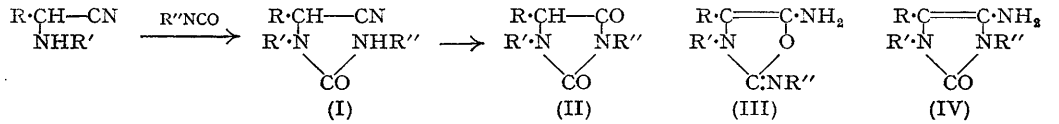
725. *Studies in the Azole Series. Part XXXIII.* The Interaction of α-Amino-nitriles and Alkyl or Aryl* iso*Cyanates.*

By A. H. Cook and G. D. Hunter.

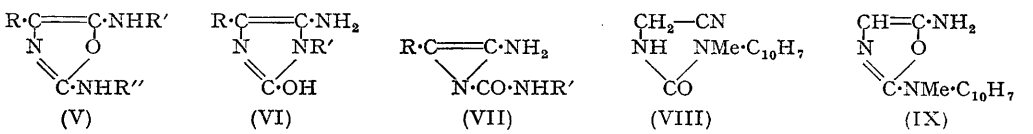
Substituted ureas obtained by the interaction of α-amino-nitriles and alkyl or aryl *iso*cyanates are converted by sodium ethoxide in ethanol into the corresponding 5-amino-oxazoles. In the case of the 5-amino-2-arylamino-oxazoles, treatment with aqueous sodium hydroxide results in the formation of dimeric products—obtained in some cases directly in admixture with 5-amino-oxazoles—which are formulated as 1-arylcarbamyl-3-*N'*-arylureido-2 : 4-di-imino-pyrrolidines.

Although the interaction of α-amino-nitriles and various organic *iso*thiocyanates has been discussed in earlier Parts of this series (Cook, Downer, and Heilbron, *J.*, 1948, 1262, 2028; Capp, Cook, Downer, and Heilbron, *J.*, 1948, 1340; Cook, Heilbron, and Smith, *J.*, 1949, 1140), little has hitherto been reported on reactions involving α-amino-nitriles and organic *iso*cyanates apart from the formation of substituted ureas (I) (Pinner and Lifschütz, *Ber.*, 1887, **20**, 2355; Pinner, *Ber.*, 1888, **21**, 2321; Mouneyrat, *Ber.*, 1900, **33**, 2393; Klages, *J. pr. Chem.*, 1902, [ii], **65**, 189; Delepine, *Bull. Soc. chim.*, 1903, **29**, 1190, 1198; Cook, Downer, and Heilbron, *J.*, 1948, 1264) and certain of the corresponding hydantoins (II). The present work shows, however, that compounds of type (III) are readily obtainable from the corresponding ureas (I).



(I) (II) (III) (IV)

The reaction between ethyl aminocyanoacetate and α-naphthyl and phenyl *iso*cyanates yielded respectively *N*-carbethoxycyanomethyl-*N'*-α-naphthyl- and -*N'*-phenyl-urea (I; R = CO_2Et, R' = H, R'' = $C_{10}H_7$ or Ph respectively). As expected, the former urea was readily converted into 5-carbethoxy-3-α-naphthylhydantoin (II; R = CO_2Et, R' = H, R'' = $C_{10}H_7$) by acid. Each of the ureas, however, was converted into a compound isomeric with the starting material when heated under reflux with ethanolic sodium ethoxide. For reasons given below, these isomers have been assigned the structures ethyl 5-amino-2-α-naphthylamino- and 5-amino-2-anilino-oxazole-4-carboxylate (V; R = CO_2Et, R' = H, R'' = $C_{10}H_7$ or Ph respectively). The former 5-amino-oxazole formed a crystalline



(V) (VI) (VII) (VIII) (IX)

monohydrochloride, a monomethyl derivative (probably V; R = CO_2Et, R' = Me, R'' = $C_{10}H_7$), and a monoacetyl derivative (V; R = CO_2Et, R' = Ac, R'' = $C_{10}H_7$). Its alternative formulation as 5-amino-2-hydroxy-1-α-naphthylglyoxaline was rendered most unlikely, first by its failure to couple with diazonium salts under a variety of conditions, and secondly by the failure of attempts to hydrolyse it to the corresponding hydantoin.

Similarly interaction of aminoacetonitrile and α-naphthyl *iso*cyanate in ether yielded *N*-cyanomethyl-*N'*-α-naphthylurea (I; R = R' = H, R'' = $C_{10}H_7$) which was smoothly

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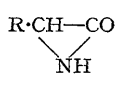
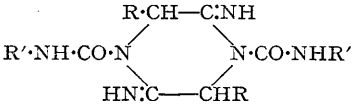
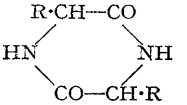
converted into 3-α-naphthylhydantoin (II; R = R′ = H, R″ = $C_{10}H_7$) and also into 5-amino-2-α-naphthylamino-oxazole (V; R = R′ = H, R″ = $C_{10}H_7$), which formed a hydrochloride but was not diazotised under any of the usual conditions. The only possible alternative structures appeared to be those of the 5-aminoglyoxaline (VI; R = H, R′ = $C_{10}H_7$) and the 2-aminoazirine (VII; R = H, R″ = $C_{10}H_7$). The latter unlikely possibility was eliminated, for *N*-cyanomethyl-*N*-methyl-*N*′-α-naphthylurea (I, R = H, R′ = Me, R″ = $C_{10}H_7$) readily gave an isomeric product, 5-amino-2-α-naphthylimino-3-methyl-4-oxazoline (III; R = H, R′ = Me, R″ = $C_{10}H_7$), an azirine structure being impossible. 1-Methyl-3-α-naphthylhydantoin was readily obtained from the corresponding urea, as with the lower homologue. *N*-Cyanomethyl-*N*′-α-naphthylurea afforded a monomethyl derivative which was not identical with the isomer (I; R = H, R′ = Me, R″ = $C_{10}H_7$) previously obtained, and was evidently *N*-cyanomethyl-*N*′-methyl-*N*′-α-naphthylurea (VIII). Treatment with sodium ethoxide afforded an isomer which must have been 5-amino-2-(*N*-methyl-α-naphthylamino)-oxazole (IX), since this time a 5-aminoglyoxaline formulation was impossible.

