

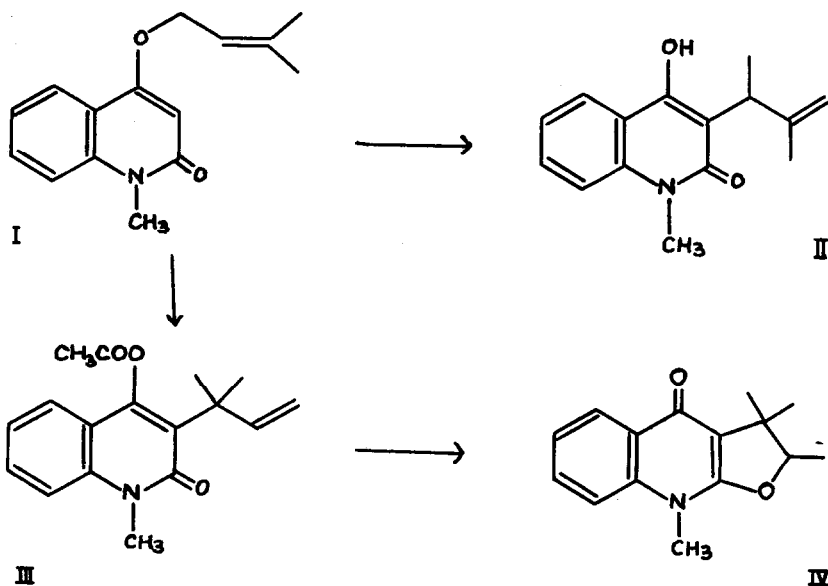
THE SYNTHESIS OF IFFLAIAMINE

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The alkaloid, ifflaiamine, was isolated from the wood of the Australian tree *Flindersia ifflaiana* F. Muell., a member of the Rutaceae. Spectroscopic studies and analogy with other quinoline alkaloids indicated that ifflaiamine was the furanoquinoline derivative (IV) (1). Because of the unusual arrangement of the isoprenoid unit we decided to confirm the structure of ifflaiamine by synthesis, and chose a route based on a Claisen rearrangement of the dimethylallyl ether (I).



Reaction of 4-hydroxy-1-methyl-2-quinolone with 1-bromo-3-methylbut-2-ene furnished the dimethylallyl ether (I). The compound rearranged readily, for example when heated briefly at 120°, but an abnormal reaction occurred exclusively giving the phenol (II) and its cyclisation products. Studies of the mechanism of the abnormal Claisen reaction of phenolic ethers show that the normal phenol is formed initially and then rearranges (2). We attempted to trap the phenolic intermediate (3) by heating the dimethylallyl ether (I) in *N*-methylpiperidine containing acetic anhydride. In this way the normal acetate (III) was obtained in high yield. Treatment of the acetate with hydrobromic acid in acetic acid at 20° gave (+)-ifflamine hydrobromide almost quantitatively, and the salt was then converted into (+)-ifflamine (IV), m.p. 128-129°. The constitution of the product was indicated by its n.m.r. spectrum which was identical with that of natural (-)-ifflamine (1).

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