868. *Thiadiazoles. Part XVI.** 5-*Substituted* 3-*Nitroamino*-1,2,4-*thiadiazoles.*

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N-Substituted *N'*-(nitroamidino)thioureas are readily synthesised by the interaction of isothiocyanate esters and nitroguanidine, and are cyclised to 5-arylamino-3-nitroamino-1,2,4-thiadiazoles by oxidation. The analogous *N*-aryl-*N'*-(nitroamidino)ureas yield 1-aminoamidino-3-arylureas on reduction; their formulation, and that of their sulphur analogues, is thus confirmed.

The readiness with which 1-substituted 3-(aminoamidino)thioureas (V) are synthesised [1] from aminoguanidine and isothiocyanate esters and cyclised to 5-substituted 3-hydrazino-1,2,4-thiadiazoles [2] suggested the analogous employment of nitroguanidine in the synthesis of 3-nitroamino-1,2,4-thiadiazoles.

In a number of cases, the established methods of preparing nitroamines have been

* Part XV, preceding paper.

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

successfully applied in the heterocyclic field. Thus, if the heterocyclic nucleus is sufficiently stable, the appropriate amine or imine may be directly nitrated: 1-nitro-2-nitroamino-2-imidazoline [3] and 2-nitroamino-1,3,4-thiadiazoles [4] have been obtained in this way. More frequently, the oxidation of nitrosamines, accessible under more restrained conditions, and the cyclisation of suitable nitroguanidino-derivatives have been employed. The chemistry of nitroamines derived from imidazoles, triazoles, and tetrazoles has been reviewed by McKay.[5]

N-Aryl-*N'*-(nitroamidino)thioureas (II) required as starting materials in the present synthesis were readily obtained by addition of isothiocyanate esters to nitroguanidine (III). Carried out in dry acetone containing an equivalent of sodium, the reaction afforded the nitroamidinothioureas (II; *e.g.*, R = Ph) as sole product in good yield. Use of alkali in aqueous acetone gave somewhat lower yields because small quantities of the corresponding urea (IV) and an unidentified by-product (probably $C_{15}H_{12}N_4S_2$) were also formed. The latter appeared to arise by the action of two mol. of phenyl isothiocyanate on nitroguanidine, since it was also the product (40%) of the action of phenyl isothiocyanate on *N*-nitroamidino-*N'*-phenylthiourea (II; R = Ph).

Although reagents usually attack nitroguanidine at the amidino- rather than the nitroamino-grouping,[5] exceptions are known.[6] The present reaction (III ⟶ II) might thus yield theoretically two isomeric addition products (II and IIa; R = Ar, X = S). The correctness of the assigned structure (II) of the nitroamidinothioureas would be demonstrated by their reduction to the known[1] 1-aminoamidino-3-arylthioureas (V; R=Ph). In view of the difficulties of catalytic and other reductions due to the presence of sulphur in thioureas, and their greater tendency to cyclisation,[7] this confirmation was obtained in the corresponding urea series (IV).

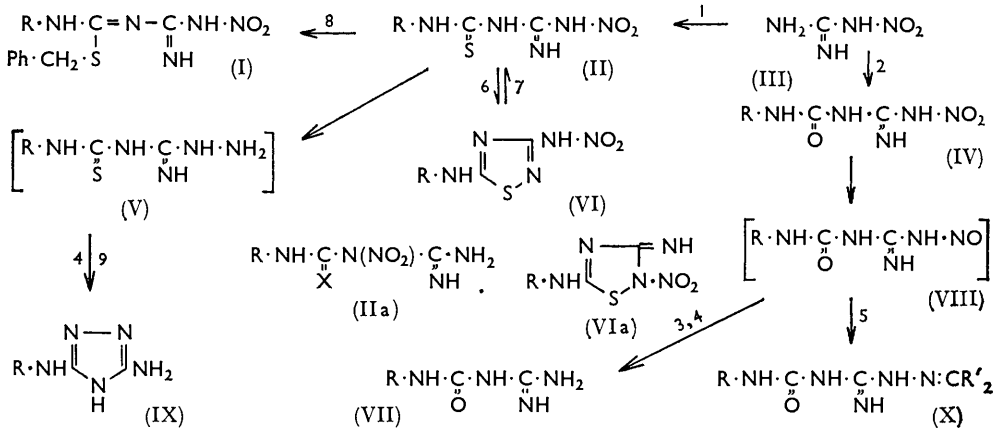
Because of the greater reactivity of aromatic isocyanates, *N*-aryl-*N'*-(nitroamidino)-ureas (IV; R = Ph, *p*-C_6H_4Me) were formed even more rapidly and in better yields than their sulphur analogues (II). Both series (II, IV) were acidic compounds, being soluble in alkalis and reprecipitated by acids, and were therefore likely to be nitroamines (II; X = O) containing a mobile hydrogen adjacent to the nitro-group, rather than the 1-amidino-3-aryl-1-nitro-isomers (IIa). Like nitroamines generally, they were thermally labile and exploded at their melting points.