Light was thrown on the structure of several compounds obtained incidentally (see Experimental section) largely as a result of investigations carried out on corresponding compounds derived from α-aminobenzyl cyanide. The latter substance readily gave, with α-naphthyl *iso*cyanate, *N*-α-cyanobenzyl-*N*′-α-naphthylurea (I; R = Ph, R′ = H, R″ = $C_{10}H_7$) which was converted by acid hydrolysis into 3-α-naphthyl-5-phenylhydantoin (II; R = Ph, R′ = H, R″ = $C_{10}H_7$), characterised as its monomethyl derivative. Treatment with sodium ethoxide under the usual conditions gave rise to two products, each isomeric with the starting material. The one formed in smaller proportion was regarded as 5-amino-2-α-naphthylamino-4-phenyloxazole (V; R = Ph, R′ = H, R″ = $C_{10}H_7$); it was characterised as a monohydrated monomethyl derivative, probably (V; R = Ph, R′ = Me, R″ = $C_{10}H_7$). It was easily convertible into the second isomer by boiling aqueous sodium hydroxide, and hydrolysis with ethanolic hydrogen chloride led to the formation of a compound of empirical formular C_8H_7ON. As a three-membered ring formulation, such as (X; R = Ph), had already been rejected in a case above, these results

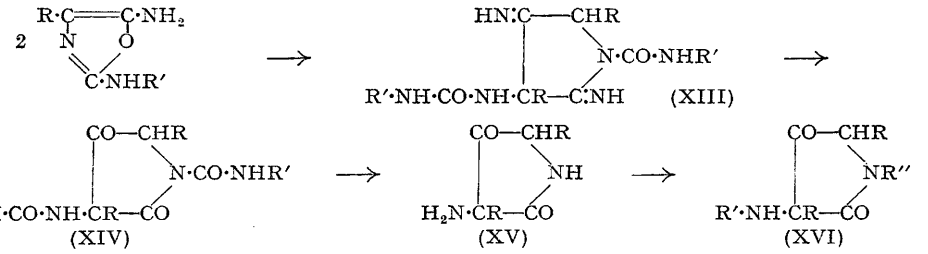

(X)


(XI)


(XII)

could only be interpreted on the basis that the compounds described here were dimeric and this indeed proved to be the case for the compound having the empirical formula C_8H_7ON. Di-imino- (XI) and diketo-piperazine (XII) structures were dismissed on account of the non-identity of the compound obtained in the present work with the known 2 : 4-diketo-3 : 5-diphenylpiperazine.

The compounds described here bore analogies to the "dibenzamidodioxytetrol" (Rügheimer, *Ber.*, 1888, **21**, 3325; 1889, **22**, 1954) which Cornforth and Huang (*J.*, 1948, 1958) have shown to be 3-benzamido-1-benzoyl-2 : 4-diketopyrrolidine. If the same type of reaction occurred in the present case, the corresponding sequence in the case of the 5-amino-oxazoles described here would be represented by the scheme :


(XIII) (XIV) (XV) (XVI)

Subsequent experiments have confirmed with reasonable certainty that this scheme

indeed describes the processes under investigation. The isomer obtained together with 5-amino-2-α-naphthylamino-4-phenyloxazole was formulated as 2 : 4-di-imino-1-α-naphthylcarbamyl-3-*N'*-α-naphthylureido-3 : 5-diphenylpyrrolidine (XIII; R = Ph, R' = $C_{10}H_7$), and the hydrolysis product $(C_8H_7ON)_2$ as 2 : 4-diketo-3 : 5-diphenylpyrrolidine (XV; R = Ph). Methylation confirmed the latter structure, a monomethyl derivative, presumably 3-amino-2 : 4-diketo-1-methyl-3 : 5-diphenylpyrrolidine (XVI; R = Ph, R' = H, R'' = Me) being obtained, while acetylation gave rise to a diacetyl derivative, presumably (XVI; R = Ph, R' = R'' = H). The compound (XV; R = Ph) moreover gave a red ferric chloride colour (cf. the colours obtained by Cornforth and Huang, *loc. cit.*, with similar compounds). The parent pyrrolidine (XIII; R = Ph, R' = $C_{10}H_7$) in its turn was characterised by a tetramethyl derivative and a diacetyl derivative. Reaction of the original 5-amino-oxazole (V; R = Ph, R' = H, R'' = $C_{10}H_7$) with ethanolic hydrogen chloride gave two further products whose composition was also in conformity with the above scheme: one was evidently 2 : 4-diketo-1-α-naphthylcarbamyl-3-*N'*-α-naphthylureido-3 : 5-diphenylpyrrolidine (XIV; R = Ph, R' = $C_{10}H_7$) while the other was undoubtedly the ethochloride of (XV; R = Ph). In view of these results, certain compounds obtained incidentally in other series (see Experimental section) have also been formulated as pyrrolidines.

