692. *Heterocyclic Compounds from Urea Derivatives. Part I. A New Synthesis of 3-Amino-5-mercapto(and -hydroxy)-1,2,4-triazoles.*

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Hydrazones derived from 1-alkyl(or -aryl)-3-(*N*-amino)amidinothioureas are synthesised by condensation of isothiocyanic esters with aminoguanidine in ketonic solvents containing an equivalent of sodium, or with the corresponding hydrazones in pyridine. Hydrolysis by strong acids cleaves and cyclises these compounds to 3-amino-5-mercapto-1,2,4-triazole in excellent yield, while alkaline hydrolysis causes ring closure to 3-amino-5-arylamino-1,2,4-triazoles, with elimination of hydrogen sulphide.

Analogous condensations involving isocyanic esters yield hydrazones derived from 1-substituted-3-(*N*-amino)amidinoureas, which afford 3-amino-5-hydroxy-1,2,4-triazole on acid hydrolysis.

AMINOGUANIDINE displays a great versatility in its chemical behaviour [1] which is partly due to the immediate proximity of the reactive amidino- and hydrazino-groups. For many years, its application in heterocyclic synthesis, notably in the triazole field, has proved very fruitful. In condensations of aminoguanidine with isocyanic and isothiocyanic esters both the amidino- [2] and the hydrazino-group [3] are potential centres for attack by these esters, and two series of compounds should be accessible, *viz.*, substituted *N*-amino-amidino-ureas or -thioureas (A; X = O or S) and *N*-amidino-*N'*-amino(thio)formylhydrazines (B; X = O or S).

(A) R·NH·CX·NH·C(:NH)·NH·NH_2 NH_2·C(:NH)·NH·NH·CX·NHR (B)

Fantl and Silbermann [4a] showed that aminoguanidine and phenyl isothiocyanate interact with simultaneous elimination of ammonia, 3-amino-5-mercapto-4-phenyl-1,2,4-triazole being formed directly. Further examples of this reaction, and of the isolation of intermediates of type B are described in recent patents.[4b] With allyl or phenyl thiocisoyanate, *N*-anilinoguanidine gave the expected amidinothiourea derivatives of type A; the allyl homologue was cyclised by alkalis to 5-allylamino-3-amino-1-phenyl-1,2,4-triazole.[4a] In Fromm's synthesis [5-9] of 1,2,4-triazoles by treatment of dithiobiurets [7-9] or their oxidation products, 3,5-di-imino-1,2,4-dithiazolidines (" thiurets ") [5,6,8,9] with hydrazine [7-9] or phenylhydrazine,[5,6] *N*-(aminoamidino)thioureas (of type A) are the precursors of the final heterocyclic products. However, cyclisation of these intermediates occurs very readily under the conditions of this synthesis,[8,9] so that they were isolated only in a few cases,[5,6,9] and sometimes merely as by-product.[8] Further, since possible alternative formulations of certain products remain undecided [5,6,8] and experimental results are in fact not always reproducible [9] (see also below), the reaction is not a reliable route to *N*-(aminoamidino)-thioureas (A). *N*-Phenylamidino-*N'*-thioformamidohydrazine, a representative of type B, has been obtained by condensing thiosemicarbazide and phenylcyanamide: the methyl ether of its thiol form was readily cyclised, with loss of methanethiol to 3,5-diamino-4-phenyl-1,2,4-triazole.[10]

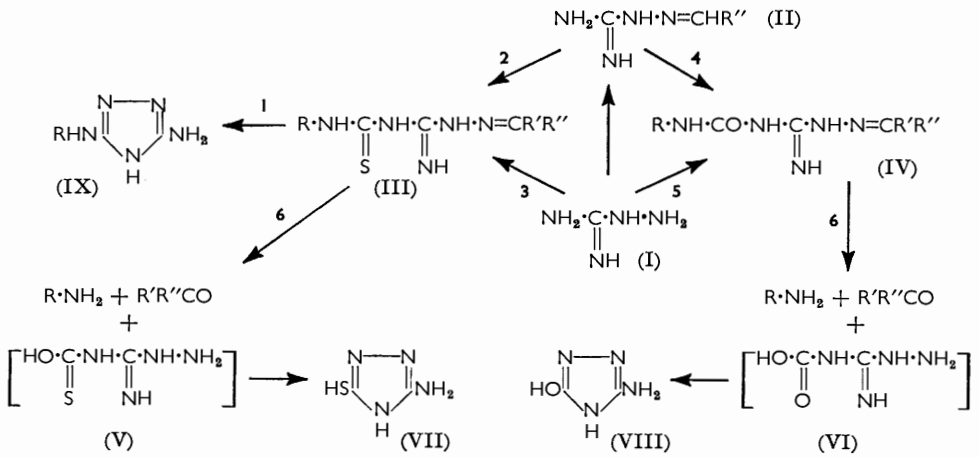
In view of the value of compounds of structure (A) and (B) in heterocyclic syntheses,

