Heterocyclic Systems Related to Pyrrocoline. Part I. 2 : 3a-*Diazaindene.*

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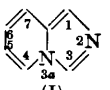
2 : 3*a*-Diazaindene (I) and various derivatives have been prepared by the cyclisation of 2-1′-acylaminoalkylpyridines. Acetylation of 2 : 3*a*-diazaindenes under Friedel–Crafts conditions has been shown to occur at the 1-position or, when this position is blocked as in 1-methyl-2 : 3*a*-diazaindene, at the 3-position. This is the reverse of the order of substitution in pyrrocoline (II).

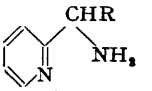
Although the chemistry of pyrrocoline (II) and its derivatives has been widely studied (Borrows and Holland, *Chem. Rev.*, 1948, **42**, 611) little is known about some of the nitrogen heterocyclic systems derived from pyrrocoline by replacement of the =CH– groups of the five-membered ring by nitrogen. Routes leading to such compounds have been examined and this paper is concerned with 2 : 3*a*-diazaindene (I) and some of its derivatives. Their preparation was achieved by the cyclisation of various 2-1′-acylaminoalkylpyridines by phosphoryl chloride.

2-Aminomethylpyridine (III; R = H) has been prepared by reduction of 2-cyanopyridine (Graf, *J. prakt. Chem.*, 1934, **140**, 39; 1936, **146**, 88; Kolloff and Hunter, *J. Amer. Chem. Soc.*, 1941, **63**, 490) but the reduction of pyridine-2-aldoxime (Craig and Hixon, *ibid.*, 1931, **53**, 4367) was found to be more satisfactory since commercial pyridine-2-aldehyde is now available.

1-Substituted 2 : 3*a*-diazaindenes were obtained from substituted 2-aminomethylpyridines. Two such amines (III; R = Me or Et) were prepared by the reduction of the


(I)


(II)



(III)

oximes of methyl and ethyl 2-pyridyl ketone and gave 1-methyl- and 1-ethyl-2 : 3*a*-diazaindene respectively.

Cyclisation of 2-formamidomethylpyridines gave 2 : 3*a*-diazaindenes which were unsubstituted at the 3-position, while substituents in this position were obtained by the use of acetyl, propionyl, and benzoyl derivatives of the amines. For example, 1-methyl-2 : 3*a*-diazaindene was obtained by cyclisation of the formyl derivative of the amine (III; R = Me) while the acetyl derivative of 2-1′-aminopropylpyridine (III; R = Et) gave 1-ethyl-3-methyl-2 : 3*a*-diazaindene. Compounds with substituents in the pyridine ring have not been prepared, but the route seems capable of extension in this way.

Attempts to prepare 2-acetamidomethylpyridine by acetylation with boiling acetic anhydride led to an oil which could not be purified, but when milder conditions were used (acetic acid and acetic anhydride at 100°) the acetyl derivative was readily obtained crystalline. It was found that acetic anhydride alone caused cyclisation together with some acetylation of the 3-methyl-2 : 3*a*-diazaindene formed.

The alkyl-substituted 2 : 3*a*-diazaindenes were obtained as liquids or low-melting solids which had a characteristic odour and darkened on storage, especially when impure. They were fluorescent under ultraviolet illumination, which was used to aid the chromatographic purification. Crystalline derivatives were formed with picric acid, methyl iodide, mercuric chloride, and silver nitrate, those with the last reagent having two molecules of the base associated with one of silver nitrate.

In view of the acetylation of 3-methyl-2 : 3*a*-diazaindene by acetic anhydride, the acetylation of the 2 : 3*a*-diazaindene system was studied under Friedel–Crafts conditions. The parent base (I) formed a monoacetyl derivative which was shown to be 1-acetyl-2 : 3*a*-diazaindene by Wolff–Kishner reduction to 1-ethyl-2 : 3*a*-diazaindene, which was also prepared by cyclisation of 2-1′-formamidopropylpyridine with phosphoryl chloride. 3-Methyl-2 : 3*a*-diazaindene was similarly shown to acetylate at the 1-position and gave the same acetyl derivative as was obtained by the action of acetic anhydride on 2-aminomethylpyridine and on 3-methyl-2 : 3*a*-diazaindene. However, 1-methyl-2 : 3*a*-diazaindene, in which the 1-position was blocked, was still acetylated, but at the 3-position. These results are in contrast with those obtained for the acetylation of pyrrocoline and its derivatives with acetic anhydride, which occurred preferentially at the 3-position and, when this was occupied, at the 1-position.