Reduction of *N*-nitroamidino-*N'*-phenylurea (IV; R = Ph) with zinc and acetic acid in the presence of a large excess of acetone gave 1-(isopropylideneaminoamidino)-3-phenylurea (X; R = Ph, R' = Me) as main product (50%), together with smaller quantities (25%) of *N*-amidino-*N'*-phenylurea (VII; R = Ph). In the absence of acetone, the latter (VII) was the only product (50%). Hydrogenation gave comparable results except that yields of the reduction product (X) were lower, and those of the urea (VII) relatively higher.

Evidence has accumulated [5,8,9] that the reduction of nitro- to amino-guanidine involves preliminary formation of nitrosoguanidine, although direct reaction may also occur in media of adequate acidity.[5,8] Guanidine, often formed in varying quantities as by-product, may arise hydrolytically from this intermediate.[10] In the present case the primary nitroso-compound (VIII) would yield the observed products (X and VII) analogously by further reduction or hydrolysis. The fact that reducing conditions are essential to the

[3] McKay and Wright, *J. Amer. Chem. Soc.*, 1948, **70**, 3990; McKay, Bryce, and Rivington, *Canad. J. Chem.*, 1951, **29**, 382.
[4] Kanaoka, *J. Pharm. Soc. Japan*, 1955, **75**, 1149; Saikachi and Kanaoka, *Yakugaku Zasshi*, 1961, **81**, 1333 (*Chem. Abs.*, 1962, **56**, 7304).
[5] McKay, *Chem. Rev.*, 1952, **51**, 301.
[6] Greer, Kertesz, and Smith, *J. Amer. Chem. Soc.*, 1949, **71**, 3005.
[7] Godfrey and Kurzer, *J.*, 1961, 5137; 1962, 3561.
[8] Lieber and Smith, *Chem. Rev.*, 1939, **25**, 213.
[9] Godfrey and Kurzer, *Chem. and Ind.*, 1962, 1584.
[10] Sugino and Yamashita, Jap.P. 172,275 (*Chem. Abs.*, 1949, **43**, 6096); *J. Chem. Soc. Japan, Pure Chem. Section*, 1949, **70**, 71 (*Chem. Abs.*, 1951, **45**, 4150).

formation of the *N*-amidino-*N'*-phenylurea (VII; R = Ph) was shown by the nearly quantitative recovery of 1-nitroamidino-3-phenylurea (IV; R = Ph) after it had been heated with acetic acid in the absence of zinc under otherwise identical conditions.



Reagents: 1, RNCS. 2, RNCO. 3, H_2–Pt. 4, Zn–AcOH. 5, Zn–AcOH–Me_2CO. 6, H_2O_2. 7, SO_2. 8, $Ph{\cdot}CH_2Cl$–NaOH. 9, $NH_2{\cdot}NH_2$.

Since the absence of rearrangement in the above reductions may reasonably be assumed, particularly under the mild conditions of hydrogenation, the observations support the formulation of the condensation products of nitroguanidine and isocyanates as nitroamines (IV), and by analogy, of their sulphur analogues as (II). As expected, the reduction of the latter (*e.g.*, II; R = Ph) gave less clear-cut results, but the isolation of small yields of 2-amino-5-anilino-1,2,4-triazole (IX; R = Ph), arising presumably through the intermediate (V) was again compatible with structure (II) but not with (IIa; X = S). The action of hydrazine (on II; R = Ph) appeared to be also predominantly reductive and gave the same results.

The oxidative cyclisation of *N*-aryl-*N'*-(nitroamidino)thioureas (II) to 5-arylamino-3-nitroamino-1,2,4-thiadiazoles (VI) was carried out with alkaline hydrogen peroxide. The presence of alkali in equimolar proportions appeared to be essential to stabilise the acidic nitroamino-moiety, since extensive decomposition, with evolution of nitrous fumes, occurred in its absence. Under alkaline conditions, however, ring closure proceeded so readily at room temperature, that the usual action of alkaline hydrogen peroxide on thioureas, *i.e.*, desulphurisation to ureas,[11] did not effectively compete with it.