[1] Lieber and Smith, *Chem. Rev.*, 1939, **25**, 213.
[2] Pinner, *Ber.*, 1889, **22**, 1600, 1609; Kurzer and Tertiuk, *J.*, 1959, 2851; Slotta, Tschesche, and Drechsler, *Ber.*, 1930, **63**, 208; Kurzer, *J.*, 1955, 2288; 1956, 2345.
[3] Freund, *Ber.*, 1896, **29**, 2510; Arndt, Milde, and Tschens her, *Ber.*, 1922, **55**, 341.
[4a] Fantl and Silbermann, *Annalen*, 1928, **467**, 283.
[4b] Fry and Lambie, B.P. 741,228; 741,280.
[5] Fromm and Vetter, *Annalen*, 1907, **356**, 190.
[6] Fromm and Weller, *Annalen*, 1908, **361**, 316.
[7] Fromm, *Ber.*, 1921, **54**, 2840; see also Arndt, *Ber.*, 1922, **55**, 12.
[8] Fromm, Kayser, Briegleb, and Föhrenbach, *Annalen*, 1922, **426**, 313, 330.
[9] Fromm, Brück, Runkel, and Mayer, *Annalen*, 1924, **437**, 106, 112.
[10] Arndt and Tschenscher, *Ber.*, 1923, **56**, 1984.

an examination of their formation from readily available aminoguanidine (I), and of some of their properties has now been undertaken. In the present work, the site of condensation of isothiocyanic esters has been restricted to the amidino-nitrogen of the aminoguanidine structure by blocking the hydrazine group. However, the hydrazones (III, IV) were not converted into the parent hydrazines (A), since their liberation by hydrolysis was accompanied by immediate cyclisation to triazoles.

Isothiocyanate and isocyanate esters reacted readily with amidinohydrazones, generally affording excellent yields of 1-substituted 3-(aminoamidino)-thioureas or -ureas (in the form of their hydrazones, III, IV). Depending on the nature of the carbonyl compound used in producing the hydrazone, and the ease with which this (*e.g.*, II) was isolated, the reaction was carried out by one of two methods. Thus, benzylideneaminoguanidine (II; R'' = Ph), separately synthesised from its constituents,[11] was directly condensed with iso(thio)-cyanate esters in hot pyridine. In the alternative procedure, intermediates (II) that were not readily isolated were employed without difficulty *in situ*. Aminoguanidine was liberated by the addition of one of its salts to an excess of the appropriate ketone (acting simultaneously as solvent and reactant), in which an equivalent of sodium had previously been dissolved. Subsequent addition of the iso(thio)cyanate ester afforded excellent yields of the required products (III, IV). The action of isothiocyanic and isocyanic esters was entirely analogous, except that, as expected, the latter reacted more vigorously. The preparation of one of the compounds now synthesised (III; R = R'' = Ph, R' = H) has previously been claimed by Fromm and his co-workers,[8] who condensed benzaldehyde with 1-(aminoamidino)-3-phenylthiourea, alleged to be one of the products of the interaction of hydrazine and 3-imino-5-phenylimino-1,2,4-dithiazolidine; in later work,[9] however, they were unable to repeat the preparation of the parent hydrazine, $Ph{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}C(:NH){\cdot}NH{\cdot}NH_2$. Since their benzylidene derivative differs from this compound (III; R = R'' = Ph, R' = H) prepared by the present direct synthesis, we think that their product was not correctly formulated.

In accordance with the pronounced basic nature of aminoguanidines, hydrazones derived from 1-substituted 3-(aminoamidino)-ureas (IV) and -thioureas (III) are monoacid bases, forming stable salts with acids. Their hydrochlorides, for example, were useful in



Reagents: 1, OH^-. 2, R·NCS. 3, R·NCS–R'R''CO. 4, R·NCO. 5, R·NCO–R'R''CO. 6, H^+.

isolating members of this series when crystallisation of the parent base was difficult, while the sparingly soluble picrates were suitable for characterisation purposes. With acetic acid, 1-phenyl-3-(isopropylideneaminoamidino)urea (IV; R = Ph, R' = R'' = Me)

[11] Thiele, *Annalen*, 1892, **270**, 1.

unexpectedly formed a hemiacetate, possibly for crystallographic reasons. Members of the amidinothiourea series (III) rapidly precipitated lead sulphide from hot alkaline sodium plumbite.

The hydrazones derived from 1-substituted 3-(aminoamidino)thioureas (III) were cleaved remarkably rapidly by dilute hydrochloric acid under very mild conditions, affording excellent yields of 3-amino-5-mercapto-1,2,4-triazole (VII), together with the appropriate amine and aldehyde or ketone. 3-(Isopropylideneaminoamidino)-1-phenylthiourea (III; R = Ph, R′ = R″ = Me), for example, gave the triazole (VII) smoothly in 75—85% yield, while aniline and acetone were isolated in the form of suitable derivatives (80 and 85%, respectively); in a side-reaction, small quantities (up to 10%) of 3-amino-5-anilino-1,2,4-triazole (IX; R = Ph) were formed, hydrogen sulphide being evolved. The more usual type of cyclisation, in which the basic skeleton of the precursor (III) remains intact, would produce, with loss of hydrogen sulphide or ammonia from potential mercapto- and amino-groups (in III), 3-amino-5-alkyl(or -aryl)amino-1,2,4-triazoles or -thiadiazoles, respectively. The present reaction, depending on the exceptionally ready removal of amine from the thioureido-grouping (in III) is therefore due to the unusually easy fission, under these conditions, of the N–C link of the terminal thioamide group in this particular structural environment. A possible mechanism of this general reaction involves preliminary hydrolytic removal of the carbonyl and amine components of the reactant (III), followed by immediate cyclisation of the intermediate hypothetical thiocarbamic acid (V), with loss of water, to the triazole (VII).

