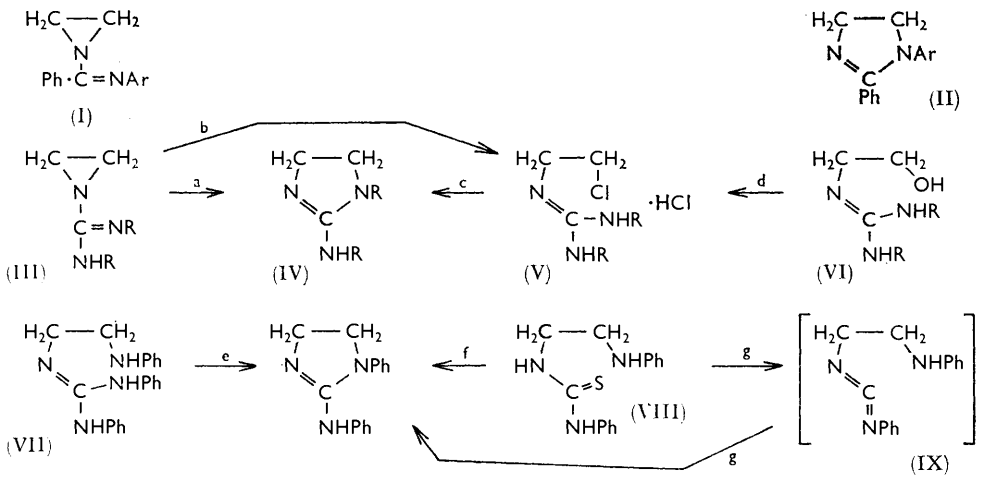
74. *2-Amino-2-imidazolines and 2-Amino-2-oxazolines. Part II.*[1]

By B. Adcock and Alexander Lawson.

1-(*NN'*-Diarylamidino)aziridines, from diarylcarbodi-imides and aziridine, have been converted into 1-aryl-2-arylamino-2-imidazolines by two independent routes, and other routes to 1-aryl-2-arylamino-2-imidazolines have been investigated. The reaction of ethylenediamine monotoluene-*p*-sulphonate with 1-aryl- (or 1-anilino-)3-nitroguanidines has been shown to yield 2-arylamino-2-imidazolines and 2-(2-phenylhydrazino)-2-imidazoline, respectively, whilst 1-(2- or 3-hydroxyalkyl)-3-nitroguanidines give 2-amino-2-oxazolines or 2-amino-5,6-dihydro-1,3-oxazines under alkaline conditions. 2-Arylamino-2-oxazolines have been prepared from ethanolamine with 1-aryl-3-nitroguanidines or by the action of methyl iodide followed by sodium ethoxide on 1-aryl-3-(2-hydroxyethyl)thioureas.

The synthesis and rearrangement of substituted aziridines have aroused renewed interest recently and have been the subject of an extensive review.[2] Following the discovery[3] that 1-(*N*-arylbenzimidoyl)aziridine (I) readily rearranges on prolonged heating with potassium iodide in acetone to give 1-aryl-2-phenyl-2-imidazoline (II), the synthesis and rearrangement of 1-(*NN'*-diarylamidino)aziridines (III) were studied.

Diphenylcarbodi-imide and di-*o*-methoxyphenylcarbodi-imide reacted readily with aziridine in ether to give 1-(*NN'*-diphenylamidino)aziridine (III; R = Ph) and 1-(*NN'*-di-*o*-methoxyphenylamidino)aziridine (III; R = C_6H_4·OMe-*o*), respectively. The free aziridines were viscous oils and were characterised as picrates or toluene-*p*-sulphonates. Prolonged treatment with potassium iodide in boiling acetone gave the rearranged products, 2-anilino-1-phenyl-2-imidazoline (IV; R = Ph) and 1-*o*-methoxyphenyl-2-*o*-methoxy-



Reagents: a, Potassium iodide in acetone: b, dry ethereal hydrogen chloride; c, ethanolic potassium hydroxide; d, thionyl chloride (R = Ph); e, polyphosphoric acid at 250°; f, methyl iodide followed by alkali; g, mercuric oxide.

anilino-2-imidazoline (IV; R = C_6H_4·OMe-*o*); whilst dry ethereal hydrogen chloride opened the aziridine ring to give 2-(2-chloroethyl)-1,3-diarylguanidine hydrochlorides (V) which were cyclised by ethanolic potassium hydroxide to 1-aryl-2-arylamino-2-imidazolines (IV).

