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SYNTHESIS OF COMPOUNDS CONTAINING THE ISOPRENE UNIT. A NEW STEREOSPECIFIC SYNTHESIS OF THE GERANYL AND FARNESYL SKELETON.

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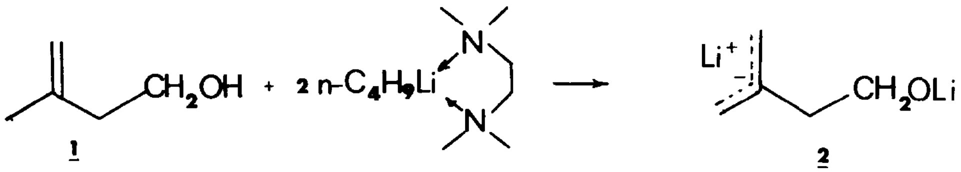
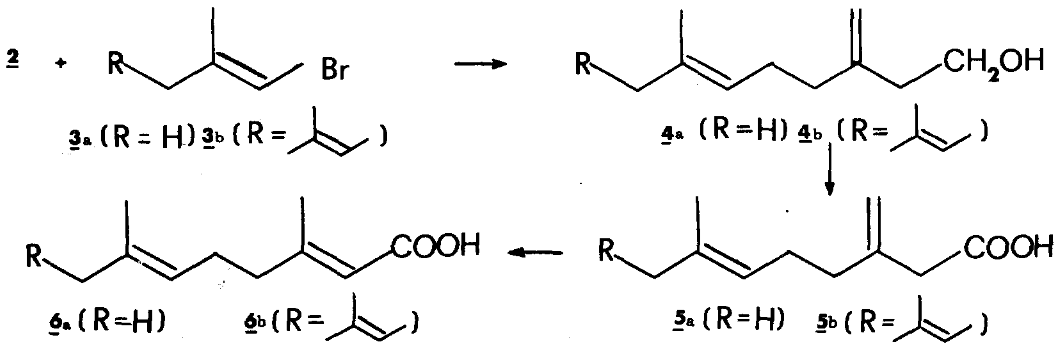
In the course of synthetic studies directed toward the synthesis of head to tail alicyclic terpenoids we have found it interesting to develop procedures which go through the repetition of a series of reactions which add one prenyl unit at a time.This synthetic approach was successfully utilized by us in a new synthesis of vitamin A and its isomers [1].

We wish now to report an attractive route which leads to the synthesis of head to tail alicyclic terpenes starting from the allyllithium species represented merely for convenience as 2.This organometallic intermediate may be easily prepared by metallation of 3-methyl-3-buten-1-ol 1. Olefins of general type $R(CH_3)C=CH_2$ can be metallated specifically on the methyl group by means of suitable organometallic derivatives [2] and treatment of 1 with n-butyllithium-TMEDA complex [3] in hexane at -78° leads to selective metallation at C_4 [4].

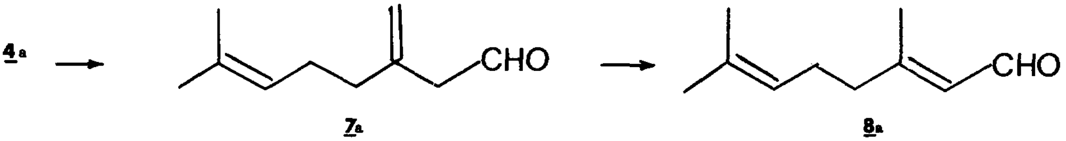


Compound 2 easily undergoes electrophilic attack by alkylhalides to give the corresponding alkylated derivatives,e.g. addition at -78° of 1-bromo-3-methyl-2-butene 3a in hexane to the suspension of 2 gives,after stirring the reaction mixture for 3 h at room temperature and working up,the expected alcohol 4a in 70% yield. The oxidation of the hydroxyl group in 4 in a two phase system involving diethyl ether and a water solution of sodium dichromate and sulphuric acid [5] gave the acid 5a (65% yield),which can be isomerized to 2-E-geranic acid 6a in quantitative yield by treatment with NaH suspension in THF at room temperature under argon. Following the same scheme the 2-E-farnesoic acid 6b was obtained,starting from geranyl bromide 3b and 2.



In another modification of this procedure the methylenic alcohol 4a was quantitatively oxidized to the corresponding aldehyde 7a by means of CrO_3-pyridine complex in methylene chloride [6].

The isomerization to 2-E-geranial 8a was quantitatively accomplished by treating the aldehyde 7a with a trace of potassium t-butylate at room temperature.



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