In addition to the above testimony in favour of pyrrolidine structures, indirect evidence was obtained from a study of certain 5-amino-3-methyloxazolines. As was expected, 5-amino-3-methyl-2-α-naphthylimino-oxazoline (III; R = H, R' = Me, R'' = $C_{10}H_7$) gave no isomer in boiling alkali. A similar result was obtained in a further case where α-methylamino-*n*-valeronitrile was converted into *N*-1-cyano-*n*-butyl-*N*-methyl-*N'*-α-naphthylurea (I; R = Pr^n, R' = Me, R'' = $C_{10}H_7$) and thence into the isomeric 5-amino-3-methyl-2-α-naphthylimino-3-*n*-propyloxazoline (III; R = Pr^n, R' = Me, R'' = $C_{10}H_7$) in the usual way. 1-Methyl-3-α-naphthyl-5-*n*-propylhydantoin (II; R = Pr^n, R' = Me, R'' = $C_{10}H_7$), obtained from the above substituted urea by acid hydrolysis, had previously been prepared by the action of α-naphthyl *iso*cyanate on α-methylamino-*n*-valeric acid (Friedmann, *Beitr. Chem. Physiol. Path.*, 1908, **11**, 172).

In order to establish the generality of these reactions, further experiments were carried out with other *iso*cyanates. Phenyl *iso*cyanate reacted readily with α-aminobenzyl cyanide and α-methylamino-*n*-valeronitrile, yielding respectively *N*-α-cyanobenzyl-*N'*-phenylurea (I; R = R'' = Ph, R' = H) (Cook, Downer, and Heilbron, *loc. cit.*) and *N*-α-cyano-*n*-butyl-*N*-methyl-*N'*-phenylurea (I; R = Pr^n, R' = Me, R'' = Ph). The former compound behaved as was expected in that, after its treatment with sodium ethoxide in dry ethanol, 5-amino-2-anilino-4-phenyloxazole (V; R = R'' = Ph, R' = H) was ultimately isolated (as its acetate), together with a much larger proportion of the corresponding 2 : 4-di-iminopyrrolidine (XIII; R = R' = Ph).

Attention was then turned to the products derived from methyl *iso*cyanate, which reacted with α-aminobenzyl cyanide and with ethyl aminocyanoacetate, giving *N*-α-cyanobenzyl-*N'*-methylurea (I; R = Ph, R' = H, R'' = Me) and *N*-carbethoxycyanomethyl-*N'*-methylurea (I; R = CO_2Et, R' = H, R'' = Me) respectively. Hydrolysis of the former urea led to 3-methyl-5-phenylhydantoin (II; R = Ph, R' = H, R'' = Me), previously obtained by methylation of 5-phenylhydantoin (Pinner, *Ber.*, 1888, **21**, 2325). Cyclisation of the same urea gave only one isomer which was designated as 5-amino-2-methylamino-4-phenyloxazole (V; R = Ph, R' = H, R'' = Me). This compound could not, however, be isomerised further, as, when warmed with alkali, it rapidly lost methylamine. Ethyl aminocyanoacetate and α-aminobenzyl cyanide afforded *N*-carbethoxycyanomethylurea (I; R = CO_2Et, R' = R'' = H) and *N*-α-cyanobenzylurea (I; R = Ph, R' = R'' = H) (Pinner and Lifschütz, *loc. cit.*) respectively. Treatment of the latter urea with sodium ethoxide in dry ethanol led to extensive decomposition and only to a small yield of 2 : 5-diamino-4-phenyloxazole (V; R = Ph, R' = R'' = H). These results suggest that the transformation of a 5-amino-oxazole into a 2 : 4-di-iminopyrrolidine as described above is a property confined to those oxazoles carrying a 2-arylamino-substituent, though it is emphasised that the corresponding 2-alkylamino-compounds have so far only received limited study.

Experimental

Compounds derived from Ethyl Aminocyanoacetate and α-Naphthyl iso*Cyanate.*—Ethyl aminocyanoacetate (25·0 g.) in ether (150 c.c.) was stirred at 0° while a solution of α-naphthyl *iso*cyanate (33·0 g.) in ether (150 c.c.) was added during 15 minutes. The bulky colourless precipitate of N-*carbethoxycyanomethyl*-N′-α-*naphthylurea* (58·0 g., 100%) was collected after 24 hours at 0°; it crystallised from ethanol in masses of small needles, m. p. 179° (Found: C, 64·9; H, 5·3; N, 14·3. $C_{16}H_{15}O_3N_3$ requires C, 64·7; H, 5·1; N, 14·1%). The urea (1·0 g.) was heated under reflux with 10% ethanolic hydrogen chloride (10 c.c.) for 1 hour, passing rapidly into solution and being replaced by a precipitate of ammonium chloride. Filtration and addition of water (60 c.c.) to the filtrate yielded 5-*carbethoxy*-3-α-*naphthylhydantoin* (0·9 g., 90%), which crystallised from aqueous methanol in colourless prisms, m. p. 85° (Found: N, 9·1. $C_{16}H_{14}O_4N_2$ requires N, 9·4%). N-*Carbethoxycyanomethyl*-N′-α-*naphthylurea* (35·0 g.) was heated under reflux with a solution of sodium ethoxide [from sodium (2·6 g.) in dry ethanol (200 c.c.)] for 2 hours, and the deep yellow solution evaporated to dryness *in vacuo*. The crystalline residue was suspended in ice-cold water (100 c.c.) and acidified with acetic acid. The precipitate of *ethyl* 5-*amino*-2-α-*naphthylamino-oxazole*-4-*carboxylate* (33·0 g., 94%) was crystallised from aqueous acetic acid in rosettes of prisms, m. p. 237° (decomp.) [Found: C, 64·7; H, 5·2; N, 13·9%; *M* (Rast), 314, 312. $C_{16}H_{15}O_3N_3$ requires C, 64·7; H, 5·1; N, 14·1%; *M*, 297]. The above 5-amino-oxazole (0·5 g.) was added to 10% ethanolic hydrogen chloride (5 c.c.), whereupon it rapidly passed into solution. Filtration and addition of ether (30 c.c.) yielded, after 24 hours at 0°, *ethyl* 5-*amino*-2-α-*naphthylamino-oxazole*-4-*carboxylate hydrochloride* (0·5 g.) in masses of colourless rods or prisms, m. p. 215° (Found: C, 57·7; H, 5·1; N, 12·1. $C_{16}H_{15}O_3N_3Cl$ requires C, 57·8; H, 4·8; N, 12·6%). The same amino-oxazole yielded a *monomethyl* derivative when treated with diazomethane in ether; this crystallised from aqueous methanol in pale yellow felted needles, m. p. 98° (decomp.) (Found: N, 13·8. $C_{17}H_{17}O_3N_3$ requires N, 13·5%). Ethyl 5-amino-2-α-naphthylamino-oxazole-4-carboxylate (0·8 g.) was heated under reflux with acetic anhydride (5 c.c.) for 5 minutes, and the solution evaporated to dryness *in vacuo*. Extraction with methanol and addition of water to the extract yielded *ethyl* 5-*acetamido*-2-α-*naphthylamino-oxazole*-4-*carboxylate* (0·1 g.), which crystallised from ethanol–water in small pale yellow prisms of the *monohydrate*, m. p. 100° (Found: N, 11·7. $C_{18}H_{17}O_4N_3,H_2O$ requires N, 11·8%).