For comparison, 2-(2-chloroethyl)-1,3-diphenylguanidine hydrochloride (V; R = Ph)

[1] Part I, Adcock, Lawson, and Miles, *J.*, 1961, 5120.
[2] Heine, *Angew. Chem., Internat. Edn.*, 1962, **1**, 528.
[3] Heine and Bender, *J. Org. Chem.*, 1960, **25**, 461.

was prepared by the action of thionyl chloride on 2-(2-hydroxyethyl)-1,3-diphenylguanidine (VI; R = Ph) in dry chloroform; the hydroxyethylguanidine being readily accessible from diphenylcarbodi-imide and ethanolamine.[1]

2-(2-Anilinoethyl)-1,3-diphenylguanidine (VII), obtained from diphenylcarbodi-imide and *N*-phenylethylenediamine, was unexpectedly resistant towards cyclisation. It was recovered unchanged after heating at 150° and after prolonged boiling with concentrated hydrochloric acid. Cyclisation to 2-anilino-1-phenyl-2-imidazoline was, however, effected by polyphosphoric acid at 250°. Polyphosphoric acid, though being a more efficient agent for cyclisation by loss of ammonia when base hydrochlorides rather than free bases are employed,[4] did not cyclise 2-(2-anilinoethyl)-1,3-diphenylguanidine hydrochloride at 210°.

The action of phenylcyanamide on *N*-phenylethylenediamine in the presence of one mole of toluene-*p*-sulphonic acid at 150° gave 2-(2-anilinoethyl)-1-phenylguanidine toluene-*p*-sulphonate. Some ammonia was evolved during the course of the reaction but none of the desired imidazoline was isolated. This salt behaved anomalously, being precipitated unchanged from solution in acid by the addition of sodium hydroxide solution.

N-Phenylethylenediamine underwent an exothermic reaction with phenylisothiocyanate, but the 1-(2-anilinoethyl)-3-phenylthiourea (VIII) could not be obtained crystalline. The impure thiourea, when heated with mercuric oxide, or with methyl iodide followed by alkali, gave 2-anilino-1-phenyl-2-imidazoline by loss of hydrogen sulphide and methanethiol, respectively; in the first case this probably occurred by way of the intermediate carbodi-imide (IX), which would readily cyclise. A similar type of reaction is the conversion of 1-substituted 3-(2-hydroxyethyl)thioureas into amino-substituted 2-amino-2-oxazolines by mercuric oxide, again probably by way of an intermediate carbodi-imide.[5,6]

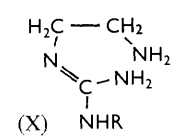
It has long been known that aliphatic amines react with 1-substituted 3-nitroguanidines to give 1,3-disubstituted guanidines;[7,8] it was therefore hoped that the action of ethylenediamine would lead to the formation of 2-(2-aminoethyl)guanidines (X), capable of cyclisation to amino-substituted 2-amino-2-imidazolines by loss of ammonia. The action of ethylenediamine on 1-nitro-3-phenylguanidine in boiling ethanol gave small yields of 2-anilino-2-imidazoline and di-(3-phenylguanidino)ethane, but the intermediate 3-phenylguanidinoethylamine could not be isolated. Substitution of the monotoluene-*p*-sulphonate of ethylenediamine for the free base improved the yield of 2-anilino-2-imidazoline and reduced the formation of basic by-products. This method has also been employed to prepare 2-*p*-chloroanilino-2-imidazoline. 1-Anilino-3-nitroguanidine reacted readily with ethylenediamine monotoluene-*p*-sulphonate to give good yields of 2-(2-phenylhydrazino)-2-imidazoline (XI) toluene-*p*-sulphonate. Only salts were obtainable owing to the ready autoxidation of the free base to highly coloured tarry material. The resistance of this substance to hydrolytic fission by prolonged treatment with hydrochloric acid, coupled with the fact that the compound exhibits strong reducing activity, supports its formulation as a disubstituted hydrazine rather than as the tautomeric hydrazone. The same compound, as its picrate, was also obtained from phenylhydrazine and 2-methylthio-2-imidazoline, showing that the alternative cyclisation to give 2-amino-1-anilino-2-imidazoline (XII) or the tetrahydrotriazine (XIII) had not taken place.

