilly, *J. Amer. Chem. Soc.*, 1953, **75**, 4053.

[9] Beyer and Badicke, *Chem. Ber.*, 1960, **93**, 826.

[10] Simons, U.S.P. 2,456,090/1948.

(X; X = S) was readily cyclised by both acids and alkalis. Like suitably substituted thiosemicarbazides in general,[2,11,12] it was converted into a 1,3,4-thiadiazole in acidic or into a 1,2,4-triazole in basic media. Thus, phosphoric acid or acetic anhydride gave 2-amino-5-anilino-1,3,4-thiadiazole (XIV) or its diacetyl derivative; and boiling alkali, eliminating ammonia or hydrogen sulphide, produced 3-mercapto- (VI; X = S) and 3-amino-5-anilino-4-phenyl-1,2,4-triazole (VII) simultaneously. Pyrolysis resulted in loss of aniline and exclusive formation of 3-anilino-5-mercapto-1,2,4-triazole (VIII; X = S).

1-(*NN'*-Diphenylamidino)semicarbazide (X; X = O), the oxygen analogue of the series, was obtained in excellent yield by the general reaction; it was sufficiently basic to yield a picrate. Pyrolysis or alkaline hydrolysis converted the compound, with loss of ammonia, into 3-anilino-5-hydroxy-4-phenyl-1,2,4-triazole (VI; X = O). It thus differs from the closely related 4-substituted 1-amidinosemicarbazides [R·NH·CO·NH·NH·C(:NH)·NH_2], which are cleaved by alkalis. Successive treatment with acetic anhydride and alkali gave 3-anilino-5-methyl-4-phenyl-1,2,4-triazole, presumably by the route X ⟶ XII ⟶ XIII postulated in the corresponding reaction of the aminoguanidine derivative (I). Phosphoric acid, however, completely degraded the semicarbazide (X; X = O) to hydrazine.

Treatment of 1-(*NN'*-diphenylamidino)-thiosemicarbazide (X; X = S) or -semicarbazide (X; X = O) with a further mol. of diphenylcarbodi-imide gave good yields of 3,5-dianilino-4-phenyl-1,2,4-triazole (IV) directly, and there was no indication that the reactions stopped at the stage corresponding to 1-amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine (III). The isolation of the postulated intermediate from the reaction involving aminoguanidine, but not in parallel experiments with thiosemicarbazide and semicarbazide, is ascribed to the stabilisation of the former more basic intermediate by salt formation and to the particular ease of crystallisation of its toluene-*p*-sulphonate. On the other hand, the ready hydrolysis of 1-amido-[13] and substituted 1-amido-groups[14] from the 1-position in 1,2,4-triazoles has been noted.

As expected, the direct action of two mol. of carbodi-imide on aminoguanidine, thiosemicarbazide, or semicarbazide, ensuring diaddition in each case, gave 3,5-diamino-4-phenyl-1,2,4-triazole (IV) in one stage. In the first example it was expedient to subject the crude product to a preliminary treatment with alkali, to convert any intermediate amidino-compound (III) into the triazole (IV).

In view of the close relationship of cyanamide, substituted cyanamides, and carbodiimides, extension of the present addition reactions to the production of the parent compounds (biguanidine and its analogues) and other of their substitution products should prove fruitful. The addition of cyanamide to thiosemicarbazide and semicarbazide has been alluded to in the patent literature,[15] but no details are available. The synthesis of 1-(phenylamidino)thiosemicarbazide[16] from phenylcyanamide appears to be the only other established variant of this general route.

Experimental

Light petroleum had b. p. 60—80°. Dimethylformamide 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-solutions.

[11] Arndt *et al.*, *Ber.*, 1921, **54**, 2089; 1922, **55**, 341; 1923, **56**, 2276.
[12] Sherman, in Elderfield's "Heterocyclic Compounds," Vol. VII, Wiley, London, 1961, pp. 587 *et seq.*
[13] Brunner, *Monatsh.*, 1915, **36**, 509.
[14] Henry and Dehn, *J. Amer. Chem. Soc.*, 1949, **71**, 2297; Otting and Staab, *Annalen*, 1959, **622**, 23
[15] Produits chimiques de Ribécourt, F.P. 993,874/1951.
[16] Arndt and Tschenscher, *Ber.*, 1923, **56**, 1984.