Under the influence of a weak acid, the direct cyclisation of hydrazones (III) to 3-amino-5-arylamino-1,2,4-triazoles (IX) became the predominant reaction: thus, 3-(isopropylideneaminoamidino)-1-phenylthiourea (III; R = Ph, R′ = R″ = Me) was slowly converted, by boiling acetic acid, into 3-amino-5-anilino-1,2,4-triazole (IX; R = Ph), only small quantities of the 3-amino-5-mercapto-derivative (VII) being formed. Boiling alkali similarly removed the carbonyl component and abstracted the elements of hydrogen sulphide from (III), affording good yields of the diaminotriazoles (IX) exclusively. The use of alkali in analogous ring-closures to 1,2,4-triazoles and 1,3,4-thiadiazoles is well established.[3,4,12]

The hydrazones of the amidinourea series (IV) were more stable than their sulphur analogues (III). They were hydrolysed by hydrochloric acid, though much more slowly, into 3-amino-5-hydroxy-1,2,4-triazole (VIII), amine and ketone, presumably by a mechanism analogous to that operating in the thiourea series. 3-(Isopropylideneaminoamidino)-1-phenylurea (IV; R = Ph, R′ = R″ = Me), for example, was largely recovered after treatment that completely cyclised the corresponding thiourea derivative (III); but it afforded the aminohydroxytriazole (VIII) on more prolonged hydrolysis. Because of the consequent increased opportunity for side-reactions, yields of triazole were somewhat lower in the urea than in the thiourea series.

As expected, cyclisation of the amidinohydrazones (IV) to substituted 3,5-diamino-1,2,4-triazoles (IX), involving elimination of water, did not occur under the influence of reagents that remove hydrogen sulphide from the thio-analogues (III). Thus, 3-(isopropylideneaminoamidino)-1-phenylurea (IV; R = Ph, R′ = R″ = Me) was recovered as the hemiacetate after being boiled with acetic acid, and resisted the action of sodium hydroxide, except that long treatment caused extensive decomposition.

The present syntheses of 3-amino-5-mercapto-1,2,4-triazole (VII) and its hydroxy-analogue (VIII) appear to be of preparative value, affording the heterocyclic compounds from readily available starting materials in a simple two-stage process in approximately 55 and 45% overall yield, respectively. In particular, the method is an improvement over existing routes to 3-amino-5-hydroxy-1,2,4-triazole, which has previously only been obtainable by the difficultly controlled interaction, at 150—210°, between dicyandiamide

[12] Arndt and Milde, *Ber.*, 1921, **54**, 2089, 2101.

and hydrazine hydrochlorides,[13] or urea and aminoguanidine hydrochloride,[13] or from the less accessible 3-hydroxy-5-nitro-1,2,4-triazole.[14]

(X) R·NH·CX·NH·CO·NH·N=CR′R″ R·NH·CX·NH·CS·NH·N=CR′R″ (XI)

On the other hand, the synthesis apparently cannot be extended to the preparation of the 3-hydroxy-5-mercapto-, 3,5-dihydroxy-, or 3,5-dimercapto-analogues, since it is doubtful if the required precursors (X and XI; X = O or S) are directly obtainable from semicarbazide and thiosemicarbazide by the present route. Acetone semicarbazone, for example, failed to react with phenyl isothiocyanate under the usual conditions. This is in agreement with the general experience [15] that isocyanic, and particularly isothiocyanic, esters do not condense with ureides and thioureides except under severe conditions, the course of the reaction then being erratic. In contrast, iso(thio)cyanates are readily added at the hydrazine residue of (thio)semicarbazide, and the cyclisation of such products to triazoles is well established.[3]

Experimental

Aqueous picric acid saturated at room temperature (approx. 0·05M) was used for preparing picrates unless otherwise stated. Light petroleum was of boiling range 60—80°. Ultraviolet absorption measurements were made with a " Unicam S.P. 500 " spectrophotometer and 0·00005M-ethanolic solutions.