Several synthetic routes to the 2-amino-2-oxazolines have been investigated. It was hoped that the action of amines on hydroxyalkylnitroguanidines (XIV; $R^2 = NO_2$) might lead to hydroxyalkylguanidines (XIV; R^2 = alkyl) capable of cyclisation to 2-(substituted amino)-2-oxazolines (XV; $n = 1$) or 2-(substituted amino)-5,6-dihydro-1,3-oxazines (XV; $n = 2$). However, the action of alkylamines in boiling ethanol on 2-(2- or 3-hydroxyalkyl)-1-nitroguanidines led, in every case, to the formation of 2-amino-2-oxazoline (XV;

[1] Snyder and Konecky, *J. Amer. Chem. Soc.*, 1958, **80**, 4388.
[5] Söderbaum, *Ber.*, 1895, **28**, 1897.
[6] Dains, Brewster, Malm, Miller, Maneval, and Sultzaberger, *J. Amer. Chem. Soc.*, 1925, **47**, 1981.
[7] Davis and Abrams, *Proc. Amer. Acad. Arts Sci.*, 1926, **61**, 437.
[8] Davis and Elderfield, *J. Amer. Chem. Soc.*, 1933, **55**, 731.

$R^1 = R^2 = H$, $n = 1$) or 2-amino-5,6-dihydro-1,3-oxazine (XV; $R^1 = R^2 = H$, $n = 2$). It was shown that the reaction did not take place by initial formation of 2-(2- or 3-hydroxyalkyl)-1-alkylguanidines (XIV; R^2 = alkyl) since triethylamine, from which there is no possibility of guanidine formation, catalysed the reaction equally well. Boiling alcoholic sodium hydroxide solution also caused cyclisation, though in poor yield with some decomposition and evolution of ammonia. Thermal cyclisation of hydroxyalkylnitroguanidines (XIV; $R^2 = NO_2$) has been reported,[9] but only under vigorous conditions. The cyclisation could occur either by preliminary decomposition of the nitroguanidine to a cyanamide or by an addition–elimination reaction of the type suggested by McKay [10] for the reaction of nitroguanidines with amines or water. The latter would appear to be more acceptable since, if a preliminary decomposition of the nitroguanidine to 2-hydroxyethylcyanamide were involved, then one might expect 2-ethyl-1-nitroguanidine to be converted into ethylcyanamide under similar conditions, a prediction which is not realised.

Alkanolamines reacting with phenyl-substituted 1-nitro-3-phenylguanidines in boiling ethanol many hours gave phenyl-substituted 2-anilino-2-oxazolines with elimination of nitrous oxide, water, and ammonia. However, on condensing 1-methyl-3-nitroguanidine with ethanolamine under the same conditions, methylamine was eliminated and 2-amino-2-oxazoline isolated as the picrate.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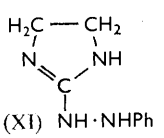
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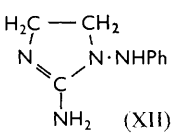
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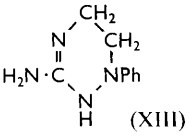
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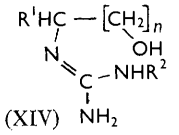
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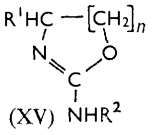
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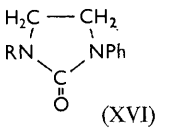
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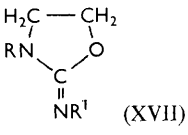
(XVII)