Ethyl 5-amino-2-α-naphthylamino-oxazole-4-carboxylate (10·0 g.) was heated under reflux with 10% aqueous sodium hydroxide (100 c.c.) until it dissolved (*ca.* 25 minutes). α-Naphthylamine was deposited and the suspension was cooled to 0°, then filtered, and the filtrate acidified with acetic acid. After 48 hours at 0°, the yellow precipitate of *diethyl* 2 : 4-*di-imino*-1-α-*naphthylcarbamyl*-3-N′-α-*naphthylureidopyrrolidine*-3 : 5-*dicarboxylate* (6·0 g., 60%), m. p. *ca.* 145° (decomp.), was filtered off and crystallised from acetic acid–water in yellow felted needles (Found: C, 64·8; H, 5·1; N, 13·8. $C_{32}H_{30}O_6N_6$ requires C, 64·7; H, 5·1; N, 14·1%). This pyrrolidine (3·0 g.) was heated under reflux with 10% ethanolic hydrogen chloride (30 c.c.) for 1 hour and the solution obtained poured into cold water (200 c.c.) and cooled to 0° for 48 hours. Filtration, extraction of the precipitate with methanol (10 c.c.), and further precipitation with water (30 c.c.) yielded 2 : 4-*diketo*-1-*naphthylcarbamyl*-3-N′-α-*naphthylureidopyrrolidine monohydrate* (1·0 g.), m. p. 80—110° (decomp.) (Found: C, 66·1; H, 4·7; N, 12·3. $C_{26}H_{22}O_5N_4$ requires C, 66·4; H, 4·7; N, 11·9%). Ethyl 5-amino-2-α-naphthylamino-oxazole-4-carboxylate (1·3 g.) was heated under reflux with 10% ethanolic hydrogen chloride (10 c.c) for 3 hours and poured into cold water (50 c.c.). The product obtained after 12 hours at 10° was a complex mixture, but fractional crystallisation from methanol–water led to the isolation of *diethyl* 3-*amino*-2 : 4-*diketopyrrolidine*-3 : 5-*dicarboxylate* in small golden prisms, m. p. 125° (decomp.) (Found: C, 45·6; H, 5·0; N, 11·8. $C_{10}H_{14}O_6N_2$ requires C, 46·5; H, 5·4; N, 10·9%).

Compounds derived from α-Aminobenzyl Cyanide and α-Naphthyl iso*Cyanate.*—A solution of α-naphthyl *iso*cyanate (33·8 g.) in ether (100 c.c.) was added during 20 minutes to a stirred solution of α-aminobenzyl cyanide (26·4 g.) in ether (250 c.c.) at 0°. The exothermic reaction rapidly produced a voluminous white precipitate of N-α-*cyanobenzyl*-N′-α-*naphthylurea* (58·5 g., 97%), which was collected after 24 hours at 0°. The urea crystallised from acetic acid in needles, m. p. 190° (decomp.) (Found: C, 75·8; H, 5·1; N, 14·3. $C_{19}H_{15}ON_3$ requires C, 75·8; H, 5·0; N, 14·0%). This urea (2·0 g.) was heated under reflux with 10% ethanolic hydrogen chloride (20 c.c.) for 75 minutes. Ammonium chloride was filtered off, and addition of water (50 c.c.) to the filtrate precipitated 3-α-*naphthyl*-5-*phenylhydantoin* (1·8 g., 90%) which crystallised from methanol in short colourless needles, m. p. 192° (Found: C, 75·7; H, 4·9; N, 9·4. $C_{19}H_{14}O_2N_2$ requires C, 75·5; H, 4·6; N, 9·3%). Acetylation of the hydantoin with

boiling acetic anhydride in presence of a trace of sulphuric acid gave a *monoacetyl* derivative which crystallised from acetic acid in silvery rods, m. p. 201° (Found, C, 73·6; H, 4·7; N, 8·1. $C_{21}H_{16}O_3N_2$ requires C, 73·3; H, 4·7; N, 8·1%).

