

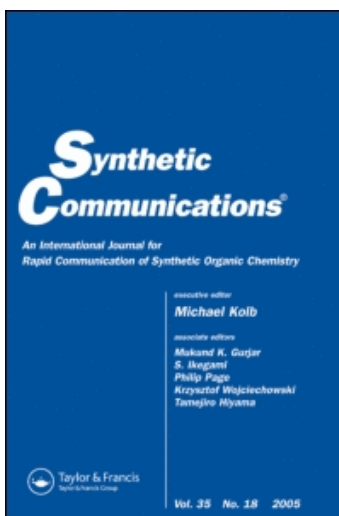
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New Approach Towards Carotane Sesquiterpenes: A Short Synthesis of (-)-Daucene

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NEW APPROACH TOWARDS CAROTANE SESQUITERPENES :
A SHORT SYNTHESIS OF (-)-DAUCENE

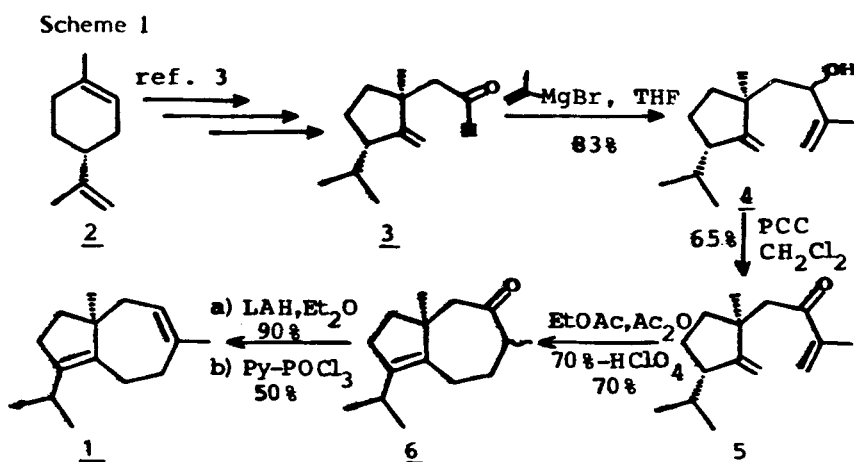
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Abstract: An enantioselective synthesis of sesquiterpene hydrocarbon (-)-daucene **1** from R-(+)-limonene involving acid catalysed enone-olefin cyclisation ($\underline{5} \rightarrow \underline{6}$) as the key step is described.

Carotanes are an interesting and growing family of bicyclic sesquiterpenes embodying an unusual hydroazulenenic skeleton.¹ The simplest member of the family and possible biogenetic precursor of many oxygenated members of this group is the hydrocarbon daucene **1**,^{1a} isolated from carrot seeds (*Daucus carota* L). Several syntheses of **1** in optically active^{2a,b} as well as racemic form^{2c,d} have been reported in recent years. Herein, we describe a new, short, enantioselective synthesis of the naturally occurring (-)-daucene **1** from abundantly available R-(+)-limonene **2**. Our approach is

general enough for adaptation to the other members of the carotane family.

The monocyclic aldehyde **3** of well defined stereochemistry and readily available from R-(+)-limonene **2**, as described by us elsewhere,³ served as the starting point of our synthesis. Addition of the Grignard reagent prepared from 2-bromopropene furnished the allylic alcohol **4** as a mixture of diastereoisomers and was oxidised to a single α,β -unsaturated ketone **5**. The key cyclisation step was smoothly carried out by exposing **5** to $\text{HClO}_4\text{-Ac}_2\text{O}$ milieu.⁴ The resulting bicyclic ketone **6** on LAH reduction and dehydration furnished the hydrocarbon daucene **1**, $[\alpha]_D^{20} (\text{C } 0.8)$, identical with the natural product. The sequence of reactions is summarised in Scheme 1.



Experimental Section

^1H NMR and ^{13}C NMR spectra were obtained on a JEOL FX-100 spectrometer. All chemical shifts are reported in units relative to Me_4Si in CDCl_3 solution. Infrared spectra were recorded on Perkin-Elmer 1310 spectrophotometer. All solvent extracts were washed with brine and dried over anhydrous Na_2SO_4 . Solvent was removed under reduced pressure on Buchi-EL rotavapor.