A further series of 2-amino-2-oxazolines (XV; $n = 1$) has been prepared from 1-aryl-3-(2-hydroxyethyl)-2-thioureas with methyl iodide and sodium ethoxide by the method previously described.[1] Previously, a small yield of 1-phenyl-2-imidazolidone was obtained as a by-product during the preparation of 2-anilino-2-oxazoline. 1-*p*-Chlorophenyl-4-ethyl-2-imidazolidone has now been obtained in a similar manner as a by-product in the preparation of 2-*p*-chloranilino-4-ethyl-2-imidazoline. Imidazolidone formation probably occurs by an independent pathway, since both 2-anilino-2-oxazoline and 2-*p*-chloranilino-4-ethyl-2-oxazoline are stable in boiling ethanolic sodium ethoxide solution. However, by heating 2-anilino-2-oxazoline (XV; $R^1 = H$, $R^2 = Ph$, $n = 1$) at 180—220°, or, better, by heating the oxazoline in a high-boiling solvent such as nitrobenzene, 1-phenyl-2-imidazolidone (XVI; R = H) may be obtained. The formation [11] of 1-substituted 2-imidazolidones by heating 3-substituted 2-imino-oxazolidines (XVII; $R^1 = H$) in an inert atmosphere to 150—215° and the formation of 1,3-disubstituted 2-imidazolidones (XVI) from 3-substituted 2-(substituted imino)-oxazolidines (XVII) at 200° in the presence of lithium chloride [12] have previously been reported, but this is the first recorded case of an oxazoline undergoing this type of reaction

Experimental

1-(NN′-*Diphenylamidino*)*aziridine*.—Aziridine (1 g.) and diphenylcarbodi-imide (4·5 g., 1 mol.) in ether (15 ml.) were heated under reflux for 1 hr. After removal of the solvent, portions

[9] Fishbein and Gallaghan, *J. Org. Chem.*, 1956, **21**, 434.
[10] McKay, *Chem. Rev.*, 1952, **51**, 301.
[11] U.S.P. 2,518,264.
[12] Gulbins and Hamann, *Angew. Chem.*, 1961, **73**, 434.

of the oily residue were converted into the *toluene*-p-*sulphonate*, needles, m. p. 138° (from ethanol–ether) (Found: C, 64·35; H, 5·9. $C_{22}H_{23}N_3O_3S$ requires C, 64·6; H, 5·6%) and the *picrate*, needles, m. p. 151° (decomp.) (from ethanol) (Found: C, 54·4; H, 4·0. $C_{21}H_{18}N_6O_7$ requires C, 54·1; H, 3·9%).

1-(NN′-*Di*-o-*methoxyphenylamidino*)*aziridine*.—Aziridine (1 g.) and di-*o*-methoxyphenylcarbodi-imide (5·9 g., 1 mol.) in ether (150 ml.) were allowed to react as above. The viscous residue, after removal of the solvent gave a *picrate*, needles, m. p. 147° (decomp.) (from ethanol) (Found: C, 52·55; H, 4·4. $C_{23}H_{22}N_6O_9$ requires C, 52·5; H, 4·2%).

2-(2-*Chloroethyl*)-1,3-*diphenylguanidine*.—(*a*) Crude 1-(*NN′*-diphenylamidino)aziridine (4 g.) in dry ether (10 ml.) was treated with dry hydrogen chloride in ether (25 ml.). The precipitate crystallised from ethanol–ether to give the *guanidine hydrochloride*, needles (5·1 g., 98%), m. p. 186—187° (Found: C, 58·1; H, 5·8; Cl, 22·9. $C_{15}H_{17}Cl_2N_3$ requires C, 58·1; H, 5·5; Cl, 23·0%). The *picrate*, prisms from ethanol, had m. p. 172° (decomp.) (Found: C, 50·1; H, 4·1; Cl, 7·6. $C_{21}H_{19}ClN_6O_7$ requires C, 50·1; H, 3·8; Cl, 7·1%).

(*b*) 2-(2-Hydroxyethyl)-1,3-diphenylguanidine [1] (0·2 g.) and thionyl chloride (0·46 g., 5 mol.) in chloroform (10 ml.) were heated on a water-bath for 15 min. Ether (15 ml.) was added to the cooled solution and 2-(2-chloroethyl)-1,3-diphenylguanidine hydrochloride crystallised as colourless needles (0·2 g., 83%).

2-(2-*Chloroethyl*)-1,3-*di*-o-*methoxyphenylguanidine*.—Crude 1-(*NN′*-di-*o*-methoxyphenylamidino)aziridine (6·9 g.) in ether was treated with an excess of ethereal hydrogen chloride. The precipitate crystallised from ethanol–ether to give the *guanidine hydrochloride*, needles (6·25 g., 73%), m. p. 149° (Found: C, 54·8; H, 5·6; Cl, 19·4. $C_{17}H_{21}Cl_2N_3O_2$ requires C, 55·1; H, 5·7; Cl, 19·2%).

