Convenient Synthesis of (+)-Decarestrictine L

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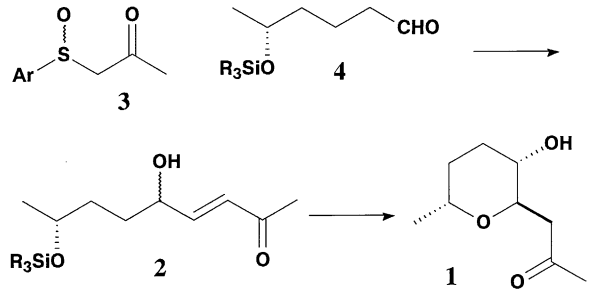
(+)-Decarestrictine L was prepared *via* intramolecular 1,4-addition of the oxy-anion, derived from trialkylsilyl ether with Bu_4NF, to the internal γ-hydroxy enone functionality, formed by the reaction of *p*-chlorobenzenesulfinylpropan-2-one with *R*-5-*t*-butyldimethylsilyloxyhexanal.

Recently, decarestrictine L (**1**) has been isolated by the German group[1] as a minor component of the decarestrictine family which is a novel class of inhibitors of cholesterol biosynthesis, and the first synthesis has been accomplished by Kibayashi *et al.*[2a] in 1993. Their synthetic method is very elegant and characteristic of their methodology using their original chiral pool derived from D-mannitol. However, they mentioned the intramolecular 1,4-addition of the oxy-anion to the 5-*alkoxy*-3-en-2-one functionality as disadvantageous (11% yield).[2a] Here, we show an interesting result in a similar synthetic strategy *via* intramolecular 1,4-addition of an oxy-anion to a 5-*hydroxy*-3-en-2-one functionality.

We have reported[3] a method to build a 5-hydroxy-3-alken-2-one functionality from aldehydes with the functionalization and three carbon elongation. Then, we envisioned to apply the method to the preparation of decarestrictine L precursor, 8-trialkylsilyloxy-5-hydroxy-3-nonen-2-one (**2**), from 5-trialkylsilyloxyhexanal (**4**) and *p*-chlorobenzenesulfinylpropan-2-one (**3**) as shown in Scheme 1.

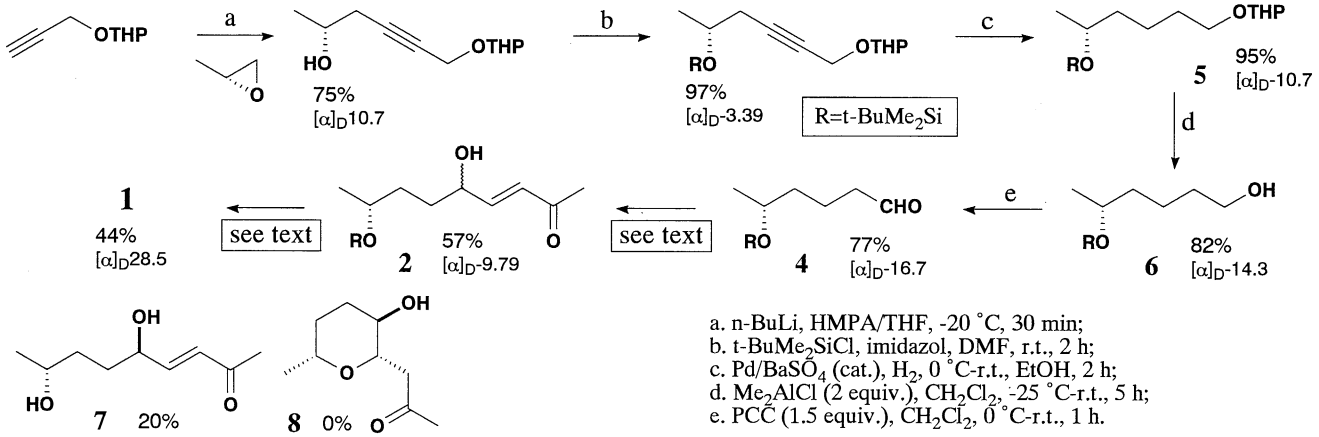
The optically active aldehyde, *R*-5-*tert*-butyldimethylsilyloxyhexanal (**4**), was prepared from *R*-(+)-propylene oxide (Merck, 99%ee) and propargyl tetrahydropyranyl ether[4] as shown in Scheme 2. The THP-protection of **5** was selectively removed by Shibasaki's method[5] to give *R*-5-*tert*-butyldimethylsilyloxyhexanol (**6**), and the alcohol **6** was converted to **4** by PCC-oxidation. *p*-Chlorobenzenesulfinylpropan-2-one (**3**) was



