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A SYNTHESIS OF (±)-OTOBAIN

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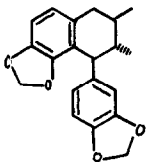
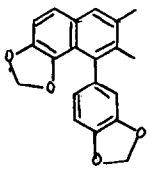
The lignan otobain (I) has been isolated from Myristica Otoba[1,2,3] and its structure and stereochemistry proved.[3,4,5] Recently Stevenson has synthesised tetradehydrootobain (II),[6] and (±)-otobain itself.[7] We wish to report a second synthesis of (±)-otobain, and the first synthesis of a lignan employing the tetralone route.



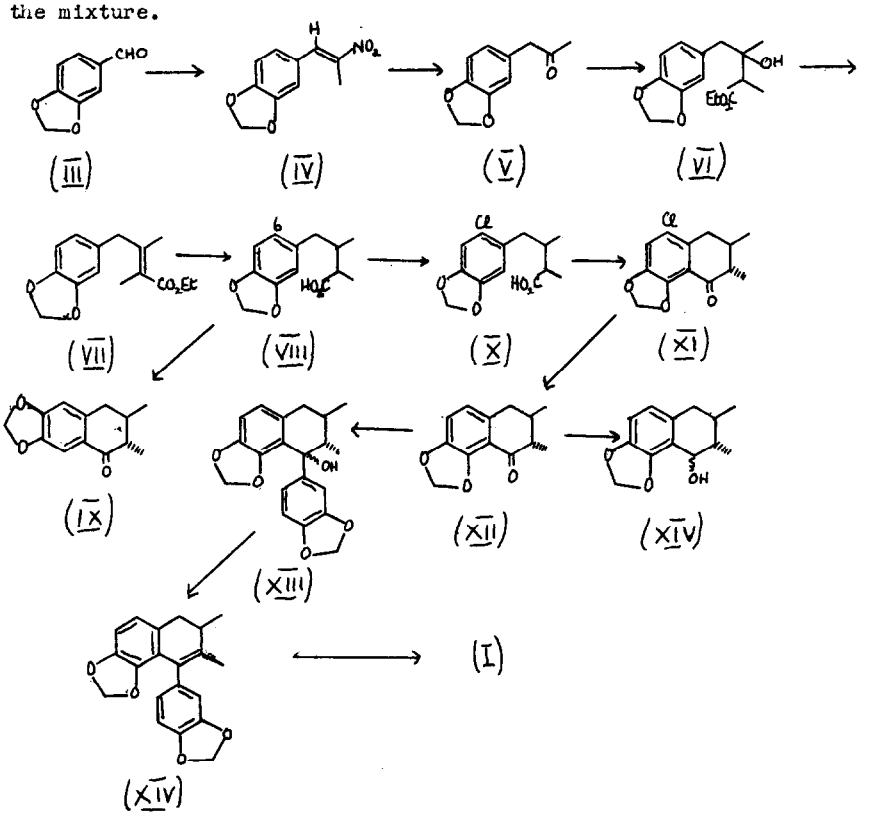
(I)



(II)

3,4-methylenedioxyphenylacetone[8] (V) obtained from piperonal (III) via the nitrostyrene (IV) was reacted with ethyl α-bromopropionate under Reformatsky conditions to afford the hydroxyester (VI). This was not isolated but dehydrated to give the unsaturated ester (VII). Hydrogenation and hydrolysis afforded the saturated acid (VIII). Direct ring closure of (VIII) would lead by substitution in the 6- position to the undesired tetralone (IX); consequently this reactive position was protected by chlorination to give the chloroacid (X). Ring closure was best achieved via the acid chloride using stannic chloride at -70°. Hydrogenolysis of the

resulting chlorotetralone (XI) using a palladium-strontium carbonate catalyst in the presence of sodium acetate afforded the tetralone (XII). This was reacted with 3,4-methyldioxyphenyl lithium in the presence of lithium bromide at -70° to afford (±)-hydroxyotobain (XIII). Hydroxyotobain has not been previously synthesised. The phenyl lithium was prepared by exchange of n-butyl lithium with 3,4-methylenedioxyphenyl bromide.[9] When the condensation reaction was carried out in the absence of lithium bromide, considerable quantities of the tetralol (XIV) were obtained; presumably by hydrogen abstraction from the traces of butyl lithium present in equilibrium in the mixture.



(±)-Hydroxy otobain (XIII) whose n.m.r. spectrum is identical with the published spectrum,[5] was dehydrated with phosphoryl chloride in pyridine to give the olefin (XV) which was reduced with sodium in isopropanol to afford (±)-otobain, m.p. 171-172° undepressed by authentic material kindly supplied by Prof. R. Stevenson. The n.m.r. spectrum was identical with the published spectrum.[3]

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