2-*Anilino*-1-*phenyl*-2-*imidazoline*.—(*a*) 2-(2-Chloroethyl)-1,3-diphenylguanidine hydrochloride (1 g.) and potassium hydroxide (0·36 g., 2 mol.) were heated in ethanol (20 ml.) for 1 hr. The mixture was cooled and potassium chloride filtered off. After removal of the solvent, the oily residue gave 2-*anilino*-1-*phenyl*-2-*imidazoline picrate*, needles (1·2 g., 80%), m. p. 148° (from aqueous alcohol) (Found: C, 54·3; H, 4·2. $C_{21}H_{18}N_6O_7$ requires C, 54·1; H, 3·9%).

(*b*) Crude 1-(*NN′*-diphenylamidino)aziridine (1·5 g.) and potassium iodide (2 g., 1·9 mol.) were heated on a water-bath in acetone (60 ml.) for 30 hr. The solvent was removed and the residue washed with cold water before being dissolved in the minimum quantity of dilute hydrochloric acid. Addition of sodium hydroxide solution precipitated an oily free base, which was extracted with chloroform and converted into the picrate (2 g., 68%), identical with that described in (*a*).

(*c*) Phenylisothiocyanate (1 g.) and *N*-phenylethylenediamine (1 g., 1 mol.) were mixed in ether (10 ml.). An exothermic reaction took place but the thiourea could not be crystallised. The crude thiourea (2 g., 1 mol.) was treated with methyl iodide (5 g., 4·75 mol.) in boiling ethanol (25 ml.) for 0·5 hr. Potassium hydroxide (5 g., 12 mol.) in water (10 ml.) was added and the mixture boiled for a further 5 hr., methanethiol being evolved. The solvent was removed *in vacuo* and the residual oil dissolved in chloroform and washed with water. The dried chloroform extract, on evaporation, gave an oily material which was converted into 2-anilino-1-phenyl-2-imidazoline picrate (1·8 g., 52%).

(*d*) Crude 1-(2-anilinoethyl)-3-phenylthiourea (2 g.) was dissolved in ethanol (20 ml.), mercuric oxide (2 g., 1·24 mol.) added, and the mixture heated on a water-bath for 1 hr. The hot solution was filtered and the residue washed with a little hot ethanol. The combined filtrate and washings were evaporated to dryness and converted into the picrate. Repeated crystallisation from ethanol and aqueous ethanol gave 2-anilino-1-phenyl-2-imidazoline picrate (1·4 g., 41%).

(*e*) 2-(2-Anilinoethyl)-1,3-diphenylguanidine (0·3 g.) in polyphosphoric acid (10 ml.) was heated at 230° for 1 hr. The mixture was neutralised with excess of ammonia and extracted with chloroform (3 × 60 ml.). The oily residue obtained on removal of the solvent gave 2-anilino-1-phenyl-2-imidazoline picrate (0·11 g., 26%).

1-o-*Methoxyphenyl*-2-o-*methoxyanilino*-2-*imidazoline*.—(*a*) 2-(2-Chloroethyl)-1,3-di-*o*-methoxyphenylguanidine hydrochloride (2 g.) in ethanol (100 ml.) was heated on a water-bath with sodium hydroxide (0·45 g., 2·1 mol.) for 2 hr. The solution was cooled and sodium chloride removed. Dry hydrogen chloride was passed in and the solvent removed *in vacuo*. The residue crystallised from ethanol–ether to give the *imidazoline hydrochloride*, prisms (1·2 g., 66%), m. p. 225° (decomp.) (Found: C, 61·1; H, 5·95. $C_{17}H_{20}ClN_3O_2$ requires C, 61·2; H, 6·0%). The

picrate formed prisms, m. p. 142° (from ethanol) (Found: C, 52·2; H, 4·1. $C_{23}H_{22}N_6O_9$ requires C, 52·5; H, 4·2%).