Aminoguanidine Series

1,2-*Diphenylbiguanidine and* 1-*Amidino*-4-*phenyl*-3,5-*diphenylimino*-1,2,4-*triazolidine*.—To a solution of aminoguanidine hydrochloride (13·25 g., 0·12 mole) in dimethylformamide (50 ml.) at 110°, diphenylcarbodi-imide (12·2 g., 0·063 mole) was added dropwise during 5 min. The golden-yellow liquid was kept at 105° during a further 5 min., allowed to cool to 30—40°, and stirred into water (200 ml.), and the slightly turbid solution was immediately treated with toluene-*p*-sulphonic acid monohydrate (19·0 g., 0·1 mole). The resulting white crystalline precipitate (product T) was collected after 10—15 minutes' storage and rinsed with a little cold water. The filtrate was treated with more toluene-*p*-sulphonic acid (24 g., 0·125 mole), and the prisms that separated slowly were collected after 48 hours' storage at 0° (18—20 g.) (filtrate F) and rinsed with ether. Crystallisation from boiling water (6 ml. per g., recovery >80%) gave prisms (15·5—18·4 g., 38—45%) of 1,2-*diphenylbiguanidine ditoluene*-p-*sulphonate dihydrate*, m. p. 210—212° (decomp.) (Found: C, 52·2; H, 5·5; N, 13·0; S, 9·9. $C_{14}H_{16}N_6,2C_7H_8O_3S,2H_2O$ requires C, 51·85; H, 5·6; N, 13·0; S, 9·9%).

Filtrate F failed to yield more toluene-*p*-sulphonate on storage at room temperature. Treatment with an excess of 0·05M-picric acid (500 ml., 0·025 mole) gave a yellow precipitate, which consisted, after crystallisation from 90% ethanol, of 1,2-diphenylbiguanidine dipicrate, m. p. and mixed m. p. (see below) 206—208° (decomp.) (10—15%, depending on the yield of ditoluene-*p*-sulphonate isolated). Alternatively, on being strongly basified with 10M-sodium hydroxide, filtrate F became purple and gradually deposited solid which consisted, after crystallisation from ethanol, of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. 234—236° (0·52 g., 5%).

A solution of the ditoluene-*p*-sulphonate dihydrate (6·48 g., 0·01 mole) in boiling water (50 ml.) was allowed to cool until an opalescence appeared. Addition of 3N-sodium hydroxide (10 ml.) gave an immediate pale-pink precipitate, which was collected at 0°, dried, and crystallised from ethanol (6—8 ml. per g.), giving needles of 1,2-*diphenylbiguanidine*, m. p. 150—152° (2 g., 75%) (Found: C, 62·9; H, 6·1; N, 31·05. $C_{14}H_{16}N_6$ requires C, 62·7; H, 6·0; N, 31·3%).

A solution of the ditoluene-*p*-sulphonate dihydrate (0·33 g., 0·0005 mole) in boiling water (10 ml.), when treated with 0·05M-picric acid (20 ml., 0·001 mole), gave the *dipicrate* (85%), forming plates, m. p. 206—208°, from 90% ethanol (Found: C, 43·3; H, 3·0; N, 22·8. $C_{14}H_{16}N_6,2C_6H_3N_3O_7$ requires C, 43·0; H, 3·0; N, 23·1%).

Product T (7—8 g.) crystallised from 90% ethanol (10—12 ml. per g., recovery 85%), forming prisms of solvated 1-*amidino*-4-*phenyl*-3,5-*diphenylimino*-1,2,4-*triazolidine toluene*-p-*sulphonate*, m. p. 219—221° (decomp.) (5·55—6·50 g., 30—35%) (Found: C, 61·3, 61·0; H, 5·2, 5·6; N, 16·7; S, 5·7. $C_{21}H_{19}N_7,C_7H_8O_3S,C_2H_5{\cdot}OH$ requires C, 61·3; H, 5·6; N, 16·7; S, 5·45%).

Addition of picric acid (0·115 g., 0·0005 mole) in ethanol (2 ml.) to a solution of the foregoing salt (0·29 g., 0·0005 mole) in boiling 80% ethanol (8 ml.) precipitated quantitatively the *picrate monohydrate*. Crystallisation from a large volume of 66% ethanol gave prisms, m. p. 223—225° (decomp.) (Found: C, 52·9; H, 3·7; N, 23·4. $C_{21}H_{19}N_7,C_6H_3N_3O_7,H_2O$ requires C, 52·6; H, 3·9; N, 22·7%).