Amidinothiourea Series

3-(*Isopropylideneaminoamidino*)-1-*phenylthiourea*.—To the deep brownish-red turbid liquid obtained on addition of sodium (2·3 g., 0·1 g.-atom) to dry acetone (150 ml.), finely powdered aminoguanidine sulphate monohydrate (15·8 g., 0·12 mole) was added. The stirred suspension was refluxed during 30 min. (colour change to pale brown), then treated with phenyl isothiocyanate (10·8 g., 0·08 mole), and stirring and refluxing were continued for another 30 min. (colour change to yellow). The cooled mixture was stirred into ice-water (1 l.), and the solidified oil collected after storage at 0°, rinsed with water, drained, stirred to a paste with ethanol (15—20 ml.), filtered off at 0°, and washed with a little ether. The resulting pale yellow crystals [m. p. 158—163° (decomp.); 12·95—14·4 g., 65—72%] were recrystallised by dissolution in acetone (12 ml. per g.), followed by vacuum-evaporation of the filtered liquid to half-bulk, and dilution with an equal volume of ethanol (recovery approx. 60% per crystallisation), thus giving prisms of 3-(*isopropylideneaminoamidino*)-1-*phenylthiourea*, m. p. 167—169° (decomp., subject somewhat to the rate of heating) [Found: C, 53·0; H, 5·8; N, 28·2; S, 13·0%; *M* (cryoscopically, in thymol), 230. $C_{11}H_{15}N_5S$ requires C, 53·0; H, 6·0; N, 28·1; S, 12·85%; *M*, 249]. The compound gave lead sulphide rapidly on being heated with alkaline sodium plumbite.

Equimolar proportions (0·001 mole) of the product and picric acid in ethanol (15 ml.) gave the *picrate* (85%), pale yellow needles, m. p. 170—172° (decomp., somewhat dependent on the rate of heating) after crystallisation from aqueous ethanol (90%) (Found: C, 42·3; H, 3·55. $C_{11}H_{15}N_5S,C_6H_3N_3O_7$ requires C, 42·7; H, 3·8%).

The use of semicarbazide hydrochloride (0·1 mole) in the above reaction, and refluxing during 3 hr., gave a liquid which deposited crystals (m. p. 184—186°; 70%) on storage. After crystallisation from water, these consisted of acetone semicarbazone, m. p. 186—188°.

3-(*Isopropylideneaminoamidino*)-1-*phenylthiourea*.—(a) *Hydrolysis by hydrochloric acid.* A suspension of the reactant (5·0 g., 0·02 mole) in N-hydrochloric acid (30 ml., 0·03 mole) was boiled during ~5 min., the distillate being collected in a solution of 2,4-dinitrophenylhydrazine (4·4 g., 0·022 mole) in concentrated sulphuric acid (10 ml.)–ethanol (120 ml.) (product, see D). The suspended reactant first softened to a colourless oil at 75—85° and then dissolved rapidly, while a little hydrogen sulphide was evolved. On cooling, the liquid deposited white crystals,

[13] Pellizzari and Roncagliolo, *Gazzetta*, 1901, **31**, I, 487.
[14] Manchot and Noll, *Annalen*, 1905, **343**, 26.
[15] Kurzer, *Chem. Rev.*, 1956, **56**, 124, 133, 134, 145, 158.

which were collected after 4 hr. at 0° (filtrate F), rinsed with a little water (m. p. 304—306°; 1·75—2·0 g., 75—85%), and recrystallised from ethanol–water (3 : 1; 50 ml. per g., recovery approx. 50%), giving white opaque prisms of 3-amino-5-mercapto-1,2,4-triazole, m. p. 300—302° (decomp., subject somewhat to the rate of heating) (Found: C, 20·6; H, 3·5; N, 48·9; S, 27·5. Calc. for $C_2H_4N_4S$: C, 20·7; H, 3·45; N, 48·3; S, 27·6%), $\lambda_{min.}$ 232 (log ε 3·50), $\lambda_{max.}$ 263 mμ (log ε 4·12).

Filtrate F was basified with 40% aqueous sodium hydroxide and steam-distilled during 10—15 min. (residual liquid : L), and the distillate was treated with 40% sodium hydroxide (20 ml., 0·2 mole) and benzoyl chloride (7·0 g., 0·05 mole). The precipitated benzanilide (3·15 g., 80%) had m. p. and mixed m. p. 160—162° (from ethanol).

The residual liquid L was neutralised with hydrochloric acid, treated with 0·05M-aqueous picric acid (100 ml., 0·005 mole) and the resulting yellow precipitate (0·8 g., 10%) crystallised from 90% ethanol, yielding yellow needles of 3-*amino*-5-*anilino*-1,2,4-*triazole picrate*, m. p. and mixed m. p. (see below) 230—232° (decomp.) (Found: C, 42·1; H, 3·4. $C_8H_9N_5,C_6H_3N_3O_7$ requires C, 41·6; H, 3·0%).

Alternatively, filtrate F was evaporated in a vacuum (to 4—5 ml.) and the separated aniline hydrochloride [1·55 g., 60%; m. p. and mixed m. p. 192—197° (decomp.), after crystallisation from ethanol–ether] filtered off at 0°. The filtrate therefrom gave 3-amino-5-anilino-1,2,4-triazole picrate, m. p. 229—231° (decomp.), as described in the foregoing paragraph.

Product D, obtained after dilution of the distillate with water (120 ml.), was acetone 2,4-dinitrophenylhydrazone (4·10 g., 85%), m. p. and mixed m. p. 124—126°.

In experiments having only the preparation of 3-amino-5-mercapto-1,2,4-triazole as objective, the reactant (0·02 mole) was dissolved in, and boiled during 1 min. with, N-hydrochloric acid (0·03 mole). The hot (vacuum-filtered) liquid deposited the product of satisfactory purity on cooling (75—80%).