(*b*) Crude 1-(*NN'*-di-*o*-methoxyphenylamidino)aziridine (1 g.) in acetone (20 ml.) was heated with potassium iodide (2 g.) on a water-bath for 24 hr. The solvent was removed and the residue washed with water (10 ml.) before conversion into the hydrochloride (0·6 g., 52%), identical with that described in (*a*).

2-(2-*Anilinoethyl*)-1,3-*diphenylguanidine*.—Diphenylcarbodi-imide (1·94 g.) and *N*-phenylethylenediamine (1·36 g., 1 mol.) were allowed to react in ethanol (10 ml.) at room temperature. After 1 hr. the precipitate crystallised from ethanol to give 2-(2-*anilinoethyl*)-1,3-*diphenylguanidine*, prisms (2·6 g., 79%), m. p. 139° (Found: C, 76·4; H, 6·8; N, 16·8. $C_{21}H_{22}N_4$ requires C, 76·5; H, 6·7; N, 16·9%).

2-(2-*Anilinoethyl*)-2-*phenylguanidine*.—*N*-Phenylethylenediamine (1 g.), toluene-*p*-sulphonic acid (1·4 g., 1 mol.) and phenylcyanamide (0·87 g., 1 mol.) were heated over a naked flame until a homogeneous melt was obtained, and then for 2 hr. on an oil-bath at 130—170°. The mixture was cooled and crystallised from ethanol to give 2-(2-*anilinoethyl*)-1-*phenylguanidine toluene*-p-*sulphonate*, needles (1·6 g., 49%), m. p. 170° (Found: C, 61·6; H, 6·2; N, 13·1. $C_{22}H_{26}N_4O_3S$ requires C, 62·0; H, 6·1; N, 13·1%).

2-*Anilino*-2-*imidazoline*.—(*a*) 1-Phenyl-3-nitroguanidine [13] (5 g.) and ethylenediamine (1·7 g., 1 mol.) were allowed to react in boiling ethanol (100 ml.) for 24 hr. when ammonia ceased to be evolved. The oily residue, after removal of the solvent, gave 2-anilino-2-imidazoline picrate (1·3 g., 12%), m. p. 193° (from aqueous alcohol), not depressed by an authentic specimen,[1] and a residue of less soluble *di*-(3-*phenylguanidino*)*ethane dipicrate*, needles (1·6 g., 15%), m. p. 235° (decomp.) (from water) (Found: C, 44·7; H, 3·7. $C_{28}H_{26}N_{12}O_{14}$ requires C, 44·5; H, 3·45%).

(*b*) 1-Phenyl-3-nitroguanidine (7 g.) in ethanol (50 ml.) was heated with ethylenediamine monotoluene-*p*-sulphonate (9 g., 1 mol.) for 48 hr. The solvent was removed *in vacuo* and the semi-solid residue dissolved in water. The solution was decolourised with charcoal, made basic with sodium hydroxide solution, and extracted with chloroform. The dried extract gave, on evaporation, 2-anilino-2-imidazoline, needles (1·2 g., 19%), m. p. 135° [from benzene–light petroleum (b. p. 60—80°)] (lit.,[1] 135°).

2-p-*Chloroanilino*-2-*imidazoline*.—This was prepared from ethylenediamine monotoluene-*p*-sulphonate and 1-*p*-chlorophenyl-3-nitroguanidine [14] as described in (*b*) above, *prisms* (33%), m. p. 156° (decomp.) [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 55·5; H, 4·9; N, 21·3. $C_9H_{10}ClN_3$ requires C, 55·3; H, 5·1; N, 21·5%). The *picrate*, needles from aqueous ethanol, had m. p. 212—213° (decomp.) (Found: C, 42·7; H, 3·1. $C_{15}H_{13}ClN_6O_7$ requires C, 42·5; H, 3·1%).

