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Total Synthesis of (3S, 6S)- (+)-3,7-Dimethyl-3-acetoxy-6-hydroxy-octa-1,7-diene

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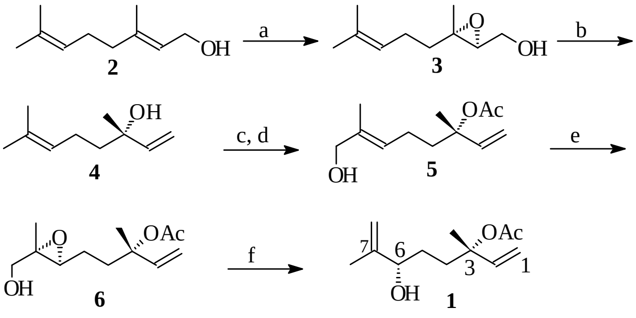
Abstract: A total synthesis of (3S, 6S)- (+)-3,7-dimethyl-3-acetoxy-6-hydroxy-octa-1,7-diene *via* the rearrangement of chiral 2,3-epoxy alcohol, with the system of Ph_3P, pyridine, I_2 and H_2O, is described.

Keywords: 2,3-Epoxy alcohol, rearrangement synthesis.

Compound **1**[1], a novel monoterpenoid, was isolated from *Mutisia spinosa (*Compositae). The structure of **1**, determined by spectroscopic techniques, corresponded to 3,7-dimethyl-3-acetoxy-6-hydroxy-octa-1,7-diene (the name of 6-hydroxy-7(9)-dehydro-6,7-dihydroneryl acetate in reference 1 is uncorrect). However the absolute configurations at C-3 and C-6 were not determined. Compound **1** was synthesized by photooxidation of linalyl acetate[2], however the authors obtained the isomer mixture of **1**. Herein we report the total synthesis of (3S, 6S)- (+)-**1** from geraniol **2** through six steps (**Scheme 1**).

Scheme 1



Reagents and conditions: a) Ti $(O^iPr)_4$, *t*-BuOOH, L- (+)-DET, CH_2Cl_2, 4Å molecular siere, CaH_2, Silica gel, -40~-20 °C, 5 h, 91%; b) Ph_3P, I_2, pyridine, Et_2O/CH_3CN (5/3), 0 °C, 1 h, then 1 equivalent H_2O added, 38 °C, 10 h, 98%; c) Ac_2O, Et_3N, rt, 10 h, 70%; d) SeO_2, *t*-BuOOH, CH_2Cl_2, rt, 2 h, 51%; e) Ti $(O^iPr)_4$, *t*-BuOOH, L- (+)-DET, CH_2Cl_2, 4Å molecular sieve, CaH_2, Silica gel, -40~-20 °C, 5 h, 78%; f) Ph_3P, I_2, pyridine, Et_2O/CH_3CN (5/3), 0 °C, 1 h, then 1 equivalent H_2O added, 38 °C, 6 h, 90%.

Geraniol **2** was epoxized by Sharpless asymmetric epoxidation [L- (+)-DET was employed][3]. By our method[4], epoxide **3** was iodinated with Ph_3P (3 equivalent), pyridine (4 equivalent) and I_2 (1.5 equivalent) in dry ether and CH_3CN, then the iodide was converted to linalool **4** by addition of 1 equivalent H_2O.Thus linalool **4** was obtained in 98% yield and >95% e.e[5].

Linalool **4** was protected with Ac_2O, Et_3N and DMAP, then SeO_2 oxidation gave allylic alcohol **5**[6]. Sharpless asymmetric epoxidation[3] of allylic alcohol **5** with L- (+)-DET led to 6S, 7S- and 6R, 7R-epoxy alcohol in a ratio of *ca.* 10:1. Rearrangement of epoxy alcohol **6** [$[\alpha]_D^{24}$ –6.4 (*c* 0.75, $CHCl_3$)] gave the title compound **1** in 90% yield as a colorless oil [$[\alpha]_D^{24}$ +6.0 (*c* 0.80, $CHCl_3$)]. The spectral data of the title compound **1** was compatible with the assigned structures[7].

Acknowledgments

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References and Notes

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5 The enantiomeric excess of linalool was measured by 400M ^{1}HNMR analysis with Eu $(hfc)_3$.

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7 spectral data:
Compound **1**: $[\alpha]_D^{24}$ +6.0 (*c* 0.80, $CHCl_3$). IR: 3435, 3075, 2974, 2941, 1736, 1647, 1251,1020, 901 cm^{-1}. EIMS (*m/z*): 152 (0.4%, M-HOAc), 137 (4), 109 (5), 93 (7), 71 (58), 67 (65), 55 (23), 43 (100). ^{1}HNMR (400MHz,$CDCl_3$): δ (ppm) 5.93 (dd, J=17.4Hz, J=10.9Hz, 1H, CH=), 5.14 (d, J=17.4Hz, 1H, CH=), 5.11 (d, J=10.9Hz, 1H, CH=), 4.93, 4.84 (s, 2H, CH_2=), 4.03 (t, J=6.4Hz, 1H, CHO), 2.00 (s, 3H, CH_3), 2.05-1.92 (m, 2H, CH_2), 1.82-1.77 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}CNMR (100MHz, $CDCl_3$): δ (ppm) 169.93, 147.06, 141.51, 113.28, 111.39, 82.73, 75.77, 35.65, 28.68, 23.63, 22.33, 17.33.

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