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The First Total Synthesis of 3-Oxo-11, 12, 13-trihydroxyeudesm-4-ene

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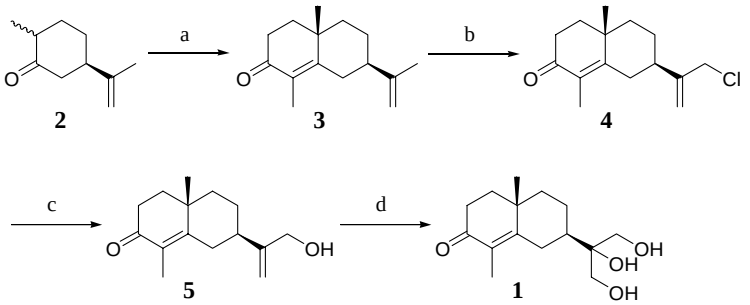
Abstract: The first total synthesis of 3-oxo-11, 12, 13-trihydroxyeudesm-4-ene, a highly oxygenated natural eudesmane, was described.

Keywords: Total synthesis, 3-oxo-11, 12, 13-trihydroxyeudesm-4-ene, eudesmane, sesquiterpene.

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

3-Oxo-11, 12, 13-trihydroxyeudesm-4-ene **1**, a highly oxygenated eudesmane, was firstly isolated from *Achillea holosericea* by Ahmed *et al.* in 2002[3]. Members of the genus *Achillea* are widely used in folk medicine for the preparation of herbal teas with antiphlogostic and spasmolytic activity[4]; extracts exhibit pharmacological activities including antibacterial[5], anti-inflammatory[6] and antiallergic[7] properties. To the best of our knowledge, the total synthesis of **1** has not been reported yet. Herein, we reported a facile total synthesis of **1** starting from (+)-dihydrocarvone **2**.



Reagents and conditions: a. Ref 8, 62%; b. Vilsmeier reagent, 30%H_2O_2, –20 °C, 1 h, 74%; c. 1) NaI, acetone, r. t., 4 h; 2) Cu_2O, DMSO, H_2O, 50-60 °C, 6 h, 68%; d. K_2OsO_4, $K_3Fe(CN)_6$, *t*-BuOH, H_2O, 0 °C, 24 h, 78%.

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(+)-Cyperone **3** (purity > 95%, determined by GC) was stereoselectively prepared from (+)-dihydrocarvone **2** in two steps[8]. Selective allylic chlorination of **3** with Vilsmeier reagent[9] afforded **4** in 74% yield. Iodination of **4** with NaI followed by treatment with Cu_2O in DMSO-H_2O (1:2) gave alcohol **5** in 68% overall yield. Dihydroxylation of **5** with $K_3Fe(CN)_6$ and a catalytic amount of K_2OsO_4 afforded 3-oxo-11, 12, 13-trihydroxyeudesm-4-ene **1** in 78% yield. The spectral data of synthetic product **1**[10] is fully consisted with literatural[3] data of natural product.

Acknowledgments

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10. Data of compound **1**: colorless oil. $[\alpha]_D^{25}$ + 21.7 (*c* 1.25, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, δ_{ppm}): 3.78-3.64 (m, 4H, H-12, H-13), 3.56 (br s, 3H, –OH), 2.79 (d, 1H, *J*=14.0 Hz, H_{eq}-6), 2.49 (m, 1H, H_{ax}-2), 2.36 (dt, 1H, *J*=17.0, 4.0 Hz, H_{eq}-2), 1.97 (t, 1H, *J*=14.0 Hz, H_{ax}-6), 1.73 (s, 3H, CH_3-15), 1.74-1.70 (m, 3H, H-1, H_{eq}-9), 1.65-1.53 (m, 3H, H-7, H-8), 1.33 (m, 1H, H_{ax}-9), 1.17 (s, 3H, CH_3-14). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 200.0 (C-3), 163.2 (C-5), 129.1 (C-4), 75.0 (C-11), 65.8 (C-13), 65.3 (C-12), 43.2 (C-7), 42.1 (C-9), 37.4 (C-1), 36.2 (C-10), 33.9 (C-2), 28.2 (C-6), 22.6 (C-14), 22.1 (C-8), 11.2 (C-15). IR (KBr/cm^{-1}): 3409, 1647, 1605, 1450, 1374, 1244, 755. MS (EI, *m/z*): 268 (M^+, 0.3), 250 (10), 237 (30), 219 (11), 202 (24), 177 (100), 161 (33), 149 (61), 91 (67), 55 (54), 43 (47).

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