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First Total Synthesis of (±)-Abieta-8, 11, 13-trien-7β-ol

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Abstract: The first total synthesis of (±)-abieta-8, 11, 13-trien-7β-ol (**7**) was accomplished *via* a strategy of AC→ABC, in which the reduction of the ketone **6** with $LiAlH_4$ gave exclusively the title compound.

Keywords: Total synthesis, (±)-abieta-8, 11, 13-trien-7β-ol, diterpene.

(±)-Abieta-8, 11, 13-trien-7β-ol (**7**)[1]was a diterpene isolated from the leaves of *J. chinensis kaizuka*[2]. To our knowledge, no total synthetic work has been reported on it. Many of this type diterpenes exhibit significant bioactivities, such as antibacterial activity[3], antitumor[4~5], and anti HIV[6]. In order to study the further relationship between the structure and bioactivities, we synthesized the title compound. To contrast with our prior work[7~10], the synthesis in this work had some differences. First, we changed the method of the introduction of isopropyl group. Second, the catalytic hydrogenation of 3-styryl and 2-propylen in compound **3** was accomplished in one step. This method can be probably applied in the synthesis of analogous compounds.

As shown in **Scheme 1**, we used α-cyclocitral **1** as A ring starting material and the compound **2** as the C ring synthon.

Condensation of compound **1** with **2** in dry THF in the presence of *n*-BuLi in a stream of argon afforded the desired compound **3** in 73% yield. Partial hydrogenation of **3** in anhydrous ethanol at room temperature over 10% Pd/C gave compound **4** in 98% yield. The reagent $BF_3{\cdot}Et_2O$ was used in the intramolecular cyclization step (B ring) at room temperature to afford the product **5** that was in *trans* form in 89% yield. The *trans*-configuration of A/B ring junction in **5** was characterized specifically by the upfield signal of the C_4-α-methyl group at 1.0 ppm. According to the literature[11], when the A/B ring is in *trans* junction, the C_4-α-methyl group is slightly deshielded by the aromatic ring C, the δ value of C_4-α-methyl group will appear at about 1.0 ppm. When A/B ring is a *cis* junction, the C_4-α-methyl group remains within the sphere of magnetic influence of aromatic ring C, the chemical shift of C_4-α-methyl group appears at about 0.40 ppm. Oxidation of compound **5** with CrO_3/HOAc afforded ketone **6** in good yield. Reduction of **6** with $LiAlH_4$ (THF, 0°C, 2h) gave exclusively the target molecule **7** as a

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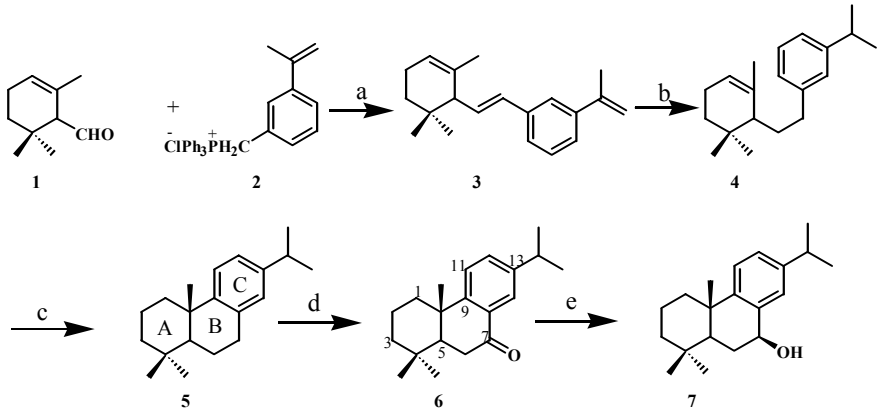
Scheme 1



1 2 3 4 5 6 7

Reagents and conditions: (a) *n*-BuLi, THF, r. t., 1h, 73%; (b) 10% Pd/C, EtOH, r. t., 30 min, 98%; (c) $BF_3{\cdot}Et_2O$, CH_2Cl_2, r. t., 24 h, 89 %; (d) CrO_3, HOAc, r. t., 30min, 93%; (e) $LiAlH_4$, THF, 0°C, 2 h, 96%.

consequence of hydride attack from the less hindered α-face. The axial 7-H of **7** exhibited a double doublet signal (*J*=10, 7 Hz) while the equatorial 7-H showed a triplet (*J*=3 Hz) according to the literature[2]. In conclusion, in the present work, a simple convergent synthetic route has been developed for the discovered diterpenoid.

Acknowledgment

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References and Notes

1. (±)-Abieta-8, 11, 13-trien-7β-ol**:** colorless oil. IR(KBr, cm^{-1}): 3398(OH). ^1H NMR (200MHz, $CDCl_3$, δ_{ppm}): 0.93 (s, H-19), 0.95 (s, H-18), 1.22 (d, *J*=6.9 Hz, H-16, H-17), 1.25 (s, H-20), 2.86 (sept, *J*=6.9 Hz, H-15), 4.79 (dd, *J*=10, 7.2 Hz, H-7), 7.07 (dd, *J*=8.0, 1.8 Hz, H-12), 7.15 (d, *J*=8.0 Hz, H-11), 7.38 (br s, H-14). ^{13}C NMR (50MHz, $CDCl_3$, δ_{ppm}): 19.1 (C-2), 21.5 (C-19), 23.9 (C-16), 24.1 (C-17), 25.3 (C-20), 30.3 (C-6), 33.1 (C-4), 33.1 (C-18), 33.6 (C-15), 38.2 (C-10), 38.7 (C-1), 41.3 (C-3), 49.2 (C-5), 71.3 (C-7), 124.3 (C-12), 125.0 (d, C-11), 125.7 (C-14), 137.7 (C-8), 146.2 (C-13), 147.3 (C-9). MS (EI, *m/z*): 286 (M^+), 271, 227, 211, 183, 162, 141, 129, 115, 91, 69, 55, 41. Found: C, 83.89; H, 10.20. $C_{20}H_{30}O$ requires C, 83.92; H, 10.49. The above data were consistent with the literature[2].
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