The 3-nitroamino-1,2,4-thiadiazoles were crystalline but exploded at their melting points. They were monobasic acids, remarkably stable towards alkalis, and, unlike their precursors (II), did not give lead sulphide with alkaline sodium plumbite. 5-Anilino-3-nitroamino-1,2,4-thiadiazole was reconverted almost quantitatively by sulphur dioxide into its parent amidinothiourea (II; R = Ph). This mild reduction thus opened the S–N link of the thiadiazole ring, the usual point of attack,[12] before affecting the nitroamino-group; it seems unlikely, therefore, that 3-nitroamino-1,2,4-thiadiazoles are reducible to their 3-hydrazino-anologues [2] and this particular aim of the present work, *i.e.*, the experimental inter-relation of the two series, was not achieved.

Ring-closure of *N*-aryl-*N'*-nitroamidinothioureas (II) at their nitroamino- instead of the imino-group would yield 1,2,4-thiadiazolidines of structure (VIa). The preferred formulation of the products as (VI) is based on their ready solubility in dilute alkalis and is supported by the results of Franchimont's colour reaction:[13] this test, widely applied by

[11] Loh and Dehn, *J. Amer. Chem. Soc.*, 1926, **48**, 2957.
[12] Kurzer, *J.*, 1955, 1, and subsequent papers.
[13] Franchimont, *Rec. Trav. chim.*, 1897, **16**, 213, 226.

McKay and his co-workers,[5] permits an empirical, though not infallible, differentiation between nitroamines and nitroimines: the exclusive development of pink rather than green colours with zinc, acetic acid, and dimethylaniline in this test by all the present compounds agreed with their containing nitroamino-groups.

Experimental

Light petroleum had boiling range 60—80°. Acetone was dried over calcium sulphate hemihydrate. Ultraviolet absorption measurements were made with a Unicam S.P. 500 spectrophotometer, and 0·00005—0·0001M-ethanolic solutions.

Thiourea Series

N-*Nitroamidino*-N′-*phenylthiourea*.—(*a*) To the suspension obtained on introducing sodium (2·3 g.) into acetone (500 ml.), nitroguanidine (10·4 g., 0·1 mole) was added, and the mixture stirred during 15 min. Phenyl isothiocyanate (13·5 g., 0·1 mole) was then added and stirring at room temperature continued during 1·5 hr. The reddish-brown liquid containing a little suspended solid was set aside during 36 hr., stirred into water (2 l.), and filtered. Acidification of the filtrate with 3N-acetic acid (50 ml.) gave a precipitate, which was collected at 0° and air-dried. Crystallisation from boiling ethanol (25 ml. per g., prolonged refluxing, and filtering, if necessary) gave a pale yellow crystalline powder of N-*nitroamidino*-N′-*phenylthiourea*, m. p. 160—161° (decomp. explosively) [yield, including material from the mother-liquors (obtained by careful partial evaporation under reduced pressure), 13·9—16·25 g., 58—68%] (Found: C, 40·9; H, 3·8; N, 29·8; S, 12·8. $C_8H_9N_5O_2S$ requires C, 40·2; H, 3·8; N, 29·3; S, 13·4%), $\lambda_{min.}$ 240 mμ (log ε 4·00), $\lambda_{max.}$ 282 mμ (log ε 4·40). The compound gave lead sulphide rapidly on being dissolved in 3N-sodium hydroxide and warmed with sodium plumbite.

(*b*) Nitroguanidine (10·4 g., 0·1 mole) dissolved almost completely on being added to water (80 ml.), 3N-sodium hydroxide (36·6 ml., 0·11 mole), and acetone (60 ml.). The stirred liquid was treated with phenyl isothiocyanate (13·5 g., 0·1 mole) in acetone (10 ml.) during 45 min., and stirring at room temperature was continued during a further 1 hr. The liquid, containing very little suspended solid, was added to 3N-hydrochloric acid (66 ml., 0·2 mole) and ice (400 ml.); the precipitate was collected after storage (to facilitate coagulation) and washed with water. The resulting air-dried pale yellow powder (15—16 g.) was refluxed briefly with ethanol (250 ml.), and the undissolved yellow residue (R) filtered off immediately. The filtrate next rapidly deposited colourless scales, which were filtered from the liquid while still hot (product U). The filtrate then gave pale yellow *N*-nitroamidino-*N′*-phenylthiourea, m. p. and mixed m. p. 159—160° (explodes) (from ethanol) (total, including material from filtrates, 10·75—12·5 g., 45—52%).

