Synthesis of Karahanaenol from Geraniol *via* an Allylsilane

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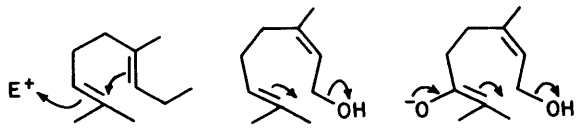
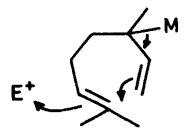
Electrophilic cyclization of an allylsilane derived from geraniol to give karahanaenol is reported and its biosynthetic implication is discussed.

In 1955, polyolefinic electrophilic cyclization was proposed as the biogenetic pathway leading to cyclic isoprenoid natural products.[1,2] Since then, many studies have been carried out to apply this cyclization to the synthesis of six-membered rings [(**1**)] of terpenes and steroids.[3] The extension of the electrophilic cyclization concept to the formation of seven-membered cyclic terpenoids has received less examination. For example, the usual suggestion for the biogenesis of karahanaenol (**4**) from geraniol (**5**) involves an electrophilic cyclization by anti-Markownikoff addition to the double bond as in (**2a**), a process not deemed to be chemically reasonable as such.[4,5] A way to overcome this problem of bond polarisation is to invoke an enolate anion (**2b**) formed by the prior oxidation of geraniol.[5] An alternative possibility is to consider the intervention of an allylic organometallic intermediate (**3**) during enzymic formation which can then cyclize in a manner consistent with bond polarization.



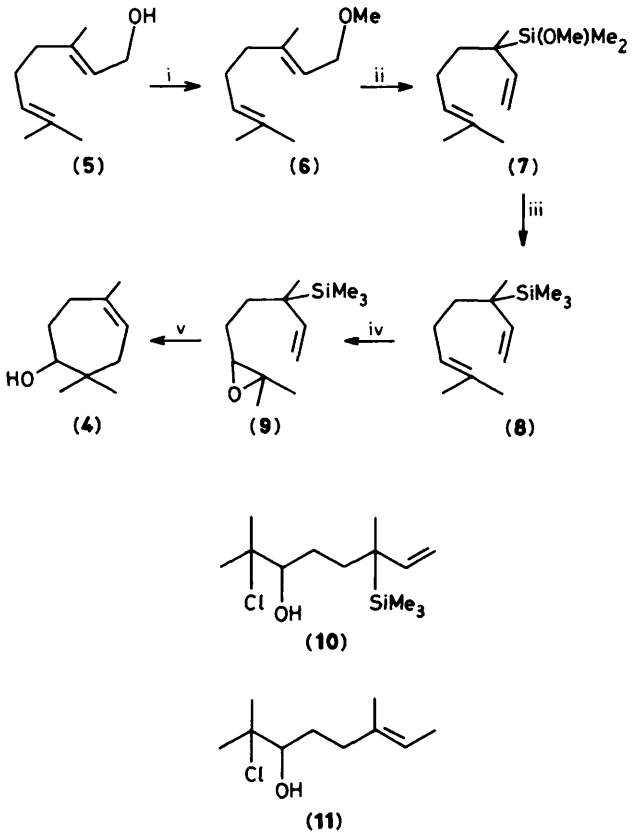
(**1**) (**2a**) (**2b**)



(**3**)

We report here the synthesis of karahanaenol (**4**) from geraniol (**5**) *via* an allylsilane according to the electrophilic cyclization concept outlined in (**3**). Recently, the allylsilane moiety has been used as an effective terminating unit in electrophilic cyclisation for the formation of six-[6] and five-membered[7] cyclic compounds.

Geraniol methyl ether (**6**), prepared by methylation of geraniol (**5**), was photolysed with dodecamethylcyclohexasilane[8] to give in 72% yield the allylsilane (**7**) as a single regioisomer.[9] Reaction of (**7**) with methyl-lithium gave the



Scheme 1. i, NaH–MeI; ii, $(Me_2Si)_6$–cyclohexane, *hν*; iii, MeLi–Et_2O; iv, MCPBA; v, $BF_3{\cdot}Et_2O$, −60 °C.

trimethylsilyl compound (**8**).[10] Epoxidation of (**8**) with *m*-chloroperbenzoic acid (MCPBA) gave exclusively the epoxide (**9**) in 83% yield (Scheme 1). When (**9**) was treated with titanium tetrachloride, the epoxide ring was opened to give the chlorohydrin (**10**) first. Longer reaction time led eventually to the formation of the proto-desilylation product (**11**) with no formation of cyclic compounds. However, treatment of (**9**) with boron trifluoride–diethyl ether for 0.5 h at −60 °C gave as the major product the cyclized product, karahanaenol (**4**) in 71% yield. The structure of (**4**) was deduced from its spectroscopic data by comparison with literature values.[11]

The present synthesis of karahanaenol from geraniol lends credence to the possibility that electrophilic cyclization of type (**3**) may account for the biogenesis of seven-membered ring monoterpenes. Similar processes can be invoked for the formation of other terpenes such as humulene where anti-Markownikoff cyclization is implicated.

We thank the N.S.E.R.C. of Canada and F.C.A.C. of Quebec for financial support of this work. The award of an International Exchange Fellowship to D. W. by the N.S.E.R.C. is gratefully acknowledged. D. W. is a Visiting Scientist from the Institute of Chemistry, Academia Sinica, Bejing, People's Republic of China.

Received, 15th May 1984; Com. 676

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