N-α-Cyanobenzyl-*N'*-α-naphthylurea (45·0 g.) was heated under reflux with a solution of sodium (3·6 g.) in dry ethanol (250 c.c.) for 2 hours, and the yellow solution evaporated to dryness *in vacuo*. The crystalline residue was suspended in water (150 c.c.) and neutralised with acetic acid. After cooling at 0° for 12 hours, the yellow precipitate (45·0 g.) was filtered off and dried over calcium chloride *in vacuo*. Extraction with hot methanol left the sparingly soluble 5-*amino*-2-α-*naphthylamino*-4-*phenyloxazole* (18·0 g., 40%), which crystallised from acetic acid in small colourless prisms, m. p. 261° (Found: C, 75·6; H, 5·0; N, 14·0. $C_{19}H_{15}ON_3$ requires C, 75·8; H, 5·0; N, 14·0%). Crystallised from dioxan, it formed a stable *compound*, m. p. 257° (decomp.), as colourless needles and prisms which were no longer soluble in dioxan (Found: C, 72·2; H, 5·9; N, 11·6. $4C_{19}H_{15}ON_3,3C_4H_8O_2$ requires C, 71·9; H, 5·7; N, 11·4%). Addition of water to the methanolic filtrates (200 c.c.) obtained above yielded a pale yellow precipitate of 2 : 4-*di-imino*-1-α-*naphthylcarbamyl*-3-N'-α-*naphthylureido*-3 : 5-*diphenylpyrrolidine* (26·5 g., 59%), which crystallised from aqueous methanol in colourless prisms (Found: C, 75·8; H, 4·9; N, 13·6. $C_{38}H_{30}O_2N_6$ requires C, 75·8; H, 5·0; N, 14·0%). On being heated, it gradually melted in the range 125—135° with effervescence which subsided at 160°, the compound then resolidifying. When heated further, it had m. p. 230—235° (decomp.). 5-Amino-2-α-naphthylamino-4-phenyloxazole with diazomethane in ether formed a *monomethyl* derivative, pale yellow prisms (from aqueous methanol), m. p. 95° (decomp.) (Found: N, 12·8. $C_{20}H_{19}O_2N_3$ requires N, 12·6%). 2 : 4-Di-imino-1-α-naphthylcarbamyl-3-N'-α-naphthylureido-3 : 5-diphenylpyrrolidine (1·0 g.) was covered with a solution of diazomethane (1·0 g.) in ether (30 c.c.); nitrogen was evolved and the solution was allowed to evaporate to dryness. The *tetramethyl* derivative crystallised from aqueous methanol in masses of small pale yellow prisms of the *solvate*, m. p. 97° (decomp.) (Found: C, 73·5; H, 6·0; N, 11·6. $C_{42}H_{38}O_2N_6,2CH_3{\cdot}OH$ requires C, 73·1; H, 6·4; N, 11·6%). The compound was very sensitive to heat, and it was not possible to dry it above room temperature or remove the methanol of crystallisation without extensive decomposition. The same pyrrolidine formed a *diacetyl* derivative when boiled with an excess of acetic anhydride for a few minutes, crystallising from aqueous pyridine in clusters of small colourless prisms, m. p. 258° (decomp.) (Found: N, 12·4. $C_{42}H_{34}O_4N_6$ requires N, 12·2%). 5-Amino-2-α-naphthylamino-4-phenyloxazole (2·0 g.) was heated under reflux with 10% ethanolic hydrogen chloride (20 c.c.) for 4 hours. The solution was filtered and cooled to 0°. Addition of water (50 c.c.) then precipitated 2 : 4-*diketo*-1-α-*naphthylcarbamyl*-3-N'-α-*naphthylureido*-3 : 5-*diphenylpyrrolidine* (1·0 g.) as a yellow solid. Crystallisation from methanol–water at 0° gave pale yellow prisms, m. p. 145—155° (decomp.) (Found: C, 76·4; H, 5·5; N, 9·4. $C_{38}H_{28}O_4N_4$ requires C, 75·5; H, 4·7; N, 9·3%). Purification was very difficult as the product appeared to decompose in the presence of most organic solvents and probably contained appreciable quantities of further degradation products.

2 : 4-Di-imino-1-α-naphthylcarbamyl-3-*N'*-α-naphthylureido-3 : 5-diphenylpyrrolidine (5·0 g.) was heated under reflux with 10% ethanolic hydrogen chloride (50 c.c.) for 1 hour. After filtration, addition of water (200 c.c.), and cooling to 0° for 12 hours, the pale yellow precipitate of 3-*amino*-2 : 4-*diketo*-3 : 5-*diphenylpyrrolidine* (2·0 g.) was collected. It crystallised from aqueous methanol in colourless prisms, m. p. 174° (decomp.) (Found: C, 72·3; H, 5·1; N, 10·9%; *M*, 310. $C_{16}H_{14}O_2N_2$ requires C, 72·2; H, 5·3; N, 10·5%; *M*, 266). This last pyrrolidine (1·0 g.) was covered with a solution of diazomethane (0·5 g.) in ether (30 c.c.) and the ether allowed to evaporate slowly. The residual 3-*amino*-2 : 4-*diketo*-1-*methyl*-3 : 5-*diphenylpyrrolidine* (1·0 g.) crystallised from aqueous methanol in pale yellow felted needles, m. p. 198° (decomp.) (Found: C, 72·5; H, 5·5; N, 10·0. $C_{17}H_{16}O_2N_2$ requires C, 72·9; H, 5·7; N, 10·0%). The same aminodiketodiphenylpyrrolidine was treated with boiling acetic anhydride for 2 minutes. Working up in the usual manner gave 1-*acetyl*-3-*acetamido*-2 : 4-*diketo*-3 : 5-*diphenylpyrrolidine* as a colourless solid which crystallised from ethanolic acetic acid in colourless rectangular plates, m. p. 215° (Found: C, 68·2; H, 4·6. $C_{20}H_{18}O_4N_2$ requires C, 68·6; H, 5·1%). 5-Amino-2-α-naphthylamino-4-phenyloxazole (0·2 g.) was dissolved in cold 10% ethanolic hydrogen chloride (10 c.c.). Ether (120 c.c.) and light petroleum (b. p. 40—60°) (20 c.c.) were added, and the filtered solution was set aside at 0° for 2 weeks. Large colourless rectangular plates of 3-*amino*-1 : 1-*diethyl*-2 : 4-*diketo*-3 : 5-*diphenylpyrrolidinium chloride* (0·1 g.), m. p. 245—255° (decomp.), were filtered off (Found: C, 65·3; H, 5·8; N, 8·5. $C_{18}H_{19}O_2N_2Cl$ requires C, 65·4; H, 5·8; N, 8·5%).

