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A SHORT SYNTHESIS OF THE ANTIFUNGAL PRINCIPLE OF *SAPIUM JAPONICUM*

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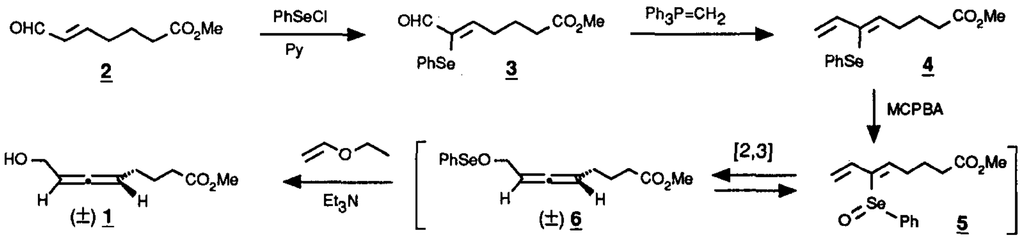
Abstract: Methyl 8-hydroxy-5,6-octadienoate (1), the antifungal principle of *Sapium japonicum*, was prepared via the oxidation and [2,3] sigmatropic rearrangement of a dienyl selenide precursor.

Sapium japonicum, a deciduous tree that is common in parts of Japan, is resistant to certain types of fungal infections. This has been attributed to the presence of methyl 8-hydroxy-5,6-octadienoate (1), a strong antifungal agent, in its leaves.[1] Several recent syntheses of allenic alcohol 1 have appeared,[2] and we now report a concise, new approach to this compound, which is shown in Scheme 1.

The α,β-unsaturated aldehyde 2 is readily available from δ-valerolactone.[3] α-Selenenylation of 2 with benzeneselenenyl chloride in pyridine[4a] provided 3 in 70% yield,[4b] followed by a Wittig reaction to afford 46% of the dienyl selenide 4. Oxidation of 4 to the corresponding selenoxide 5 and subsequent [2,3] sigmatropic rearrangement[5,6] was expected to provide the desired product 1 after hydrolysis of the selenenic ester 6. However, pyrolysis of the relatively stable selenoxide 5 under a variety of conditions produced complex mixtures of selenenylated products containing little or none of the allenic alcohol 1. Enol ethers have been previously employed to scavenge selenenic electrophiles formed during selenoxide eliminations.[7,8] In the present case, transselenenylation of an added enol ether with 6 would drive the rearrangement to completion and prevent competing additions of the selenenic ester, or related Se (II) electrophiles, to the allene moiety. Thus, oxidation of 4 with m-chloroperbenzoic acid (MCPBA) and treatment of the crude selenoxide 5 with triethylamine and ethyl vinyl ether afforded 47% of 1.[9] Scheme 1 therefore provides a simple, three-step synthesis of the racemic[10] allenic alcohol 1 from aldehyde 2.

Scheme 1



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2. a) Rodini, D.J.; Snider, B.B. *Tetrahedron Lett.* **1980**, *21*, 3857. b) Huguet, J.; Reyes, M. del C. *Tetrahedron Lett.* **1990**, *31*, 4279. c) Gooding, O.W.; Beard, C.C.; Jackson, D.Y.; Wren, D.L.; Cooper, G.F. *J. Org. Chem.* **1991**, *56*, 1083.
3. Gleason, J.G.; Bryan, D.B.; Kinzig, C.M. *Tetrahedron Lett.* **1980**, *21*, 1129.
4. a) Zima, G.; Liotta, D. *Synth. Commun.* **1979**, *9*, 697. b) Compound 3 was isolated as a pure geometric isomer with the (Z)-configuration, as determined by NOE between the aldehyde proton and the olefinic proton.
5. For a review of [2,3] sigmatropic rearrangements of selenium compounds, see: Reich, H.J. *Organoselenium Chemistry*; Liotta, D., Ed., Wiley: New York, 1987, Ch. 8.
6. Only a few previous examples of allenic alcohol formation by the rearrangement of dienyl selenoxides are known: a) Lerouge, P.; Paulmier, C. *Tetrahedron Lett.* **1984**, *25*, 1987. b) Back, T.G.; Lai, E.K.Y.; Muralidharan, K.R. *J. Org. Chem.* **1990**, *55*, 4595.
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8. The use of either secondary or tertiary amines in the absence of ethyl vinyl ether gave very low yields of 1. For secondary amines as scavengers of Se (II) electrophiles, see: Reich, H.J.; Wollowitz, S.; Trend, J.E.; Chow, F.; Wendelborn, D.F. *J. Org. Chem.* **1978**, *43*, 1697.
9. Selenide 4 was treated with excess MCPBA in chloroform for 15 min, followed by washing with aqueous $NaHCO_3$, drying and concentration of the mixture. The crude selenoxide 5 was stirred in ethyl vinyl ether containing ca. 12 eq. of triethylamine at room temperature for 12 h, the solution was evaporated, and the product 1 isolated by flash chromatography over silica-gel. Its identity was confirmed by its IR, ^{1}H-NMR and high and low resolution mass spectra.
10. An attempted enantioselective preparation of 1 using chiral oxaziridines as oxidants instead of MCPBA resulted in low (< 10%) enantiomeric excesses. This procedure was previously employed for the enantioselective synthesis of allylic alcohols from allylic selenides: Davis, F.A.; Stringer, O.D.; McCauley Jr., J.P. *Tetrahedron* **1985**, *41*, 4747.

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