Product U (0·9—1·3 g., 4—6%) consisted, after crystallisation from ethanol, of minute needles of *N*-nitroamidino-*N′*-phenylurea, m. p. 203—205° (decomp.) (Found: C, 43·3; H, 4·3; N, 32·0. Calc. for $C_8H_9N_5O_3$: C, 43·05; H, 4·0; N, 31·4%). Its ultraviolet absorption curve was coincident with that of authentic material (see below).

The yellow by-product R [m. p. 237—240° (decomp.); 2·2—2·6 g., 14—17%] gave, on crystallisation from dimethylformamide (steam-bath)–ethanol (10 ml. each, per g., recovery 50%), or from dimethyl sulphoxide–ethanol (10 and 40 ml. per g., recovery 50%), greenish-yellow needles or prisms, respectively, m. p. 263—266° (decomp.) (Found: C, 56·95; 56·2; H, 4·5; 4·3; N, 17·5; 18·0; S, 20·3; 20·85. $C_{15}H_{12}N_4S_2$ requires C, 57·7; H, 3·8; N, 17·95; S, 20·5%). The product was soluble in 3N-sodium hydroxide but insoluble in cold or hot 3N-hydrochloric acid. It gave lead sulphide with alkaline sodium plumbite.

N-*Nitroamidino*-N′-*phenylthiourea*.—(*a*) S-*Benzyl derivative*. A solution of the reactant (2·39 g., 0·01 mole) in ethanol (20 ml.) and 1·5N-sodium hydroxide (13·3 ml., 0·02 mole) was treated with benzyl chloride (1·26 g., 0·01 mole) and stirred at room temperature during 2 hr. The liquid was added to water (80 ml.) and treated with acetic acid (5 ml.). The aqueous layer was decanted from the precipitated oil, which was washed with water and covered with a little ethanol and ether. The resulting solid (2 g.), which was formed slowly on storage, crystallised from ethanol (see note below)–light petroleum (b. p. 40—80°; 20 ml. each), giving the S-*benzyl derivative* as an opaque powder, m. p. 97—99° (1·05 g., 32%) (Found: C, 55·4; H, 4·5.

$C_{15}H_{15}N_5O_2S$ requires C, 54·7; H, 4·55%). On prolonged storage, the material decomposed with loss of toluene-ω-thiol. A small ethanol-insoluble residue (0·13 g., 6%) was *N*-nitroamidino-*N'*-phenylurea, m. p. and mixed m. p. (see below) 202—204°.

(*b*) *Action of hydrazine.* The thiourea (1·2 g., 0·005 mole) dissolved in ethanol (10 ml.), with gentle evolution of hydrogen sulphide on addition of hydrazine hydrate (0·5 g., 0·01 mole). The liquid was set aside at room temperature overnight, a small quantity of greyish-blue powder filtered off (0·15 g.), and the filtrate allowed to evaporate to dryness spontaneously at room temperature. The residue was redissolved in boiling water (25 ml.), *just* acidified with 3N-acetic acid, and treated with 0·05M-picric acid (50 ml., 0·0025 mole); it gave 3-amino-5-anilino-1,2,4-triazole picrate as yellow needles (0·50 g., 25%), m. p. and mixed m. p.[1] 230—232° (decomp.) (from 90% ethanol).

(*c*) *Action of aniline.* The thiourea (2·4 g., 0·01 mole) dissolved with gentle effervescence in aniline (10 ml.) at 100°. The liquid was kept at this temperature during 3 hr. (slight evolution of ammonia), the aniline removed [by steam-distillation or by two successive extractions with N-hydrochloric acid (120 and 60 ml.)], and the residual resinous paste stirred with ethanol (10 ml.). The resulting crude solid (1·5 g.), collected after storage at 0°, gave *NN'*-diphenylthiourea, m. p. and mixed m. p. 152—153° (0·96 g., 42%, from ethanol). The filtrates therefrom contained an unidentified mixture, forming a solid whose m. p. varied from 100° to 120°.

