822. *Heterocyclic Compounds from Urea Derivatives. Part VIII.*[1] *Addition Products of* NN′*-Di(isopropylideneamino)guanidine and Isothiocyanate Esters, and Their Cyclisation*

By Frederick Kurzer and K. Douraghi-Zadeh

Aryl isothiocyanates react additively with *NN′*-di(isopropylideneamino)-guanidine in acetone, giving good yields of 1,3-di(isopropylideneamino)-2-(substituted-anilino)thioformylguanidines. These are readily cyclised to 3-arylamino-5-isopropylidenehydrazino-1,2,4-triazoles by the action of sodium hydroxide or dimethylformamide. Hydrochloric acid, on the other hand, yields chiefly 3-isopropylidenehydrazino-5-mercapto-1,2,4-triazole, some reactions of which are described.

The structure of 3-anilino-5-hydrazino-1,2,4-triazole, previously based on degradative evidence, is confirmed by the alternative synthesis of its 5-(3,5-dimethylpyrazol-1-yl) derivative by the hydrazinolysis of 3,5-dimethyl-1-[*N*-(anilino-*S*-methylthioformyl)amidino]pyrazole.

In continuation of our study of the addition of systems containing twinned double bonds to *NN′*-diaminoguanidine,[1] the behaviour of isothiocyanate esters in this reaction

[1] F. Kurzer and K. Douraghi-Zadeh, *J.*, 1965, 3912.

has been examined. As in the case of aminoguanidine,[2] the initial addition occurs at the central imino- or at a hydrazino-group (of I) in the presence or absence, respectively, of blocking substituents on the hydrazino-groups.[1] This Paper describes the addition of isothiocyanates to diaminoguanidine thus substituted (II), and the cyclisation of the resulting addition products.

Aryl isothiocyanates reacted smoothly with *NN'*-di(isopropylideneamino)guanidine (II; R = R' = Me) in boiling acetone, giving 1,3-di(isopropylideneamino)-2-(substituted-anilino)thioformylguanidines (IV; R = R' = Me) in 70—80% yields. Their alternative formulation (as IVa) is excluded by the results of their conversion into 1,2,4-triazoles of established structure (see below). A procedure employing the dihydrazone (II; R = R' = Me) prepared *in situ*, used in the analogous addition of carbodi-imides,[1] was not advantageous in the present reaction; yields were lower than those from the two-stage process (I ⟶ II ⟶ IV), and the adduct (IV) tended to cyclise to (VI) in the alkaline environment. *NN'*-Di(benzylideneamino)guanidine (II; R = H, R' = Ph) unexpectedly failed to undergo the addition-reaction under the standard conditions, being substantially recovered after treatment with phenyl isothiocyanate in acetone or benzene containing triethylamine as catalyst. Small yields of the desired adduct (IV; R = H, R' = Ph) were obtained on performing the addition in dimethylformamide.

The formal structural resemblance of the diaminothioformylhydrazones (IV) now described to the corresponding addition compounds (XV) [1] of carbodi-imides is reflected in the similarity of their general chemical behaviour, particularly their cyclisation. The adducts (IV) gave salts such as picrates; they thus retained their net basic character, in spite of the presence of the acidic anilinothioformyl function in their structure. They were desulphurised by alkaline sodium plumbite as expected. Their ultraviolet spectra, containing well-defined maxima at 254—255 and 295—300 mμ, superficially resembled those of their analogues (XV); the better definition of their maxima, and their considerable bathochromic displacement can presumably be ascribed to the sulphur-containing grouping in the molecule.

