A Simple Synthesis of β-Cuparenone and Related Sesquiterpenoids

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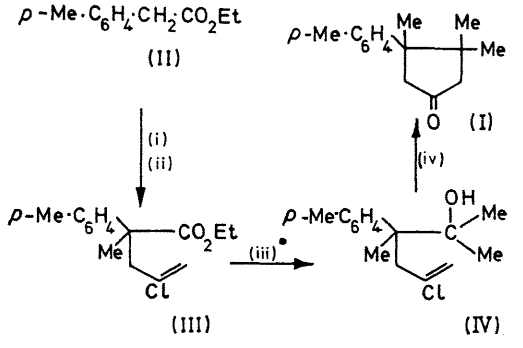
We describe a potentially general approach to the synthesis of the arylcyclopentane framework found in many sesquiterpenes of the order *Cupressales*.[1] From the essential oil of "mayur pankhi" Chetty and Dev isolated (+)-α-cuparenone and an isomer, (+)-β-cuprarenone, which was assigned structure (I) on the basis of somewhat tenuous i.r. spectral data and reduction to cuparene.[2] (±)-Cuparene and (±)-α-cuparenone have been synthesized by Raphael *et al.*[3] in a multi-step sequence beginning with 3-methyl-3-*p*-tolylcyclohexanone. We have developed an efficient and unambiguous synthesis of β-cuparenone, verifying structure (I), based on our recently described cyclanone annelation.[4]

Stepwise alkylation of ethyl *p*-tolylacetate (II)[5] by 2,3-dichloropropene and methyl iodide in liquid ammonia with sodamide proceeded in 71 and 76% yields, respectively, to give (III),† b.p. 96—97°/0·15 mm. whose i.r., n.m.r., and mass spectra were in accord with expectations. Treatment of (III) with ethereal methyl-lithium afforded oily (IV)† (80% yield), showing O–H (2·82 μm.) and no C=O absorption; the n.m.r. spectrum was also confirmatory. When the carbinol (IV) reacted with cold 90% H_2SO_4,



(i) NH_2^-, 2,3-dichloropropene; (ii) MeI, NH_2^-; (iii) MeLi; (iv) 90% H_2SO_4, 0°, 20 min.

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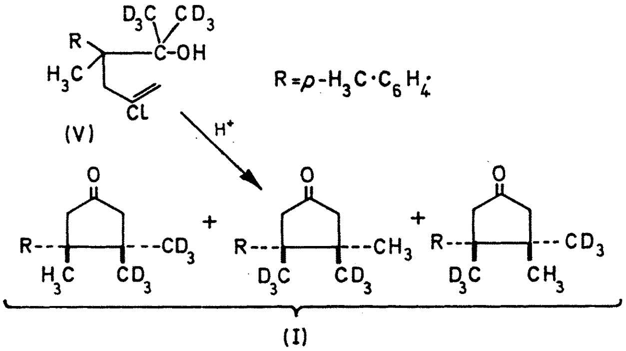
† Satisfactory elemental analyses were obtained for all new compounds.

followed by quenching in ice water and working-up, β-cuparenone (I) was the sole ketone isolated (34% yield, *via* alumina chromatography); its spectral properties were identical with those of natural (I)‡ and it gave the expected semicarbazone, m.p. 210—212° (reported[2]: 213.5—215°). The above reaction sequence also provides access to cuparene,[2] β-cuparenol,[2,6] and related compounds.



Cycloalkanone syntheses of this type are susceptible to rapid ionic rearrangements during product formation. Thus, carbinol (V) leads to (I) with no loss of deuterium but complete scrambling of the three alkyl-bound methyl groups (n.m.r.). The propensity for carbonium-ion rearrangement prior to ring closure places limitations on our cyclic ketone synthesis[4] where isomeric ketones could arise, but suggests useful extensions[4b] as well, some of which we plan to report subsequently.

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