(*d*) *Action of phenyl isothiocyanate.* A solution of the thiourea (1·2 g., 0·005 mole) in acetone (10 ml.) and N-sodium hydroxide (5 ml., 0·005 mole) was treated with phenyl isothiocyanate (0·68 g., 0·005 mole) and heated on the steam-bath during 1 hr., yellow solid gradually separating. This was collected at 0° (0·9 g.), washed with acetone, and crystallised from dimethylformamide (10 ml. at 100°)–ethanol (10 ml.), forming greenish-yellow needles, m. p. (and mixed m. p. with R, see above) 264—267° (decomp.) (0·62 g., 40%, calc. as $C_{15}H_{12}N_4S_2$).

(*e*) *Reduction.* A suspension of the thiourea (1·2 g., 0·005 mole) and zinc shavings (3 g.) in water (50 ml.), ethanol (10 ml.), and acetic acid (20 ml.) was stirred on the steam-bath during 1 hr. (slow evolution of hydrogen sulphide). It was then filtered and treated with 0·05M-picric acid (100 ml., 0·005 mole), and the resulting picrate A collected. The filtrate thereform deposited, on storage in the open, a further crop of picrate B (0·5 g.) which was collected at 0°. Crystallisation from 90% ethanol gave needles (0·36 g., 18%) of 3-amino-5-anilino-1,2,4-triazole picrate, m. p. and mixed m. p.[1] 229—232° (decomp.) (Found: C, 42·2; H, 2·8. Calc. for $C_8H_9N_5,C_6H_3N_3O_7$: C, 41·6; H, 3·0%). Fraction A was a mixture of picrates that could only be partially separated and was not identified.

N-*Nitroamidino*-N'-p-*tolylthiourea.*—The stirred opalescent solution obtained on dissolving nitroguanidine (5·2 g., 0·05 mole) in acetone (25 ml.), water (15 ml.), and 3N sodium hydroxide (16·7 ml., 0·05 mole) was treated, during 30 min., with *p*-tolyl isothiocyanate (7·5 g., 0·05 mole) in acetone (15 ml.). After 1 hour's further stirring, the clear yellow liquid was added to 3N-hydrochloric acid (50 ml., 0·15 mole) and ice (pH 1). The resulting precipitate was collected after 2 hr., washed, and air-dried (11·5 g.). The product was refluxed with ethanol (50 ml. per g.), and the undissolved material U filtered off at room temperature. Rapid evaporation of the filtrate to a third of its bulk in a vacuum gave, on cooling, prisms (5·05—5·6 g., 40—44%) of N-*nitroamidino*-N'-p-*tolylthiourea*, m. p. 168—170° (explodes) (Found: C, 42·7; H, 4·0; N, 27·5; S, 11·7. $C_9H_{11}N_5O_2S$ requires C, 42·7; H, 4·3; N, 27·7; S, 12·65%), $\lambda_{min.}$ 245 mμ (log ε 4·01), $\lambda_{max.}$ 282 mμ (log ε 4·41). Addition of the ethanolic filtrate to water (10 vol.) gave a precipitate of the same material of satisfactory purity [m. p. 167—170° (explodes); 2·0 g., bringing the total yield to 56—60%].

Alternatively, crystallisation of the crude product from dimethylformamide–ethanol (3 and 6 ml. per g., recovery 60—70%) gave the solvated *nitro-thiourea*, m. p. 128—129° (decomp., after softening at 100°) (Found: C, 44·5; H, 5·6; N, 25·8; S, 9·3. $C_9H_{11}N_5O_2S,H{\cdot}CO{\cdot}NMe_2$ requires C, 44·2; H, 5·5; N, 25·8; S, 9·8%).

The residue U (up to 1·75 g., 15%) was *N*-nitroamidino-*N'*-*p*-tolylurea, m. p. and mixed m. p. (see below) 212—214° (decomp.) (needles, from ethanol). Its ultraviolet absorption curve was coincident with that of an authentic specimen (see below). In some experiments, the crude material was almost entirely ethanol-soluble, no urea being obtained as by-product.

5-*Anilino*-3-*nitroamino*-1,2,4-*thiadiazole.*—A solution of *N*-nitroamidino-*N'*-phenylthiourea (4·80 g., 0·02 mole) in ethanol (40 ml.) and 3N-sodium hydroxide (7·3 ml., 0·022 mole) was treated, at room temperature, with 6% hydrogen peroxide (12·5 ml., 0·022 mole). The liquid, whose temperature rose spontaneously to 45—50°, was set aside for 15 min., then stirred into