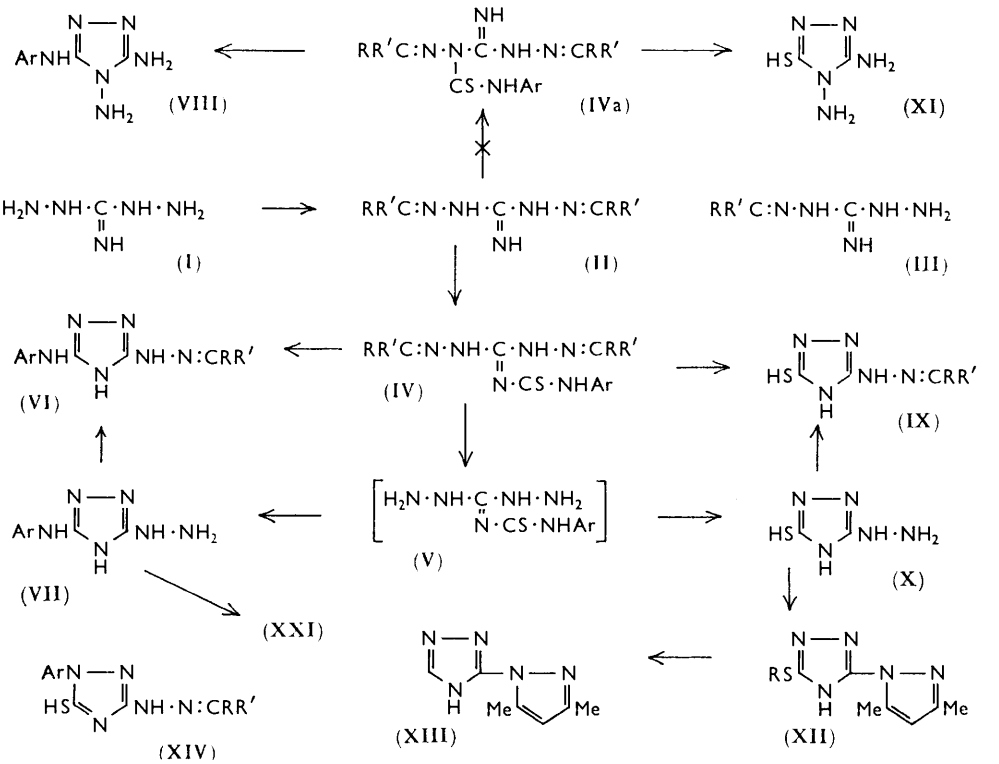
1,3-Di(isopropylideneamino)-2-anilinothioformylguanidines (IV; R = R' = Me) were cyclised in excellent yield by strong alkalis to 3-arylamino-5-hydrazino-1,2,4-triazoles (VII; *e.g.*, Ar = Ph), best isolated as hydrazones (VI). The same ring-closure occurred in hot dimethylformamide, though less completely, part of the reactant being cleaved to *NN'*-di(isopropylideneamino)guanidine. For this reason, dimethylformamide was not generally suitable as a solvent for the initial addition-reaction (II ⟶ IV; R = R' = Me), the cyclic end-product (VI) being obtained in one stage.

The formulation of the resulting 3-arylamino-5-hydrazino-1,2,4-triazoles (VII), also produced in the acidic cyclisation of 1,3-di(isopropylideneamino)-2-(*NN'*-diarylamidino)-guanidines (XV) [1] has so far been based on their chemical properties and on degradative evidence.[1] Their structure has now been further confirmed by the following synthesis. 3,5-Dimethyl-1-[*N*-(anilinothioformyl)amidino]pyrazole (XVI), prepared [3] from phenyl isothiocyanate and 1-amidino-3,5-dimethylpyrazole, was converted, on successive *S*-methylation (to XVII) and hydrazinolysis, into 3-anilino-5-(3,5-dimethylpyrazol-1-yl)-1,2,4-triazole (XXI) in low yield. The identity of this product with material obtained by the action of acetylacetone on 3-anilino-5-hydrazino-1,2,4-triazole (VII), arising in the present cyclisations, confirms the structure of the latter as (VII). Its alternative formulation as the isomeric 3,4-diamino-1,2,4-triazole (VIII) being thus excluded, the representation of the original addition products as (IVa) is also inadmissible.

The above hydrazinolysis is attended by parallel reactions, resulting in 3-amino-5-anilino-1,2,4-triazole (XXII) (up to 20%) and 3,5-dimethylpyrazole (XXIII) (up to 45%). The consequent low yields of the reaction (XVII ⟶ XXI) do not, however, appear to weaken the argument upon which the structural assignment is based, particularly in view

[2] L. E. A. Godfrey and F. Kurzer, *J.*, 1960, 3437; 1961, 5137.
[3] F. L. Scott and J. Reilly, *J. Amer. Chem. Soc.*, 1952, **74**, 4562

of the known mobility of *N*-amidino-groups attached to pyrazole [4-6] and triazole [7] nuclei. Thus, the formation of the three products of the hydrazinolysis is accounted for by a mechanism involving the initial replacement of the *S*-methylthiol-group (of XVII) and cyclisation, with loss of ammonia, of the resulting intermediate (XVIII), with or without simultaneous cleavage into two nuclei. Studies of the hydrazinolysis of nitroguanidine [8] and, more particularly, of 1-amidino-2,3-dimethylpyrazole [4-6] have provided data suggesting



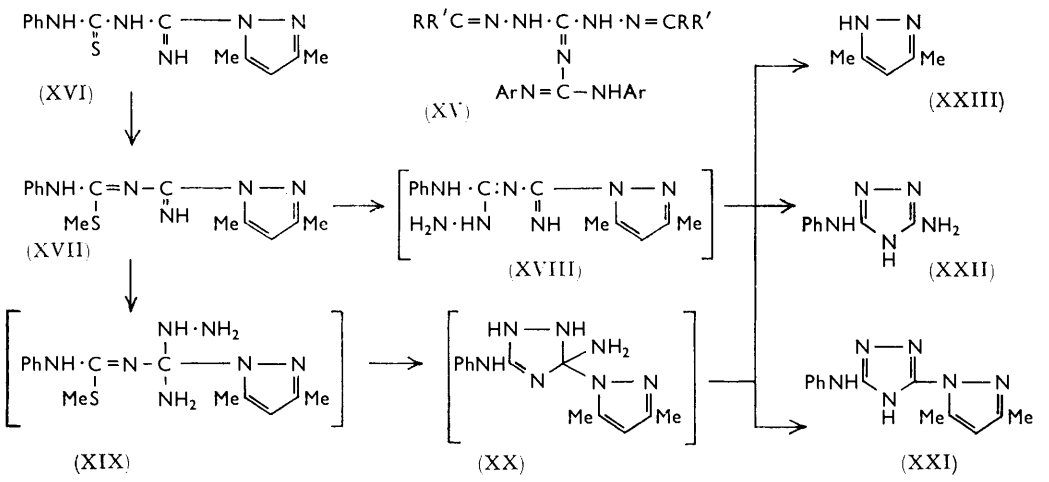
that the initial attack of hydrazine in these comparable systems occurs additively at an (amidino)imino-group. On this basis, the present reaction may be visualised to proceed by the route (XVII) ⟶ (XIX) ⟶ (XX). Loss of ammonia from the precursor (XX) yields the desired pyrazolyl-triazole (XXI), whilst fission of the molecule, with the appropriate transfer of hydrogen, furnishes the products (XXII) and (XXIII).

