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A Facile Synthesis of the C-11 isomer of 5-*epi*-Kudtriol

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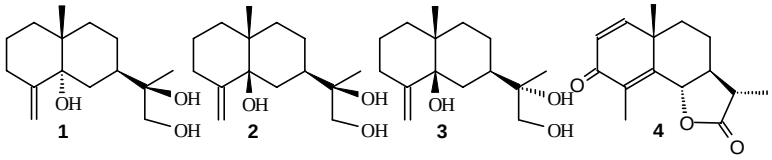
Abstract: The C-11 isomer of natural trihydroxyl sesquiterpene 5-*epi*-kudtriol has been synthesized starting from (+)-dihydrocarvone *via* asymmetric dihydroxylation as a key step.

Keywords: Asymmetric synthesis, asymmetric dihydroxylation, 5-epi-kudtriol.

Eudesmane derivatives contain a number of naturally occurring compounds. Among them many compounds possess intriguing biological properties[1,2].

Kudtriol **1** and 5-epi-kudtriol **2** was first isolated from the aerial parts of *Jasania glatinosa* by Tereasa *et al* [3], and their structures were determined as (-)-eudesm-4(14)-en-5α,11,12-triol and (+)-eudesm-4(14)-en-5β,11,12-triol respectively by spectroscopic methods .

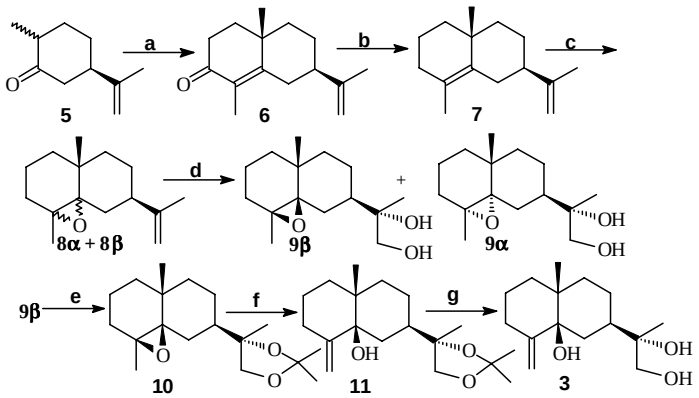


Although previous paper reported the synthesis of **2** from α-santonin **4** in eleven steps[4], an efficient and flexible synthetic route leading to this type of derivatives is still required to clarify the absolute configuration. Herein, we developed a new, general approach to synthesize the C-11 isomer **3** of **1** from (+)-dihydrocarvone **5** in eight steps by the use of the Sharpless asymmetric dihydroxylation as key reaction, and compared the stereochemistry with **2**.

As shown in **Scheme 1,** (+)-α-cyperone **6** was easily prepared from (+)-dihydrocarvone in two steps[5]. Deoxygenation[6] of **6** with $AlCl_2H$ afforded diene **7,** which was converted to the inseparable epoxides **8α** and **8β** by regioselective epoxidation[7] with 0.9 eq mCPBA. The mixture was treated with commercially available AD-mix-α[8] in *t*-BuOH-H_2O to afford diols **9α** in 64% yield and **9β** in 34% yield, which could be carefully separated by chromatography on silica gel. The diastereoselectivity was determined by analysis of the ^1H NMR (400 MHz) data. Next, the rearrangement of oxirane ring in these epoxides was invalid regardless of using LDA, $Al(O\text{-}iPr)_3$[9] or $Ti(O\text{-}iPr)_4$[10]**.** We assumed that the dihydroxyl group was responsible for these results.

After protection with acetone[11], **9β** could convert to allylic alcohol **11** smoothly with 5 eq LDA in ether. Removal of the protecting group in **10** in 1Mol·L^{-1} HCl , the title compound **3** was achieved in 90% yield. The structure of all compounds were confirmed with ^{1}HNMR, IR, MS spectral data[12].

Scheme 1



Reagents and conditions: a. ref 5, 50%; b. $AlCl_2H$, ether, rt, 3h, 85%; c. mCPBA (0.9 eq), CH_2Cl_2, 0°C, 2h, 84% of **8α** and **8β**; d. AD-mix-α, 0°C, 24h, 95% ; e. $(MeO)_2CMe_2$, p-TsOH, acetone, rt, 3h, 80%; f. LDA, ether, rt, 84%; g. 1 Mol·L^{-1} HCl, THF, reflux, 3h, 90%.

Acknowledgments

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12. Spectral data of **3**: Compound **3**: $[\alpha]_D^{11}$ –42.3 (c 0.36, $CHCl_3$); ^{1}H NMR (400 MHz , $CDCl_3$) : δ (ppm) 1.02 (s, 3H, 10-Me), 1.13 (s, 3H, 11-Me), 3.43 and 3.63 (dd, 2H, AB, J= 7.9Hz, 12-H), 4.94(brs, 1H, 14 - H), 5.07(brs, 1H, 14 –H); EIMS: *m/z* (%): 254 (M^+, 3), 239 (3), 236 (5), 222 (2), 205 (15), 187 (12), 161 (56), 147 (27), 43 (100); IR: 3400, 2932, 2869, 1641, 1449, 1378, 1281, 1028cm^{-1}.

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