A solution of the solvated toluene-*p*-sulphonate (0·59 g., 0·001 mole) in boiling 80% ethanol (15 ml.), cooled to ~35° and treated with 3N-sodium hydroxide (1 ml., 0·003 mole), gave a greenish-yellow liquid which deposited needles on being stirred. They were collected at 0° (0·32—0·35 g., 85—95%) and crystallised from ethanol (20 ml., recovery 60%), to yield needles of 1-*amidino*-4-*phenyl*-3,5-*diphenylimino*-1,2,4-*triazolidine*. Its decomposition temperature was ill-defined between 200 and 210° (rate-dependent, after severe sintering at 160—165°) (Found: C, 68·2; H, 4·9; N, 27·0. $C_{21}H_{19}N_7$ requires C, 68·3; H, 5·1; N, 26·6%).

3,5-*Dianilino*-4-*phenyl*-1,2,4-*triazole*.—A solution of aminoguanidine hydrochloride (1·10 g., 0·01 mole) in dimethylformamide (10 ml.), treated with diphenylcarbodi-imide (4·25 g., 0·022 mole), was kept at 100° during 30 min., then stirred into ice-cold N-ammonia or N-sodium hydroxide (40 ml.). The resinous precipitate coagulated and hardened somewhat on storage; the supernatant aqueous phase was decanted and the residual viscous air-dried material stirred with ethanol (10 ml.). The white powder that remained undissolved, and more that separated on storage at 0°, crystallised from ethanol as prisms (1·45 g., 45%) of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (with analysed sample, from thiosemicarbazide, see below) 235—236°.

In another experiment, the crude powder was first refluxed in 3N-sodium hydroxide (25

ml.)–ethanol (50 ml.) during 30 min., and the product isolated by dilution with water; the yield of the above triazole rose to 60%.

Reactions of 1,2-*Diphenylbiguanidine*.—(*a*) *Stability in acids and alkalis*. A solution of the ditoluene-*p*-sulphonate dihydrate (1·94 g., 0·003 mole) in 3N-ethanolic (80%) sodium hydroxide (25 ml.) [or the suspension obtained in 3N-aqueous sodium hydroxide (15 ml.)] gave, after 1 hour's refluxing, removal of most of the ethanol by distillation under reduced pressure, and dilution with water, the base (70%), m. p. and mixed m. p. 150—152° (from ethanol–light petroleum). The alkaline-ethanolic solution became intense reddish-violet to dark-brown on contact with air.

When the ditoluene-*p*-sulphonate dihydrate (0·003 mole) was kept in 100% orthophosphoric acid (6 ml.) at 140° during 1 hr., and the solution diluted with ice–water (40 ml.), 75% of the salt was recovered directly and another 15% as dipicrate, from the mother-liquors.

(*b*) *Pyrolysis*. Melted 1,2-diphenylbiguanidine (1·34 g., 0·005 mole) was kept at 160° during 15 min. Ammonia was copiously evolved, and droplets (of aniline) appeared on the cooler parts of the vessel. The whole was dissolved in water (40 ml.), and approximately one-third of the bulk of the liquid distilled off (distillate D). The residual solution deposited oil on cooling; this solidified on storage and stirring. It was collected at 0° (aqueous filtrate F), and crystallised from ethanol–light petroleum (1 : 1; b. p. 40—80°), yielding needles (0·60 g., 48%) of 3-*amino*-5-*anilino*-4-*phenyl*-1,2,4-*triazole*, m. p. 196—198° (Found: C, 66·4; H, 5·3; N, 27·2. $C_{14}H_{13}N_5$ requires C, 66·9; H, 5·2; N, 27·9%), $\lambda_{min.}$ 232 (log ε 3·89), $\lambda_{max.}$ 256 mμ (log ε 4·02). Its *picrate*, obtained quantitatively in ethanol, when crystallised from a large volume of 66% ethanol, formed needles, m. p. 269—271° (decomp., after darkening from 260°) (Found: C, 50·1; H, 3·35. $C_{14}H_{13}N_5,C_6H_3N_3O_7$ requires C, 50·0; H, 3·3%).

Filtrate F, treated with 0·05M-picric acid (100 ml., 0·005 mole), gave a yellow precipitate which was boiled with 90% ethanol (30 ml.) and filtered hot. The undissolved powder was 3-amino-5-anilino-4-phenyl-1,2,4-triazole picrate (0·1 g.), m. p. and mixed m. p. (see above) 268—271° (decomp.). The filtrate therefrom deposited 3-amino-5-anilino-1,2,4-triazole picrate, m. p. and mixed m. p.[1] 229—231° (decomp.) (0·65 g., 32%) (Found: C, 42·0; H, 3·4. Calc. for $C_8H_9N_5,C_6H_3N_3O_7$: C, 41·6; H, 3·0%).