In hydrochloric acid, the cyclisation of 2-anilinothioformyl-1,3-di(isopropylideneamino)-guanidine (IV; Ar = Ph; R = R′ = Me) occurred predominantly with elimination of aniline, affording good yields of 3-hydrazino-5-mercapto-1,2,4-triazole (X) (or a suitable hydrazone, IX). The identification of this product as the hydrazino-compound (X) rather than the isomeric diamine (XI) provides yet further evidence for the formulation of its open-chain precursor as (IV) and not (IVa). 3-Anilino-5-isopropylidenehydrazino-1,2,4-triazole (VI; Ar = Ph; R = R′ = Me) was a by-product of this reaction, arising in the alternative ring-closure proceeding with loss of hydrogen sulphide. A third possible

[4] F. L. Scott, C. M. F. Murphy, and J. Reilly, *Nature*, 1951, **167**, 1037; F. L. Scott, M. T. Kennedy, and J. Reilly, *ibid.*, 1952, **169**, 72.
[5] F. L. Scott, D. G. O'Donovan, and J. Reilly, *J. Amer. Chem. Soc.*, 1953, **75**, 4053.
[6] F. Kurzer and L. E. A. Godfrey, *Angew. Chem.*, 1963, **75**, 1158; *Angew. Chem. Internat. Edn.*, 1963, **2**, 460.
[7] L. E. A. Godfrey and F. Kurzer, *J.*, 1962, 3561.
[8] R. Phillips and J. F. Williams, *J. Amer. Chem. Soc.*, 1928, **50**, 2465.

cyclisation, resulting in (XIV) with loss of ammonia, did not occur, being obviously prevented by the stability of the hydrazino-groups of (IV), one of which needs to be cleaved in this change.

3-Hydrazino-5-mercapto-1,2,4-triazole (X) and its isomer, 3,4-diamino-5-mercapto-1,2,4-triazole (XI), are the main products of the hydrazinolysis of *NN'*-dithiocarbamoylhydrazine;[9-11] they were originally distinguished from one another by their power of forming mono- and di-benzylidene derivatives, respectively,[10b] and later by additional reactions.[11] The structure of (X) has been confirmed by its synthesis from 4-amino-1-thioformamido-3-*S*-methylisothiosemicarbazide, $H_2N{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}C(SMe){:}N{\cdot}NH_2$,[12] and



by *X*-ray crystallography.[13] Accordingly, 3-hydrazino-5-mercapto-1,2,4-triazole (X) has now been converted by means of acetylacetone [14] almost quantitively into the corresponding 3-(3,5-dimethylpyrazol-1-yl) derivative (XII; R = H), and thence into the methylthio-compound (XII; R = Me). Oxidative removal of the mercapto-group from (XII; R = H) gave the parent heterocycle, 3-(3,5-dimethylpyrazol-1-yl)-1,2,4-triazole (XIII), identical with the product directly synthesised recently from 3-hydrazino-1,2,4-triazole by Kröger, Etzold, and Beyer.[15] The acidic hydrogen peroxide [16] employed in this desulphurisation (XII ⟶ XIII) tended to degrade the heterocyclic reactant to hydrazine, and conditions had to be carefully controlled to prevent this degradation from becoming the main reaction.

During the preparation of *NN'*-di(benzylideneamino)guanidine (II; R = H, R' = Ph), required in this work, conditions that favour the formation of the monobenzylidene-compound (III; R = H, R' = Ph) were also examined. Dihydrazone formation occurred so rapidly, however, that the use of even a large excess of diaminoguanidine (2·5 moles) did not suppress it entirely. *N*-Amino-*N'*-(benzylideneamino)guanidine (III), unlike the

