

FORMAL TOTAL SYNTHESIS OF DITERPENE ALKALOIDS ATISINE,
GARRYINE AND VEATCHINE

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Hydrophenanthrene synthesis was examined by thermolysis of 1-cyano-4-methoxy-1-(4-methoxycarbonyl-4-vinyl)pentylbenzocyclobutene (**1**) which was prepared as follows. 2-Bromo-5-methoxybenzaldehyde was treated with cyanoacetic acid to give the corresponding cinnamic acid, whose reduction with sodium borohydride, followed by decarboxylation, afforded 2-bromo-5-methoxyphenylpropionitrile. Treatment of this nitrile with sodium amide in liq. ammonia gave 1-cyano-4-methoxybenzocyclobutene (**2**). The condensation of **2** with methyl 4-iodo-1-methyl-1-vinylvalerate, prepared from methyl methylacetoacetate in four steps, in the presence of sodium amide furnished the starting material (**1**). Thermolysis of **1** in dry benzene below 230° in an autoclave gave (±)-4α-cyano-1,2,3,4,4a,9,10,10a-octahydro-7-methoxy-1α-methoxycarbonyl-1β-methylphenanthrene (**3**) in stereoselective and regioselective manner. On the other hand, thermolysis of **1** over 230° afforded regioselectively **3** and 10aβ-epimer (**4**). The former product (**3**) was converted into the latter (**4**) by oxidation with chromic acid, followed by bromination, dehydrobromination with N-phenylbenzamidine and hydrogenation. The structure of **4** was confirmed by conversion into the known (±)-1α-carboxy-1,2,3,4,4a,10,10aβ-octahydro-7-methoxy-1β-methylphenanthrene.

Catalytic reduction of **4** gave the lactam, which was reduced with lithium aluminum hydride to afford 16,17-imino-13-methoxy-5β,10α-podocarpene-8,11,13-triene. This compound was correlated with diterpene alkaloids, atisine, garryine and veatchine. Thus, a formal total synthesis of these alkaloids has been accomplished.