A Short Synthesis of (+)-Isophyllocladene and (+)-Phyllocladene

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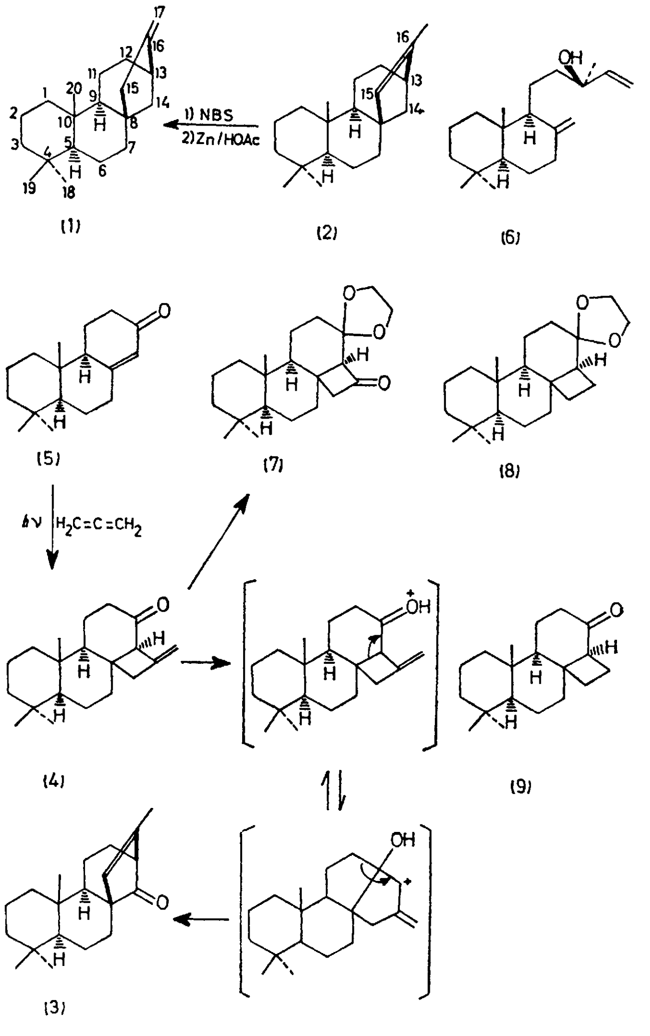
Summary Rearrangement of the ketone (**4**) obtained by photochemical cycloaddition of allene to $\Delta^{8(14)}$-podocarpen-13-one (**5**) leads to (+)-Δ^{15}-isophyllocladen-14-one (**3**), which can be converted into (+)-isophyllocladene (**2**) or (+)-phyllocladene (**1**).

Phyllocladene (**1**) and isophyllocladene (**2**) occur in the leaf oil of various conifers.[1] Since the elucidation of their structures,[2] several multistep syntheses have been published.[3]

We now report that isophyllocladenone (**3**) is readily obtained from the cycloaddition product (**4**) of allene and (+)-$\Delta^{8(14)}$-podocarpen-13-one (**5**), a degradation compound of manool (**6**).[4]

Cycloaddition of allene to the α,β-unsaturated ketone (**5**) on irradiation at low temperature is entirely regio- and stereo-specific.[5] The structure of the adduct is confirmed by the following evidence; ketalisation of (**4**) in the presence of a very small amount of *p*-toluenesulphonic acid, and ozonolysis gave the cyclobutanone (**7**), m.p. 142—144°, $\nu(C{=}O)$: 1775 cm^{-1}. Its circular dichroism ($\Delta\epsilon$ −0·97; λ_{max} 298 nm) and n.m.r. spectrum are in agreement with the proposed structure. Wolff–Kishner reduction of the cyclobutanone (**7**) yields a crystalline ketal (**8**). Hydrolysis of the ketal gives the ketone (**9**) (m.p. 67—68°; $[\alpha]_D$ ($CHCl_3$) + 30°, $\Delta\epsilon$ +0·83; λ_{max} 299 nm) identical in all respects with a sample of known stereochemistry.[4b] The cyclobutane ring is therefore in the β-configuration.

Compound (**4**) rearranges to isophyllocladenone (**3**) when refluxed for 3 h in benzene in the presence of a large amount of *p*-toluenesulphonic acid (1:1 by weight).[6] After chromatography and recrystallisation, a 50% yield of isophyllocladenone (**3**) is obtained. The n.m.r. spectrum and Cotton effect are in agreement with the expected structure, which is completely established by Wolff–Kishner reduction of (**3**)[7] to (+)-isophyllocladene (**2**) (m.p. 109—110°; $[\alpha]_D$ ($CHCl_3$) + 22°, $\Delta\epsilon$ +1·2; λ_{max} 209 nm).[8] *N*-bromosuccinimide bromination of isophyllocladene, followed by reduction with Zn–AcOH gives (+)-phyllocladene (**1**), as a crystalline compound (m.p. 95—96°, $[\alpha]_D$ ($CHCl_3$) +12°; $\Delta\epsilon$ −3; λ_{max} 203 nm).[8] The i.r. spectra of (**1**) and (**2**) are identical with those published in the literature.[9] The phyllocladene skeleton can therefore be built in two steps from a tricyclic precursor (**5**).



(*Received*, 28*th January* 1975; *Com.* 100.)

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