(b) *Alkaline hydrolysis.* The reactant (2·49 g., 0·01 mole) dissolved gradually when refluxed in 1·5N-aqueous sodium hydroxide (30 ml.) during 15 min. The filtered liquid remained clear when cooled to 0°; acidification by 2N-acetic acid yielded hydrogen sulphide and a crystalline precipitate (m. p. 156—158°; 1·49 g., 85%) which consisted, after crystallisation from ethanol–light petroleum, of prismatic needles of 3-amino-5-anilino-1,2,4-triazole, m. p. and mixed m. p. 160—162° with authentic material [16] (from *S*-benzyl-*N*-cyano-*N'*-phenylisothiourea and hydrazine) (Found: C, 55·4; H, 5·5; N, 40·8. Calc. for $C_8H_9N_5$: C, 54·9; H, 5·1; N, 40·0%).

The *picrate* (85%, from equimolar proportions of the reactants, in ethanol) formed yellow plates, m. p. 231—233° (decomp.) (from 90% ethanol) (Found: C, 42·0; H, 3·1. $C_8H_9N_5,C_6H_3N_3O_7$ requires C, 41·6; H, 3·0%).

(c) *Hydrolysis by acetic acid.* The reactant (2·49 g., 0·01 mole) dissolved within 15 min. when refluxed in 2N-acetic acid (25 ml., 0·05 mole), hydrogen sulphide being evolved. The solution was refluxed during a further 30 min., cooled, and basified with concentrated aqueous ammonia. The separated 3-amino-5-anilino-1,2,4-triazole (70%), collected at 0°, had m. p. and mixed m. p.[16] 159—161° (from ethanol). The aqueous filtrate therefrom, on spontaneous partial evaporation to small bulk, was neutral and deposited 3-amino-5-mercapto-1,2,4-triazole, m. p. 302—304° (decomp.) (15%).

Alternatively, the clear hydrolysate, when cooled to 0°, deposited needles, which were collected (aqueous filtrate : F) and crystallised from a little ethanol–light petroleum. They were 3-*amino*-5-*anilino*-1,2,4-*triazole diacetate*, m. p. 122—125° (decomp.) (Found: C, 49·2; H, 5·8; N, 23·5. $C_8H_9N_5,2C_2H_4O_2$ requires C, 48·8; H, 5·8; N, 23·7%). The diacetate was also obtained (60%) by dissolving the authentic base [16] (0·001 mole) in hot 2N-acetic acid (0·006 mole); it showed no m. p. depression with the above material. The aqueous filtrate F deposited 3-amino-5-mercapto-1,2,4-triazole, m. p. 302—304° (12—15%), on spontaneous partial evaporation.

3-*Amino*-5-*benzylmercapto*-1,2,4-*triazole*.—A solution of 3-amino-5-mercapto-1,2,4-triazole (1·16 g., 0·01 mole) in N-sodium hydroxide (10 ml.) was treated with benzyl chloride (1·52 g., 0·012 mole), diluted with ethanol (20 ml.), and kept at 60—70° during 10 min. The solution was evaporated to a third of its bulk in a vacuum at 50—60°, then diluted with water (20 ml.), and the precipitated solidified oil collected at 0°. Crystallisation from benzene–ethanol (20 : 1; 20 ml.) gave white prisms of the sulphide, m. p. 109—111° (1·48 g., 72%). The analytical specimen was recrystallised from chloroform–light petroleum (Found: C, 52·7;

[16] Fromm and Kapeller-Adler, *Annalen*, 1928, **467**, 240, 266.

H, 5·0; N, 27·5. Calc. for $C_9H_{10}N_4S$: C, 52·4; H, 4·85; N, 27·2%). Fromm and Kapeller-Adler [16] who prepared this compound from the substituted cyanamide $(Ph{\cdot}CH_2{\cdot}S)_2C{=}N{\cdot}CN$ and hydrazine give m. p. 109°.

3-*Amino*-5-p-*chlorobenzylthio*-1,2,4-*triazole* was similarly prepared by using 4-chlorobenzyl chloride (1·93 g., 0·012 mole). Crystallisation from ethanol–light petroleum (1 : 3) gave plates, m. p. 142—144° (1·95 g., 82%) (Found: C, 45·1; H, 3·4; N, 23·6; Cl, 14·5. $C_9H_9ClN_4S$ requires C, 44·9; H, 3·7; N, 23·3; Cl, 14·75%).

Di-(3-*amino*-1,2,4-*triazol*-5-*yl*) *Disulphide*.—A solution of 3-amino-5-mercapto-1,2,4-triazole (0·58 g., 0·005 mole) in N-sodium hydroxide (5 ml., 0·005 mole) was treated with 0·2M-aqueous bromine (12·5 ml., 0·0025 mole), which was decolorised immediately. The pale-brown product which crystallised was collected at 0° (m. p. 228—230°; 0·37 g., 65%) and gave, after crystallisation from water (carbon), colourless needles of the disulphide, m. p. 232—236° (decomp., somewhat subject to the rate of heating), $\lambda_{min.}$ 244 mμ (log ε 3,37), shallow $\lambda_{max.}$ 270 mμ (log ε 3·46). Arndt and Milde [12] give m. p. 240° (decomp.).