[9] F. Arndt and F. Bielich, *Ber.*, 1923, **56**, 809.
[10] (*a*) E. Fromm and E. Layer, *Annalen*, 1923, **433**, 1; (*b*) E. Fromm and L. Wetternick, *ibid.*, 1926, **447**, 300, 311.
[11] E. Hoggarth, *J.*, 1952, 4817.
[12] E. S. Scott and L. F. Audrieth, *J. Org. Chem.*, 1954, **19**, 742.
[13] M. E. Senko, U.S. Atomic Energy Comm. UCRL. 3521 (1956) (*Chem. Abs.*, 1957, **51**, 5496); M. E. Senko and D. H. Templeton, *Acta Cryst.*, 1958, **11**, 808.
[14] L. Jacobs in " Heterocyclic Compounds," ed. R. C. Elderfield, Vol. 5, Wiley, New York, 1957, p. 48.
[15] C. F. Kröger, G. Etzold, and H. Beyer, *Annalen*, 1963, **664**, 164.
[16] E. R. Buchmann, A. O. Reims, and H. Sargent, *J. Org. Chem.*, 1941, **6**, 764.

dihydrazone (II), was water-soluble and was isolated as the picrate only. It was characterised by its conversion into *NN'*-di(benzylideneamino)guanidine, into its 3,5-dimethylpyrazolyl derivative, and into a mixed dihydrazone (cf. Experimental section).

The reactions of diaminoguanidine now described recall the parallel behaviour of aminoguanidine;[2] thus, the addition products of aminoguanidine hydrazones and isothiocyanate esters yield chiefly 3-amino-5-arylamino- or 3-amino-5-mercapto-1,2,4-triazoles on cyclisation in alkaline or acid media, respectively. The present reactions involving diaminoguanidine thus proceed entirely analogously, affording the corresponding hydrazino- instead of amino-triazoles. An unexpected difference, *viz.*, the inertness of *NN'*-di(benzylideneamino)guanidine towards isothiocyanate, not shared by (benzylideneamino)guanidine, may be caused by steric effects.

Experimental

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

N-*Amino*-N'-(*benzylideneamino*)*guanidine*.—A stirred suspension of *NN'*-diaminoguanidine hydriodide (2·17 g., 0·01 mole) and sodium carbonate (0·53 g., 0·005 mole) in 66% aqueous ethanol (12 ml.) was treated with benzaldehyde (0·85 g., 0·008 mole) in 50% ethanol (8 ml.) on a steam-bath. Solution occurred rapidly and heating was continued for 15 min. The liquid was added to ice–water, and the pale yellow solid (filtrate F) crystallised from a little 80% ethanol, giving ivory felted scales (0·32 g., 30%) of *NN'*-di(benzylideneamino)guanidine, m. p. 178—179° (lit.,[17] 176 to 180°) (Found: C, 67·8; H, 5·7. Calc. for $C_{15}H_{15}N_5$: C, 67·9; H, 5·7%).

Filtrate F was acidified (to Congo Red) with concentrated hydrochloric acid and treated with 0·05M-aqueous picric acid (160 ml., 0·008 mole). The resulting precipitate gave, on crystallisation from 75% ethanol, felted needles (1·45 g., 45%) of N-*amino*-N'-(*benzylideneamino*)-*guanidine picrate*, m. p. 201—203° (decomp.) (Found: C, 41·8; H, 3·6; N, 28·6. $C_8H_{11}N_5,C_6H_3N_3O_7$ requires C, 41·4; H, 3·45; N, 27·6%).

The use of a larger excess of diaminoguanidine hydriodide (0·02 mole) gave a reaction mixture which, on dilution with water, deposited only a little dihydrazone (up to 10%). Treatment of the filtrate with picric acid (0·02 mole) in 50% ethanol gave a mixture of picrates. Crystallisation from 80% ethanol (200 ml.), and removal of the material that had separated above 30°, gave *N*-amino-*N'*-(benzylideneamino)guanidine picrate, m. p. and mixed m. p. 201—203° (decomp.) (72—80%). Subsequent fractions were *NN'*-diaminoguanidine picrate, m. p. and mixed m. p. 188—189° (decomp.) (lit.,[18] m. p. 191°).

N-Amino-*N'*-(benzylideneamino)guanidine picrate, on being dissolved in 80% ethanol containing a little benzaldehyde, gave *NN'*-di(benzylideneamino)guanidine picrate, m. p. and mixed m. p. 248—250° (decomp.) (from 85% ethanol), almost quantitatively (Found: C, 51·5; H, 3·8; N, 22·6. Calc. for $C_{15}H_{15}N_5,C_6H_3N_3O_7$: C, 51·0; H, 3·6; N, 22·7%) [lit.,[19] m. p. 240—242° (decomp.)].

The above picrate, on being recrystallised from 80% aqueous ethanol containing 15% acetone gave platelets of N-*benzylideneamino*-N'-(*isopropylideneamino*)*guanidine picrate*, m. p. 213—215° (decomp.) almost quantitatively (Found: C, 46·0; H, 4·3. $C_{11}H_{15}N_5,C_6H_3N_3O_7$ requires C, 45·7; H, 4·0%). The above picrate (0·0003 mole), on being dissolved in 80% aqueous ethanol containing 2% acetylacetone (10 ml.) and heating, gave platelets of 1-[N-(*benzylideneamino*)*amidino*]-3,5-*dimethylpyrazole picrate*, m. p. 198—199° (decomp.), nearly quantitatively (Found: C, 48·6; H, 4·0. $C_{13}H_{15}N_5,C_6H_3N_3O_7$ requires C, 48·5; H, 3·8%).