Distillate D, on being acylated [40% sodium hydroxide (5 ml.) and benzoyl chloride (1 ml.)], gave benzanilide, m. p. and mixed m. p. 162—164° (0·29 g., 30%).

(*c*) *With aniline*. A solution of 1,2-diphenylbiguanidine (1·08 g., 0·004 mole) in aniline (10 ml.) was boiled during 30 min., cooled, treated with water (20 ml.), and steam-distilled to remove the aniline. The residual mixture was separated into the aqueous (A) and the oily (O) phase. The former (A), treated with 0·05M-picric acid (40 ml., 0·002 mole), gave a precipitate which was fractionated (as in *b*, above) into the picrates of 3-amino-5-anilino-4-phenyl-1,2,4-triazole (8%), m. p. and mixed m. p. 269—271° (decomp.), and 3-amino-5-anilino-1,2,4-triazole (20%), m. p. and mixed m. p. 229—231° (decomp.). (Found: C, 42·4; H, 2·8%). The oil (O), when crystallised from ethanol–light petroleum (b. p. 40—80°), gave 3-amino-5-anilino-4-phenyl-1,2,4-triazole (12%), m. p. and mixed m. p. 196—198°. The filtrate therefrom gave more 3-amino-5-anilino-1,2,4-triazole, isolated as the picrate (20%).

(*d*) *With acetic anhydride*. The ditoluene-*p*-sulphonate dihydrate (3·24 g., 0·005 mole) was refluxed in acetic anhydride (10 ml.) during 15 min., and the solution added to water (40 ml.). The solution was basified with 10M-sodium hydroxide (20 ml., 0·2 mole) and refluxed during 5 min. The resulting powdery precipitate, collected at 0° and crystallised from ethanol (carbon), was 3-anilino-5-methyl-4-phenyl-1,2,4-triazole (0·75 g., 60%), m. p. 228—230° (lit., m. p. [6] 227—228°).

(*e*) *With diphenylcarbodi-imide*. A solution of 1,2-diphenylbiguanidine ditoluene-*p*-sulphonate dihydrate (3·24 g., 0·005 mole) in dimethylformamide (6 ml.) was treated with diphenylcarbodi-imide (0·97 g., 0·005 mole) and kept at 100° during 30 min., then stirred into water (25 ml.). The resulting white pasty mass, from which the supernatant water was drained (aqueous phase A), was stirred with cold ethanol (6—8 ml.), giving a white powder which consisted, after crystallisation from ethanol, of (solvated) 1-amidino-4-phenyl-3,5-diphenylimino-1,2,4-triazolidine toluene-*p*-sulphonate, m. p. and mixed m. p. 219—221° (1·23 g., 42%) (Found: C, 61·1; H, 4·95%).

The aqueous phase, A, with 0·05M-picric acid (100 ml., 0·005 mole) gave the dipicrate of the starting material, m. p. and mixed m. p. 206—208° (plates from 90% ethanol) (1·63 g., 45%).

Reactions of 1-*Amidino*-4-*phenyl*-3,5-*diphenylimino*-1,2,4-*triazolidine*.—(*a*) *Alkaline hydrolysis*.

A solution of the solvated toluene-*p*-sulphonate (0·29 g., 0·0005 mole) in ethanol (5 ml.)–3N-sodium hydroxide (5 ml.) was refluxed during 20 min., the resulting bright blue solution beginning to deposit solid while boiling. The product was collected at 0° and consisted, after crystallisation from ethanol, of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 234—236° (0·14 g., 85%).

(*b*) *Aminolysis.* A solution of the reactant (1·17 g., 0·002 mole) in aniline (5 ml.) was refluxed during 1 hr., treated with water (10 ml.) and aqueous ammonia (*d* 0·88; 1 ml.), and steam-distilled until the aniline had been removed. The residual suspension was basified with 3N-sodium hydroxide (1 ml.) and allowed to cool to ~30°, the solid (S) collected, and the filtrate acidified with 3N-acetic acid and treated with 0·05M-picric acid (50 ml., 0·0025 mole). The precipitate was phenylguanidine picrate, m. p. and mixed m. p.[17] 219—221° (decomp.) (from 90% ethanol; 0·51 g., 70%) (Found: C, 43·3; H, 3·2. Calc. for $C_7H_9N_3,C_6H_3N_3O_7$: C, 42·9; H, 3·3%). Solid S was 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 234—236° (0·62 g., 95%, from ethanol).

