

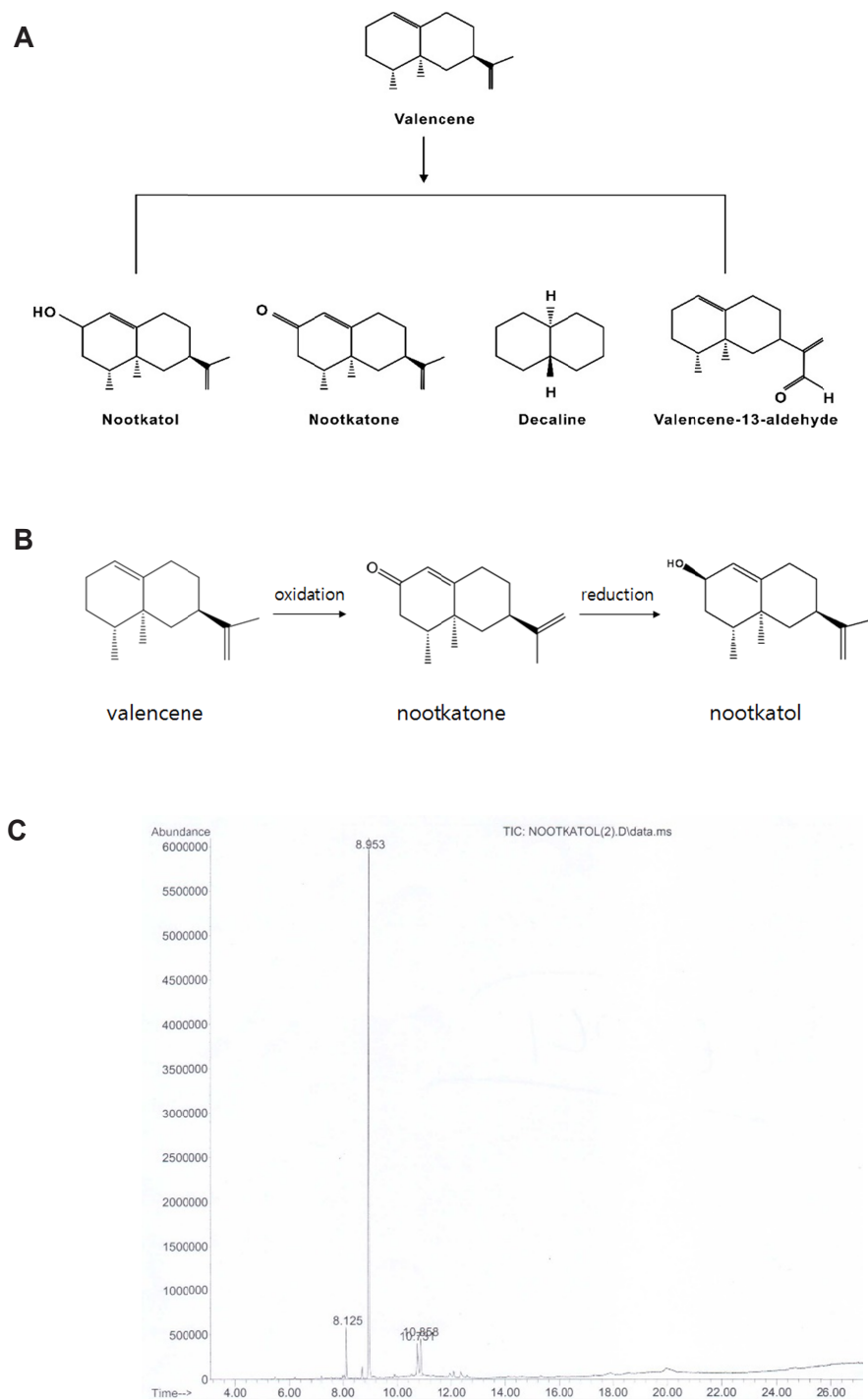
SUPPLEMENTARY MATERIALS AND METHODS

Valencene derivatives

Nootkatone is produced by valencene oxidation, during which nootkatol is a precursor to nootkatone. Decalin is a saturated analog of naphthalene, and all functional groups and double bonds in its chemical structure were removed, with only the two-ring structure of valencene remaining. Valencene-13-aldehyde was synthesized by adding an aldehyde functional group at the thirteenth carbon position of valencene.

Nootkatol synthesis

Eight grams (40 mmol) of valencene ($C_{15}H_{24}$; MW, 204 g) was dissolved in 200 ml of ethyl acetate. t-BHT (40 g), sodium bicarbonate (2 g), and sodium hypochlorite (40 mmol) were added and stirred for 8 h at 5–10°C. Sodium bisulfite (40 g) was added to the mixture and left overnight. Water layers were washed with ethyl acetate, and the dry reaction solution was distilled to synthesize nootkatone at a yield of 7.0 g (80.3% purity). To synthesize nootkatol, 8.72 g of nootkatone ($C_{15}H_{22}O$, MW, 218; 40 mmol) was dissolved in 50 ml of methanol (solution A). Another solution using 2.16 g (4 mmol) of sodium methoxide and 1.512 g (40 mmol) of $NaBH_4$ (sodium borohydride) in 50 ml of methanol (solution B) was prepared. Solution B was mixed with solution A, and the two reacted at 25°C for 3 h. After the reaction, cold water was added to the reaction mixture, and excess $NaBH_4$ was removed by adding 20 ml of 10% HCl. This solution was extracted thrice with ether and washed thrice with water. After drying the ether solution with anhydrous sodium sulfate, the solvent was removed and nootkatol was synthesized at a yield of 7.8 g (89.4% purity). The synthesis strategy is briefly described schematically in Supplementary Fig. 1B. Purity of the synthesized nootkatol was confirmed by gas chromatography-mass spectrometry (GC-MS). GC-MS data were obtained using an HP GC-MSD unit (6890 series; Hewlett-Packard, Palo Alto, CA, USA) with an HP-5MS capillary column (60.0 m \times 250 μ m \times 0.25 μ m, Hewlett-Packard). The results are shown in Supplementary Fig. 1C.



Supplementary Fig. 1. Chemical structures of valencene derivatives and synthesis of nootkatol. (A) The structure of various valencene derivatives, nootkatol, nootkatone, decaline and valencene-13-aldehyde. (B) Schematic diagram depicting nootkatol synthesis. (C) Total ion chromatogram of synthesized nootkatol. The main compound, nootkatol (89.4%, Rt [min] = 8.953), and its minor components are indicated.