Compounds derived from other α-*Amino-nitriles and* α-*Naphthyl* iso*Cyanate*.—α-Naphthyl *iso*-

cyanate (39·0 g.) in ether (150 c.c.) was added to a stirred solution of aminoacetonitrile (13·0 g.) in chloroform (60 c.c.) at 0° during 15 minutes. The exothermic reaction rapidly produced a voluminous white precipitate of N-*cyanomethyl*-N′-α-*naphthylurea* (51·5 g., 99%) which was collected after 24 hours at 0°. It crystallised from methanol in masses of colourless needles, m. p. 183° (Found : C, 69·3; H, 4·9; N, 18·4. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9; N, 18·7%). The above urea (1·0 g.) was converted by boiling 10% ethanolic hydrogen chloride into 3-α-*naphthylhydantoin* (0·9 g.) which crystallised from methanol in large colourless rhombs, m. p. 219° (Found : N, 12·7. $C_{13}H_{10}O_2N_2$ requires N, 12·4%). *N*-Cyanomethyl-*N*′-α-naphthylurea (30·0 g.) was added to a solution of sodium ethoxide [from sodium (3·4 g.) in dry ethanol (200 c.c.)] and heated under reflux for 1·5 hours. Evaporation to dryness *in vacuo* yielded a colourless crystalline solid which was suspended in water (150 c.c.) and neutralised with acetic acid. The precipitate of 5-*amino*-2-α-*naphthylamino-oxazole* (30·0 g., 100%) crystallised from methanol in plates, m. p. 193° (decomp.)(Found: C, 69·3; H, 5·1; N, 18·7. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9; N, 18·7%). The compound gradually decomposed when heated in camphor (Rast) (Found : *M*, 281. $C_{13}H_{11}ON_3$ requires *M*, 225). The above oxazole (1·0 g.) was shaken with 10% ethanolic hydrogen chloride (10 c.c.) at room temperature; it rapidly passed into solution and was replaced by a colourless precipitate of 5-*amino*-2-α-*naphthylamino-oxazole hydrochloride* (1·1 g.) which was collected after 1 week at 0° and crystallised from methanol–ether in colourless rods, m. p. 217° (decomp.) (Found : C, 59·9; H, 4·9; N, 15·7. $C_{13}H_{12}ON_3Cl$ requires C, 59·7; H, 4·6; N, 16·1%).

5-Amino-2-α-naphthylamino-oxazole (10·0 g.) was suspended in 10% aqueous sodium hydroxide (100 c.c.) and warmed to 80°; the oxazole rapidly passed into solution and was replaced by a bulky precipitate of α-naphthylamine. Heating was continued for 5 minutes before cooling to 0° and removal of α-naphthylamine by filtration. The filtrate was acidified with acetic acid and kept at 0° for 24 hours. 2 : 4-*Di-imino*-1-α-*naphthylcarbamyl*-3-N′-α-*naphthylureidopyrrolidine* (0·8 g., 8%) was collected and crystallised from aqueous methanol in yellow felted needles, m. p. 161—163° (decomp.) (Found : C, 68·8; H, 5·0; N, 18·7. $C_{26}H_{22}O_2N_6$ requires C, 69·3; H, 4·9; N, 18·7%).

N-Methylaminoacetonitrile (7·0 g.) in ether (300 c.c.) was stirred at 0° while a solution of α-naphthyl *iso*cyanate (17·0 g.) in ether (100 c.c.) was added during 10 minutes. The colourless precipitate of N-*cyanomethyl*-N-*methyl*-N′-α-*naphthylurea* (20·5 g., 85%) was collected after 24 hours at 0°, and crystallised from benzene, forming long, thin needles, m. p. 126° (Found : C, 70·4; H, 5·6; N, 17·9. $C_{14}H_{13}ON_3$ requires C, 70·3; H, 5·4; N, 17·6%). Heating this compound under reflux with 10% ethanolic hydrogen chloride for 2 hours gave 1-*methyl*-3-α-*naphthylhydantoin*, massive, irregular colourless prisms, m. p. 183 (from methanol) (Found : N, 11·9. $C_{14}H_{12}O_2N_2$ requires N, 11·7%). The same urea (12·0 g.) was heated under reflux for 1·5 hours with a solution of sodium ethoxide [from sodium (1·2 g.)] in dry ethanol. The solution was evaporated to dryness *in vacuo*, the residue suspended in water (50 c.c.) and neutralised with acetic acid, and the precipitate collected after 6 hours at 0°. 5-*Amino*-3-*methyl*-2-α-*naphthyliminooxazoline* (10·0 g., 83%) crystallised from methanol in thin rectangular plates, m. p. 163° (Found : C, 70·7; H, 5·7; N, 17·3. $C_{14}H_{13}ON_3$ requires C, 70·3; H, 5·4; N, 17·6%). After being boiled with 10% aqueous sodium hydroxide for a short period, it was recovered unchanged on acidification, though in small yield.