1S-methyl-3S-isopropyl-2-methylene-1S-[2'-hydroxy-3'-methyl but-3'-enyl]cyclopentane.4: Into a 50 mL three necked RB flask, fitted with dry nitrogen gas inlet, pressure equilizing addition funnel and mercury seal, magnesium turnings (170 mg, 7.0 mmol) were placed and dry THF (20 mL) was introduced. To this mixture 2-bromopropene (970 mg, 8.0 mmol) was slowly added and stirring continued until all the magnesium dissolved. A solution of the aldehyde 3 (1.0 g, 5.55 mmol) in 5 mL of dry THF was slowly added to it and the reaction mixture was stirred at RT for 1h. The reaction was quenched by addition of saturated NH_4Cl solution and extracted with diethylether (3 x 50 mL). The combined organic extract was washed, dried and concentrated to give an oily liquid which was distilled at $120^\circ\text{C}/0.1$ mm to furnish an epimeric mixture of allylic alcohols 4.

(1.0 g, 83%), $[\alpha]_D^{25} - 53.3$ (C 2.0), IR(neat): 3400, 3050, 890 cm^{-1} ; ^1H NMR: (mixture of hydroxy epimers) 4.9 - 4.6 (m, 8H), 4.2 - 4.0 (m, 2H), 2.6 - 1.2 (m, 22H), 1.08 (s, 3H), 1.0 (s, 3H), 0.95 (d, $J = 7$ Hz, 6H), 0.75 (d, $J = 7$ Hz, 6H). Anal. Calcd. for $\text{C}_{15}\text{H}_{26}\text{O}$: C, 81.02, H, 11.79; Found: C, 81.12, H, 11.81.

1S-methyl-3S-isopropyl-2-methylene-1S-[3'-methyl-3'-

enyl-but-2'-one]cyclopentane.5: To a suspension of pyridiniumchlorochromate (1.1 g, 60 mmol) in dry dichloromethane (5 mL) containing 1.0 g of activated molecular sieves (4 A), was added allylic alcohol 4 (1.0 g, 4.5 mmol) in dry dichloromethane (5 mL) at 0°C . The reaction mixture was brought to room temperature, stirred for an additional 1h, diluted with dry ether (20 mL) and filtered through a small florisil (3 g) column. Removal of solvent gave an oily liquid which was distilled at $110^\circ\text{C}/0.1$ mm to furnish enone 5 (645 mg, 65%), $[\alpha]_D^{25} - 62.2$ (C 2.0), IR(neat): 1680, 890 cm^{-1} ; ^1H NMR: 5.90 (br s, 1H), 5.70 (br s, 1H), 4.75 (t, 2H), 3.0 - 2.0 (m, 3H), 1.8 (s, 3H), 1.75 - 1.2 (m, 5H), 1.05 (s, 3H), 0.95 (d, $J = 7$ Hz, 3H), 0.75 (d, $J = 7$ Hz, 3H); ^{13}C NMR: 201.0, 162.7, 145.8, 123.8, 103.3, 50.4, 47.4, 44.5, 36.9, 28.5, 27.0, 22.9, 21.6, 17.4, 16.1. Anal. Calcd. for $\text{C}_{15}\text{H}_{24}\text{O}$: C, 81.76, H, 10.98; Found: C, 81.82, H, 10.97.

1S,4-dimethyl-8-isopropyl-bicyclo[5.3.0]deca-7-ene-3-

one 6: To a solution of enone 5 (500 mg, 2.3 mmol) in 10 mL of ethylacetate was added 1 mL of acetic anhydride and 0.1 mL of 70% perchloric acid. The reaction mixture was stirred at room temperature for 5 min. The reaction mixture was then quenched with saturated Na_2CO_3 solution and organic layer was separated. The aqueous layer was once again extracted with ethylacetate (25 mL) and the combined organic extracts were washed, dried and concentrated to give an oily liquid which was chromatographed on silicagel (20 g) column to furnish the bicyclic ketone 6 (350 mg, 70%), bp. $110^\circ\text{C}/0.1$ mm, $[\alpha]_{\text{D}}^{25} -15$ (c 1.0), IR(neat): 1700 cm^{-1} ; $^1\text{H NMR}$: (methyl epimeric mixture) 2.7 - 1.4 (m, 24H), 1.2 - 0.8 (series of s and d, 24H). Anal. Calcd. for $\text{C}_{15}\text{H}_{24}\text{O}$: C, 81.76, H, 10.98. Found: C, 81.80, H, 10.94.