2-*Anilinothioformyl*-1,3-*di*(*benzylideneamino*)*guanidine*.—A solution of *NN'*-di(benzylideneamino)guanidine (1·33 g., 0·005 mole) in dimethylformamide (3 ml.) containing a drop of benzaldehyde was treated with phenyl isothiocyanate (0·68 g., 0·005 mole) and kept at 100° for 6 hr. Addition to water (50 ml.) gave an oil which solidified on storage at 0° (2 g.) and

[17] F. L. Scott, D. A. O'Sullivan, and J. Reilly, *J. Appl. Chem.*, 1952, **2**, 184.
[18] G. Pellizzari and C. Cantoni, *Ber.*, 1905, **38**, 283; *Gazzetta*, 1905, **35**, I, 291.
[19] R. A. Henry, H. D. Lewis, and G. B. L. Smith, *J. Amer. Chem. Soc.*, 1950, **72**, 2015; E. Lieber, S. Schiff, R. A. Henry, and W. G. Finnegan, *J. Org. Chem.*, 1953, **18**, 218.

was digested with cold methanol (8 ml.). The remaining white solid (m. p. 186—189°; 0·34 g., 17%) gave, on crystallisation from ethanol (250 ml. per g., followed by distillation to half volume), pale yellow prisms of the *substituted guanidine*, m. p. 190—192° (Found: C, 65·4; H, 5·0; N, 20·5; S, 8·2. $C_{22}H_{20}N_6S$ requires C, 66·0; H, 5·0; N, 21·0; S, 8·0%). It had $\lambda_{min.}$ 245 mμ (log ε 4·13); $\lambda_{max.}$ 273 mμ (4·42); $\lambda_{min.}$ (shallow) 301 (4·22). The warmed methanol extracts, treated with picric acid (0·92 g., 0·004 mole) in ethanol, gave *NN'*-di(benzylideneamino)-guanidine picrate, m. p. and mixed m. p. 248—250° (from 80% ethanol) (36%).

Interaction of the above reactants in refluxing anhydrous benzene (100 ml.), or acetone (100 ml.), containing triethylamine (0·5 ml.) for 1 hr., and removal of most of the solvent in a vacuum, deposited the starting material, m. p. and mixed m. p. 178—179° (85%).

2-*Anilinothioformyl*-1,3-*di*(*isopropylideneamino*)*guanidine*.—(*a*) A solution of *NN'*-di(isopropylideneamino)guanidine [1] (3·38 g., 0·02 mole) in acetone (80 ml.) was treated with phenyl isothiocyanate (2·70 g., 0·02 mole) and refluxed for 2 hr. It was distilled to small volume (*ca.* 20 ml.) and diluted with hot ethanol (20 ml.). The crystals which separated on cooling were collected at 0° (m. p. 115—117°; total, including material from the filtrates, 4·35—4·85 g., 72—80%) and gave on, crystallisation from ethanol (6 ml. per g., recovery 80%), elongated prisms of 2-*anilinothioformyl*-1,3-*di*(*isopropylideneamino*)*guanidine*, m. p. 118—120° (Found: C, 55·5; H, 6·4; N, 28·1; S, 10·7. $C_{14}H_{20}N_6S$ requires C, 55·3; H, 6·6; N, 27·6; S, 10·5%). The compound gave lead sulphide when boiled with sodium plumbite in 3N-sodium hydroxide. It had $\lambda_{min.}$ 228 mμ (log ε 4·25), $\lambda_{max.}$ 254 (4·47), $\lambda_{min.}$ 274 (4·23), $\lambda_{max.}$ 296 (4·38).

Its *picrate*, obtained quantitatively in ethanol containing 10% acetone, and recrystallised therefrom, had m. p. 164—166° (decomp.) (Found: C, 45·05; H, 4·6. $C_{14}H_{20}N_6S,C_6H_3N_3O_7$ requires C, 45·0; H, 4·3%).

(*b*) To the suspension obtained on introducing sodium (0·46 g., 0·02 g.-atom) into acetone (100 ml.), *NN'*-diaminoguanidine hydriodide [20] (5·4 g., 0·025 mole) was added. The resulting clear stirred liquid was refluxed for 15 min., treated successively with phenyl isothiocyanate (2·7 g., 0·02 mole) and triethylamine (5 ml.), and refluxing was continued for 1 hr. Most of the solvent was removed in a vacuum, the residue stirred into ice–water (100 ml.), and the semi-solid precipitate digested with ice-cold methanol (10 ml.). The resulting powder was the substituted guanidine, m. p. and mixed m. p. (see above) 118—120° (total, 2·45 g., 40%) (from ethanol).

Evaporation of the digestion and crystallisation filtrates gave 3-anilino-5-isopropylidene-hydrazino-1,2,4-triazole (up to 0·46 g., 10%), m. p. and mixed m. p.[1] 228—230° (decomp.) (from ethanol containing a little acetone) (Found: C, 57·8; H, 6·3. Calc. for $C_{11}H_{14}N_6$: C, 57·4; H, 6·1%).