Experimental

2-*Aminomethylpyridine*.—This amine, b. p. 95—98°/20 mm., was prepared in 81% yield by reduction of pyridine-2-aldoxime with zinc powder and acetic acid (Craig and Hixon, *loc. cit.*). By the action of boiling 98% formic acid (6 c.c.) on the amine (2 g.) for 3 hr., 2-*formamidomethylpyridine* was obtained as a pale yellow oil (1·95 g., 77%), b. p. 160—161°/4 mm. (Found : C, 61·9; H, 6·2; N, 21·0. $C_7H_8ON_2$ requires C, 61·7; H, 5·9; N, 20·6%). The *picrate* formed prisms, m. p. 158°, from benzene (Found : C, 43·2; H, 3·0. $C_7H_8ON_2,C_6H_3O_7N_3$ requires C, 42·7; H, 3·0%). The amine (3 g.) with acetic anhydride (5 c.c.) in acetic acid (15 c.c.) at 100° for 30 min. gave 2-*acetamidomethylpyridine* as a pale yellow liquid (3·7 g., 89%), b. p. 160—163°/5 mm., which solidified, and crystallised from benzene–light petroleum (b. p. 60—80°) as plates, m. p. 59—60° (Found : C, 64·0; H, 6·8. $C_8H_{10}ON_2$ requires C, 64·0; H, 6·7%).

2 : 3a-*Diazaindene*.—2-Formamidomethylpyridine (1·95 g.) and phosphoryl chloride (4 c.c.) were heated under gentle reflux in benzene (12 c.c.) for 4 hr. The benzene and the excess of phosphoryl chloride were removed under reduced pressure and the residue was decomposed with water, basified, and extracted with chloroform. Fractionation of the dried extract gave the crude base (1·35 g., 80%), b. p. 120—125°/3 mm., which solidified and rapidly darkened. It was purified by evaporation at 80—90°/2 mm. on to a " cold finger " condenser, followed by chromatography on alumina in benzene containing 1% of methanol, and re-evaporation. 2 : 3a-*Diazaindene* was obtained as needles, m. p. 54—55°, having a strong light blue fluorescence under ultraviolet light (Found : C, 71·4; H, 5·2. $C_7H_6N_2$ requires C, 71·2; H, 5·1%). The *picrate* formed needles, m. p. 216° (decomp.), from ethanol (Found : C, 45·0; H, 3·0. $C_7H_6N_2,C_6H_3O_7N_3$ requires C, 45·0; H, 2·6%), and a *compound* with silver nitrate crystallised from water as needles, m. p. 178° (Found : C, 41·7; H, 2·9. $AgNO_3,2C_7H_6N_2$ requires C, 41·4; H, 3·0%).

1-*Acetyl*-2 : 3a-*diazaindene*.—2 : 3*a*-Diazaindene (0·83 g.) in carbon disulphide (15 c.c.) was added to a mixture of aluminium chloride (3·75 g.) and acetyl chloride (2·2 g.) in carbon disulphide (35 c.c.). The whole was stirred and boiled under reflux for 4 hr. and the solvent was removed by distillation from the water-bath. The residue was decomposed with ice-water, and an excess of sodium hydroxide solution (30%) was added before the resulting mixture was extracted with chloroform. Evaporation of the chloroform gave 1-*acetyl*-2 : 3a-*diazaindene* (0·8 g., 71%) which crystallised from *cyclo*hexane as cream needles, m. p. 129°, having a violet fluorescence in ultraviolet light (Found : C, 67·7; H, 5·0; N, 17·6. $C_9H_8ON_2$ requires C, 67·5; H, 5·0; N, 17·5%).

