907. *Heterocyclic Systems Related to Pyrrocoline. Part II.*[1] *The Preparation of Polyazaindenes by Dehydrogenative Cyclisations.*

By J. D. Bower and G. R. Ramage.

Some heterocyclic systems based on pyrrocoline (I), but having additional nitrogen atoms in the five-membered ring, have been prepared by dehydrogenation of pyridine derivatives.

In Part I[1] the preparation was described of 2 : 3*a*-diazaindene, one of the heterocyclic systems formally to be obtained by replacing =CH– groups of the five-membered ring of pyrrocoline (I) by nitrogen atoms. Three other, previously unknown systems of this class, namely 1 : 2 : 7*a*- and 1 : 3 : 3*a*-triazaindene and 1 : 7*a*-diazaindene (II, III, and IV respectively; R = H in each case) have now been prepared. These have in common a nitrogen atom at the 3-position of pyrrocoline (I), and cyclisation to form the five-membered ring was conveniently effected by dehydrogenation of suitably substituted pyridine derivatives so that a N–N bond was formed with the ring-nitrogen atom.

1 : 2 : 7*a*-Triazaindene (II; R = H) and its 3-methyl derivative (II; R = Me) were prepared by oxidation of the hydrazones (V; R = H and Me respectively) obtained by the action of hydrazine hydrate on pyridine-2-aldehyde and methyl 2-pyridyl ketone respectively. Distillation of the crude hydrazone (V; R = H) gave a residue of pyridine-2-aldazine (VI; R = H) which was also formed by the action of pyridine-2-aldehyde on the hydrazone. Methyl 2-pyridyl ketone hydrazone (V; R = Me) similarly reacted with the parent ketone and gave the azine (VI; R = Me). The azines were also formed as by-products during the oxidation of the hydrazones (V; R = H and Me) by alkaline

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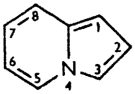
[1] Part I, Bower and Ramage, *J.*, 1955, 2834.

potassium ferricyanide, but the cyclisations proceeded readily and gave good yields of 1 : 2 : 7*a*-triazaindene (II; R = H) and its 3-methyl derivative (II; R = Me) respectively. These products were obtained as water-soluble, crystalline materials which exhibited a blue fluorescence in ultraviolet light. Methiodides were readily formed and silver nitrate combined in equimolecular proportions to form complexes. Fargher and Furness [2] found that 1 : 2 : 3*a*-triazaindene formed a similar type of complex, whereas two moles of 2 : 3*a*-diazaindene combine with one mole of silver nitrate (Part I).[1]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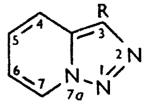
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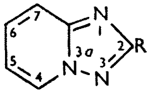
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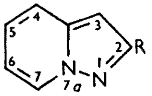
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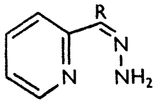
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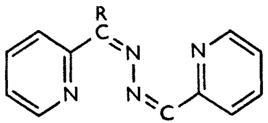
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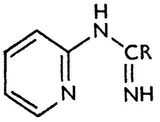
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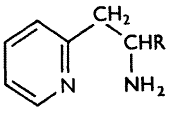
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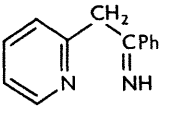
(IX)

Since this work was completed, Boyer, Borgers, and Wolford [3] have reported the preparation of the compounds (II; R = H and Ph) by the oxidation of the appropriate hydrazones by silver oxide.

Derivatives of 1 : 3 : 3*a*-triazaindenes (III) were prepared by the dehydrogenation of *N*-2-pyridylamidines (VII). The three substituted triazaindenes (III; R = Me, Ph, and *p*-tolyl) were prepared from the corresponding amidines (VII) which were obtained by the method of Oxley, Partridge, and Short [4] who prepared *N*-2-pyridylbenzamidine (VII; R = Ph) by the reaction of benzonitrile with 2-aminopyridine in the presence of aluminium chloride. The amidine (VII; R = Ph or *p*-tolyl) was readily cyclised by lead tetra-acetate in boiling acetic acid, and the products were obtained on dilution with water. It was more convenient to cyclise *N*-2-pyridylacetamidine (VII; R = Me) in boiling benzene since the product was very soluble in water, differing in this respect from the aryl-substituted compounds. Since the amidine (VII; R = H) has not yet been prepared, the parent member (III; R = H) was not obtained.

