

A New Approach to the Formal Synthesis of (\pm)- α -Cedrene

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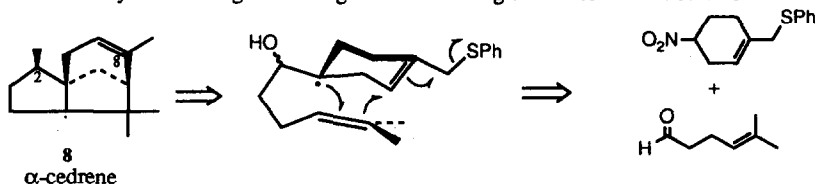
Abstract: A tandem radical cyclization, which proceeds via an addition/elimination mechanism, has been applied to the synthesis of norcedrenone 7, a precursor for the synthesis of (\pm)- α -cedrene 8.

α -Cedrene 8 has been obtained from cedar-wood oil and vetiver oil.¹ This interesting sesquiterpene possesses a relatively rare tricyclo[5.3.1.0^{1,5}]undecane skeleton. A number of strategies for the synthesis of α -cedrene have been studied and briefly summarized.² Previously, we demonstrated that a tandem radical cyclization via hydrogen atom transfer is a very useful method to construct a Δ^2 -cedrene skeleton. However, since this reaction is terminated by the formation of a C-H bond, the resulting products cannot retain useful functionalities as a result of the transfer.³ Therefore, our previous method is limited to the Δ^2 -cedrene which is a minor naturally occurring isomer. We now report a new approach to the synthesis of norcedrenone 7⁴ which is a precursor for the synthesis of (\pm)- α -cedrene 8. The new method involves a tandem radical cyclization through an addition/elimination mechanism.

Our approach is based on the following hypotheses:

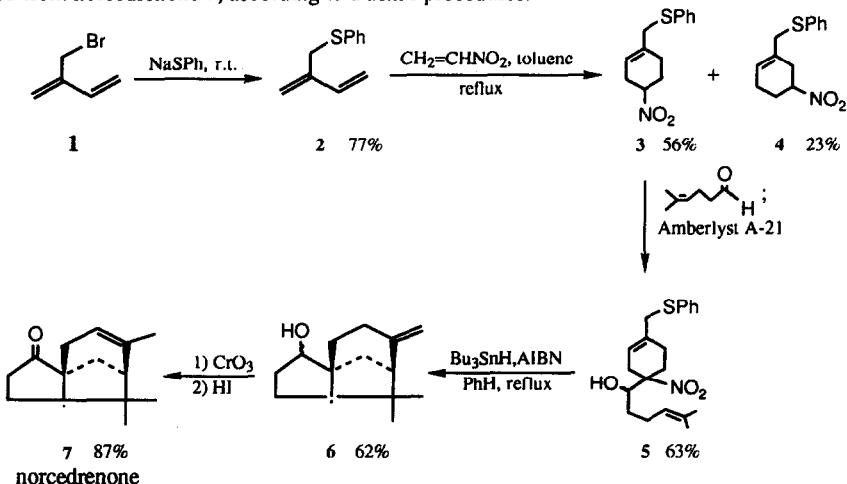
- 1) A tandem radical cyclization reaction is very efficient to construct the cedrene skeleton.
- 2) The position at carbon-8 in the cedrene molecule must be functionalized during/or after the reaction of cyclization.

A directed synthetic design involving these two strategic features is outlined below.



The 2-(phenylthiomethyl)-1,3-butadiene 2 was obtained in 77% yield from the reaction of 2-(bromomethyl)-1,3-butadiene 1⁵ with sodium thiophenoxide at room temperature for 12 h. The cycloaddition of 2 with nitroethylene in refluxing toluene for 15 h gave a mixture of 1-(phenylthiomethyl)-4-nitrocyclohexene 3 and 1-(phenylthiomethyl)-5-nitrocyclohexene 4 in 79% yield. The ratio of the two isomers was determined to be 2.5:1 based on the ¹H NMR integration of the vinyl protons at 5.40 ppm and 5.49 ppm, respectively. The cyclization precursor 5 was readily obtained in 63% yield from the addition of 3 to 5-methyl-4-hexenal catalyzed by Amberlyst A-21 at room temperature for 24 h. The tandem radical cyclization of 5 was effected by the treatment with tributyltin hydride 6 in the presence of 20 mol% of

azobisisobutyronitrile (AIBN) in benzene at 80°C for 8 h. A mixture of secondary alcohols **6** was obtained in 62% isolated yield. Subsequent oxidation of the mixture **6** with Jones reagent at 0–5°C, followed by the treatment with a catalytic amount of HI in benzene at 30°C for 24 h, gave 87% yield of norcedrenone **7** (based on the data from MP, ¹H NMR, ¹³C NMR, IR, and HRMS studies).⁷ (±)- α -Cedrene **8** could be obtained from norcedrenone **7**, according to Buchi's procedures.⁴



In conclusion, we have successfully developed a novel method and used it in the synthesis of norcedrenone **7**, a precursor to (±)- α -cedrene **8**. Further applications of this method should allow convenient syntheses of naturally occurring tricyclo[5.3.1.0^{1,5}]undecanes such as (±)- α -biotol and (±)- β -biotol.

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References and Notes:

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- Norcedrenone **8**: mp 58–60°C (lit.⁴ mp 57–59°C); IR ν_{max} (CHCl₃ cm⁻¹) 1736 (C=O); ¹H NMR (CDCl₃) δ 1.06(s, 3H, -Me), 1.14(s, 3H, -Me), 1.48–1.55(m, 1H), 1.60–1.95(m, 5H), 1.68(s, 3H, -Me), 2.02–2.13(m, 1H), 2.27–2.63(m, 3H), 5.25(br.s, 1H, =CH); ¹³C NMR (CDCl₃) 21.56(t), 24.71(q), 26.60(q), 27.51(q), 34.82(t), 37.40(t), 40.57(t), 48.04(s), 54.35(d), 57.44(s), 58.34(d), 117.37(d), 140.12(s); Exact mass calcd for 204.1514, found 204.1519(M⁺).

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