3-*Methyl*-2 : 3a-*diazaindene*.—2-Acetamidomethylpyridine (2·9 g.), by the phosphoryl chloride treatment, gave an oil (1·6 g., 62%), b. p. 112—117°/4 mm., which solidified but rapidly darkened and became oily again. Repeated crystallisation from *cyclo*hexane gave 3-*methyl*-2 : 3a-*diazaindene* as prisms, m. p. 55°, which had a blue fluorescence in ultraviolet light (Found : C, 72·2; H, 6·1. $C_8H_8N_2$ requires C, 72·7; H, 6·1%). The *picrate* was obtained as prisms, m. p. 221° (decomp.), after crystallisation from a large volume of ethanol (Found : C, 46·5; H,

3·2. $C_8H_8N_2,C_6H_3O_7N_3$ requires C, 46·5; H, 3·1%). Methyl iodide in boiling acetone formed a hydrated derivative which was dried at 100°/3 mm. and then gave the ***methiodide***, m. p. 184° (Found: C, 38·9; H, 4·1. $C_9H_{11}N_2I$ requires C, 39·4; H, 4·0%). The *compound* with silver nitrate crystallised from water as needles, m. p. 189—190° (Found: C, 43·8; H, 3·6. $AgNO_3,2C_8H_8N_2$ requires C, 44·3; H, 3·7%).

1-*Acetyl*-3-*methyl*-2 : 3a-*diazaindene*.—(*a*) 3-Methyl-2 : 3*a*-diazaindene (0·9 g.) was acetylated with acetyl chloride (1·2 g.) and aluminium chloride (2·6 g.) in carbon disulphide (50 c.c.) as described above. Evaporation of the chloroform gave a dark residue which crystallised from benzene–light petroleum (b. p. 60—80°) as brown needles (0·9 g., 75%), m. p. 138°. Recrystallisation gave 1-*acetyl*-3-*methyl*-2 : 3a-*diazaindene* as fawn needles, m. p. 139°, having a violet fluorescence in ultraviolet light (Found: C, 69·3; H, 5·9. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·8%).

(*b*) 2-Aminomethylpyridine (1·2 g.) was boiled under reflux with acetic anhydride (5 c.c.) for 5 hr. Removal of the excess of acetic anhydride, treatment of the residue with water and alkali, chloroform extraction, and evaporation gave a solid. The product from the benzene extract of this crystallised from benzene–light petroleum (b. p. 60—80°) as yellow-brown needles (0·7 g., 36%), m. p. 136—138°. Recrystallisation gave fawn needles, identical with those obtained by method (*a*), m. p. and mixed m. p. 139°.

(*c*) 3-Methyl-2 : 3*a*-diazaindene (0·3 g.) was heated under reflux for 5 hr. with acetic anhydride (3 c.c.). A similar process to that used above gave a chloroform extract, the material from which was separated by chromatography into 3-methyl-2 : 3*a*-diazaindene (0·06 g.), identified as the methiodide, and 1-acetyl-3-methyl-2 : 3*a*-diazaindene (0·14 g.), m. p. 139°.

3-*Phenyl*-2 : 3a-*diazaindene*.—Cyclisation of 2-benzamidomethylpyridine (1·1 g.; Graf, *J. prakt. Chem.*, **1936**, **146**, 88) gave a dark oil which, on evaporation at 140°/2 mm. on to a "cold finger" condenser followed by crystallisation from *cyclo*hexane, gave 3-*phenyl*-2 : 3a-*diazaindene* (0·62 g., 61%) as prisms, m. p. 109° (Found: C, 80·1; H, 5·2. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2%). The *picrate* formed needles, m. p. 185—186°, from ethanol (Found: C, 53·9; H, 3·0. $C_{13}H_{10}N_2,C_6H_3O_7N_3$ requires C, 53·9; H, 3·1%).

2-1′-*Aminoethylpyridine*.—Methyl 2-pyridyl ketoxime, m. p. 120°, from methyl 2-pyridyl ketone (Gilman, Tolman, and Massie, *J. Amer. Chem. Soc.*, **1946**, **68**, 2399) was reduced by the method used (above) for the preparation of 2-aminomethylpyridine and gave 2-1′-aminoethylpyridine (86%), b. p. 197—201°/760 mm. 2-1′-*Formamidoethylpyridine* (78%) was obtained as a pale yellow liquid, b. p. 156°/4 mm. (Found: C, 63·9; H, 7·0. $C_8H_{10}ON_2$ requires C, 64·0; H, 6·7%), and 2-1′-*acetamidoethylpyridine* crystallised from *cyclo*hexane as needles, m. p. 107° (Found: C, 66·2; H, 7·4. $C_9H_{12}ON_2$ requires C, 65·8; H, 7·4%). The action of propionic anhydride on the amine for 75 min. on the water-bath gave the propionyl derivative as an oil, b. p. 155—158°/5 mm., which formed deliquescent needles when cool. The *picrate* of 2-1′-propionamidoethylpyridine formed prisms, m. p. 128°, from benzene (Found: C, 47·2; H, 4·1. $C_{10}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 47·2; H, 4·2%). Benzoylation of 2-1′-aminoethylpyridine by the Schotten–Baumann method gave 2-1′-*benzamidoethylpyridine* as needles, m. p. 93° [from light petroleum (b. p. 60—80°)] (Found: C, 74·9; H, 6·2. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%).