After several projected syntheses had been unsuccessful, the 1 : 7*a*-diazaindenes (IV; R = H and Ph) were obtained in reasonable yield from the amines (VIII; R = H and Ph respectively) by ferricyanide oxidation. The amine (VIII; R = Ph) was prepared by reduction of 2-phenacylpyridine oxime. Evidence supporting structure (IV; R = H) for the parent compound was provided by a molecular-weight determination and the formation of pyrazole-3-carboxylic acid on oxidation of the diazaindene by potassium permanganate. The ultraviolet absorption spectra of this and other polyazaindene systems afforded evidence confirming the structures of the new systems and this work is given in the following paper.

In the dehydrogenative cyclisations both the triazaindene systems were prepared by removal of the two hydrogen atoms. Several analogous cyclisations have been described, *e.g.*, the formation of 2 : 5-diphenyl-1 : 3 : 4-oxadiazole by ferricyanide oxidation of benzaldehyde benzoylhydrazone [5] and the preparation of benziminazoles and benzoxazoles

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[2] Fargher and Furness, *J.*, 1915, **107**, 688.

[3] Boyer, Borgers, and Wolford, *J. Amer. Chem. Soc.*, 1957, **79**, 678.

[4] Oxley, Partridge, and Short, *J.*, 1947, 1110.

[5] Stollé and Münch, *J. prakt. Chem.*, 1904, **70**, 393.

by lead tetra-acetate oxidation of Schiff's bases from *o*-diamines and *o*-aminophenols respectively.[6]

The formation of the 1 : 7*a*-diazaindene system, however, differs in that four hydrogen atoms were removed. That this did not proceed through the imine [7] (by the removal of two hydrogen atoms) and a subsequent cyclisation of the type discussed above was suggested by the failure to cyclise the imine (IX). It appeared likely that cyclisation first gave a dihydro-compound which was then dehydrogenated. A similar procedure has been applied to the preparation of 1 : 3*a*-diazaindene from its dihydro-derivative and is described in the following paper.

EXPERIMENTAL

Pyridine-2-aldehyde Hydrazone (V; R = H).—Pyridine-2-aldehyde (5·0 g.) and 90% hydrazine hydrate (10 c.c.) were heated together at 90—100° for 30 min. 30% Sodium hydroxide solution (10 c.c.) was added to the cooled solution which was then extracted with ether. The extract was dried (KOH) and fractionation gave the crude hydrazone (4·3 g.), b. p. 124—128°/5 mm., as a pale yellow liquid which, on redistillation, gave *pyridine-2-aldehyde hydrazone*, b. p. 127°/5 mm. (Found: C, 59·7; H, 6·0; N, 34·2. $C_6H_7N_3$ requires C, 59·5; H, 5·8; N, 34·7%). *Pyridine-2-aldehyde 4-phenylthiosemicarbazone*, prepared from the hydrazone and phenyl *iso*thiocyanate in boiling benzene, formed felted needles, m. p. 191—192°, from methanol (Found: C, 60·7; H, 4·4. $C_{13}H_{12}N_4S$ requires C, 60·9; H, 4·7%). The residue from the first distillation of the hydrazone, the *aldazine* (VI; R = H), crystallised from ethanol as yellow plates, m. p. 152° (Found: C, 69·0; H, 5·0. $C_{12}H_{10}N_4$ requires C, 68·6; H, 4·8%), and was also prepared from the hydrazone by reaction with pyridine-2-aldehyde.

