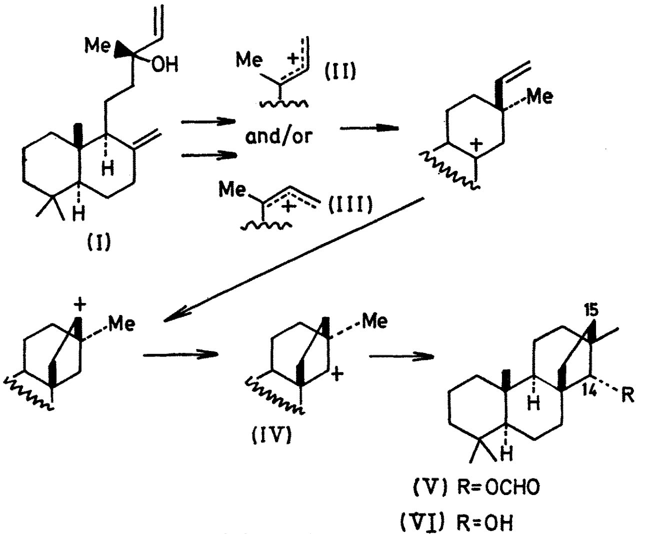
The Mechanism of the Transformation of Manool into 14α-Hibyl Formate

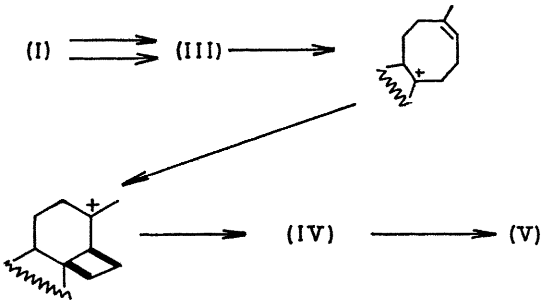
By JEAN-LOUIS FOURREY, JUDITH POLONSKY,* and ERNEST WENKERT
(*Institut de Chimie des Substances Naturelles, C.N.R.S., 91-Gif-sur-Yvette, France*)

Summary The formolysis of [15-^{14}C]isomanool has been found to lead to [14-^{14}C]-14α-hibyl formate. This finding is compatible with only one of several mechanisms suggested for the unusual structural change.

THE formolysis of manool (I)[1,2] has been shown recently to yield tricyclic dienes[3] and the tetracyclic formate (V) [isolated as 14α-hibol (VI)]. Two plausible mechanisms were advanced to describe the unusual double cyclization leading to (V): scheme A, reminiscent of the biosynthetic route to the tetracarbocyclic diterpenes, and scheme B, an intuitively preferable,[1] but chemically less precedented route. In order to differentiate between the two schemes, it was decided to carry out a formolysis of [15-^{14}C]isomanool (VII) and to ascertain the position of the radioactive carbon in the product. Scheme A would require radioactivity to appear in 14α-hibol (VI) at C-15, while scheme B would place the label into C-14.

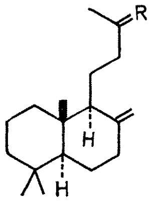


Scheme A

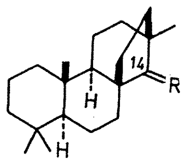


Scheme B

The following synthesis and formolysis of isomanool (VII) and degradation of 14α-hibol (VI) represent the reactions upon which the labelling experiments were based. Sodium hydride-induced condensation of the manool degradation product (VIII)[4] with the phosphonoacetic ester[5] derived from triethyl phosphite and methyl bromoacetate yielded the acrylic ester (IX) whose reduction with lithium aluminium hydride produced isomanool (VII).[6] Formolysis of the latter under conditions previously employed for manool[1] followed by lithium aluminium hydride reduction afforded a mixture from which 14α-hibol could be isolated. Jones oxidation of the latter and interaction of phenyl-lithium with the resultant ketone (X) gave carbinol (XI), m.p. 104—105°, $[\alpha]_D$ $-44\cdot4°$ ($c = 1\cdot15$, chloroform), whose Kuhn–Roth oxidation led to benzoic acid.



(VII) R=$C^{15}HC^{16}H_2OH$
(VIII) R=O
(IX) R=$CHCO_2Me$



(X) R=O
(XI) R=OH,Ph

The reaction sequence was repeated starting with the phosphonoacetic ester ($1\cdot8 \times 10^6$ d.p.m./mmole) prepared from methyl bromo[2-^{14}C]acetate. The intermediate (X) ($1\cdot42 \times 10^6$ d.p.m./mmole) was diluted to $2\cdot62 \times 10^5$ d.p.m./mmole with non-radioactive ketone and converted into carbinol (XI) ($2\cdot56 \times 10^5$ d.p.m./mmole) and subsequently into benzoic acid with radioactivity count of $2\cdot46 \times 10^5$ d.p.m./mmole. These facts show conclusively that C-15 of isomanool becomes C-14 of the hibane skeleton and that the formic acid-induced transformations of isomanool (VII) and, hence, of manool (I) into 14α-hibyl formate (V) proceed by way of scheme B. Furthermore these experiments illustrate the first instance of the formation of a medium-sized ring, albeit not its isolation, in the solvolysis of an olefinic alcohol derivative.[7]

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