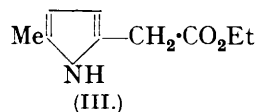
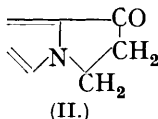
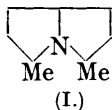


135. *The Lupin Alkaloids. Part IX. The Synthesis of 5 : 5'-Dimethyldi(1 : 2)pyrrolidine.*

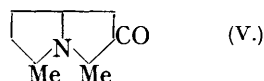
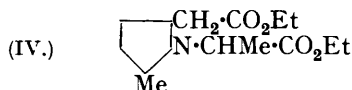
By G. R. CLEMO and T. P. METCALFE.

OF the structures for norlupinane consistent with the *n*-propyl *n*-amyl ketone obtained by Karrer and co-workers (*Helv. Chim. Acta*, 1928, 11, 1062) from lupinine, two, *viz.*, octahydropyridocoline and methyloctahydropyrrocoline, have already been synthesised (J., 1932, 2959; 1935, 1743) and a third, 5 : 5'-dimethyldi(1 : 2)pyrrolidine (I), has now been prepared.



The method used by Clemo and Ramage (J., 1931, 53) for the preparation of 3-keto-4 : 5-dihydrodi(1 : 2)pyrrole (II) was first tried, but it was not found possible to condense potassium-2-methylpyrrole with  $\beta$ -bromobutyronitrile.

*Ethyl 2-methylpyrrole-5-acetate* (III) was then prepared by the method used by Sohl and Shriner (*J. Amer. Chem. Soc.*, 1933, 55, 3831) for the preparation of ethyl 1-methylpyrrole-5-acetate. The ester side chain was proved to be in position 5 by conversion into the dimethylpyrrole and degradation of this by means of hydroxylamine to acetyl-acetonedioxime. The ester (III) was catalytically hydrogenated and condensed with ethyl  $\alpha$ -bromopropionate, yielding *ethyl 2-methylpyrrolidine-5-acetate-1- $\alpha$ -propionate* (IV). The Dieckmann ring closure of this gave 4-keto-5 : 5'-dimethyldi(1 : 2)pyrrolidine (V), but the Clemmensen reduction of this gave the 4-hydroxy-compound. This result agrees with that recorded for the reduction of 3-keto-2-methyloctahydropyrrocoline in Part VIII (J., 1935, 1743), which also has a methyl group in the  $\alpha$ -position to the carbonyl group. The Wolff reduction (*Annalen*, 1912, 394, 86), however, gave 5 : 5'-dimethyldi(1 : 2)pyrrolidine as a colourless stable liquid.



The stability of the bases increases in the order : octahydropyridocoline, methyloctahydropyrrocoline, 5 : 5'-dimethyldi(1 : 2)pyrrolidine, and there is a corresponding fall in their boiling points : 38—40°/1 mm.; 32—35°/1 mm.; 25°/1 mm.

Theoretically there should be eight stereoisomerides of the base (I), but in this work no evidence has been found of the occurrence of more than one form of (I), or of its derivatives such as (V).

## EXPERIMENTAL.

*Ethyl 2-Methylpyrrole-5-acetate*.—Diazoacetic ester (7 g.) was added, with shaking, during  $\frac{1}{4}$  hour to 2-methylpyrrole (9 g.) and copper-bronze (0.4 g.) at 100°, and the mixture kept at this temperature for a further hour. After filtration the dark brown liquid was distilled; 2-methylpyrrole (5.15 g.) was recovered, and *ethyl 2-methylpyrrole-5-acetate* (4.5 g.) obtained as a very pale yellow oil, b. p. 129—130°/12 mm. (Found: C, 64.7; H, 7.5.  $C_9H_{13}O_2N$  requires C, 64.7; H, 7.8%).

*Ethyl 2-Methylpyrrolidine-5-acetate*.—The pyrrole ester (9.4 g.), in a mixture of glacial acetic acid (20 c.c.) and ethyl alcohol (6 c.c.), was shaken for 36 hours with platinum oxide (0.5 g.) in hydrogen at 100 lb./sq. in. After filtration and removal of solvents, the residue was basified (50% potassium hydroxide solution), extracted with ether, and distilled, giving 7.7 g. of an oil, b. p. 98°/12 mm. (Found: C, 63.0; H, 9.8.  $C_9H_{17}O_2N$  requires C, 63.2; H, 9.9%). The *picrate* formed yellow prisms, m. p. 112°, very soluble in alcohol, and the *picrolonate*, yellow prisms with oblique ends, m. p. 194° (Found: C, 52.2; H, 6.0.  $C_9H_{17}O_2N, C_{10}H_8O_5N_4$  requires C, 52.4; H, 5.7%).