(*c*) The triazolidine failed to yield the 4,6-dimethylpyrimidin-2-yl derivative when heated with an excess of acetylacetone at 100° or refluxed with an equimolar quantity of this reagent in ethanol (both during 2 hr.), being converted instead into 3,5-dianilino-4-phenyl-1,2,4-triazole (in 80 and 90% yield, respectively). The toluene-*p*-sulphonate (solvate) was recovered entirely in this reaction.

Thiosemicarbazide Series

1-(NN′-*Diphenylamidino*)*thiosemicarbazide.*—Thiosemicarbazide (13·65 g., 0·15 mole) was dissolved in dimethylformamide (75 ml.) at 105—110°, the liquid allowed to cool to 70°, and diphenylcarbodi-imide (14·55 g., 0·075 mole) added: the temperature of the temporarily pink, then yellow liquid rose to 105°. The solution was kept on the steam-bath during 5 min., cooled to 30—40°, and then stirred into ice-water (400 ml.). After 2 hr. at room-temperature, and 12 hr. at 0°, the aqueous phase was decanted from coagulated white solid, which was then stirred with warm ethanol (15 ml.). After 6 hr. at 0°, the white powdery solid (15—17 g.) was collected and rinsed with a little ethanol (ethanolic extracts E). Crystallisation from ethanol (3 ml. per g.) gave prismatic columns (12·8—15·4 g., 60—72%) of 1-(NN′-*diphenylamidino*)-*thiosemicarbazide*, m. p. 146—148° (Found: C, 58·9; H, 5·0; N, 24·9; S, 11·2. $C_{14}H_{15}N_5S$ requires C, 58·9; H, 5·3; N, 24·6; S, 11·2%). With boiling aqueous sodium plumbite in 3N-sodium hydroxide the compound gave a first yellow, then black precipitate.

The ethanolic mother-liquors therefrom were evaporated in a vacuum to half-volume and deposited plates, which consisted, on further crystallisation from ethanol, of 3-anilino-5-mercapto-1,2,4-triazole, m. p. 286—290° (decomp.) (0·9—1·3 g., 6—9%) (Found: C, 49·7; H, 4·5; N, 29·2; S, 16·7. Calc. for $C_8H_8N_4S$: C, 50·0; H, 4·2; N, 29·2; S, 16·7%) (lit., m. p. 275°[18] or 268°[19]).

The ethanolic extracts E deposited, on partial spontaneous evaporation, small quantities (0·6—0·85 g., 5—7%) of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see below) 233—235°.

3,5-*Dianilino*-4-*phenyl*-1,2,4-*triazole.*—A solution of thiosemicarbazide (0·91 g., 0·01 mole) in dimethylformamide (5 ml.), treated with diphenylcarbodi-imide (4·25 g., 0·022 mole), was kept at 100° during 20 min., then stirred into water (50 ml.). The aqueous phase was decanted from the resulting sticky resinous precipitate, which was then stirred with cold ethanol (8 ml.). The resulting white powder gave, on crystallisation from ethanol (60 ml. per g., recovery 85%) or ethanol–acetone (1 : 2, 20 ml. per g., recovery 70%), prisms (total, 2·15 g., 65%), disintegrating on drying to a white powder, of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. 236—237° (lit., m. p.[7] 234°) [Found: C, 73·5; H, 5·1; N, 21·6%; *M* (cryoscopically, in thymol), 305. Calc. for $C_{20}H_{17}N_5$: C, 73·4; H, 5·2; N, 21·4%; *M*, 327]. The material became grey on exposure to air. The *picrate*, formed almost quantitatively in ethanol, consisted of yellow needles, m. p. 243—244° (decomp.) (from a large volume of ethanol) (Found: C, 56·6; H, 3·7. $C_{20}H_{17}N_5,C_6H_3N_3O_7$ requires C, 56·1; H, 3·6%).

A solution of the triazole (0·50 g., 0·0015 mole) in boiling ethanol (40 ml.) was treated with toluene-*p*-sulphonic acid monohydrate (0·57 g., 0·003 mole) in water (1 ml.) and distilled to

[17] Smith, *J. Amer. Chem. Soc.*, 1929, **51**, 477.
[18] Arndt, *Ber.*, 1922, **55**, 14.
[19] Fromm, *Annalen*, 1922, **426**, 327.

one-third bulk. The crystals were collected after storage at 0° during 24 hr. (0·64 g., 85%), recrystallised from ethanol (30 ml. per g.), and slowly gave prisms of the *toluene*-p-*sulphonate*, m. p. 238—240° (decomp.) (Found: C, 64·85; H, 5·0; N, 14·15; S, 6·5. $C_{20}H_{17}N_5,C_7H_8O_3S$ requires C, 64·9; H, 5·0; N, 14·0; S, 6·4%).