Scheme 1.

prepared by mCPBA-oxidation of *p*-chlorophenylthioacetone formed by treatment of *p*-chlorothiophenol with chloroacetone in the presence of Na_2CO_3 (2 equiv.) in acetone. The aldehyde **4** was treated with 4 equiv. of the sulfoxide **3** in the presence of 3 equiv. of diethylamine in acetonitrile at 50 °C for 2 h to give 8-*tert*-butyl-dimethylsilyloxy-5-hydroxy-3-nonen-2-one (**2**) in 57% yield as a diastereomeric mixture (5*R*:5*S*=1:1).[6] The trialkylsilyl group of **2** was removed by treatment with tetrabutylammonium fluoride (1.5 equiv.) in THF for 1.5 h at room temperature to afford decarestrictine L (**1**)[7] and the water soluble diol **7** in 44% and 20% yields respectively.

It is interesting to note that only the desired **1** was obtained by the treatment of diastereomeric mixture of **2** with tetrabutylammonium fluoride. Therefore, the yield of decarestrictine L (**1**) is looked upon as 88% based on 5*S*,8*R*-**2**. However, we can not rationalize why two diastereomers of **2** behaved so differently.



a. n-BuLi, HMPA/THF, -20 °C, 30 min;
b. t-$BuMe_2SiCl$, imidazol, DMF, r.t., 2 h;
c. Pd/$BaSO_4$ (cat.), H_2, 0 °C-r.t., EtOH, 2 h;
d. Me_2AlCl (2 equiv.), CH_2Cl_2, -25 °C-r.t., 5 h;
e. PCC (1.5 equiv.), CH_2Cl_2, 0 °C-r.t., 1 h.

Scheme 2.

References and Notes

1 S. Grabley, P. Hammann, K. Hütter, R. Kirsch, H. Kluge, R. Thiericke, M. Mayer, and A. Zeeck, *J. Antibiot.*, **45**, 1176 (1992).

2 a) N. Machinaga and C. Kibayashi, *Tetrahedron Lett.*, **34**, 5739 (1993); b) The latest paper on (±)-decarestrictine L synthesis: J. S. Clark and G. A. Whitlock, *Tetrahedron Lett.*, **35**, 6381 (1994).

3 J. Nokami, A. Nishimura, M. Sunami, and S. Wakabayashi, *Tetrahedron Lett.*, **28**, 649 (1987).

4 J. Nokami, T. Taniguchi, S. Gomyô, and T. Kakihara, *Chem. Lett.*, **1994**, 1103.

5 Y. Ogawa and M. Shibasaki, *Tetrahedron Lett.*, **25**, 663 (1984).

6 Some of paired signals (the ratio of 1:1) were observed in ^{1}H and ^{13}C-NMR spectra. For example, ^{1}H NMR ($CDCl_3$,400 MHz) δ 1.15 and 1.17 (each d, J=4.7 Hz, -C<u>H</u>3, 3H), 2.77 and 3.35 (each br, -O<u>H</u>, 1H), 3.89 and 3.96 (each m, -C<u>H</u>(OSiR3)-, 1H), 4.29 and 4.34 (each m, -C<u>H</u>(OH)-, 1H).

7 ^{1}H and ^{13}C NMR spectral data and the optical rotation ($[\alpha]_D$) were in full agreement with those reported in Ref. 1 and in Ref. 2a respectively. All the optical rotations shown in Scheme 2 were measured in $CHCl_3$ (c ca. 1.0).