2-(2-*Phenylhydrazino*)-2-*imidazoline*.—(*a*) 1-Anilino-3-nitroguanidine [15] (5 g.) and ethylenediamine monotoluene-*p*-sulphonate (5·95 g., 1 mol.) were allowed to react in boiling ethanol (100 ml.) for 12 hr. whilst ammonia was evolved. The solvent was removed and the residue crystallised from ethanol–ether to give 2-(2-*phenylhydrazino*)-2-*imidazoline toluene*-p-*sulphonate*, needles (6·8 g., 76%), m. p. 176° (turning pink on exposure to air) (Found: C, 55·0; H, 5·5; N, 15·6. $C_{16}H_{20}N_4SO_3$ requires C, 55·2; H, 5·7; N, 16·1%). The *picrate*, needles from ethanol, had m. p. 198° (decomp.) (Found: C, 44·3; H, 4·0. $C_{15}H_{15}N_7O_7$ requires C, 44·4; H, 3·7%).

(*b*) 2-Methylthio-2-imidazoline hydriodide (2 g.) and phenylhydrazine (0·9 g., 1·02 mol.) were heated on a water-bath in ethanol (20 ml.) for 5 hr., until methanethiol ceased to be evolved. The solvent was removed under reduced pressure and the residue washed with ether. The crude hydriodide was converted into 2-(2-phenylhydrazino)-2-imidazoline picrate (0·6 g., 48%).

2-*Amino*-2-*oxazoline*.—(*a*) 1-(2-Hydroxyethyl)-3-nitroguanidine [16] (0·6 g.) in ethanol (20 ml.) was heated under reflux with methylamine (0·26 g., 2·1 mol.) for 5 hr. The excess of methylamine was removed *in vacuo* and ethanolic picric acid added to the residue to give 2-amino-2-oxazoline picrate, needles (0·9 g., 70%), m. p. 186° (from ethanol) (lit.,[17] 186°) (Found: C, 34·4; H, 3·1. Calc. for $C_9H_9N_5O_8$: C, 34·3; H, 2·9%).

(*b*) 1-Methyl-3-nitroguanidine [13] (1·5 g.) in ethanol (20 ml.) was treated with ethanolamine (0·6 g., 1·2 mol.) on a steam-bath for 24 hr. The solvent was removed and the residue

[13] McKay and Wright, *J. Amer. Chem. Soc.*, 1947, **69**, 3028.
[14] U.S.P. 2,559,085.
[15] Henry, *J. Amer. Chem. Soc.*, 1950, **72**, 5343.
[16] McKay and Milks, *J. Amer. Chem. Soc.*, 1950, **72**, 1616.
[17] Gabriel, *Ber.*, 1889, **22**, 1150.

converted into the picrate. Repeated crystallisation from ethanol gave 2-amino-2-oxazoline picrate (0·75 g., 19%).

2-Amino-5,6-dihydro-1,3-oxazine.—1-(3-Hydroxypropyl)-3-nitroguanidine [18] (2 g.) in ethanol was heated under reflux with methylamine (1·6 g., 4 mol.) for 3 hr. The excess of methylamine was removed *in vacuo*, together with the solvent, and the oily residue converted into 2-amino-5,6-dihydro-1,3-oxazine picrate, needles (0·7 g., 17%), m. p. 196° (decomp.) after sintering at 185° (from aqueous alcohol) (lit.,[9] 188—200°) (Found: C, 36·4; H, 3·4. Calc. for $C_{10}H_{11}N_5O_8$: C, 36·5; H, 3·3%).

2-p-*Chloranilino-2-oxazoline.*—(*a*) 1-(*p*-Chlorophenyl)-3-nitroguanidine [14] (1·6 g.) and ethanolamine (0·5 g., 1·1 mol.) in ethanol (25 ml.) were heated under reflux for 96 hr. The solvent was removed *in vacuo* and the residue extracted with dilute hydrochloric acid. Addition of sodium hydroxide solution precipitated 2-(*p*-chloranilino)-2-oxazoline, needles (0·35 g., 24%), m. p. 161° [from benzene–light petroleum (b. p. 60—80°)] (lit.,[19] 163°) (Found: C, 54·7; H, 4·7; N, 14·3. Calc. for $C_9H_9ClN_2O$: C, 55·0; H, 4·6; N, 14·2%). The *picrate*, needles from aqueous ethanol, had m. p. 182° (decomp.) (Found: C, 42·25; H, 3·1. $C_{15}H_{12}ClN_5O_8$ requires C, 42·3; H, 2·8%).

(*b*) 2-*p*-Chloranilino-2-oxazoline was prepared in 26% yield by the action of methyl iodide followed by sodium ethoxide on 1-(2-hydroxyethyl)-3-*p*-chlorophenylthiourea, as described in a previous Paper.[1]

The Table lists oxazolines produced by these methods.