Methyl 2-Pyridyl Ketone Hydrazone (V; R = Me).—Methyl 2-pyridyl ketone (5·0 g.) and 100% hydrazine hydrate (8 c.c.) were heated at 90—100° for 2½ hr. The cooled solution deposited a solid which was removed and combined with the material obtained by extraction with ether. Crystallisation of the product (5·5 g.) from benzene–light petroleum (b. p. 60—80°) gave the *hydrazone* as needles, m. p. 77—78° (Found: C, 62·1; H, 6·45. $C_7H_9N_3$ requires C, 62·2; H, 6·7%). *Methyl 2-pyridyl ketone 4-phenylthiosemicarbazone* formed very pale yellow needles, 178—179°, from ethanol (Found: C, 61·9; H, 5·05. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2%).

1 : 2 : 7a-*Triazaindene* (II; R = H).—Pyridine-2-aldehyde hydrazone (5·7 g.), potassium ferricyanide (33·5 g.), sodium hydrogen carbonate (8·6 g.), and water (220 c.c.) were heated together at 90—100° for 45 min. The solid azine (1·6 g.) was removed and 30% sodium hydroxide solution (20 c.c.) was added to the filtrate which was then extracted with chloroform. Distillation of the extract gave a fraction (2·9 g., 51%), b. p. 142—145°/7 mm., which solidified. Chromatography on alumina in a 1% solution of methanol in benzene, followed by evaporation at 110°/4 mm. on to a " cold-finger " condenser, gave 1 : 2 : 7a-*triazaindene* as prisms, m. p. 39—40° (Found: C, 60·2; H, 4·3. $C_6H_5N_3$ requires C, 60·5; H, 4·2%). The *methiodide* formed plates, m. p. 176°, from propanol (Found: C, 32·2; H, 3·3. $C_7H_8N_3I$ requires C, 32·2; H, 3·1%), and the 1 : 1 *compound* with silver nitrate was obtained as needles, m. p. 136° (decomp.), from very dilute nitric acid (Found: C, 25·5; H, 2·1. $C_6H_5N_3,AgNO_3$ requires C, 24·9; H, 1·7%).

3-*Methyl*-1 : 2 : 7a-*triazaindene* (II; R = Me).—Potassium ferricyanide (18·8 g.) and sodium hydrogen carbonate (4·9 g.) in water (150 c.c.) were added to methyl 2-pyridyl ketone hydrazone (3·5 g.). The mixture was heated at 90—100° for 30 min. to complete the reaction, which began at once. Filtration of the cooled mixture gave *methyl 2-pyridyl ketazine* (VI; R = Me) (0·1 g.) which formed yellow needles, m. p. 54°, on crystallisation from aqueous methanol (Found: C, 70·3; H, 6·0. $C_{14}H_{14}N_4$ requires C, 70·6; H, 5·9%). The filtrate was basified and extracted with chloroform. Fractionation of the extract gave an oil (2·75 g., 79%), b. p. 116—120°/2 mm., which soon solidified and was crystallised from benzene–light petroleum (b. p. 60—80°) and then evaporated at 100°/2 mm. on to a " cold-finger " condenser. 3-*Methyl*-1 : 2 : 7a-*triazaindene* was obtained as needles, m. p. 84—85°, which had a faint deep blue fluorescence under ultraviolet light (Found: C, 62·9; H, 5·0. $C_7H_7N_3$ requires C, 63·1; H,

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[6] Stephens, *Nature*, 1949, **164**, 342; Stephens and Bower, *J.*, 1949, 2971; 1950, 1722.

[7] Wibaut and de Jong, *Rec. Trav. chim.*, 1949, **68**, 485.

5·3%). The 1 : 1 *compound* with silver nitrate crystallised from water as needles, m. p. 195° (decomp.) (Found: C, 28·5; H, 2·2. $C_7H_7N_3,AgNO_3$ requires C, 27·7; H, 2·3%).