(*c*) A solution of *NN'*-di(isopropylideneamino)guanidine [1] (1·69 g., 0·01 mole) in dimethylformamide (10 ml.), treated with phenyl isothiocyanate (1·35 g., 0·01 mole), was kept at 100° for 1 hr., and stirred into ice–water. The solidified oil gave, on crystallisation from acetone–ethanol (1 : 3; 40 ml. per g.), successive crops of 3-anilino-5-isopropylidenehydrazino-1,2,4-triazole, m. p. and mixed m. p.[1] 228—230° (decomp.) (total, 1·2 g., 52%) (Found: C, 56·6; H, 6·0%).

2-*Anilinothioformyl*-1,3-*di*(*isopropylideneamino*)*guanidine*. (a) *Reaction with sodium hydroxide*. A solution of the reactant (0·61 g., 0·002 mole) in 3N-sodium hydroxide (3·3 ml.)–ethanol (12 ml.) was refluxed for 1 hr., and distilled to half bulk in a vacuum. Acidification with 3N-acetic acid gave hydrogen sulphide and a white precipitate which consisted, after crystallisation from acetone–ethanol (1 : 3; 40 ml. per g., with addition of carbon and kieselguhr), of felted needles of 3-anilino-5-isopropylidenehydrazino-1,2,4-triazole, m. p. and mixed m. p.[1] 228—230° (decomp.) (total, 0·385 g., 84%). After 15 minutes' refluxing, the yield of this triazole was 45%, one-third of the reactant being recovered from the mother-liquors.

(b) *Reaction with dimethylformamide*. A solution of the reactant (1·22 g., 0·004 mole) in dimethylformamide (8 ml.) was kept at 100° for 2 hr., and stirred into ice–water. The solidified oil was collected at 0° (filtrate F) and crystallised from acetone–ethanol, giving 3-anilino-5-isopropylidenehydrazino-1,2,4-triazole, m. p. and mixed m. p.[1] 228—230° (decomp.) (0·39 g., 42%). Filtrate F, on acidification with 3N-hydrochloric acid and treatment with 0·05M-picric acid (0·003 mole) gave *NN'*-di(isopropylideneamino)guanidine picrate, m. p. and mixed m. p.[1] 198—200° (decomp.) (from 85% ethanol) (0·35 g., 22%).

(c) *Reaction with hydrochloric acid*. A solution of the reactant (3·04 g., 0·01 mole) in ethanol

[20] G. I. Keim, R. A. Henry, and G. B. L. Smith, *J. Amer. Chem. Soc.*, 1950, **72**, 4944.

(5 ml.)–water (5 ml.)–3N-hydrochloric acid (5 ml., 0·015 mole) was refluxed for 8—10 min. (slight evolution of hydrogen sulphide), slowly distilled at atmospheric pressure to half-bulk, and diluted with acetone (3 ml.). The separated crystals, collected at 0° (filtrate G) and crystallised from acetone–ethanol–water (2 : 2 : 1, 30 ml. per g.), gave needles (total, 1·1 g., 65%) of 3-*isopropylidenehydrazino*-5-*mercapto*-1,2,4-*triazole*, m. p. 256—258° (decomp.) (Found: C, 35·4; H, 5·1; N, 41·5; S, 18·8. $C_5H_9N_5S$ requires C, 35·1; H, 5·3; N, 40·9; S, 18·7%).

Filtrate G was basified with concentrated ammonia; the solid which separated gradually gave, on crystallisation from acetone–ethanol (1 : 3), felted needles of 3-anilino-5-isopropylidenehydrazino-1,2,4-triazole, m. p. and mixed m. p.[1] 228—230° (decomp.) (0·18—0·28 g., 8—12%).

In some experiments, the distilled-down reaction mixture was set aside without addition of acetone; the separated product (0·6 g.) gave, on crystallisation from 50% ethanol, 3-hydrazino-5-mercapto-1,2,4-triazole as a crystalline powder (0·16—0·2 g., 12—15%), m. p. 247—248° (decomp., somewhat rate-dependent) (Found: C, 19·1; H, 3·9; N, 52·9; S, 24·4. Calc. for $C_2H_5N_5S$: C, 18·3; H, 3·8; N, 53·4; S, 24·4%). The m. p. is given variously between 240° and 248° in the literature.[9-12] The remainder of the product was isolated from the filtrate as the less soluble 3-isopropylidenehydrazino-compound (40—45%) as above.

3-(3,5-*Dimethylpyrazol*-1-*yl*)-5-*mercapto*-1,2,4-*triazole*.—A solution of 3-isopropylidenehydrazino-5-mercapto-1,2,4-triazole (0·86 g., 0·005 mole) in 3N-hydrochloric acid (6 ml., 0·018 mole) was distilled to small bulk (*ca.* 3 ml.) during 10 min., then diluted with ethanol (3 ml.). On being treated with acetylacetone (1·2 g., 0·012 mole), the liquid was filled with crystals. The mixture was heated to boiling, and the product collected at 0° [m. p. 293—294° (decomp.); 0·92 g., 95%]. Crystallisation from a large volume of ethanol gave opaque granular 3-(3,5-*dimethylpyrazol*-1-*yl*)-5-*mercapto*-1,2,4-*triazole*, m. p. 294—296° (decomp.) (Found: C, 43·5; H, 4·8; S, 16·9. $C_7H_9N_5S$ requires C, 43·1; H, 4·6; S, 16·4%).

