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A SHORT STEREOSELECTIVE SYNTHESIS OF (-)-SERRICORNIN

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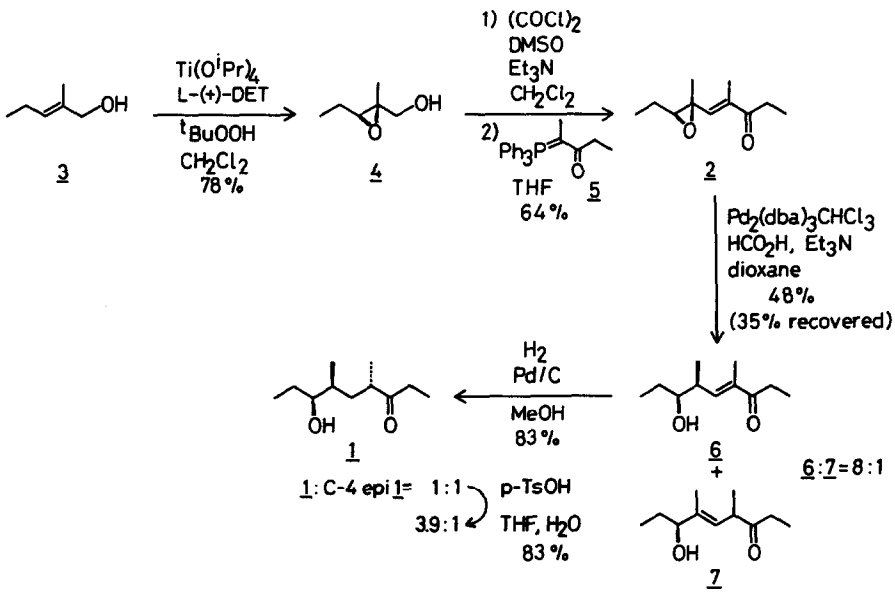
Summary: Palladium-catalyzed reduction of (+)-(*E*)-(6*S*,7*S*)-4,6-dimethyl-6,7-epoxy-4-nonen-3-one with formic acid gave (-)-(*E*)-(6*S*,7*S*)-4,6-dimethyl-7-hydroxy-4-nonen-3-one, which was hydrogenated to give (-)-serricornin.

(-)-Serricornin 1 is a sex pheromone produced by *Lasioderma serricorne F.*, a female cigarette beetle, which is a serious pest of cured tobacco leaves.[1] Although several syntheses of (-)-1 have been reported,[2] they require more than ten steps from easily available starting materials. Recently we have reported a stereoselective preparative method for optically active acyclic building blocks which have vicinal hydroxy and methyl groups by palladium-catalyzed hydrogenolysis of alkenyloxiranes.[3] Based on this methodology we have accomplished a very concise five-step synthesis of (-)-1.

Epoxydation of (*E*)-2-methyl-2-penten-1-ol (3) using *t*-BuOOH in the presence of $Ti(O^iPr)_4$ and diethyl L-tartrate as a catalyst at -23°C gave the chiral oxirane 4 ($[\alpha]_D^{24}$ =



-17.9° ($CHCl_3$, c 3.63)) in 78% yield. Swern oxidation of **4** followed by Wittig reaction with phosphorane **5** gave the (*E*)-alkenyl oxirane **2**[4] in 64% yield from **4**. Reaction of **2** with HCO_2H-Et_3N in the presence of $Pd_2(dba)_3CHCl_3$ (5 mol%) and trimethyl phosphite (5 mol%) at room temperature for 3 h gave the alcohol **6**[5] and a small amount of **7** (48% yield, **6**:**7** = 8:1) with recovery of **4** (35%). After separation of **6** by column chromatography on SiO_2, hydrogenation of the olefin **6** using Pd/C in MeOH gave (-)-serricornin **1**[6] and its C-4 epimer (1:1) in 83% yield. The ratio of **1** and its C-4 epimer was raised to 3.9:1 by acid catalyzed epimerization[7] (*p*-TsOH in THF-H_2O (1:1) at 50°C for 5 h). The synthesis of (-)-**1** described here is the shortest and one of the most practical method among those reported. This research was financially supported by Shorai Foundation for Science and Technology.

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4. **2**: $[\alpha]_D^{24}$ = +139° ($CHCl_3$, *c* 2.12); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.08-1.17 (m, 6H), 1.42 (s, 3H), 1.85 (s, 3H), 2.64 (q, *J* = 7.0 Hz, 2H), 2.55 (t, *J* = 6.5 Hz, 1H), 6.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 22.4 MHz) 8.2 (q), 10.1 (q), 12.1 (q), 16.6 (q), 21.8 (t), 30.1 (t), 58.7 (s), 65.0 (d), 137.2 (d), 139.9 (s), 201.7 (s); IR (neat) 2975, 1680, 1460, 1380, 1220, cm^{-1}; MS: m/z 183, 165, 53, 137, 124, 109, 97, 91, 81, 67, 56, 53; HRMS $C_{11}H_{18}O_2$ caled m/z 182.1307, found m/z 182.1302.
5. **6**: $[\alpha]_D^{24}$ = -34.7° ($CHCl_3$, *c* 0.53); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.90-1.20 (9H), 1.81 (d, *J* = 1.4 Hz, 3H), 2.27 (s, 1H), 2.65-2.76 (m, 3H), 2.70 (q, *J* = 7.5 Hz, 2H), 3.33-3.53 (m, 1H), 6.52 (dd, *J* = 10.0, 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 22.4 MHz) 8.8 (q), 10.2 (q), 30.5 (t), 39.4, (d), 76.4 (d), 136.0 (s), 144.0 (d), 202.7 (s); IR (neat) 3400, 2950, 2925, 1710, 1660, 1460, 1380, 1045, 980, 735 cm^{-1}; MS: m/z 185, 167, 155, 137, 126, 109, 97, 93, 81, 69, 58, 56, 53. The enantiomeric excess of **6** was found to be 88-96% by NMR analysis of its (*R*)-MTPA ester.[8]
6. (-)-Serricornin (**1**) was obtained as a mixture of open-chain form **1** and its intramolecular hemiacetal form by ^1H NMR and ^{13}C NMR, which are in accordance with the literature. M. Mori, T. Chuman, and K.Kato, *Tetrahedron Lett.*, **25**, 2553 (1984).
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