

Surprisingly, diisobutylaluminum hydride reduction of **6** in THF¹⁴ was unsuccessful in sharp contrast to the similar reaction results in the dendrolasin synthesis¹⁵. Instead, an alternative procedure employing aluminum chloride-lithium aluminum hydride (1:3)¹⁶ worked quite well producing the desired homoallylic alcohol **7** in 61% yield from **5**. The active reducing agent appears to be aluminum hydride (AlH₃) produced in situ. Two methylene triplets appeared in the nmr spectrum at δ 3.52 and 2.18 confirming the structural assignment.

The standard Sharpless epoxidation of the homoallylic alcohol **7** gave rise to the epoxyalcohol **8** in 77% yield. One of the vinylic proton signals disappeared in the nmr spectrum and a new triplet at δ 2.92 was assigned to the H-4 signal.

Oxidation of the epoxyalcohol **8** was accomplished by a careful reaction with chromium trioxide-pyridine complex in dichloromethane¹⁷ for 30 minutes yielding relatively clean epoxyaldehyde **9**. The unstable epoxyaldehyde **9** was converted to rose furan(**1**) by passing through a silica gel column with pentane-ether (5:1) as the eluting solvent. The overall yield from **8** was 33%. The nmr spectrum displayed typical furan peaks at δ 7.19 and 6.13.

The facile conversion of the epoxyaldehyde **9** to the furan **1** under mild conditions suggests a possible biogenetic routes for **1**.

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Chiral Guaiazulenes from Limonene*

Eun Lee and Jong In Hong

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151. Received October 20, 1986

Limonene is one of the cheapest chiral starting material in the natural product synthesis. Both (R)-(+)- and (S)-(-)-limonene are readily available and one synthetic sequence can be applied to the synthesis of both optical isomers of a target molecule. This report concerns with a synthesis of a chiral guaiazulenic intermediate from (R)-(+)-limonene, in which the original chiral center is preserved at the hydroazulene ring junction.

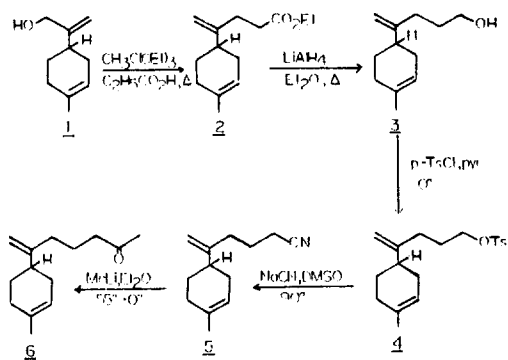
(R)-(+)-Limonene is known to produce chiral 1-formyl-5-isopropenyl-2-methyl-1-cyclopentene when it is subjected to selective epoxidation, hydrolysis to the diol, cleavage by periodate, and intramolecular condensation with piperidine and acetic acid¹. If the ketone **6** is used as the starting material in the same sequence of reactions, one would obtain the

ketoaldehyde **10**, which should serve as an ideal substrate for aldol condensation to form hydroazulene derivatives.

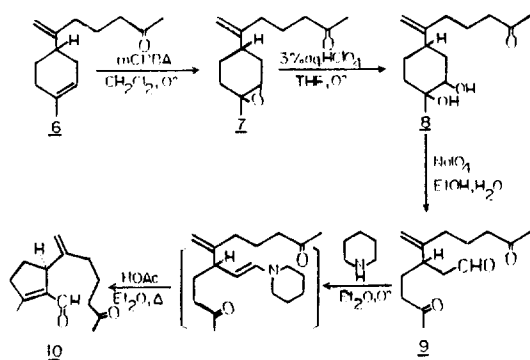
The ene reaction of (R)-(+)-limonene with methyl vinyl ketone in the presence of aluminum chloride at room temperature was reported to afford the ketone **6**², but we could not obtain the product of useful purity under the conditions reported. Various other Lewis acid catalysts were tested and zinc bromide³ was found to provide a small yield (<10%) of the ketone **6** in acceptable purity. Since other direct routes employing metalated (R)-(+)-limonene⁴ did not turn out to be practical, a conventional reaction sequence from (+)-limonen-10-ol(**1**)⁴ was devised.

Thus (+)-limonen-10-ol(**1**) was subjected to orthoester Claisen rearrangement to provide the ethyl ester **2**, which was reduced to the alcohol **3**. The corresponding tosylate **4** was converted to the homologous nitrile **5**, which afforded the ketone **6** upon treatment with methylolithium. (Scheme 1) The overall yield of **6** was 55% from **1**.

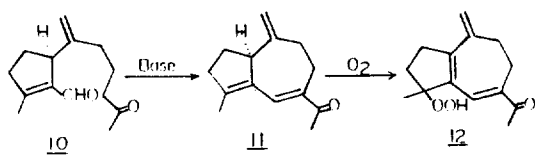
* Dedicated to Professor Sae-Hee Chang on the occasion of his both birthday.



Scheme 1



Scheme 2



Scheme 3

Careful reaction of **6** with one equivalent of *m*-chloroperoxybenzoic acid produced the monoepoxide **7**⁵, which was converted to the diketonaldehyde **9** via the diol **8** by acid

catalyzed hydration and periodate cleavage. Successive treatment of **9** with piperidine and acetic acid cleanly provided the ketoaldehyde **10** in an overall yield of 42%. (Scheme 2) A sharp singlet at δ 9.90 in the nmr spectrum of **10** was contrasted with a triplet at δ 9.67 in that of **9**⁶.

With the intermediate **10** on hand, various aldol conditions were studied for the final seven-membered ring cyclization. The reactions in alcoholic hydroxide and carbonate afforded reasonable yields (50–65%) of the hydroazulenic product **11**, but the best yield (82%) was obtained when **10** was reacted with 1.1 equivalents of sodium hydroxide in refluxing benzene containing 0.6 equivalent of dibenzo-18-crown-6. In the nmr spectrum of **11**⁷, the appearance of a vinylic singlet at δ 7.21 instead of an aldehydic signal was most diagnostic. The methyl signal at δ 2.20 in the spectrum of **10** shifted upfield at δ 1.82. The mass spectrum showed M^+ peak at m/e 202 (12.4% relative to the base peak at 43).

When **11** was allowed to stand in air, a crystalline product slowly formed, and the structure was assigned as the hydroperoxide **12**. (Scheme 3) The vinylic singlet appeared at δ 6.21 and the methyl singlet at δ 1.42 in the nmr spectrum of **12**. It will be interesting to see whether the chirality is preserved in **12**. Shorter routes to **11** are being investigated, which will serve as a precursor in the synthesis of other guaiazulenes. **Acknowledgement.** This research was supported by a grant(1983) from Korea Research Foundation.

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5. Mixture of isomers.
6. The structural assignment of **10** was confirmed by an independent synthesis via a nitrile analog of **7**. The alternative cycloheptenecarbaldehyde structure can be safely discarded.
7. ϵ_{305} (MeOH) = 13.600, $\Delta\epsilon_{311}$ = +1.2, $\Delta\epsilon_{347}$ = -1.2