The diacetyl derivative, obtained in 90% yield in boiling acetic anhydride, had m. p. 218—220° (from ethanol) (lit., m. p.[7] 218°) (Found: C, 68·5; H, 5·5. Calc. for $C_{24}H_{21}N_5O_2,C_2H_5{\cdot}OH$: C, 68·3; H, 5·9%).

Reactions of 1-(NN′-*Diphenylamidino*)*thiosemicarbazide*.—(*a*) *With phosphoric acid*. The reactant (0·86 g., 0·003 mole), dissolved in 100% orthophosphoric acid (10 ml.), was kept at 120° during 1 hr. The cooled clear solution was stirred into ice (50 g.) and aqueous ammonia (*d* 0·88; 20 ml.), and the flocculent precipitate collected after 2 hr. Crystallisation from boiling water (100 ml. per g.) gave plates (0·49 g., 85%) of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. and mixed m. p.[2] 205—206°.

(*b*) *With acetic anhydride*. A solution of the reactant (0·86 g., 0·003 mole) in acetic anhydride (5 ml.) was kept at 100° during 5 min., then stirred into water (12 ml.). The precipitate, which was collected after 48 hr. at 0° and crystallised from ethanol, was the diacetyl derivative of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. and mixed m. p.[2] 274—276° (after shrinking at 270°) (0·18 g., 22%). The yield was not improved, when the time of heating was extended to 30 min.

(*c*) *With sodium hydroxide*. A solution of the reactant (1·43 g., 0·005 mole) in 3N-sodium hydroxide (10 ml., 0·03 mole) was refluxed during 30 min. (evolution of ammonia), then stirred into ice and acetic acid (2·4 g., 0·04 mole), and the precipitate was collected and cautiously dried at room-temperature. Crystallisation of the soft material from ethanol (5—8 ml.) gave prisms of 3-anilino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. 204—206° (0·37 g., 28%) (the m. p. is variously given between 206° and 210° in the literature [7,20]) (Found: C, 62·6; H, 4·1; N, 21·4. Calc. for $C_{14}H_{12}N_4S$: C, 62·7; H, 4·5; N, 20·9%).

Alternatively, crystallisation of the crude product from boiling water (12—15 ml.) gave pale yellow needles (m. p. 190—195°; 0·30 g., 24%) which consisted, after crystallisation from ethanol–light petroleum (b. p. 40—80°), of 3-amino-5-anilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see above) 195—198° (Found: C, 67·1; H, 5·3; N, 27·5. Calc. for $C_{14}H_{13}N_5$: C, 66·9; H, 5·2; N, 27·9%).

(*d*) *Pyrolysis*. Finely powdered 1-(*NN*′-diphenylamidino)thiosemicarbazide (1·43 g., 0·005 mole), placed in a bath at 200° and kept at this temperature during 15 min., changed in appearance without melting and droplets of aniline condensed in the cooler parts of the vessel. The residue, ground with cold ethanol (5—8 ml.) and collected at 0° (0·69 g., 72%) (filtrate F), was 3-anilino-5-mercapto-1,2,4-triazole, m. p. 286—288° (from ethanol) (lit., m. p. 275° [18] or 268° [19]).

Filtrate F gave, after evaporation to small volume, removal of a trace more of the above thiol, and treatment with ethanolic picric acid, a little (0·12 g., 5%) 3-amino-5-anilino-4-phenyl-1,2,4-triazole picrate, m. p. and mixed m. p. (with material obtained in the pyrolysis of 1,2-diphenylbiguanidine) 269—271° (decomp., after darkening from 260°).

(*e*) *With diphenylcarbodi-imide*. A solution of 1-(*NN*′-diphenylamidino)thiosemicarbazide (1·43 g., 0·005 mole) and diphenylcarbodi-imide (0·97 g., 0·005 mole) in dimethylformamide (4 ml.) was kept at 100° during 30 min. The sticky semisolid resinous white material was stirred with water (2 × 10 ml.), ground with a little ethanol (5 ml.), and collected. Crystallisation of the white powder (1·4 g.) from ethanol (50 ml.) gave flat prisms (1·18 g., 72%) of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. 233—235°. Attempts to isolate the (assumed) intermediate 4-phenyl-3,5-diphenylimino-1-thiocarbamoyl-1,2,4-triazolidine by employing more restrained conditions (*e.g.*, 5 min. at 40—50°) were unsuccessful, the same product, m. p. 233—235°, being obtained in comparable yields.