N-2-*Pyridylacetamidine* (VII; R = Me).—Aluminium chloride (7·5 g.) was added to a mixture of 2-aminopyridine (4·7 g.) and acetonitrile (3·3 g.). After the vigorous reaction had subsided the mixture was heated at 200° (bath) for 15 min., cooled, and decomposed with water (25 c.c.), and neutral material was removed by ether. The aqueous solution was then made strongly alkaline and extracted with ether.

The extracts from four such experiments were combined, dried (Na_2SO_4), and on fractionation gave 2-aminopyridine (5·2 g., 27%) followed by the crude amidine (11·9 g., 44% on initial aminopyridine), b. p. 126—127°/3 mm., which solidified. This was sufficiently pure for conversion into the triazaindene, but a sample was purified by chromatography on alumina in benzene containing 1% of ethanol. After a yellow impurity had passed through, the product was eluted with ethanol and evaporation twice over phosphoric oxide at 80°/2 mm. gave *N*-2-pyridylacetamidine as deliquescent prisms, m. p. 67—68°. The *picrate* formed felted yellow needles, m. p. 188—189°, from methanol (Found: C, 42·7; H, 3·1. $C_7H_9N_3,C_6H_3O_7N_3$ requires C, 42·9; H, 3·3%). The derivative with phenyl *iso*thiocyanate, N-*phenyl*-N′-(N-2-*pyridylacetimidoyl*)*thiourea*, formed needles, m. p. 134°, from benzene (Found: C, 62·2; H, 4·8. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2%).

N-2-*Pyridyl*-p-*toluamidine* (VII; R = *p*-tolyl).—The process used to prepare *N*-2-pyridylbenzamidine [4] was applied to *p*-tolunitrile and gave N-2-*pyridyl*-p-*toluamidine* (53%), which crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 127° (Found: C, 73·9; H, 6·2. $C_{13}H_{13}N_3$ requires C, 73·9; H, 6·2%).

2-*Methyl*-1 : 3 : 3a-*triazaindene* (III; R = Me).—*N*-2-Pyridylacetamidine (2·2 g.) was heated under reflux in benzene (25 c.c.) with lead tetra-acetate (7·4 g.) for 30 min. The cooled, filtered solution was extracted with 30% sodium hydroxide solution, and the organic layer was separated and distilled. A fraction (1·7 g., 78%), b. p. 130—135°/27 mm., which solidified, was redistilled (b. p. 137°/32 mm.) and evaporated at 70°/3 mm. on to a " cold-finger " condenser and gave 2-*methyl*-1 : 3 : 3a-*triazaindene* as deliquescent prisms, m. p. 49—50° (Found: C, 63·0; H, 5·7. $C_7H_7N_3$ requires C, 63·1; H, 5·3%). The *picrate* formed prisms, m. p. 177—178°, from methanol (Found: C, 43·0; H, 2·8. $C_7H_7N_3,C_6H_3O_7N_3$ requires C, 43·1; H, 2·8%).

2-*Phenyl* 1 : 3 : 3a-*triazaindene* (III; R = Ph).—Lead tetra-acetate (4·4 g.) and *N*-2-pyridylbenzamidine [4] (1·97 g.) were boiled for 10 min. in acetic acid (15 c.c.), and the solution was then poured into water. The dried precipitate was crystallised from light petroleum (b. p. 40—60°), and the resulting crystals (1·25 g.), m. p. 139°, were purified by evaporation at 150°/2 mm., followed by chromatography on alumina in benzene–ethanol (95 : 5 v/v). Further crystallisation gave 2-*phenyl*-1 : 3 : 3a-*triazaindene* as prisms, m. p. 141° (Found: C, 73·7; H, 4·6. $C_{12}H_9N_3$ requires C, 73·8; H, 4·6%). The *picrate* formed felted yellow needles, m. p. 168°, from ethanol (Found: C, 51·2; H, 3·6. $C_{12}H_9N_3,C_6H_3O_7N_3,C_2H_6O$ requires C, 51·1; H, 3·9%).