1-*Methyl*-2 : 3a-*diazaindene*.—2-1′-Formamidoethylpyridine with phosphoryl chloride gave a crude product (70%), b. p. 100—105°/1·5 mm. Redistillation, followed by chromatography on alumina in benzene containing 1% of methanol, and evaporation at 70°/3 mm. on to a "cold finger" condenser gave 1-*methyl*-2 : 3a-*diazaindene* as needles, m. p. 64—65° (Found: C, 72·7; H, 6·2. $C_8H_8N_2$ requires C, 72·7; H, 6·1%). The *methiodide* crystallised as needles, m. p. 209°, from acetone (Found: C, 39·2; H, 4·0. $C_9H_{11}N_2I$ requires C, 39·4; H, 4·0%).

1-Methyl-2 : 3*a*-diazaindene was acetylated by the Friedel–Crafts procedure and the product (88%) solidified to yellow needles, m. p. 54—56°. Crystallisation from light petroleum (b. p. 60—80°), evaporation at 100°/3 mm., and recrystallisation gave 3-*acetyl*-1-*methyl*-2 : 3a-*diazaindene* as pale yellow needles, m. p. 66—67° (Found: C, 69·0; H, 5·9. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·8%). The crystals had a violet fluorescence in ultraviolet light.

1 : 3-*Dimethyl*-2 : 3*a*-*diazaindene*.—Cyclisation of 2-1′-acetamidoethylpyridine (1·6 g.) gave 1 : 3-dimethyl-2 : 3a-diazaindene as a yellow oil (1·09 g., 76%), b. p. 120—125°/5 mm., which solidified to deliquescent prisms. The *picrate* formed plates, m. p. 254° (decomp.), on crystallisation from a large volume of ethanol (Found: C, 48·2; H, 3·5. $C_9H_{10}N_2,C_6H_3O_7N_3$ requires C, 48·0; H, 3·5%).

3-*Ethyl*-1-*methyl*-2 : 3a-*diazaindene*.—(*a*) 2-1′-Propionamidoethylpyridine was cyclised and

gave a yellow oil (89%), b. p. 118—124°/4 mm. Redistillation gave 3-*ethyl*-1-*methyl*-2 : 3a-*diazaindene* as a yellow oil, b. p. 130°/5 mm. (Found : C, 74·9; H, 7·6. $C_{10}H_{12}N_2$ requires C, 75·0; H, 7·6%). The *mercurichloride* formed needles, m. p. 203—204° (decomp.), from ethanol (Found : C, 27·8; H, 2·9. $C_{10}H_{12}N_2,HgCl_2$ requires C, 27·8; H, 2·8%). The *compound* with silver nitrate, prepared from an aqueous suspension, formed needles, m. p. 175° (decomp.), from aqueous methanol (Found : C, 48·5; H, 5·2. $AgNO_3,2C_{10}H_{12}N_2$ requires C, 49·0; H, 4·9%).

(*b*) Wolff–Kishner reduction (cf. Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487). 3-Acetyl-1-methyl-2 : 3*a*-diazaindene (0·22 g.), potassium hydroxide (1·0 g.), 90% hydrazine hydrate (0·75 c.c.), and ethylene glycol (7·5 c.c.) were heated under reflux for 1 hr. The temperature of the mixture was raised to 190° by distillation and maintained for 5 hr. An insoluble red intermediate was formed, but this disappeared during the treatment. Water (15 c.c.) was added to the cooled solution which was then extracted with chloroform. The oil obtained on evaporation of the extract was chromatographed in benzene on alumina and then converted into a mercurichloride and a silver nitrate derivative (31% yield). These were crystallised from ethanol and aqueous methanol respectively, and were identical with the mercurichloride and silver nitrate derivative of 3-ethyl-1-methyl-2 : 3*a*-diazaindene.