(-)-Daucene 1 : In to a two-necked, 25 mL RB flask fitted with a rubber septum and mercury seal was placed LAH (50 mg, excess) in dry ether (10 mL). To this suspension, bicyclic ketone 6 (250 mg, 1.14 mmol) in dry ether (5 mL) was slowly added through a syringe. The reaction mixture was stirred for 30 min. A few drops of ethylacetate were then added to destroy excess hydride. The reaction mixture was diluted with water

and extracted with ether (3 x 25 mL). The ethereal layer was washed and dried. Removal of solvent gave epimeric mixture of bicyclic hydroxy olefin (225 mg, 90%), IR(neat): 3400 cm^{-1} ; $^1\text{H NMR}$: 3.8 (m, 1H), 2.6 - 1.3 (series of m, 13H) 1.05 - 0.80 (series of s and d, 12H). Anal. Calcd. for $\text{C}_{15}\text{H}_{26}\text{O}$: C, 81.02, H, 11.79. Found: C, 81.12, H, 11.81. This material was directly employed for the next step.

The mixture of hydroxy olefins (50 mg, 0.225 mmol) in dry pyridine (1.0 mL) was placed in a 5 mL RB flask fitted with a drying tube. To this stirred solution was added phosphorousoxychloride (0.2 mL) at $0-5^\circ\text{C}$ and the mixture was stirred for 12 h at room temperature. The reaction mixture was diluted with pentane (10 mL) and slowly quenched with water (2 mL) to hydrolyze the excess phosphorousoxychloride. The reaction mixture was extracted with pentane (3 x 10 mL), washed and dried. Removal of solvent gave an oily residue which was charged on a AgNO_3 silicagel (5 g) column. Elution with pentane removed less polar impurities. Further, elution with 20% benzene-pentane furnished pure (-)-daucene 1, (23 mg, 50%), $[\alpha]_{\text{D}}^{25} -20^\circ$ (C 1.0)^{1a}; IR(neat): 2970, 830 cm^{-1} ; $^1\text{H NMR}$: 5.37 (t, 1H), 2.8 - 1.8 (m, 11H), 1.73 (br s, 3H), 0.99 (d, J = 7 Hz, 3H), 0.92 (d, J = 7 Hz, 3H), 0.91 (s, 3H). The IR and NMR

spectra of our material were found to be identical with the authentic spectrum supplied by Professor Seto.⁵

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References

1. (a) G.V. Figulevskii and V.I. Kivaleva, Doklady Akad. Nauk S.S.S.R., 1961, 141, 1384. (b) M.C. Sriraman, B.A. Nagasampagi, R.C. Pandey and Sukh Dev, Tetrahedron, 1973, 29, 985. (c) J.S. Glasby, Encyclopaedia of the Terpenoides, John Wiley & Sons Limited, 1982. (d) M. Miski, A. Ulubelen, T.J. Mabry, W.H. Watson, I. Vickovic and M. Holub, Tetrahedron, 1984, 40, 5197. (e) K. Pandita, S.G. Agarwal, R.K. Thappa and K.L. Dhar, Indian J. Chem. Sect. B, 1984, 23, 956. (f) M.G. Valle, G. Appendino, G.M. Nano and V. Picci, Phytochemistry, 1987, 26, 253.

2. (a) M. Yanasaki, *J. Chem. Soc., Chem. Commun.*, 1972, 606. (b) H. De Broissia, J. Levisalle and H. Ruddler, *Bull. Soc. Chim. Fr.*, 1972, 4314. (c) P. Naegeli and R. Kaiser, *Tetrahedron Lett.*, 1972, 2013. (d) H. Seto, Y. Fujimoto, T. Tatsumo and H. Yoshioka, *Synthetic Commun.*, 1985, 1217.
3. G. Mehta and N. Krishna Murthy, *Tetrahedron Lett.*, 1987, in press.
4. N.H. Anderson and H.S. Uh, *Tetrahedron Lett.*, 1973, 2079.
5. We thank Professor Seto for his help in making available comparison spectra.