2-(Substituted amino)-2-oxazolines (XV; $n = 1$) and their derivatives.

			Yield		Found (%)				Reqd. or Calc. (%)		
R^1	R^2	Method	(%)	M. p.	C	H	N	Formula	C	H	N
H	Ph	A	16·5	121° [a]	66·5	6·2	17·4	$C_9H_{10}N_2O$	66·7	6·2	17·3
	Picrate			187 [b]	45·8	3·3		$C_{15}H_{13}N_5O_8$	46·0	3·3	
Et	Ph										
	Picrate	A	20	135 [c]	48·7	4·2		$C_{17}H_{17}N_5O_8$	48·7	4·1	
Et	*p*-Cl·C_6H_4	A	35	112 [d]	58·8	5·7	12·65	$C_{11}H_{13}ClN_2O$	58·9	5·8	12·5
	,,	B	24	113 [d, e]							
	Picrate			164 [f]	45·0	3·65		$C_{17}H_{16}ClN_5O_8$	45·0	3·5	
H	*p*-MeO·C_6H_4	B	65	121—122 [g]	62·5	6·3	14·8	$C_{10}H_{12}N_2O_2$	62·6	6·3	14·6
	Picrate			165 [f]	45·9	3·6		$C_{16}H_{15}N_5O_9$	45·6	3·6	

[a] From chloroform–light petroleum (b. p. 40—60°) (lit.[1] m. p. 119—120°). [b] From aqueous ethanol (lit.,[1] m. p. 187°). [c] From ethanol (lit.,[1] m. p. 135°). [d] From benzene–light petroleum (b. p. 60—80°). [e] A non-basic residue from this preparation crystallised from benzene–light petroleum (b. p. 60—80°) to give 1-*p*-chlorophenyl-4-ethyl-2-imidazolidone, needles (17%), m. p. 147° (Found: C, 59·0; H, 5·7; N, 12·5. $C_{11}H_{13}ClN_2O$ requires C, 58·9; H, 5·8; N, 12·5%). [f] From ethanol. [g] From chloroform–light petroleum (b. p. 40—60°) (lit.,[19] m. p. 120°).

1-(p-*Chlorophenyl*)-3-(2-*hydroxyethyl*)*thiourea.*—*p*-Chlorophenylisothiocyanate (20 g.) and ethanolamine (7·2 g., 1 mol.) were allowed to react in ethanol (40 ml.). After 2 hr. the crystalline material gave the *thiourea*, needles (25 g., 92%), m. p. 127° (from ethanol) (Found: C, 46·85; H, 4·8. $C_9H_{11}ClN_2OS$ requires C, 46·8; H, 4·8%).

New thioureas prepared in this way were 1-(p-*chlorophenyl*)-3-(1-*hydroxymethylpropyl*)*thiourea* needles (78%), m. p. 120° (from ethanol) (Found: C, 51·3; H, 5·6. $C_{11}H_{15}ClN_2OS$ requires C, 51·1; H, 5·8%) and 1-(2-*hydroxyethyl*)-3-(p-*methoxyphenyl*)*thiourea*, prisms (79%), m. p. 146—147° (from benzene–ethanol) (Found: C, 53·6; H, 6·0. $C_{10}H_{14}N_2O_2S$ requires C, 53·3; H, 6·2%).

1-*Phenyl*-2-*imidazolidone.*—2-Anilino-2-oxazoline (1·9 g.) in nitrobenzene (30 ml.) was heated under reflux for 4 hr. The solvent was steam-distilled and the aqueous residue extracted with chloroform. The chloroform extract was washed with dilute hydrochloric acid and water, dried, and evaporated. The residue crystallised from chloroform–light petroleum (b. p. 40—60°) to give 1-phenyl-2-imidazolidone, needles (0·63 g., 33%), m. p. 162—163°, not depressed by an authentic specimen.[1]

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[18] Fishbein and Gallaghan, *J. Amer. Chem. Soc.*, 1954, **76**, 3217.
[19] Najer, Chabrier, and Giudicelli, *Bull. Soc. chim. France*, 1959, 352.