1-(*Isopropylideneaminoamidino*)-3-p-*tolylthiourea*.—Interaction of the reactants [except for the use of *p*-tolyl isothiocyanate (11·9 g., 0·08 mole)] and isolation of the product as described for the phenyl homologue, gave a solid product [m. p. 152—154° (decomp.); 13·5 g., 64%] which crystallised from ethanol (12 ml. per g.) as plates of the substituted *thiourea*, m. p. 160—162° (decomp., subject somewhat to the rate of heating) (Found: C, 54·3; H, 6·2; N, 27·6. $C_{12}H_{17}N_5S$ requires C, 54·75; H, 6·5; N, 26·6%). It gave a *picrate*, needles (from 1 : 3 aqueous ethanol), m. p. 175—177° (decomp.) (Found: C, 44·5; H, 3·7. $C_{12}H_{17}N_5S,C_6H_3N_3O_7$ requires C, 43·9; H, 4·1%)

This hydrazone (2·63 g., 0·01 mole) in N-hydrochloric acid (12 ml.) (3 min. at 95°) gave (cf. above) 3-amino-5-mercapto-1,2,4-triazole (84%) (Found: C, 21·1; H, 3·5%), *p*-toluidine hydrochloride (68%), acetone 2,4-dinitrophenylhydrazone, and 3-amino-5-anilino-1,2,4-triazole picrate (3%).

In boiling 1·5N-sodium hydroxide (30 ml.) during 20 min. it (0·01 mole) gave 3-amino-5-*p*-toluidino-1,2,4-triazole (1·70 g., 90%), m. p. 179—180° (needles, from water). Fromm *et al.*[9] give m. p. 178—180°.

1-(*Isobutylideneaminoamidino*)-3-*phenylthiourea*.—Sodium (1·15 g., 0·05 g.-atom) was introduced into ethyl methyl ketone (80 ml.), and the resulting brown suspension treated with aminoguanidine sulphate monohydrate (7·9 g., 0·06 mole) and refluxed with stirring during 20 min. After addition of phenyl isothiocyanate (5·4 g., 0·04 mole), refluxing was continued during 45 min. The mixture was stirred into water (500 ml.), and the separated *thiourea* collected, stirred with ethanol (12—15 ml.) (yield, 6·8 g., 65%) and crystallised from ethyl methyl ketone (20 ml.) and then from ethanol (10 ml. per g.) as plates, m. p. 153—155° (decomp.) (Found: C, 55·2; H, 6·6; N, 26·85; S, 12·0. $C_{12}H_{17}N_5S$ requires C, 54·75; H, 6·5; N, 26·6; S, 12·2%). Its *picrate* (92%) formed yellow prisms, m. p. 148—150° (decomp.), from much ethanol (Found: C, 43·7; H, 4·0. $C_{12}H_{17}N_5S,C_6H_3N_3O_7$ requires C, 43·9; H, 4·1%). In N-hydrochloric acid it gave 3-amino-5-mercapto-1,2,4-triazole (78%), benzanilide (73%), and ethyl methyl ketone 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 111—113° (from ethanol).

1-(*Benzylideneaminoamidino*)-3-*phenylthiourea*.—A solution of (benzylideneamino)guanidine [11] (1·62 g., 0·01 mole) in pyridine (6 ml.) was treated with phenyl isothiocyanate (1·35 g., 0·01 mole), kept at 100° during 20 min., and stirred into ice-water containing concentrated hydrochloric acid (6 ml.). The precipitate was collected, stirred with warm ethanol (10 ml.), filtered off (2·38 g., 80%), and crystallised from boiling ethanol (30 ml. per g., recovery 60%), giving off-white prisms of 1-(*benzylideneaminoamidino*)-3-*phenylthiourea*, m. p. 168—170° (sintering at 166°) (Found: C, 60·4; H, 5·0; N, 23·1; S, 11·3. $C_{15}H_{15}N_5S$ requires C, 60·6; H, 5·05; N, 23·6; S, 10·8%). Fromm *et al.*[8] gave m. p. 223°. We obtained a *picrate*, m. p. 170—172° (decomp.) (from aqueous ethanol) (Found: C, 48·2; H, 3·5. $C_{15}H_{15}N_5S,C_6H_3N_3O_7$ requires C, 47·9; H, 3·4%).

Hydrolysis of the product (0·0033 mole) by N-hydrochloric acid (6 ml.) yielded 3-amino-5-mercapto-1,2,4-triazole (66%), aniline (as benzanilide, 64%), and benzaldehyde (as 2,4-dinitrophenylhydrazone, 78%).

