

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*

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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.

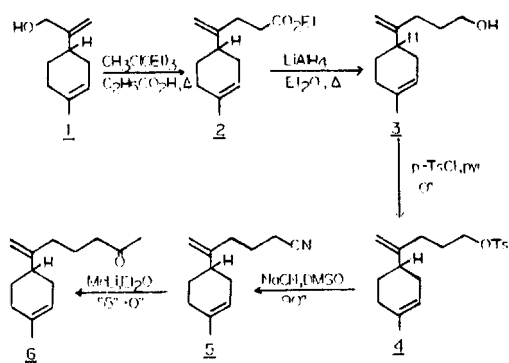
(R)-(+)-Limonene is known to produce chiral 1-formyl-5-isopropenyl-2-methyl-1-cyclopentene when it is subjected to selective epoxidation, hydrolysis to the diol, cleavage by periodate, and intramolecular condensation with piperidine and acetic acid¹. If the ketone **6** is used as the starting material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

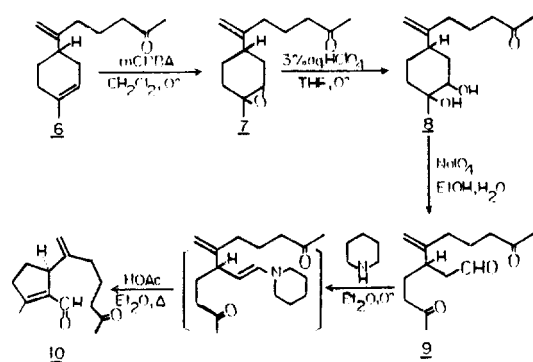
The ene reaction of (R)-(+)-limonene with methyl vinyl ketone in the presence of aluminum chloride at room temperature was reported to afford the ketone **6**², but we could not obtain the product of useful purity under the conditions reported. Various other Lewis acid catalysts were tested and zinc 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**)⁵ 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**.

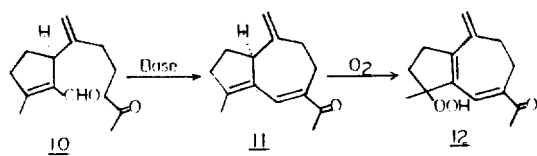
* Dedicated to Professor Sae-Hee Chang on the occasion of his both birthday.



Scheme 1



Scheme 2



Scheme 3

Careful reaction of **6** with one equivalent of *m*-chloroperoxybenzoic acid produced the monoepoxide **7**, 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**.

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**, 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