## The Total Synthesis of Dasycarpidone and 3-epi-Dasycarpidone

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WE recently reported<sup>1</sup> the synthesis of the ring system of the group of indole alkaloids typified by uleine<sup>2</sup> (Ia) and dasycarpidone<sup>3,2b</sup>(Ib). We have now succeeded in extending our synthetic approach and have obtained thereby racemic dasycarpidone and 3-epi-dasycarpidone<sup>2b</sup> (Ic), in each case identified by i.r., u.v., mass spectroscopic, and t.l.c. comparisons with the natural alkaloids.



Oxidation<sup>4</sup> of 3-ethyl-4-methylpyridine (IIa) with selenium dioxide in refluxing pyridine gave 3-ethylisonicotinic acid (IIb) in 72% yield (m.p. **198—200°**). Transformation into the corresponding ester (IIc) (b.p.  $90-94^{\circ}/2$  mm.) was achieved in 80% yield by successive treatment with thionyl chloride and methanol. Claisen condensation of this ester (IIc) with methyl propionate was effected with sodium hydride in 67% yield.

The resultant  $\beta$ -keto-ester (IId) (b.p. 102–110°/ 0.4 mm.) was hydrolysed and decarboxylated with refluxing aqueous H<sub>2</sub>SO<sub>4</sub>-HOAc to give the ketone (IIe) (b.p.  $102-110^{\circ}/4$  mm.). Conversion into an enamine (pyrrolidine in refluxing benzene) was followed, without purification, by reaction<sup>5</sup> with benzenediazonium chloride to give the phenylhydrazone (IIf) (m.p. 212-213°). Fischer indolisation, catalysed by syrupy phosphoric acid, gave the indole (III) in 70% yield (amorphous,  $\lambda_{\max}$ 227, 322 m $\mu$ ; log  $\epsilon$  4·33, 4·26,  $\nu_{max}$  1640 cm.<sup>-1</sup>). The methiodide of (III) gave a single alcohol (IVa) (m.p. 169-175°) on reduction with potassium borohydride. The production of only the desired  $\Delta^3$ -piperideine is consistent with published data<sup>6</sup> on the reduction of 3-substituted pyridinium The transformation of the conjugated salts. ketone (IVb) (m.p. 96–100°,  $\lambda_{max}$  236, 315 m $\mu$ ; log  $\epsilon$  4.10, 4.28  $\nu_{max}$  3200, 1625 cm.<sup>-1</sup>), the manganese dioxide oxidation product of (IVa), into the required enamine (V) was more difficult than for the corresponding de-ethyl analogue.<sup>1</sup>

It was necessary to subject the compound to treatment with dimsyl sodium at 95° for 36 hr. followed by work-up using ammonium chloride in order to obtain the intermediate, (m.p. 151-153°,  $\lambda_{\max} 242, 322 \text{ m}\mu; \log \epsilon 4.09, 4.20, \nu_{\max} 1665 \text{ cm}.^{-1}$ ).

Cyclisation of the intermediate resulted from treatment with 50% acetic acid at 100°. A readily separable mixture of dasycarpidone (Ib) and 3-epidasycarpidone (Ic) (m.p. 164-166°) was obtained in which the epi-base predominated to the extent of 5:1. Professor L. J. Dolby has kindly informed us that he has synthesised dasycarpidone and epidasycarpidone by a totally different approach.

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