3-(3,5-*Dimethylpyrazol*-1-*yl*)-5-*methylthio*-1,2,4-*triazole*.—A solution of the foregoing 5-thiol (0·39 g., 0·002 mole) in methanol (15 ml.) containing sodium (0·046 g., 0·002 g.-atom) was treated with iodomethane (2·8 g., 0·02 mole) and refluxed for 1 hr. The liquid was concentrated in a vacuum (to *ca.* 3 ml.) and stirred into ice–water (20 ml.). The precipitate yielded, after crystallisation from ethanol–light petroleum (1 : 1), hexagonal prisms of the *substituted* 1,2,4-*triazole*, m. p. 124—125° (0·28 g., 68%) (Found: C, 45·4; H, 4·9; N, 34·2; S, 15·6. $C_8H_{11}N_5S$ requires C, 45·9; H, 5·3; N, 33·5; S, 15·3%).

Interaction of the above reactants in the absence of sodium, during 30 min., followed by slow dilution of the concentrated liquid with ether, gave the corresponding *hydriodide*, forming white felted needles (from a little ethanol–ether), m. p. 224—226° (decomp., after darkening from 200°) (0·48 g., 72%) (Found: C, 29·2; H, 3·7; I, 38·3. $C_8H_{11}N_5S$,HI requires C, 28·5; H, 3·6; I, 37·7%).

3-(3,5-*Dimethylpyrazol*-1-*yl*)-1,2,4-*triazole*.—A stirred suspension of 3-(3,5-dimethylpyrazol-1-yl)-5-mercapto-1,2,4-triazole (0·39 g., 0·002 mole) in ethanol (6 ml.) at 45° was treated with 15% hydrogen peroxide (1·35 ml., 0·006 mole)–concentrated hydrochloric acid (0·6 ml., 0·006 mole) in one portion. The resulting clear liquid was kept at 50° for 15 min., basified (to pH 8) with concentrated ammonia, and allowed to evaporate partially at room temperature. The separated solid was rinsed with water (2 ml.) (filtrate N), and gave ivory-white prisms of 3-(3,5-dimethylpyrazol-1-yl)-1,2,4-triazole, m. p. 180—181° (from ethanol–light petroleum) (lit.,[15] 178—180°) (total, 0·18 g., 56%) (Found: C, 51·2; H, 5·5. Calc. for $C_7H_9N_5$: C, 51·5; H, 5·5%). Addition of 0·05M-picric acid (0·002 mole) to filtrate N precipitated hydrazine dipicrate, m. p. and mixed m. p.[2] 289—292° (decomp.) (0·15 g., 15%). Under more severe conditions (15 min. at 100°, followed by distillation of the liquid to 3 ml.), the above products were formed in 10 and 75% yield, respectively.

3,5-*Dimethyl*-1-[N-(*anilino*-S-*methylthioformyl*)*amidino*]*pyrazole*.—(a) *Preparation.* A solution of 3,5-dimethyl-1-[*N*-(anilinothioformyl)amidino]pyrazole[3] (10·92 g., 0·04 mole) in methanol (40 ml.)–methyl iodide (22·7 g., 0·16 mole) was refluxed for 1 hr., distilled to half bulk, and slowly diluted with ether (30 ml.). The resulting white solid (m. p. 91—94°; 14·9 g., 90%) gave, on crystallisation from methanol–ether (3 and 12 ml. per g.; recovery 60%), small needles of the *hydriodide*, m. p. 93—95° (Found: C, 39·7; H, 4·35; I, 31·2. $C_{14}H_{17}N_5S$,HI requires C, 40·5; H, 4·3; I, 30·6%).

(b) *Hydrazinolysis.* (i) A stirred solution of the foregoing hydriodide (2·08 g., 0·005 mole) in methanol (100 ml.)–water (5 ml.) was treated at room temperature during 1 hr. with hydrazine hydrate (0·25 g., 0·005 mole) dissolved in 50% aqueous methanol (25 ml.), and stirring at room

temperature was continued for 3 days. The liquid, which had partly evaporated, deposited white solid (m. p. 260—262°; 0·14 g., 11%), giving needles of 3-anilino-5-(3,5-dimethylpyrazol-1-yl)-1,2,4-triazole, m. p. and mixed [1] m. p. 262—264° (from ethanol) (Found: C, 61·25; H, 5·6. Calc. for $C_{13}H_{14}N_6$: C, 61·4; H, 5·5%).