1-(*Benzylideneaminoamidino*)-3-*methylthiourea*.—Interaction of (benzylideneamino)guanidine [11] (8·1 g., 0·05 mole) and methyl isothiocyanate (3·65 g., 0·05 mole) in pyridine (25 ml.) at 100° during 30 min., and addition of the liquid to ice and hydrochloric acid gave a sticky orange

oil. The supernatant liquid was decanted, and the oil was washed with water and stirred with 3N-ethanolic hydrochloric acid (20 ml., 0·06 mole). The resulting crystalline suspension was set aside at 0°, and the solid then collected, rinsed with ether, and twice crystallised from boiling ethanol (4 ml. per g.). The *hydrochloride* thus obtained formed prisms, m. p. 180—183° (decomp.) (5·7 g., 42%) (Found: C, 43·5; H, 5·3; N, 25·45; Cl, 12·6. $C_{10}H_{13}N_5S$,HCl requires C, 44·2; H, 5·2; N, 25·8; Cl, 13·1%). The *picrate*, crystallised from a large volume of 50% aqueous ethanol, had m. p. 191—193° (decomp.; sintering at 188°) (Found: C, 41·1; H, 3·5. $C_{10}H_{13}N_5S,C_6H_3N_3O_7$ requires C, 41·4; H, 3·45%).

The hydrochloride (0·01 mole) in boiling N-hydrochloric acid (15 ml.) gave 3-amino-5-mercapto-1,2,4-triazole (87%), methylamine (as picrate, 78%), and benzaldehyde (as 2,4-dinitrophenylhydrazone, 92%).

Amidinourea Series

1-(*Isopropylideneaminoamidino*)-3-*phenylurea*.—To the suspension obtained on introducing sodium (4·6 g., 0·2 g.-atom) into acetone (320 ml.), aminoguanidine sulphate monohydrate (29·0 g., 0·22 mole) was added, and the stirred mixture refluxed during 30 min. The source of heat was withdrawn, phenyl isocyanate (19·0 g., 0·16 mole) added dropwise during 15 min., refluxing continued during 10 min., and the mixture added to ice-water (1·5 l.). The precipitated oil solidified when stirred for 1 hr., was collected, and immediately dissolved in hot benzene (20—25 ml.). The deep green warm liquid, which was quickly separated from droplets of water, deposited crystals on storage; these were collected at 0° and rinsed with benzene–light petroleum, then light petroleum (m. p. 120—124°) (yield, 22—24 g., 59—65%). Vacuum-evaporation of the filtrates to small bulk gave more material (1—3 g.). Crystallisation from ethanol–light petroleum (3 and 10 ml. per g., recovery approx. 75%) gave needles of 1-(*isopropylideneaminoamidino*)-3-*phenylurea*, m. p. 124—126° (Found: C, 56·7; H, 6·5; N, 29·85. $C_{11}H_{15}N_5O$ requires C, 56·65; H, 6·4; N, 30·0%). Specimens crystallised from benzene occluded some of this solvent, giving high carbon values on analysis.

The *hydrochloride* was formed (85%) on addition to the reactant (0·23 g., 0·001 mole) in ethanol (3 ml.) of 3N-ethanolic hydrochloric acid (1 ml., 0·003 mole), followed by dilution with ether (10 ml.). Crystallisation from ethanol–light petroleum gave needles, m. p. 191—192° (decomp.) (Found: C, 48·8; H, 5·8; Cl, 12·8. $C_{11}H_{15}N_5O$,HCl requires C, 49·0; H, 5·9; Cl, 13·2%). Specimens crystallised from ethanol–ether sintered at 124—128° before melting at 190—192°, probably owing to solvation. The *picrate* had m. p. 210—212° (decomp.) (from large volumes of ethanol–water) (Found: C, 44·3; H, 3·7. $C_{11}H_{15}N_5O,C_6H_3N_3O_7$ requires C, 44·2; H, 3·9%).

A solution of the product (2·33 g., 0·01 mole) in boiling 2N-acetic acid (25 ml., 0·05 mole) deposited crystals on cooling. After being collected at 0° (m. p. 140—144°; 1·9 g., 72%) and crystallised from ethanol, they consisted of white opaque prisms of the *hemiacetate*, m. p. 143—145° (Found: C, 54·6; H, 6·7; N, 26·4. $C_{11}H_{15}N_5O,\frac{1}{2}C_2H_4O_2$ requires C, 54·75; H, 6·5; N, 26·6%). The same product resulted (40—60%) after 30 minutes' boiling of the above solution. For characterisation it was converted into the picrate, m. p. and mixed m. p. 210—213° (decomp.) (Found: C, 44·8; H, 4·2%), and into the base, m. p. and mixed m. p. 123—125° (yield 50%).

Acid Hydrolysis of 1-(*Isopropylideneaminoamidino*)-3-*phenylurea*.—(*a*) The reactant (4·66 g., 0·02 mole) dissolved on being heated with 2N-hydrochloric acid (18 ml., 0·036 mole). The solution was distilled to half-volume, diluted with water (10 ml.), and again distilled to small volume (12—15 ml.; residual liquid, R). The distillate, collected in a solution of 2,4-dinitrophenylhydrazine in concentrated sulphuric acid and ethanol, gave acetone 2,4-dinitrophenylhydrazone, m. p. 124—126° (4·33 g., 91%). The liquid R, on being basified strongly and steam-distilled gave aniline (isolated as benzanilide, 70%).