1-*Methyl*-3-*phenyl*-2 : 3a-*diazaindene*.—2-1 -Benzamidoethylpyridine on cyclisation gave 1-*methyl*-3-*phenyl*-2 : 3a-*diazaindene*, which crystallised from aqueous methanol as cream needles, m. p. 120° (Found : C, 81·1; H, 5·8. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8%).

2-1′-*Aminopropylpyridine*.—Reduction of ethyl 2-pyridyl ketoxime (from ethyl 2-pyridyl ketone; Bertucat, *Compt. rend.*, 1951, **232**, 1758) by zinc and acetic acid gave a 92% yield of 2-1′-*aminopropylpyridine*, b. p. 110°/31 mm. (Found : C, 70·7; H, 9·0. $C_8H_{12}N_2$ requires C, 70·5; H, 8·9%). 2-1′-*Formamidopropylpyridine* had b. p. 146°/2 mm. (Found : C, 65·8; H, 7·5. $C_9H_{12}ON_2$ requires C, 65·8; H, 7·4%), and 2-1′-*acetamidopropylpyridine* was obtained as deliquescent prisms, m. p. 83° (Found : C, 67·3; H, 8·1. $C_{10}H_{14}ON_2$ requires C, 67·4; H, 7·9%).

1-*Ethyl*-2 : 3a-*diazaindene*.—(*a*) Cyclisation of 2-1′-formamidopropylpyridine (1·48 g.) gave 1-*ethyl*-2 : 3a-*diazaindene* (1·12 g., 85%), b. p. 116°/2 mm., which darkened on storage (Found : C, 73·4; H, 7·2. $C_9H_{10}N_2$ requires C, 73·9; H, 6·9%). The *picrate* formed prisms, m. p. 203° (decomp.) (Found : C, 47·9; H, 3·5. $C_9H_{10}N_2,C_6H_3O_7N_3$ requires C, 48·0; H, 3·5%), and the *picrolonate* gave needles, m. p. 222° (Found : C, 55·6; H, 4·7. $C_9H_{10}N_2,C_{10}H_8O_5N_4$ requires C, 55·6; H, 4·4%), both from ethanol. A *compound* with silver nitrate was obtained as needles, m. p. 152—153°, from water (Found : C, 46·9; H, 4·4. $AgNO_3,2C_9H_{10}N_2$ requires C, 46·8; H, 4·4%).

(*b*) Reduction of 1-acetyl-2 : 3*a*-diazaindene (0·22 g.) by the modified Wolff–Kishner method gave an oil which was converted into a picrate, picrolonate, and a compound with silver nitrate, which were identical with the corresponding derivatives obtained as above.

1-*Ethyl*-3-*methyl*-2 : 3a-*diazaindene*.—(*a*) 2-1′-Acetamidopropylpyridine gave 1-*ethyl*-3-*methyl*-2 : 3a-*diazaindene* (80%), b. p. 115—123°/2 mm., which when redistilled had b. p. 120°/2 mm. (Found : C, 75·3; H, 7·7. $C_{10}H_{12}N_2$ requires C, 75·0; H, 7·6%). The *mercurichloride* formed diamond-shaped plates, m. p. 210—211° (decomp.), from ethanol (Found : C, 28·3; H, 3·2. $C_{10}H_{12}N_2,HgCl_2$ requires C, 27·8; H, 2·8%). The *methiodide* formed needles, m. p. 200°, from acetone (Found : C, 43·6; H, 5·0. $C_{11}H_{15}N_2I$ requires C, 43·7; H, 5·0%), and the *picrate* was obtained as diamond-shaped plates, m. p. 259° (decomp.), from ethanol (Found : C, 49·4; H, 3·8. $C_{10}H_{12}N_2,C_6H_3O_7N_3$ requires C, 49·4; H, 3·9%).

(*b*) Reduction of 1-acetyl-3-methyl-2 : 3*a*-diazaindene. The modified Wolff–Kishner procedure used above gave an oil which, after chromatography, was converted into a picrate and a mercurichloride (yield 33%). The former had m. p. 258—259°, not depressed on admixture with the picrate of 1-ethyl-3-methyl-2 : 3*a*-diazaindene, and the latter, m. p. 210—211°, was identical with the corresponding mercurichloride.

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