3N-hydrochloric acid (12 ml.) and ice (120 g.). The white precipitate was collected, washed with water, and air-dried [m. p. between 156 and 160° (explodes); 4·25—4·5 g., 90—95%]. Crystallisation from boiling ethanol (30 ml. per g., removal of insoluble by-product by filtration, if necessary) (recovery, including material from mother-liquors, over 80%) gave plates of *5-anilino-3-nitroamino-1,2,4-thiadiazole*, m. p. 159—161° (explodes) (Found: C, 41·0; H, 3·0; N, 28·9; S, 13·2. $C_8H_7N_5O_2S$ requires C, 40·5; H, 2·95; N, 29·5; S, 13·5%), $\lambda_{min.}$ 234 mμ (log ε, 3·86), $\lambda_{max.}$ 278 mμ (log ε 4·34). The compound did not give lead sulphide with boiling sodium plumbite in 3N-sodium hydroxide. It was stable to alkalis, being reprecipitated by 3N-hydrochloric acid almost quantitatively from its solution in 3N-sodium hydroxide (0·2 g. in 12 ml.) that had been refluxed during 30 min.

Attempts to perform the foregoing oxidation in acidified ethanol (0·005 mole of reactant in 25 ml. of solvent at 55—60°) were unsuccessful: the deep-orange liquid evolved nitrous fumes. Slow addition to the thiourea derivative, dissolved in chloroform (0·005 mole in 200 ml.) at room temperature, of equimolar quantities of bromine (in chloroform) gave, mostly, sticky resins.

Reduction of 5-Anilino-3-nitroamino-1,2,4-thiadiazole.—A solution of the thiadiazole (0·71 g., 0·003 mole) in ethanol (10 ml.)—0·5N-sodium hydroxide (12 ml., 0·006 mole) at 35° was treated with a slow stream of sulphur dioxide during 20 min. The precipitate which formed after a few minutes was collected after storage at 0°. It was *N*-nitroamidino-*N'*-phenylthiourea, m. p. and mixed m. p. 162—163° (decomp.) (pale yellow powder, from ethanol; 0·60 g., 84%) [mixed m. p. with starting material, 142° (decomp.)].

3-Nitroamino-5-p-toluidino-1,2,4-thiadiazole.—*N*-Nitroamidino-*N'*-*p*-tolylthiourea (1·26 g., 0·005 mole) in ethanol (12 ml.) and 0·5N-sodium hydroxide (10 ml., 0·005 mole) was oxidised with 6% hydrogen peroxide (3·1 ml., 0·0055 mole), and was isolated as described for the 5-anilino-analogue. Crystallisation from ethanol (40 ml. per g., slow dissolution) gave prismatic needles (total, 0·94 g., 75%) of *3-nitroamino-5-p-toluidino-1,2,4-thiadiazole*, m. p. 169—170° (explodes) (Found: C, 42·9; H, 3·65; N, 27·6; S, 12·1. $C_9H_9N_5O_2S$ requires C, 43·0; H, 3·6; N, 27·9; S, 12·75%), $\lambda_{min.}$ 235 mμ (log ε, 3·92), $\lambda_{max.}$ 277 mμ (log ε 4·35).

Urea Series

N-Nitroamidino-N'-phenylurea.—(*a*) *Preparation.* To the stirred suspension obtained on addition of sodium (1·15 g., 0·05 g.-atom) to acetone (250 ml.), nitroguanidine (5·2 g., 0·05 mole) was added, and stirring continued during 0·5 hr. The suspension was treated with phenyl isocyanate (6·25 g., 0·0525 mole) during 15 min., and stirring at room temperature continued during 30 min. Any undissolved residue was removed and the clear liquid added to water (1 l.) containing 3N-acetic acid (25 ml.). The resulting white air-dried precipitate (9—10 g.) dissolved on being refluxed (for 15 min.) with ethanol (1—1·2 l.); the filtered (carbon) liquid gave prisms of *N-nitroamidino-N'-phenylurea*, m. p. 203—205° (decomp.) (total, including material from mother-liquors, 8·4—9·1 g., 75—82%) (Found: C, 43·0; H, 4·2; N, 31·5. $C_8H_9N_5O_3$ requires C, 43·05; H, 4·0; N, 31·4%), $\lambda_{min.}$ 220 (log ε 4·06), $\lambda_{max.}$ 226 (log ε 4·09), $\lambda_{min.}$ 242 (log ε 3·89), $\lambda_{max.}$ (principal) 274 mμ (log ε 4·44).

