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THE SYNTHESIS OF BELLENDINE

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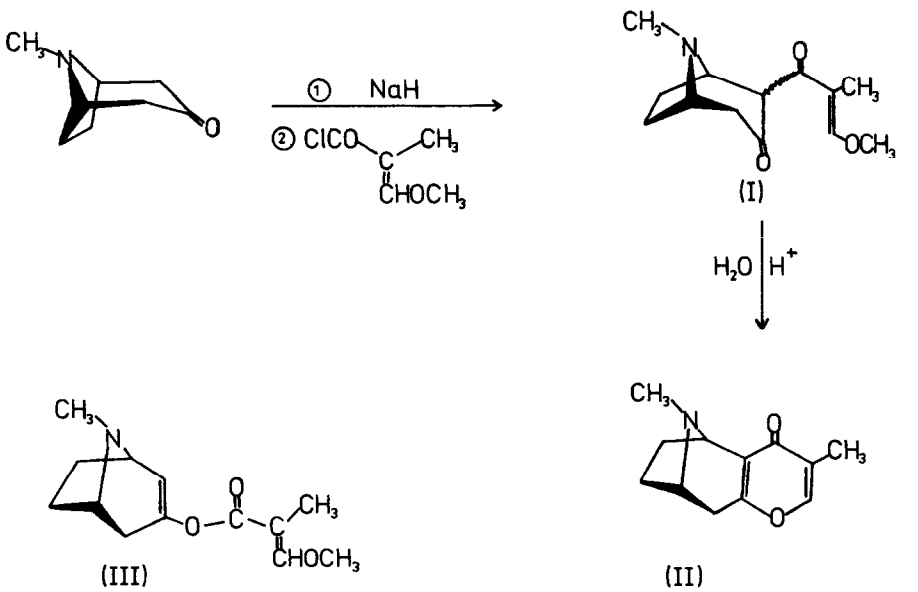
Bellendine was the first alkaloid to be isolated[1] from the Proteaceae, a plant family widely distributed in the southern hemisphere, and its structure was shown to be (II) by direct methods of X-ray crystallography[2]. The plant from which it was obtained, Bellendena montana, contains other alkaloids of analogous structure, and several other tropane or pyranotropane alkaloids related to it have subsequently been isolated from New Caledonian[3], Queensland[4], or Tasmanian[4] endemic species.

We have synthesised racemic bellendine by the following process:



Tropinone in dry benzene was refluxed with sodium hydride for 20 hours, then 3-methoxy-methacryloyl chloride[5] in dry benzene was added at 10°C. The mixture was refluxed for 15

minutes, cooled, and shaken with saturated aqueous ammonium chloride, then the aqueous solution was extracted with benzene, the combined extracts were evaporated, and the residue was purified by PTLC on silica gel in 10% methanol-chloroform. Material from the high R_f band was removed and hydrolysed by warming briefly on a water bath with dilute sulphuric acid. The base was recovered in low overall yield from the neutralised solution and purified by PTLC. The crystalline product, further purified by sublimation, had UV, IR, NMR and mass spectra identical with those of bellendine. It melted at 128.5° alone and at 153° when mixed with (+) bellendine (m.p. 162°).

In addition to (I) and some unchanged tropinone, the acylation produced a considerable amount of crystalline product which, from its spectroscopic properties and ready hydrolysis to tropinone, corresponded to the O-acyl derivative (III) of the latter [$\nu_{C=O}$ 1715, $\nu_{C=C}$ 1650 cm^{-1}; λ_{max} 243 nm, ε_{max} 2,750; τ 8.27 (s, 3H), 7.50 (s, 3H), 6.15 (s, 3H), 4.41 (d, H), 6.50 (m, 2H); M^+, 237].

The method of synthesis is being extended to the preparation of other pyranotropane-type alkaloids[4] from proteaceous plants.

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