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SYNTHESIS OF (6S,7S)-TRANS-LAUREDIOL AND ITS [9,10-$^2H_2$]-ANALOGUE

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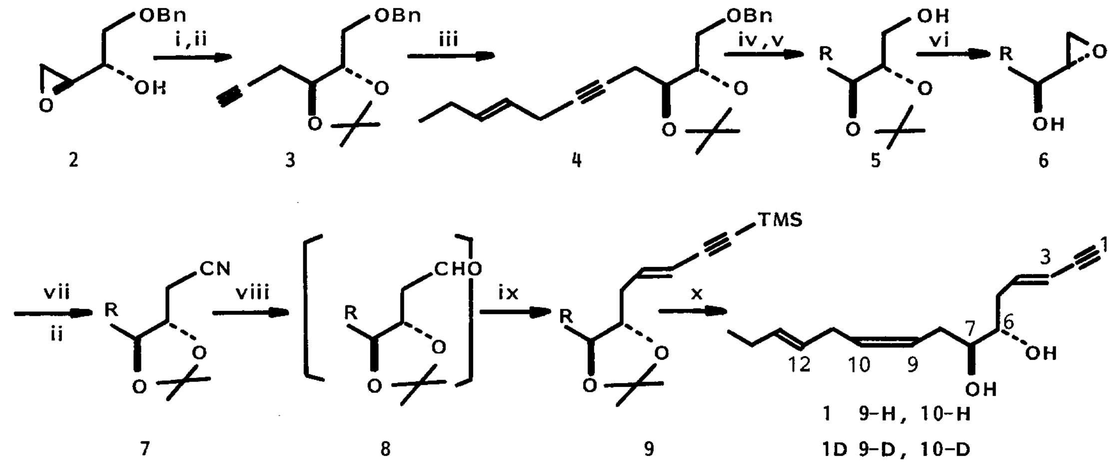
Abstract. A total synthesis of (6S,7S)-trans-laurediol and its [9,10-$^2H_2$]-analogue, starting from (2R,3R)-(+)-tartaric acid, is described.

The marine red algae of the genus Laurencia are the major source of a variety of halogenated cyclic ethers containing enyne or allene side chains.[1] Laurediols, a mixture of (6R,7R)- and (6S,7S)-enantiomers of trans(=3E,9Z,12E)- and cis(=3Z,9Z,12E)-pentadeca-3,9,12-trien-1-yne-6,7-diols,[2a] have been proposed to be one of the biosynthetic precursors[1b,2] of these metabolites. As one of our continuing studies on synthesis of marine natural products,[3] we describe herein the first synthesis of the title compounds (**1**) and (**1D**), which will be useful for studies of the biosynthesis and biomimetic synthesis.

The synthesis involves transformation of (2R,3R)-(+)-tartaric acid into a key intermediate (**2**), corresponding to the C(5)-C(8) unit with two asymmetiric centers of **1**, followed by sequential elongation at the both terminals of **2**. Thus the tartaric acid was converted into (2S,3S)-1-benzyloxy-3,4-epoxy-2-butanol[4] (**2**), $[\alpha]_D$ +14.5°, (51%), by a modification of the known procedure.[4]

Elongation of two-carbon unit [C(9)-C(10)] was achieved by treatment of **2** with the lithium acetylide-ethylenediamine complex,[5] giving acetylene glycol, which easily formed its acetonide (**3**). Further treatment of **3** with base (LDA but not BuLi) and then with (E)-2-pentenyl bromide effected formation of undecenyne (**4**). Hydrogenation of **4** over Lindlar catalyst afforded the corresponding undecadiene, which underwent the Birch reduction to give (5Z,8E)-undecadiene-1,2,3-triol 2,3-acetonide (**5**) (52% from **2**), $[\alpha]_D$ -9.3° ($CHCl_3$), MS, m/z 240 (M^+), constituing the C(5)-C(15) unit of **1**. Deuteration of **4** under the same conditions followed by the reduction produced the corresponding [5,6-$^2H_2$]-analogue (**5D**), $[\alpha]_D$ -11.7°, MS, m/z 242 (M^+) and 240 ($\sim$0%).

Transformation of **5** into **1** was commenced by formation of epoxy alcohol (**6**), which was smoothly performed by mesylation of **5** and subsequent treatment with acid and then with base. Compound **6** was treated with magnesium cyanide[6] to give glycol nitrile, which again formed its acetonide (**7**). Hydride reduction of **7** followed by careful treatment with acid (SiO_2, -20 °C, 3 min) gave rise to highly labile β-alkoxy aldehyde (**8**), which was immediately submitted to Wittig reaction. The resulting trimethylsilylpentadecatrienynediol acetonide (**9**) was deprotected smoothly to give **1**, $[\alpha]_D$ -27.0° (CCl_4), (22% from **5**), which was identical with an authentic sample, $[\alpha]_D$ +27.2° (CCl_4), derived from laurencin[7] in all respects except the sign of the optical rotation. The deuterated compound (**5D**) was transformed in the same manner as **5** to give **1D**,[8] $[\alpha]_D$ -23.6° (CCl_4); MS, m/z 236 (M^+) and 234 (∿0%).



Scheme. Bn = benzyl; R = (2Z,5E)-octadienyl. Reagents: i) LiC≡CH•EDA, DMSO, 20 °C, 1.5 h (78%): ii) $Me_2C(OMe)_2$, PPTS, 20 °C (98%): iii) LDA, THF-HMPA; C_5H_9Br (73%): iv) H_2, $Pd-BaSO_4$, EtOH (95%): v) $Li-NH_3$, THF-MeOH, -78 °C (99%): vi) MsCl, Et_3N, CH_2Cl_2; 2M HCl, MeOH; $Ba(OH)_2$, $CH_2Cl_2-H_2O$ (96%): vii) NaCN, $MgSO_4$, $MeOH-H_2O$, 35 °C, 19 h (88%): viii) DIBAH, hexane; SiO_2, -20 °C, 3 min: ix) $TMS-C{\equiv}CCH_2PPh_3Br$, BuLi, THF: x) Bu_4NF, THF; 2M HCl, MeOH (27% from **7**).

References and Notes

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8) **1D**: IR (neat), 3440, 2240, 2090, 1640, and 970 cm^{-1}; ^1H NMR ($CDCl_3$), δ 0.97 (3H, t, J = 7 Hz, 15-H), 1.82 (2H, br, OH), 2.01 (2H, br qui, J = 7 Hz, 14-H), 2.29 and 2.34 (each 1H, dd, J = 14, 5 and 14, 7 Hz, 8-H), 2.39 (2H, m, 5-H), 2.76 (2H, br d, J = 6 Hz, 11-H), 2.83 (1H, d, J = 2.5 Hz, 1-H), 3.51 and 3.57 (each 1H, dt, J = 7, 4 and 7, 5 Hz, 6- and 7-H), 5.39 and 5.50 (each 1H, dt, J = 15, 7 and 15, 6 Hz, 13- and 12-H), 5.63 (1H, br dd, J = 16 and 2.5 Hz, 3-H), and 6.29 (1H, dt, J = 16 and 7 Hz, 4-H).

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