(*b*) *Reduction in presence of acetone.* To a stirred solution of the urea (1·12 g., 0·005 mole) in acetone (150 ml.), zinc shavings (5 g.) were added; the suspension was diluted with acetic acid (20 ml.) and water (20 ml.), and stirred and refluxed for 6 hr., more 50% acetic acid (20 ml.) being added after 3 hr. The mixture was filtered, the solid rinsed with boiling acetone (50 ml.) and then water (200 ml.), the filtrate basified with 3N-ammonia, and most of the acetone removed by distillation in a vacuum. On storage at 0°, the residual liquid deposited a solid (0·8 g.) which gave, on crystallisation from ethanol (5 ml.)–light petroleum (1 : 1, b. p. 40—60°, 60—80°; 15 ml.), prismatic needles (0·6 g., 52%) of 1-(isopropylideneamino)amidino-3-phenylurea, m. p. and mixed m. p.[1] 123—125° (Found: C, 56·9; H, 6·15. Calc. for $C_{11}H_{15}N_5O$: C, 56·65; H, 6·4%).

Alternatively, filtrate F, after removal of most of the acetone as before, was treated with 0·05M-aqueous picric acid (150 ml., 0·0075 mole), and the yellow precipitate collected at 0° (2·3 g.). Crystallisation from 66% ethanol (300 ml.), followed by chilling, gave prisms (1·27 g., 55%) of 1-(isopropylideneamino)amidino-3-phenylurea picrate, m. p. and mixed m. p.[1] 208—210° (decomp.) (Found: C, 43·8; H, 4·1. Calc. for $C_{11}H_{15}N_5O,C_6H_3N_3O_7$: C, 44·2; H, 3·9%). The filtrate therefrom gave, on vacuum-evaporation to one-third bulk, a further crop of yellow

solid [m. p. 225—227° (decomp.); 0·51 g., 25%], affording *N*-amidino-*N'*-phenylurea picrate, m. p. and mixed m. p. (see below) 235—236° (decomp.) (from 80% ethanol) (Found: C, 42·0; H, 3·2. Calc. for $C_8H_{10}N_4O,C_6H_3N_3O_7$: C, 41·3; H, 3·2%).

(*c*) *Reduction in absence of acetone.* The urea (1·12 g., 0·005 mole) and powdered zinc (5 g.) were suspended in acetic acid (20 ml.), water (50 ml.), and ethanol (10 ml.), and the stirred mixture kept at room temperature during 1 hr. and at 70—80° during 2 hr. The mixture was filtered at room temperature (removal of zinc and zinc acetate) and the filtrate F was treated with toluene-*p*-sulphonic acid monohydrate (1·9 g., 0·01 mole) and set aside in a basin during 24 hr. The plates (0·56 g., 32%) that separated were *N*-amidino-*N'*-phenylurea toluene-*p*-sulphonate, m. p. and mixed m. p. with authentic material (see below) 224—226° (decomp.) (from 75% ethanol).

Alternatively, treatment of filtrate F with 0·05M-aqueous picric acid (100 ml., 0·005 mole) gave an immediate precipitate (1·3 g.) which afforded, on crystallisation from 80% ethanol, felted needles (1·06 g., 52%) of *N*-amidino-*N'*-phenylurea picrate, m. p. and mixed m. p. (see below) 236—238° (decomp.) (Found: C, 42·1; H, 3·6; N, 23·6. Calc. for $C_8H_{10}N_4O,C_6H_3N_3O_7$: C, 41·3; H, 3·2; N, 24·1%).

N-Nitroamidino-*N'*-phenylurea (0·67 g., 0·003 mole), suspended in acetic acid (12 ml.), water (25 ml.), and ethanol (5 ml.), and kept on the steam-bath during 3 hr., was recovered (90%).

(*d*) *Hydrogenation.* A solution of the urea (2·23 g., 0·01 mole) in dimethylformamide (150 ml.) containing Adams platinum oxide catalyst [14] (0·1 g.) was agitated at room temperature during 24 hr. in hydrogen at 40 atm. in a stainless-steel vessel. The decanted liquid was heated with benzaldehyde (1 g.) and acetic acid (5 ml.) on a steam-bath during 45 min., distilled to small bulk (20—30 ml.) in a vacuum at $<50°$, and stirred into water (100 ml.) and ammonia (*d* 0·88; 5 ml.), and the resulting grey precipitate A was collected at 0°. The filtrate therefrom was treated with 0·05M-picric acid (200 ml., 0·01 mole): the resulting precipitate consisted, after crystallisation from 80% ethanol, of *N*-amidino-*N'*-phenylurea picrate, m. p. and mixed m. p. (see below) 236—238° (decomp.) (1·71 g., 42%).

