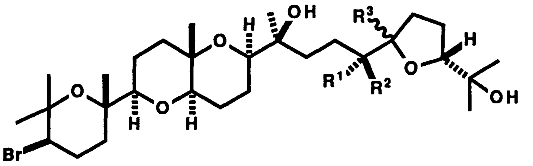
CHEMISTRY LETTERS, pp. 1847-1848, 1988.

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

Koji NOZAKI and Haruhisa SHIRAHAMA*
Department of Chemistry, Faculty of Science, Hokkaido University,
Sapporo 060

cis- and trans-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-O-dimethoxybenzylidene-3,7-dimethyloct-6-en-2-ol respectively.

Recently marine triterpene ethers, thyrsiferol (**1**)[1] and venustatriol (**2**),[2] 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.[3] During studies on the syntheses of both the compounds we found that bishomoallylic alcohols could be stereoselectively epoxidized to give either α- or β-epoxide.[4] This finding led us to the successful completion of the syntheses[3a] and the efficient synthesis of teurilene.[5] Now we describe a novel stereocontrolled epoxidation of a trishomoallylic alcohol and stereoselective synthesis of tetrahydrofuran moieties of **1** and **2**.



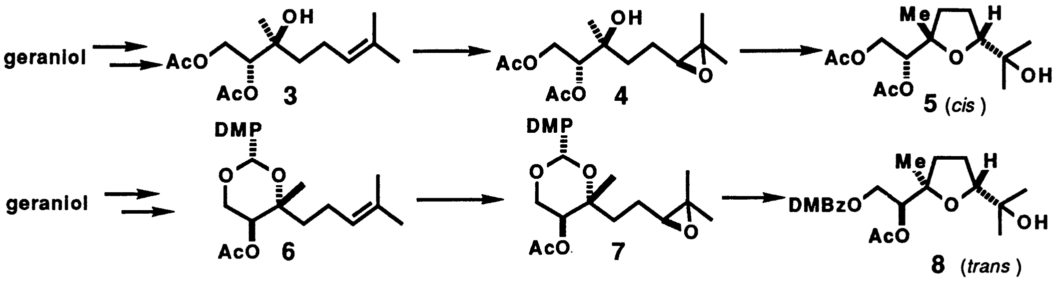
**1** $R^1 = H$, $R^2 = OH$, $R^3 = \alpha\text{-}CH_3$
**2** $R^1 = OH$, $R^2 = H$, $R^3 = \beta\text{-}CH_3$

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[7] to give cis-tetrahydrofuran derivative **5**[8] and its diastereoisomer in 80% and 10% yields, respectively.[9] 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**.

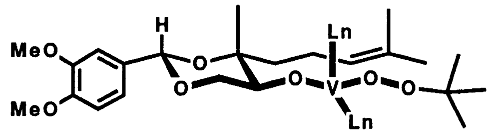
Another trans-tetrahydrofuran derivative **8** was derived as follows. A properly protected triol **6**[10] was dissolved in 1,2-dichloroethane and stirred with excess TBHP, VAA and 3A molecular sieves for 8 h at ambient temperature[7] to afford epoxide **7** and its diastereoisomer in 64% and 10% yields,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

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 p-toluenesulfonic 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**.



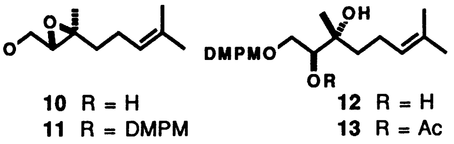
**DMP** = 3,4-dimethoxyphenyl, **DMBz** = 3.4-dimethoxybenzoyl



**9**

References

1) J.W. Blunt, M.P. Hartshorn, T.J. McLennan, M.H.G. Munro, W.T. Robinson, and S.C. Yorke, Tetrahedron Lett., <u>1978</u>, 69; T. Suzuki, M. Suzuki, A. Furusaki, T. Matsumoto, A. Kato, Y. Imanaka, and E. Kurosawa, ibid., <u>26</u>, 1329 (1985).
2) S. Sakemi, T. Higa, C.W. Jefford, and G. Bernardinelli, Tetrahedron Lett., <u>27</u>, 4287 (1986).
3) Synthetic studies on **1** and/or **2** :a) M. Hashimoto, T. Kan, K. Nozaki, M. Yanagiya, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., <u>29</u>, 1143 (1988); b) M. Hashimoto, T. Kan. M. Yanagiya, H. Shirahama, and T. Matsumoto, ibid., <u>28</u>, 5665 (1987);c) E.J. Corey and D.C. Ha, ibid., <u>29</u>, 3171 (1988);(d) C.A. Broka, L. Hu, W.J. Lee, and T. Shen, ibid., <u>28</u>, 4993 (1987).
4) An example previously reported : T. Fukuyama, B. Vranesic, D.P. Negri, and Y. Kishi, Tetrahedron Lett., <u>1978</u>, 2741.
5) M. Hashimoto, M. Yanagiya, and H. Shirahama, Chem. Lett., <u>1988</u>, 645.
6) Synthesized from geraniol according to Hanson's procedure : R.M. Hanson, Tetrahedron Lett., <u>25</u>, 3783 (1984).
7) Sharpless oxidation conditions : K.B. Sharpless and R.C. Michaelson, J. Am. Chem. Soc., <u>95</u>, 6136 (1973).
8) $^1$H NMR (CDCl$_3$, 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).
9) The ratio of the diastereoisomers was estimated by NMR peak height.
10) The trishomoallylic alcohol **6** was prepared as follows.



**10** R = H
**11** R = DMPM
**12** R = H
**13** R = Ac

**10**[7]→**11** 3,4-dimethoxybenzylchloride,[11] DMF, NaH, rt., **11**→**12** HClO$_4$, DMF,rt.,[6] **12**→**13** Ac$_2$O, py, CH$_2$Cl$_2$, rt., **13**→**6** i) DDQ,[12] 3A molecular sieves, benzene, rt. ii) K$_2$CO$_3$, MeOH, rt. **DMPM** = 3,4-dimethoxybenzyl

11) A stereoselective oxidation of a trishomoallylic alcohol appeared recently.[3c]
12) Y. Oikawa, T. Tanaka, K. Horita, T. Yoshioka, and O. Yonemitsu, Tetrahedron Lett., <u>25</u>, 5393 (1984).
13) Y. Oikawa, Y. Yoshioka, and O. Yonemitsu, Tetrahedron Lett., <u>23</u>, 889 (1982).

( Received July 29, 1988 )