N-Cyanomethyl-*N*′-α-naphthylurea (5·0 g.) and methyl sulphate (3·0 g.) were heated under reflux in dry acetone (100 c.c.) in the presence of potassium carbonate (10·0 g.) for 4 hours. The suspension was filtered, treated with water (100 c.c.), and cooled to 0° for 18 hours. The bulky, colourless precipitate of N-*cyanomethyl*-N′-*methyl*-N′-α-*naphthylurea* (5·0 g.) was slowly formed, and crystallised from methanol in a voluminous mass of colourless felted needles, m. p. 198° (Found : C, 70·0; H, 5·0; N, 17·6. $C_{14}H_{13}ON_3$ requires C, 70·3; H, 5·4; N, 17·6%). This urea (3·0 g.) was heated under reflux for 2 hours with a solution of sodium ethoxide [from sodium (0·3 g.) in ethanol (30 c.c.)], and the solution evaporated to dryness *in vacuo*. The residue was suspended in water (30 c.c.), neutralised with acetic acid, and cooled to 0° for 3 hours. 5-*Amino*-2-N-*methyl*-α-*naphthylamino-oxazole* (2·5 g.) was filtered off; it crystallised from methanol in sheaves of colourless spears, m. p. 191—192° (decomp.) (Found : N, 18·3. $C_{14}H_{13}ON_3$ requires 17·6%).

α-Methylamino-*n*-valeronitrile (11·3 g.) in ether (50 c.c.) was added to a solution of α-naphthyl *iso*cyanate (17·5 g.) in ether (50 c.c.) at 0° during 5 minutes. After cooling at 0° for 18 hours, the bulky precipitate of N-n-*cyano*-n-*butyl*-N-*methyl*-N′-α-*naphthylurea* (28·8 g., 100%) was filtered off and crystallised from benzene, forming large colourless rods, m. p. 151° (Found: C, 73·2; H, 6·8; N, 14·9. $C_{17}H_{19}ON_3$ requires C, 72·6; H, 6·8; N, 14·9%). Heating it under reflux for 2 hours with 10% ethanolic hydrogen chloride yielded 1-methyl-3-α-naphthyl-5-*n*-propylhydantoin,

colourless rectangular plates, m. p. 153° (from methanol) (Found: C, 72·1; H, 6·8; N, 10·0. Calc. for $C_{17}H_{18}O_2N_2$: C, 72·3; H, 6·4; N, 9·9%). The same urea (1·9 g.) was added to a solution of sodium ethoxide [from sodium (0·15 g.) in dry ethanol (25 c.c.)] and heated under reflux for 2 hours. Evaporation to dryness and acidification gave a precipitate of *5-amino-3-methyl-2-α-naphthylimino-4-n-propyloxazoline* (1·9 g., 100%), which crystallised from methanol in thick, massive rods, m. p. 198° (Found: N, 14·6. $C_{17}H_{19}ON_3$ requires N, 14·9%). It was much more stable to hydrolysis than any of the other compounds obtained in this series, being recovered substantially unchanged after 3 hours' refluxing with ethanolic hydrogen chloride; neither isomer nor dimer was obtained.

Compounds derived from α-Amino-nitriles and Phenyl iso*Cyanate.*—A solution of phenyl *iso*cyanate (11·6 g.) in ether (100 c.c.) was added during 5 minutes to a solution of ethyl aminocyanoacetate (12·5 g.) in ether (50 c.c.) at 0°. After 18 hours at 0°, the bulky precipitate of *N-cyanocarbethoxymethyl-N′-phenylurea* (21·5 g., 89%) was filtered off and crystallised from methanol, forming long, thin, colourless needles, m. p. 167—169° (Found: C, 57·9; H, 5·4; N, 16·9. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3; N, 17·0%). A solution of sodium ethoxide [from sodium (0·5 g.) in dry ethanol (50 c.c.)] was added to the above urea (5·0 g.). After 2 hours' heating under reflux the orange solution was evaporated to dryness *in vacuo*, and the crystalline residue treated with water (35 c.c.) and neutralised with acetic acid. The colourless precipitate of *ethyl 5-amino-2-anilino-oxazole-4-carboxylate* (4·1 g., 82%) was filtered off; crystallisation from aqueous methanol gave pale yellow cubes, m. p. 211—212° (Found: C, 58·3; H, 5·4; N, 17·0. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3; N, 17·0%).

