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Stereoselective Synthesis of Tetrahydrofuran Moieties of Thyrsiferol and Venustatriol. Stereocontrolled Epoxidation of Bishomo- and Trishomo-allylic Alcohols

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<u>cis</u>- and <u>trans</u>-2-(1,2-Diacetoxyethyl)-5-(1-hydroxy-1-methylethyl)-2-methyltetrahydrofurans were stereoselectively derived from 1,2-diacetoxy-3,7-dimethyloct-6-en-3-ol and 1,3-0-dimethoxybenzylidene-3,7-dimethyloct-6-en-2-ol respectively.

Recently marine triterpene ethers, thyrsiferol  $(1)^{1}$  and venustatriol (2),<sup>2)</sup> have become of interest to synthetic chemists because of the strong cytotoxicity and the antiviral activity, respectively, and of their unique shape of the molecules.<sup>3)</sup> During studies on the syntheses of both the compounds we found that bishomoallylic alcohols could be stereoselectively epoxidized to give either  $\alpha$ - or  $\beta$ -epoxide.<sup>4)</sup> This finding led us to the successful completion of the syntheses<sup>3a)</sup> and the efficient synthesis of teurilene.<sup>5)</sup> Now we describe a novel stereocontrolled epoxidation of a trishomoallylic alcohol and stereoselective synthesis of tetrahydrofuran moieties of 1 and 2.



The readily available triol diacetate  $3^{6}$  was treated with excess t-butyl hydroperoxide (TBHP) and a catalytic amount of vanadylacetylacetonate (VAA) in dichloromethane at room temperature for 3 h<sup>7</sup>) to give <u>cis</u>-tetrahydrofuran derivative  $5^{8}$  and its diastereoisomer in 80% and 10% yields, respectively.<sup>9</sup>) The stereochemistry of 5 was revealed by the existence of NOE between 2-Me and 5-H. The reaction should proceed through stereoselective oxidation of bishomoallylic alcohol 3 to 4.

Another <u>trans</u>-tetrahydrofuran derivative 8 was derived as follows. A properly protected triol  $6^{10}$  was dissolved in 1,2-dichloroethane and stirred with excess TBHP, VAA and 3A molecular sieves for 8 h at ambient temperature<sup>7</sup> to afford epoxide 7 and its diastereoisomer in 64% and 10% yields, respectively.<sup>9</sup>

Stereoselective oxidation 11) of this trishomoallylic alcohol **6** was considered to proseed through a transition state as 9. The epoxide 7 was converted to an acetate, and treatment of the acetate with dichlorodicyanobenzoquinone (DDQ) in dichloromethane containing a little water followed by stirring with ptoluenesulfonic acid for 1 min gave  $8^{8}$  in 66% yield.

Both of the tetrahydrofuran derivatives 5 and 8 are considered to be important building blocks in the Corey route 3c) for the syntheses of 1 and 2.



DMP = 3,4-dimethoxyphenyl, DMBz = 3.4-dimethoxybenzoyl



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  8) <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ) of 5 : 1.10, 1.24, 1.26, 2.03, 2.09(each 3H, s), 1.75-2.05(4H, m), 3.81(1H, dd, J=6, 9), 3.95(1H, dd, J=8, 12), 4.67(1H, dd, J=2, 12), 5.09(1H, dd, J=2, 8).
  8 : 1.13, 1.22, 1.29, 2.08, 3.93, 3.94(each 3H, s), 1.7-2.1(4H, m), 3.82(1H, t, J=8.5), 4.37(1H, dd, J=8.5, 12), 4.59(1H, dd, J=2.5, 12), 5.33(1H, dd, J=2.5, 8.5), 6.89(1H, d, J=9), 7.52(1H, d, J=2), 7.64(1H, dd, J=2, 9). 7.64(1H, dd, J=2, 9).9) The ratio of the diastereoisomers was estimated by NMR peak height.
- 10) The trishomoallylic alcohol 6 was prepared as follows.



 $10^{7} \rightarrow 11$  3,4-dimethoxybenzylchloride,<sup>11)</sup> DMF, NaH, rt., 11 $\rightarrow$ 12 HCIO<sub>4</sub>, DMF,rt.,<sup>6)</sup> 12 $\rightarrow$ 13 Ac<sub>2</sub>O, py, CH<sub>2</sub>Cl<sub>2</sub>, rt., 13 $\rightarrow$ 6 i) DDQ,<sup>12)</sup> 3A molecular sieves, benzene, rt. ii) K<sub>2</sub>CO<sub>3</sub>, MeOH, rt. **DMPM** = 3,4-dimethoxybenzyl

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