Interaction of 4-*Phenylthiosemicarbazide and Diphenylcarbodi-imide*.—To a solution of the thiosemicarbazide (5·0 g., 0·03 mole) in dimethylformamide (10 ml.) at 20°, the carbodi-imide (5·8 g., 0·03 mole) was added dropwise during 5 min., with external cooling so as to keep the temperature below 60°. The clear yellow liquid was set aside at room temperature during 30 min., then added to water (150 ml.) and stirred during 1 hr. The aqueous phase was decanted and the air-dried resinous product dissolved in methanol (50 ml.). On storage, and partial

[20] Guha and Sen, *J. Indian Chem. Soc.*, 1927, **4**, 46; Guha and Chakraborty, *ibid.*, 1929, **6**, 109; Arndt and Milde, *Ber.*, 1921, **54**, 2110; Fromm, *Annalen*, 1923, **433**, 12.

evaporation, the solution became deep purple and slowly deposited crystals. They were separated, by N-sodium hydroxide, into insoluble (1·5 g., 15%) 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 234—236° (from ethanol), and soluble (4·2 g., 52%) 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see above) 204—206° (reprecipitated by 3N-hydrochloric acid and crystallised from ethanol).

Semicarbazide Series

1-(NN′-*Diphenylamidino*)*semicarbazide*.—A stirred suspension of semicarbazide hydrochloride (11·15 g., 0·1 mole) in dimethylformamide (100 ml.) at 80° was treated dropwise with diphenylcarbodi-imide (9·7 g., 0·05 mole) in dimethylformamide (10 ml.) during 30 min., dissolution being complete when all the reagent had been added. The liquid was kept at 80—85° for another 30 min., allowed to cool, stirred into water (200 ml.), filtered (solid S), and basified with 3N-sodium hydroxide (40 ml.). The brown liquid slowly deposited a powdery solid which was collected at 0° and crystallised from ethanol (3—4 ml. per g.), yielding a white opaque powder (total, including material from the mother-liquors, 12·8—15·0 g., 75—88%) of solvated 1-(NN′-*diphenylamidino*)*semicarbazide* (with dimethylformamide *), m. p. 119—121° (decomp., somewhat subject to the rate of heating) (Found: C, 59·85, 59·8; H, 6·5, 6·7; N, 24·2, 24·6. $C_{14}H_{15}N_5O$,H·CO·NMe_2 requires C, 59·65; H, 6·4; N, 24·6%). Its ultraviolet absorption curve was coincident with that of the non-solvated base (see below).

Solid S (0·4—0·5 g.) was 1,3-diphenylurea, m. p. and mixed m. p. 236—238° (from ethanol).

The dimethylformamide-solvated compound (3·42 g., 0·01 mole) dissolved slowly on being refluxed in acetone (180 ml.). The filtered liquid deposited refractive flat prisms (3·10 g., 95%) of solvated 1-(NN′-*diphenylamidino*)*semicarbazide* (with acetone), m. p. 94—96° (decomp.) (Found: C, 62·55; H, 6·8; N, 21·7. $C_{14}H_{15}N_5O$,Me_2CO requires C, 62·4; H, 6·4; N, 21·4%). Crystallisation from diethyl ketone did not yield a comparable solvate.

The acetone-solvated product (1·64 g., 0·005 mole), when crystallised from ethanol (10 ml.), gave opaque needles of the non-solvated *base*, m. p. 150—154° (decomp., somewhat subject to the rate of heating) (0·87 g., 65%) (Found: C, 62·7, 62·5; H, 5·7, 6·1; N, 26·05. $C_{14}H_{15}N_5O$ requires C, 62·45; H, 5·6; N, 26·0%), $\lambda_{min.}$ 230 (log ε 4·02), $\lambda_{max.}$ 262 mμ (log ε 4·38). The material was reconvertible into the solvate, m. p. 118—121°, on crystallisation from ethanol containing a few drops of dimethylformamide (Found: C, 59·7; H, 6·5%).

A solution of the dimethylformamide-solvated compound (0·34 g., 0·001 mole) in cold 0·2N-hydrochloric acid (6 ml., 0·0012 mole), when treated with 0·05M-picric acid (40 ml., 0·002 mole), slowly deposited a granular precipitate (85%), which gave, on crystallisation from ethanol–light petroleum (b. p. 40—80°), yellow prisms of the *picrate*, m. p. 110—112° (decomp.) (Found: C, 48·45; H, 4·45; N, 21·0. $C_{14}H_{15}N_5O$,$C_6H_3N_3O_7$,C_2H_5·OH requires C, 48·5; H, 4·4; N, 20·6%).