*Ethyl 2-Methylpyrrolidine-5-acetate-1- $\alpha$ -propionate*.—The pyrrolidine ester (6.2 g.),  $\alpha$ -bromopropionic ester (7.8 g.), and potassium carbonate (10 g.) were heated together on the water-bath for 5 hours. Water was added, and the oil extracted with ether, dried, and distilled (7.3 g., b. p. 150—151°/12 mm.) (Found: C, 62.0; H, 9.2.  $C_{14}H_{25}O_4N$  requires C, 62.0; H, 9.2%).

*4-Keto-5:5'-dimethyl-di(1:2)pyrrolidine*.—The di-ester (5.4 g.) was added to potassium (2 g.) powdered under xylene (15 c.c.). After the first vigorous reaction had abated, the whole was heated for 5 hours on the water-bath, alcohol added to dissolve unused potassium, then water (8 c.c.) and concentrated hydrochloric acid (50 c.c.), and the solution heated for 18 hours on the water-bath. After evaporation to dryness the residue was basified with potassium hydroxide solution (50%), and the *ketone* extracted with ether and distilled as a colourless oil (1.9 g., b. p. 65°/1 mm.) which became yellow after 2 hours (Found: C, 70.2; H, 9.9.  $C_9H_{15}ON$  requires C, 70.6; H, 9.8%). The *picrate* formed yellow needles, m. p. 186° (Found: C, 47.4; H, 4.4.  $C_9H_{15}ON, C_8H_3O_7N_3$  requires C, 47.1; H, 4.7%), and the *picrolonate*, yellow rectangular prisms, m. p. 217° (Found: C, 54.9; H, 5.7.  $C_9H_{15}ON, C_{10}H_8O_5N_4$  requires C, 54.7; H, 5.5%).

*4-Hydroxy-5:5'-dimethyl-di(1:2)pyrrolidine*.—The ketone (0.5 g.) in concentrated hydrochloric acid (10 c.c.) was refluxed for 21 hours with amalgamated zinc (5 g.). The solution was then evaporated to dryness, and the residue basified with potassium hydroxide solution (50%) and steam-distilled. The distillate was acidified (hydrochloric acid) and evaporated to dryness, the residue basified with potassium hydroxide solution (50%) and extracted with ether, and the extract distilled (0.35 g., b. p. 68—70°/1 mm.) (Found: C, 69.6; H, 11.2.  $C_9H_{17}ON$  requires C, 69.7; H, 11.0%). The *picrolonate* formed yellow lozenge-shaped crystals, m. p. 205° (Found: C, 54.5; H, 6.1.  $C_9H_{17}ON, C_{10}H_8O_5N_4$  requires C, 54.4; H, 6.0%).

*5:5'-Dimethyl-di(1:2)pyrrolidine*.—The ketone (2.4 g.) and hydrazine hydrate (1.6 g. of 95%) were refluxed for 15 hours, the hydrazone dried in ethereal solution, and the ether removed. The residue (1.2 g.) was heated at 160—180° for 11 hours in a sealed tube with sodium ethoxide (from sodium, 1.4 g., and absolute alcohol, 10 c.c.). Water (10 c.c.) and excess of hydrochloric acid were added, and the solution evaporated to dryness. The *base* was liberated by potassium hydroxide solution (50%), extracted with ether, dried, and distilled, yielding 0.65 g. of a colourless mobile liquid, b. p. 25°/1 mm. (Found: C, 77.9; H, 12.5.  $C_9H_{17}N$  requires C, 77.7; H, 12.2%), which had a very penetrating odour and was easily soluble in water, giving a solution alkaline to litmus. The *picrate* formed yellow rectangular prisms, m. p. 249° (Found: C, 48.6; H, 5.5.  $C_9H_{17}N, C_8H_3O_7N_3$  requires C, 48.9; H, 5.4%), and the *picrolonate*, stout brown prisms, m. p. 180° (Found: C, 56.8; H, 6.4.  $C_9H_{17}N, C_{10}H_8O_5N_4$  requires C, 56.6; H, 6.2%).

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