Chinese Chemical Letters Vol. 15, No. 2, pp 141 – 142, 2004
http://www.imm.ac.cn/journal/ccl.html

First Total Synthesis of (±)-3-(5-Hydroxy-4, 7, 8-trimethyl-3E, 8-nonadiene)-Δ^2-butenolide

Tao ZHANG, Yi LI, Li Zeng PENG, Hua Wei LIU, Tian Sheng MEI, Yu Lin LI *

National Laboratory of Applied Organic Chemistry and Institute of Organic Chemistry
Lanzhou University, Lanzhou 730000

Abstract: An efficient total synthesis of (±)-3-(5-hydroxy-4,7,8–trimethyl–3E,8–nonadiene)–Δ^2–butenolide **1**, an unusual homosesquiterpene, starting from geraniol **2** through ten steps are described.

Keywords: Total synthesis, Δ^2–butenolide, homosesquiterpene.

Compound **1**, an unusual homosesquiterpene from the plant *Gochnatia glutinosa* grown in Argentina[1]. Its structure was determined by spectroscopic methods, however, the absolute configuration of C-8 and C-10 remained unsolved. As far as we know, neither biological activity nor a total synthesis of **1** has been reported. Here we wish to describe the first total synthesis of (±)-**1**.

Our synthetic route started from geraniol **2** as outlined in **Scheme 1**, and involved three key steps: (1) alkylation of α, β-unsaturated ester[2], (2) addition of the lithium derivative of iodide to aldehyde[3], (3) Corey's oxidative lactionization method[4].

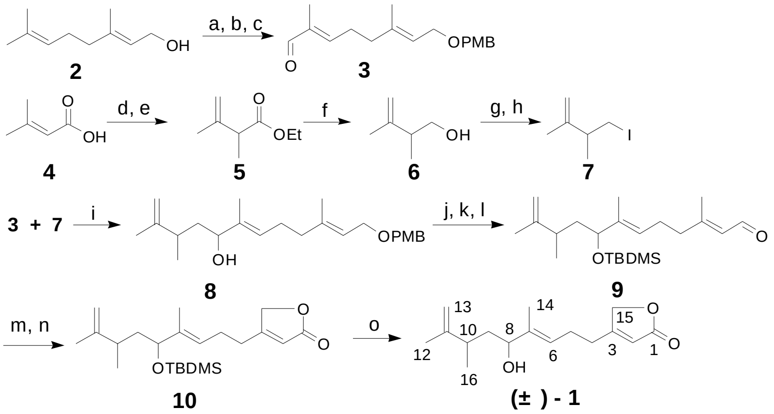
p-Methoxy benzyl protected geraniol was converted to the aldehyde **3** using SeO_2/*t*-BuOOH system followed by Swern oxidation. Esterification of senecioic acid **4** and subsequent alkylation of α, β-unsaturated ester gave the ester **5**. Reduction of ester **5** with $LiAlH_4$ in ether gave alcohol **6**, which was converted *via* its tosate into iodide **7**[5]. Addition the lithium derivative of iodide **7** to aldehyde **3** led to epimer **8**, which was protected with TBDMSCl and followed by selective remove *p*-methoxy benzyl protective group and oxidation by PCC to afford aldehyde **9**. Treatment of aldehyde **9** with 1.1 eqive. of trimethylsiylcyanide (TMSCN) in CH_2Cl_2 at 0°C in the presence of catalytic amount of potassium cyanide/18-crown-6 complex gave the corresponding O-trimethylsilylcyanohydin which was followed by oxidation *in situ* using PDC in DMF at room temperature (Corey's oxidative lactionization method) to afford the Δ^2-butenolide **10** in 51% yield. After deprotection of **10** by treatment with PPTS in EtOH[6], the title compound **1** was obtained. The spectral data of synthetic compound (±) **1** was coincided with those of natural compound **1**. We believe that our strategy for

---

* E-mail: liyl@lzu.edu.cn

synthesis of compound (±) **1** makes possible for the asymmetric synthesis of natural compound **1**.

Scheme 1



Reagent and conditions: a) *p*-$MeOC_6H_4CH_2O(C{=}NH)CCl_3$, PPTS, CH_2Cl_2, r.t., 85%; b) SeO_2, *t*-BuOOH, CH_2Cl_2, r.t., 51%; c) Swern oxidation, 81%; d) Oxalyl chloride, then EtOH, CH_2Cl_2, 0°C, 95%; e) LDA, MeI, THF, -78 °C , 90%; f) $LiAlH_4$, Ether, 0 °C, 87%; g) *p*-TsCl, Py, 0 °C, 92%; h) NaI, CH_3COCH_3, reflux, 80%; i) Li, THF, 0 °C, 78%; j) TBDMSCl, Imid., DMF, r.t., 91%; k) DDQ, CH_2Cl_2 /H_2O (20:1), 0 °C, 86%; l)PCC, NaOAc, CH_2Cl_2, r.t., 80%; m) Me_3SiCN, KCN, 18-Crown -6, CH_2Cl_2, 0 °C; n) PDC, DMF, r.t.; o)PPTS, EtOH, r.t., 70%.

Acknowledgments

This work was financial supported by the National Natural Science Foundation of China (Grant No. 20072012) and the Special Research Grant for Doctoral Sites in Chinese Universities (Grant No. 20010730001).

References and Notes

1. M. I. Ybarra, C. A. N. Catalan, J. G. Diaz, W. Herz, *Phytochemistry*, **1994**, *35*, 1585.
2. D. M. Walba, W. N. Thurmes, R. C. Haltiwanger, *J. Org. Chem.*, **1988**, *53*, 1046.
3. G. Pattenden, L. Roberts, A. J. Blake, *J. Chem. Soc. Perkin. Trans. 1*, **1998**, 863.
4. E. J. Corey, G. Schmidt, *Tetrahedron Lett.*, **1980**, *21*, 731.
5. J. D. White, G. N. Reddy, G. O. Spessard, *J. Am. Chem. Soc.*, **1988**, *110*, 1624.
6. C. Prakash, S. Saleh, I. A. Blair, *Tetrahedron Lett.*, **1989**, *30*, 19.
7. Spectral data: Compund **1**, IR (KBr): v 3433, 1780, 1745, 1638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 5.85 (s, 1 H, CH=), 5.36 (t, 1 H, $J = 6.5$ Hz, CH=), 4.74 (s, 2 H, CH_2=), 4.71 (s, 2 H, CH_2O), 4.03-3.96 (m, 1 H, C*H*OH), 2.50-2.45 (m, 2 H, CH_2), 2.38-2.33 (m, 2 H, CH_2), 1.67 (S, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.54-1.44 (m, 2 H, CH_2), 1.02 (d, 3 H, $J = 7.0$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 169.8 (C-1), 150.3 (C-11), 139.4 (C-7), 122.7 (C-6), 119.2 (C-3), 115.7 (C-2), 109.9 (C-13), 76.1 (C-8), 73.6 (C-15), 40.2 (C-9), 38.4 and 37.8 (C-12 and C-14), 28.4 and 25.2 (C-4 and C-5), 20.0 (C-10), 18.8 (C-16); EIMS, *m/z*: 249 (M-15, 1.1).

Received 20 January, 2003