α-Aminobenzyl cyanide (12·5 g.) in ether (100 c.c.) was cooled to 0°, and a solution of phenyl *iso*cyanate (11·5 g.) in ether (100 c.c.) added during 10 minutes. A voluminous white precipitate rapidly appeared, and the *N*-α-cyanobenzyl-*N′*-phenylurea (22·5 g., 94%) was collected after 72 hours at 0°. The urea crystallised from ethanol in colourless hairs, m. p. 155°. The same compound (12·5 g.) was heated with a solution of sodium ethoxide [from sodium (1·2 g.) in dry ethanol (200 c.c.)] under reflux for 1·5 hours. The yellow solution was evaporated to dryness *in vacuo*. The crystalline residue, suspended in ice-cold water (80 c.c.), was neutralised with acetic acid, and the resulting yellow precipitate collected after 12 hours at 0°. This solid was stirred with hot methanol (100 c.c.) and cooled to 0° for a further 12 hours. The colourless residue of 5-amino-2-anilino-4-phenyloxazole (1·7 g.) was collected; it crystallised from acetic acid as the *acetate* in colourless hexagonal plates, m. p. 217° (decomp.) (Found: C, 65·9; H, 5·4. $C_{17}H_{17}O_3N_3$ requires C, 65·6; H, 5·5%). Addition of cold water (100 c.c.) to the methanolic filtrates obtained above yielded a yellow precipitate of *2 : 4-di-imino-3 : 5-diphenyl-1-phenylcarbamyl-3-N′-phenylureidopyrrolidine hydrate* (9·5 g.), yellow prisms (from methanol–water), m. p. 94° (decomp.) (Found: C, 69·5; H, 5·6. $C_{30}H_{26}O_2N_6,H_2O$ requires C, 69·2; H, 5·4%).

α-Methylamino-*n*-valeronitrile (6·0 g.) in ether (20 c.c.) was cooled to 0°, and a solution of phenyl *iso*cyanate (6·5 g.) in ether (30 c.c.) added during 5 minutes. The colourless solution was kept at 0° for 24 hours, and a crystalline solid gradually deposited. This precipitate (4·7 g.) was filtered off, and addition of light petroleum (b. p. 40—60°) to the filtrate gave a further 5·0 g. of crystalline solid (total yield 84%). *N-α-Cyano-n-butyl-N-methyl-N′-phenylurea* crystallised from benzene containing 10% light petroleum (b. p. 40—60°) in long, thin, colourless rods, m. p. 77° (Found: N, 18·2. $C_{13}H_{17}ON_3$ requires N, 18·2%).

Compounds derived from α-Amino-nitriles and Methyl iso*Cyanate.*—A solution of methyl *iso*cyanate (3·0 g.) in ether (50 c.c.) was added to α-aminobenzyl cyanide (6·5 g.) in ether (50 c.c.) at 0° during 5 minutes. The crystalline precipitate of *N-α-cyanobenzyl-N′-methylurea* (8·3 g., 87%) was collected after 72 hours at 0° and recrystallised from methanol in long, thin, colourless needles, m. p. 166° (Found: C, 63·2; H, 5·9; N, 22·1. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8; N, 22·2%). This urea (6·7 g.) was heated with a solution of sodium ethoxide [from sodium (0·85 g.) in dry ethanol (50 c.c.)] under reflux for 1·5 hours. The dark solution was evaporated to dryness *in vacuo*, and the residue neutralised with aqueous acetic acid. After 13 hours at 0°, the yellow precipitate of *5-amino-2-methylamino-4-phenyloxazole* (3·2 g., 48%) was filtered off. Crystallisation was effected from acetic acid–light petroleum (b. p. 40—60°), giving small colourless needles, m. p. *ca.* 240° (decomp.) (Found: C, 64·3; H, 5·5. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8%). Heating the original urea with ethanolic hydrogen chloride gave, in the usual way, 3-methyl-5-phenylhydantoin which crystallised from aqueous methanol in square plates, m. p. 160°.

Ethyl aminocyanoacetate (10·5 g.) in ether (65 c.c.) was treated with an equivalent amount of methyl *iso*cyanate in ether (50 c.c.), added at 0° during 5 minutes. After cooling at 0° for 24 hours, the colourless precipitate of *N-cyanocarbethoxymethyl-N′-methylurea* (12·5 g., 78%) was

filtered off. It crystallised from methanol in long, thin, colourless needles, m. p. 164° (Found: C, 45·6; H, 5·9; N, 22·7. $C_7H_{11}O_3N_3$ requires C, 45·4; H, 5·9; N, 22·7%).

Compounds derived from α-Amino-nitriles and Sodium Cyanate.—α-Aminobenzyl cyanide (20·0 g.) was dissolved in 50% aqueous acetic acid and the solution cooled to 0°. Finely powdered sodium cyanate (10·0 g.) was added during 15 minutes with stirring. *N*-α-Cyanobenzylurea (26·5 g., 100%) was collected after 24 hours at 0°. After crystallisation from water, it had m. p. 177°. This urea (12·0 g.) was heated with a solution of sodium (1·6 g.) in dry ethanol (100 c.c.) under reflux for 1·5 hours. The solution became dark green and ammonia was steadily evolved. Evaporation to dryness *in vacuo* yielded a gum which was suspended in cold water and neutralised with acetic acid. After cooling to 0° for 24 hours, the yellow precipitate of 2 : 5-*diamino*-4-*phenyloxazole* (1·9 g., 16%) was filtered off and well washed with water (Found: C, 60·9; H, 4·9. $C_9H_9ON_3$ requires C, 61·7; H, 5·1%). It was insoluble in most organic solvents, but dissolved to a moderate extent in acetic acid, with partial decomposition.

Ethyl aminocyanoacetate (3·5 g.) was dissolved in 50% aqueous acetic acid (30 c.c.) at 0°. Finely powdered sodium cyanate (1·75 g.) was added during 8 minutes with stirring; a bulky white precipitate was soon formed. After cooling at 0° for 24 hours, N-*carbethoxycyanomethylurea* (3·3 g., 63%) was filtered off. It crystallised from methanol in long, thin, colourless needles, m. p. 166° (Found: C, 42·4; H, 5·5; N, 24·9. $C_6H_9O_3N_3$ requires C, 42·1; H, 5·3; N, 24·6%).

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