(ii) Interaction of the above reactants in refluxing 60% aqueous methanol (30 ml.) during 3 hr., followed by vacuum-evaporation of the liquid to half bulk, gave the pyrazolyl-triazole, m. p. and mixed m. p. 262—264° (4%). The filtrate therefrom was diluted with ethanol (8 ml.) and treated with a solution of picric acid (1·15 g., 0·005 mole) in ethanol (10 ml.). The separated solid was collected (filtrate P) and gave, on crystallisation from 80% ethanol, prisms of 3-amino-5-anilino-1,2,4-triazole picrate, m. p. and mixed m. p.[2] 230—232° (decomp.) (0·4 g., 20%) (Found: C, 41·3; H, 2·9. Calc. for $C_8H_9N_5,C_6H_3N_3O_7$: C, 41·6; H, 3·0%).

Filtrate P deposited, on spontaneous partial evaporation, a further crop of picrate (1·2 g.) which consisted, after crystallisation from very little ethanol, of granules of 3,5-dimethylpyrazole picrate, m. p. 158—160° (lit.,[21] 166—167°) (0·73 g., 45%) (Found: C, 40·9; H, 3·5; N, 22·5. Calc. for $C_5H_8N_2,C_6H_3N_3O_7$: C, 40·6; H, 3·4; N, 21·5%).

1,3-*Di*(*isopropylideneamino*)-2-p-*toluidinothioformylguanidine*.—(*a*) A solution of *NN'*-di-(isopropylideneamino)guanidine (1·69 g., 0·01 mole) and *p*-tolyl isothiocyanate (1·49 g., 0·01 mole) in acetone (50 ml.) was refluxed for 1 hr. and then successively distilled to quarter, and very small bulk. The separated solid was collected at 0° (m. p. 128—132°; total, 2.30 g., 72%); it gave, on crystallisation from acetone–ethanol, needles of the *guanidine derivative*, m. p. 132—134° (Found: C, 56·6; H, 7·2; N, 26·0; S, 9·7. $C_{15}H_{22}N_6S$ requires C, 56·6; H, 6·9; N, 26·4; S, 10·1%), $\lambda_{min.}$ 230 mμ (log ε 4·29), $\lambda_{max.}$ 255 (4·46), $\lambda_{min.}$ 274 (4·27), $\lambda_{max.}$ 295 (4·39).

(*b*) Interaction of the reactants (0·01 mole each) in dimethylformamide (10 ml.) at 100° during 1·5 hr., addition of the liquid to ice–water, and trituration of the partially solidified oil with methanol (8 ml.) gave a white solid (2 g.). Fractional crystallisation from ethanol–acetone (8 : 1) gave 1,3-di(isopropylideneamino)-2-*p*-toluidinothioformylguanidine, m. p. and mixed m. p. [with (*a*)] 132—134° (total, 1·2 g., 38%), and the more soluble 3-isopropylidenehydrazino-5-*p*-toluidino-1,2,4-triazole, m. p. and mixed m. p.[1] 254—255° (decomp.) (from ethanol–acetone, 1 : 1) (total, 0·78 g., 32%).

2-p-*Bromoanilinothioformyl*-1,3-*di*(*isopropylideneamino*)*guanidine*.—The use of *p*-bromophenyl isothiocyanate (4·3 g., 0·02 mole) under the conditions of the foregoing experiment (*a*) gave a solid (m. p. 155—156°; total 5·0 g., 65%), which formed, after crystallisation from acetone (10 ml. per g., recovery 75%), needles of the *substituted guanidine*, m. p. 152—154° (Found: C, 43·5; H, 4·8; Br, 21·3; N, 22·1. $C_{14}H_{19}BrN_6S$ requires C, 43·9; H, 5·0; Br, 20·9; N, 21·9%), $\lambda_{min.}$ 225 mμ (log ε 4·26), $\lambda_{max.}$ 255 (4·52), $\lambda_{min.}$ 276 (4·25), $\lambda_{max.}$ 300 (4·40).

3-p-*Bromoanilino*-5-*isopropylidenehydrazino*-1,2,4-*triazole*.—*NN'*-Di(isopropylideneamino)-guanidine (0·85 g., 0·005 mole) and *p*-bromophenyl isothiocyanate (1·07 g., 0·005 mole) in dimethylformamide (5 ml.) were kept at 100° for 2 hr., and stirred into water (30 ml.). The resulting oil solidified on being stirred, was collected at 0° (filtrate H), digested with cold methanol (8 ml.), and the resulting crystalline solid collected at 0° [m. p. 239—242° (decomp.); 0·83 g., 55%]. Crystallisation from acetone–ethanol gave felted needles of 3-p-*bromoanilino*-5-*isopropylidenehydrazino*-1,2,4-*triazole*, m. p. 246—248° (decomp.) (Found: C, 43·2; H, 4·25; Br, 25·65; N, 27·45. $C_{11}H_{13}BrN_6$ requires C, 42·7; H, 4·2; Br, 25·9; N, 27·2%), $\lambda_{min.}$ 220 mμ (log ε 4·05), $\lambda_{max.}$ 265 (4·48).

Filtrate H, treated with 0·05M-picric acid (50 ml., 0·0025 mole), gave *NN'*-di(isopropylideneamino)guanidine picrate, m. p. and mixed m. p.[1] 199—200° (decomp.) (from ethanol) (0·52 g., 26%).

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