Interaction of semicarbazide hydrochloride and diphenylcarbodi-imide in the molar ratio 1 : 2 in dimethylformamide during 1·5 hr. gave, by the usual procedure (see above), 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. 235—237° (52%).

Reactions of 1-(NN′-*Diphenylamidino*)*semicarbazide*.—(*a*) *Pyrolysis*. The finely powdered semicarbazide derivative (solvated, with dimethylformamide) (0·86 g., 0·0025 mole), when placed in a bath at 160°, melted and evolved ammonia. The clear melt was kept at 160—180° during 30 min., the cooled material dissolved in boiling ethanol (8 ml.), and the solution slowly diluted with light petroleum. The resulting needles (m. p. 210—212°; 0·51 g., 80%) were 3-anilino-5-hydroxy-4-phenyl-1,2,4-triazole, m. p. 212—214° (from ethanol) (lit.,[7,21] m. p. 212—213°) (Found: C, 66·5; H, 4·7. Calc. for $C_{14}H_{12}N_4O$: C, 66·7; H, 4·8%).

(*b*) *With sodium hydroxide*. A solution of the solvated semicarbazide derivative (3·42 g., 0·01 mole) in 3N-sodium hydroxide (20 ml.)–ethanol (10 ml.) was refluxed during 1 hr., ammonia being evolved. The liquid was acidified with 3N-acetic acid (to pH 6), and the resulting precipitate (m. p. 208—210°; 2·28 g., 90%) collected at 0°. Crystallisation from ethanol (10 ml. per g., recovery 75%) gave needles of 3-anilino-5-hydroxy-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see above) 211—213°.

(*c*) *With phosphoric acid*. A solution of the semicarbazide derivative (0·86 g., 0·0025 mole)

* Dimethylformamide as a constituent of solvates has previously been observed; see, for example, Petersen and Domagk, G.P. 965,723/1957.

[21] Busch and Blume, *J. prakt. Chem.*, 1906, **74**, 547.

in 100% orthophosphoric acid (6 ml.) was kept at 120° for 1 hr., then added to ice (60 g.) and aqueous ammonia (*d* 0·88; 15 ml.), and the filtered liquid treated with 0·05M-picric acid (100 ml., 0·005 mole). The precipitate (92%) was hydrazine dipicrate, m. p. and mixed m. p.[2] 288—292° (decomp., after darkening from 260°) (from 90% ethanol).

(*d*) *With acetic anhydride.* A solution of the semicarbazide derivative (1·71 g., 0·005 mole) in acetic anhydride (8 ml.) was refluxed during 15 min., stirred into water (20 ml.), and carefully treated with 10N-sodium hydroxide (20 ml.). The resulting mixture was boiled during 10 min.; ammonia was evolved, and the precipitated oil solidified. The resulting white solid, collected at 0° and crystallised from ethanol (20 ml. per g.), gave needles of 3-anilino-5-methyl-4-phenyl-1,2,4-triazole, m. p. 228—230° (0·75 g., 60%) (Found: C, 72·4; H, 5·8; N, 21·7. Calc. for $C_{15}H_{14}N_4$: C, 72·0; H, 5·6; N, 22·4%) (lit.,[6] m. p. 227—228°). The *picrate* formed needles, m. p. 192—195° (decomp.) (Found: C, 52·8; H, 4·2. $C_{15}H_{14}N_4,C_6H_3N_3O_7,C_2H_5{\cdot}OH$ requires C, 52·6; H, 4·4%).

(*e*) *With diphenylcarbodi-imide.* A solution of the solvated semicarbazide derivative (3·42 g., 0·01 mole) in dimethylformamide (10 ml.) was treated with diphenylcarbodi-imide (2·15 g., 0·011 mole) and kept at 100° during 45 min., then stirred into water. After removal of the supernatant aqueous phase, the sticky gum was converted, by being stirred with ethanol (10 ml.), into a white powder (m. p. 228—230°; 1·83 g., 56%) consisting of 3,5-dianilino-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 235—236° (from ethanol).

The same triazole was formed (52%) and isolated in the usual manner (m. p. and mixed m. p. 228—230°) when semicarbazide hydrochloride had reacted with 2 mol. of diphenylcarbodi-imide in dimethylformamide at 100° during 1 hr.

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