Product A (0·5 g.) was treated with picric acid (1·15 g., 0·005 mole) in hot ethanol (20 ml.). The crude picrate was refluxed with 66% ethanol (120 ml.), and a small insoluble residue removed. The filtrate gave 1-(benzylideneamino)amidino-3-phenylurea picrate (0·61 g., 12%), m. p. and mixed m. p.[1] 208—212° (Found: C, 49·3; H, 3·7; N, 21·65. Calc. for $C_{15}H_{15}N_5O,C_6H_3N_3O_7$: C, 49·4; H, 3·5; N, 21·95%).

Hydrogenation as above, but in dimethylformamide (100 ml.) and acetone (200 ml.) at 60 atm., removal of most of the solvent in a vacuum, addition to water (100 ml., precipitation of unchanged reactant), and treatment of the filtrate with aqueous picric acid, gave up to 22% yields of 1-(isopropylideneamino)amidino-3-phenylurea picrate, m. p. and mixed m. p.[1] 210—212° (decomp.) (Found: C, 44·3; H, 4·2. Calc. for $C_{11}H_{15}N_5O,C_6H_3N_3O_7$: C, 44·2; H, 3·9%).

N-*Nitroamidino*-N'-p-*tolylurea* was prepared as the corresponding phenyl homologue, by using *p*-tolyl isocyanate (7·0 g., 0·0525 mole). The crude air-dried product (10 g.) was crystallised by being refluxed with ethanol (400 ml. per g.); the filtered solution deposited silky felted needles (72%), m. p. 213—214° (decomp.) (Found: C, 46·3; H, 5·0; N, 28·9. $C_9H_{11}N_5O_3$ requires C, 45·6; H, 4·6; N, 29·5%), $\lambda_{min.}$ 220, $\lambda_{max.}$ 231, $\lambda_{min.}$ 246, and $\lambda_{max.}$ (principal) 278 mμ (log ε 4·08, 4·12, 3·95, and 4·44, respectively).

N-*Amidino*-N'-*phenylurea*.—To the suspension obtained on introducing sodium (0·46 g., 0·02 g.-atom) into acetone (50 ml.), guanidine thiocyanate (2·35 g., 0·02 mole) was added; the resulting reddish-brown liquid was treated with phenyl isocyanate (2·4 g., 0·02 mole) during 10 min., and the liquid was set aside and allowed to evaporate partially during 12 hr., then stirred into water (100 ml.). The filtered liquid F was acidified with acetic acid and treated with toluene-*p*-sulphonic acid monohydrate (7·6 g., 0·04 mole). The crystalline precipitate [m. p. 215—220° (decomp.); 5·3 g., 76%] crystallised from 75% ethanol (carbon) (15 ml. per g., recovery 80%), giving minute prisms of N-*amidino*-N'-*phenylurea toluene*-p-*sulphonate*, m. p. 224—227° (decomp.) (Found: C, 50·9; H, 4·4; N, 16·4; S, 9·55. $C_8H_{10}N_4O,C_7H_8O_3S$ requires C, 51·4; H, 5·1; N, 16·0; S, 9·1%).

The picrate obtained by addition to the acidified filtrate F, of 0·05M-aqueous picric acid (400 ml., 0·02 mole) and crystallisation from 80% ethanol (400 ml.), formed prismatic needles

[14] Adams, Voorhees, and Shriner, *Org. Synth.*, Coll. Vol. I, Wiley, New York, 1941, p. 463.

(5·9 g., 72%), m. p. 236—238° (decomp.) (Found: N, 24·5. Calc. for $C_8H_{10}N_4O,C_6H_3N_3O_7$: N, 24·1%) (lit.,[15] m. p. " darkening from 230°, decomposing at higher temperatures ").

Franchimont Tests.—The nitroamino-compound was treated, in glacial acetic acid solution, with a little zinc dust and a few drops of 1% dimethylaniline in glacial acetic acid. The following colours were produced: Blue-pink, by *N*-nitroamidino-*N'*-phenylurea, *N*-nitroamidino-*N'*-*p*-tolylurea. Cyclamen, by *N*-nitroamidino-*N'*-phenylthiourea, *N*-nitroamidino-*N'*-*p*-tolylthiourea. Rose-pink, by 5-anilino-3-nitroamino-1,2,4-thiadiazole, 3-nitroamino-5-*p*-toluidino-1,2,4-thiadiazole.

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[15] Pellizzari, *Gazzetta,* 1923, **53**, 384, 391.