(*b*) A solution of the reactant (0·015 mole) in 2N-hydrochloric acid (0·025 mole) was refluxed during 30 min., basified with N-aqueous sodium hydroxide (0·03 mole), and distilled to 25 ml. Acidification and further reduction in volume (to 20 ml.) gave a residual liquid which, after rapid vacuum-filtration, deposited needles, which were collected at 0°. Spontaneous evaporation of the combined filtrates and washing liquids afforded a further quantity of crude product, m. p. 280—285° (decomp.) (total, 1·10 g., 73%). Crystallisation from water (10 ml. per g.) gave prismatic needles of 3-amino-5-hydroxy-1,2,4-triazole, m. p. and mixed m. p. 286—290° (decomp.), which became pinkish in air (Found: C, 24·5; H, 3·6; N, 55·3. Calc. for $C_2H_4N_4O$: C, 24·0; H, 4·0; N, 56·0%). Its ultraviolet absorption spectrum was an almost

straight line of negative slope, which is defined approximately by the following points: λ, 215 mμ (log ε 3·75); 230 mμ (3·25); 240 mμ (2·65); 260 mμ (1·05). Authentic material for comparison was obtained in very low yield by the fusion of aminoguanidine hydrochloride and urea by the method of Pellizzari and Roncagliolo.[13]

(*c*) Dissolution of the urea (0·005 mole) during 3 min. with hot 2N-hydrochloric acid (0·0075 mole) gave a product which consisted, after crystallisation, of the hydrochloride of the starting material, m. p. 191—192° (decomp.) (50%).

A boiling suspension of the triazole (0·25 g., 0·0025 mole) in ethanol (25 ml.), treated with picric acid (0·57 g., 0·0025 mole) dissolved in hot ethanol (6 ml.), gave a clear liquid within 10 min. The filtered solution slowly deposited solid which consisted, after crystallisation from ethanol (50 ml. per g.), of yellow plates (78%) of the *picrate*, m. p. and mixed m. p. (with a specimen similarly prepared from authentic [13] 3-amino-5-hydroxy-1,2,4-triazole) 210—212° (decomp.) (Found: C, 29·8; H, 2·4. $C_2H_4N_4O,C_6H_3N_3O_7$ requires C, 29·2; H, 2·1%). The m. p. of 3-amino-5-hydroxy-1,2,4-triazole picrate prepared from 3-hydroxy-5-nitro-1,2,4-triazole [14] has been given as 204°; the specimen was described as easily soluble in ethanol.

1-(4-*Biphenylyl*)-3-(*isopropylideneaminoamidino*)*urea*.—A stirred suspension of sodium (0·575 g., 0·025 g.-atom) in acetone (40 ml.) was refluxed with aminoguanidine sulphate monohydrate (3·95 g., 0·03 mole) during 30 min., then treated with 4-biphenylyl isocyanate (3·9 g., 0·02 mole) during 1 min., and refluxing was continued during 30 min. The mixture was stirred into ice-water, and the resulting solidified oil ground with 80% ethanol (10 ml.), collected (6 g.) and crystallised by dissolution in acetone, and dilution of the filtered partly evaporated solution with ethanol. The product thus obtained (m. p. 168—172°; 4·0 g., 65%) gave, on further crystallisation from ethanol (20 ml. per g.), 1-(4-*biphenylyl*)-3-(*isopropylideneaminoamidino*)*urea*, m. p. 170—172° (decomp.) (Found: C, 66·6; H, 6·2; N, 23·0. $C_{17}H_{19}N_5O$ requires C, 66·0; H, 6·15; N, 22·65%). The *picrate* (95%) formed yellow prisms, m. p. 216—219° (decomp.), from large volumes of ethanol–water (Found: C, 51·35; H, 3·9. $C_{17}H_{19}N_5O,C_6H_3N_3O_7$ requires C, 51·3; H, 4·1%).

1-(*Benzylideneaminoamidino*)-3-*phenylurea*.—A solution of (benzylideneamino)guanidine [11] (1·62 g., 0·01 mole) in pyridine (6 ml.) was treated dropwise with phenyl isocyanate (1·19 g., 0·01 mole), and the resulting warm (40—50°) liquid set aside at room temperature during 30 min., then stirred into ice and concentrated hydrochloric acid. The precipitated oil solidified and was rinsed with water and crystallised from boiling ethanol (15 ml.), yielding prisms of the substituted *amidinourea*, m. p. 159—161° (1·97 g., 70%) (Found: C, 63·8; H, 5·65; N, 25·5. $C_{15}H_{15}N_5O$ requires C, 64·05; H, 5·3; N, 24·9%).

This compound (0·001 mole) in hot ethanol (5 ml.) with ethanolic 3N-hydrochloric acid (1 ml.) gave needles of the *hydrochloride*, m. p. 197—198° (decomp.) (from ethanol) (Found: C, 57·0; H, 5·1; N, 21·65; Cl, 11·5. $C_{15}H_{15}N_5O,HCl$ requires C, 56·7; H, 5·0; N, 22·05; Cl, 11·2%). The *picrate*, crystallised from a large volume of 50% aqueous ethanol, had m. p. 206—210° (decomp.) (Found: C, 49·4; H, 3·6. $C_{15}H_{15}N_5O,C_6H_3N_3O_7$ requires C, 49·4; H, 3·5%).

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