Chinese Chemical Letters Vol. 13, No. 2, pp 119– 120, 2002
http://www.imm.ac.cn/journal/ccl.html

Synthesis of Cholest-5-en-24-oxo-3b, 19-Diacetate

Wei Gang LU, Ming Yan WANG, Jing Yu SU, Long Mei ZENG*

School of Chemistry and Chemical Engineering, Zhongshan University, Guangzhou 510275

Abstract: Cholest-5-en-24-oxo-3ß, 19-diacetate was synthesized starting from stigmasterol **3** *via* seven step reactions in 21.0% overall yield. It can be served as a key intermediate for the synthesis of many biologically active 19-hydroxylated sterols.

Keywords: Hydroxylated sterol, synthesis, irradiation, ozonolization.

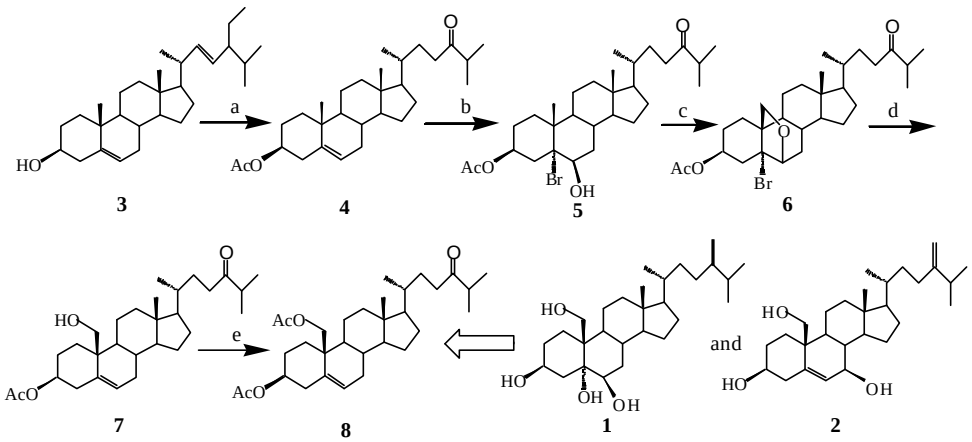
Two biologically active 19-hydroxylated sterols, 24-methylenecholesta-3β, 5α, 6β, 19-tetrol **1**, 24-methylenecholesta-5-ene-3β, 7β, 19-triol **2**, were isolated from the soft corals, *Nephthea albida and Nepthea tiexieral verseveldt* by L. M. Zeng[1,2]. **1** showed strong anti-inflamatory activity comparable with dexamethone and **2** showed potent anti-leukemic activity (IC_{50} 0.01 μg/mL). We have designed a synthetic route for the synthesis of **1** and **2** as shown in **Scheme 1**. In this route, cholest-5-en-24-oxo-3ß, 19-diacetate **8** is a key intermediate. Herein, we report the synthesis of **8**.

Compound **4** was synthesized from **3** referring to the literature[2]. **4** was converted to compound **5** with NBA containing catalytic amount of $HClO_4$ in dark in 60% yield. In this reaction, temperature played an important role, since it is an exothermic reaction. In our studies we found that the favorable temperature was between 10° C~20° C, and raising temperature would lead to decrease the yield of **5**. Compound **5** was treated with LTA and iodine by irradiation to give the epoxide **6**[3,4]. The reaction mixture was hydrolyzed directly with Zn/AcOH in 95% ethanol[5], then the resulting material was purified by flash column chromatography over silica gel to afford **7** in 46% yield.

The ^{1}HNMR spectrum of **7** was very similar to that of **4** except that δ_H 1.061 (19-methyl) was replaced by δ_H 3.616, d, J = 11.5Hz and δ_H 3.830, d, J = 11.5Hz (an oxygen bearing methylene group). The ^{1}HNMR spectrum of **8** showed the signals of 19-methylene protons (19-CHa and 19-CHb) moved to lower field at δ 3.976 and 4.460 owing to the deshielding effect of the acetyl group[6].

Scheme 1

* E-mail: ceszlm@zsu.edu.cn



a) Ref. 5; b) NBA/dioxane-H_2O, H^+; c) $Pb(AcO)_4/I_2$, hν; d) Zn/AcOH; e) Ac_2O/Py.

Acknowledgment

We are grateful to the National Natural Science Foundation of China (No. 29932030) and Natural Science Foundation (No. 970154) of Guangdong Province for financial support for this work.

References and Notes

1. G. Y. S. Wang, F. Y. Li, L. M. Zeng, *Chem. J. Chin. Univ.*, **1992**, *13*, 623.
2. J. G. Cui, J. Y. Su, L. M. Zeng, *Steroids*, **2001**, *66*, 33.
3. S. Ohnishi, T. Kosaki, Y. Osawa, *Steroids*, **1990**, *55*, 5.
4. W. J. Rodewald, J. R. Jaszczynski, R. R. Sicinski, *Polish J. Chem.*, **1978**, *52*, 501.
5. M. Numazawa, A. Mutsumi, N. Asano, Y. Ito, *Steroids*, **1993**, *58*, 40.
6. Compound 8: mp 106 ~ 108°C; IR (KBr) ν: 2939, 1745, 1739, 1709, 1250, 1038, 980 cm^{-1}; ^{1}HNMR ($CDCl_3$, 500MHz, ppm) δ: 0.687 (s, 3H), 0.911 (d, 3H, *J* = 6.5Hz), 1.091 (d, 6H, *J* = 7.0Hz), 2.025 (s, 3H), 2.046 (s, 3H), 2.606 (m, 1H, *J* = 7.0Hz), 3.976 (d, 1H, *J*=11.5Hz), 4.460 (d, 1H, *J* = 11.5Hz), 4.621 (m, 1H), 5.626 (brs, 1H); FABMS *m/z*: 519 (M^++H).

Received 11 June, 2001