Chinese Chemical Letters Vol. 12, No. 5, pp. 407 – 408, 2001

First Total Synthesis of 5α-Hydroxy-isopterocarpolone

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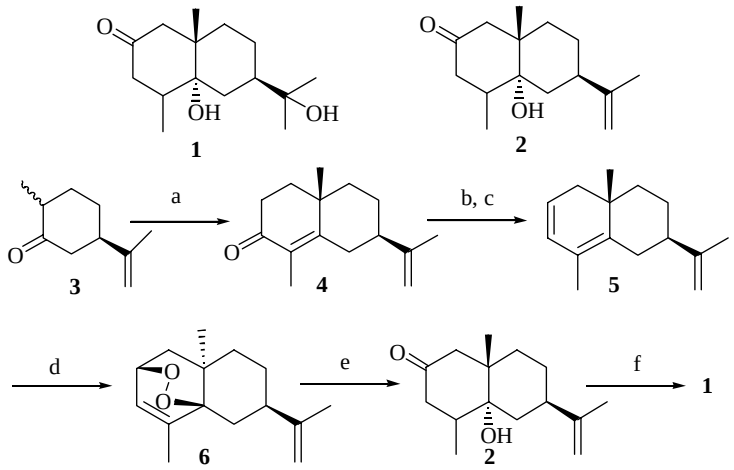
Abstract: The first total synthesis of 5α-hydroxy-isopterocarpolone has been described.

Keywords: Total synthesis, 5α-hydroxy-isopterocarpolone.

Sesquiterpenic compounds of the Eudesmane family have attracted considerable attention due to their intriguing biological properties[1,2], particularly significant antifeedant activity, cell growth inhibitory and plant growth regulating activities.

In 1996, J. Hu and co-workers[3] had isolated eudesmane sesquiterpene 5α-hydroxy-isopterocarpolone **1** from the aerial parts of chinese folk medicine *Artemisia eriopoda* and elucidated its structure by spectropic methods. Herein, we reported the first total synthesis of **1** starting from (+)-dihydrocarvone **3** (**Scheme 1**). In this synthetic route, the key intermediate α-rotunol **2**, which was isolated from the crude drug "Ko-bushi" by Hikino *et al.*[4], has also been synthesized.

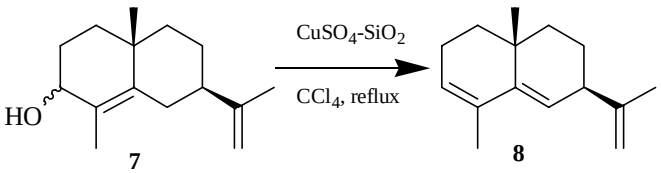
Scheme 1



a. Ref 5, 50%; b. $TsNHNH_2$, benzene, r. t., 5 h, 90%; c. BuLi, THF, -78°C – 0°C, 12 h, 92%; d. $^1O_3$, CH_2Cl_2 2 h, 71%; e. K_2CO_3, MeOH, r. t., 12 h, 60%; f. 10% H_2SO_4, THF, reflux, 5 h, 48%.

As shown in **Scheme 1**, (+)-cyperone **4** (Purity > 95%, determined by GC) was stereoselectively prepared from (+)-dihydrocarvone in two steps[5]. Hydrazone formation of **4** with tosylhydrazine followed by treatment with excess *n*-butyl lithium (6eq) in anhydrous THF under the Shapiro conditions[6] gave triene **5** in one pot. It is worth to note that dehydration[7] of the alcohol **7** with $CuSO_4$-SiO_2 only afford the undesired heteroannular triene **8** exclusively (**Scheme 2**). Oxidation of the triene **5** with singlet oxygen afforded the desired endo-peroxide **6** as single product in 71% yield[8], in which the peroxide bridge should have the α-configuration for the steric hindrance of angular methyl group restrict the approach of singlet oxygen from the site undergoing reaction. Reduction cleavage of peroxide with K_2CO_3 gave the natural α-rotunol **2** in 60% yield, which was then hydrolyzed with 10% sulfuric acid to form 5α-hydroxy-isopterocarpolone **1** in 48% yield directly. The spectral data[9] of synthetic product **1** is fully consisted with literature[3] data of natural product.

Scheme 2



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Acknowledgments

We are grateful for the financial supports from NNSFC (Grant No. 29732060).

References and notes

1. T. A. Van Beek, A. De Grot, *Recl. Trav. Chim. Pays-Bas*, **1986**, *105*, 513.
2. M. Ando, K. Isogai, H. Azami, N. Hirata, Y. Yanagi, *J. Nat. Prod.*, **1991**, *54*, 1017.
3. J. F. Hu, S. P. Bai, Z. J. Jia, *Phytochemistry*, **1996,** *43*, 815.
4. H. Hikino, K. Aota, D. Kuwano, T. Takemoto, *Tetrahedron*, **1971**, *27*, 4831.
5. Z. M. Xiong, J. Yang, Y. L. Li, *Tetrahedron Asymmetry*, **1996**, *7*, 2607.
6. For reviews of alkene formation from tosylhydrazone, see: R. H. Shapiro, *Org. React.* (N. Y.), **1976**, *23*, 405.
7. T. Nishiguchi, N. Machida, E. Yamamoto, *Tetrahedron lett.*, **1987**, *28*, 4565.
8. For cycloaddition using singlet oxygen with diene, see:
   a) W. Adam, M. Prein, *Acc. Chem. Res.*, **1996**, *29*, 275.
   b) H. H. Wasserman, J. L. Ives, *Tetrahedron*, **1981**, *37*, 1825.
9. Spectra data of **1**: $[\alpha]_D^{15}$ +34 (c 2.5, $CHCl_3$), ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm) 1.01 (s, 3H, Me-10), 1.11 (s, 3H, Me-11), 1.25 (s, 3H, Me-11), 2.03 (s, 3H, Me-4), 2.10 (d, 1H, *J* = 16.4 Hz, H-1), 2.17 (d, 1H, *J* = 16.4 Hz, H-1), 3.50 (brs, 2H, OH), 5.83 (s, 1H, H-3); EIMS: *m/z* (%): 252 (M^+, 13), 237 (25), 234 (20), 217 (10), 205(30), 194 (50), 147 (21), 139 (100), 43 (80); IR (Film): 3447, 3420, 1720, 1670, 1131, 1049, 860 cm^{-1}.

Received 14 August, 2000