2-p-*Tolyl*-1 : 3 : 3a-*triazaindene* (III; R = *p*-tolyl).—A similar process to the above gave 2-p-*tolyl*-1 : 3 : 3a-*triazaindene* (60%) as needles, m. p. 173°, from aqueous ethanol (Found: C, 74·5; H, 5·2. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%).

2-(β-*Aminophenethyl*)*pyridine* (VIII; R = Ph).—Concentrated hydrochloric acid (30 c.c.) was added, in portions during about 5 min., to 2-phenacylpyridine oxime [8] (7·5 g.) and zinc (15·0 g.) in boiling methanol (200 c.c.). Boiling was continued for a further 10 min. before the mixture was filtered and the filtrate concentrated. A large excess of 30% sodium hydroxide solution was added and the product was isolated by ether. A fraction (4·5 g.), b. p. 157—162°/2 mm., on redistillation gave 2-(β-*aminophenethyl*)*pyridine* as a yellow oil, b. p. 160°/2 mm. (Found C, 79·2; H, 7·5. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1%). The *picrate* formed prisms, m. p. 148°, from methanol (Found: C, 53·1; H, 4·1. $C_{13}H_{14}N_2,C_6H_3O_7N_3$ requires C, 53·4; H, 4·0%). The *benzoyl* derivative formed needles, m. p. 148°, from ligroin (Found: C, 78·8; H, 6·0. $C_{20}H_{18}ON_2$ requires C, 79·4; H, 6·0%).

1 : 7a-*Diazaindene* (IV; R = H).—Potassium ferricyanide (142 g.), sodium hydrogen carbonate (36·5 g.), and 2-2′-aminoethylpyridine [9] (12·8 g.) were heated in water (435 c.c.) at 90—100° for 4 hr. A 30% solution of sodium hydroxide (60 c.c.) was added to the cooled solution before extraction with chloroform. The material left on evaporation of the chloroform

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[8] Scheuing and Winterhalder, G.P. 594,849.

[9] Kirchner, McCormick, Cavallito, and Miller, *J. Org. Chem.*, 1949, **14**, 388.

was extracted with benzene, and the benzene extract was concentrated and chromatographed on alumina. The fast-moving wide band, having a blue-violet fluorescence in ultraviolet light, was collected and gave, on distillation, 1 : 7a-*diazaindene* (2·6 g.), b. p. 108°/25 mm. [Found: C, 70·9; H, 5·3; N, 23·8%; *M* (cryoscopic, in benzene), 118. $C_7H_6N_2$ requires C, 71·2; H, 5·1; N, 23·7%; *M*, 118]. The *picrate* formed needles, m. p. 151° (decomp.), from ethanol and was dried over phosphoric oxide at 60°/2 mm. for 30 min. before analysis (Found: C, 45·6; H, 3·8. $C_7H_6N_2,C_6H_3O_7N_3,C_2H_6O$ requires C, 45·8; H, 3·8%).

Oxidation of the diazaindene (0·5 g.) in water (200 c.c.) at 50—55° with potassium permanganate (3·7 g.), filtration, and evaporation of the acidified filtrate to dryness, followed by extraction of the residue with acetone and evaporation gave pyrazole-3-carboxylic acid (0·15 g.), which crystallised from dilute hydrochloric acid as prisms, m. p. and mixed m. p. 211—212° (ethyl ester, m. p. and mixed m. p. 159—160°). The authentic sample of acid was prepared by the method of Pechmann and Burkard.[10]

2-*Phenyl*-1 : 7a-*diazaindene* (IV; R = Ph).—2-(β-Aminophenethyl)pyridine (1·5 g.), potassium ferricyanide (12·5 g.), and sodium hydrogen carbonate (3·2 g.) were heated at 90—100° in water (50 c.c.) for 3 hr. The cooled solution deposited a solid (1·3 g.) which, after several crystallisations from aqueous methanol, gave 2-*phenyl*-1 : 7a-*diazaindene* as needles, m. p. 109° (Found: C, 80·3; H, 5·2; N, 14·7. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%).

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[10] Pechmann and Burkard, *Ber.*, 1900, **33**, 3594.