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Stereoselective Synthesis of (+)-Δ^5-Dehydrosugiyl Methyl Ether

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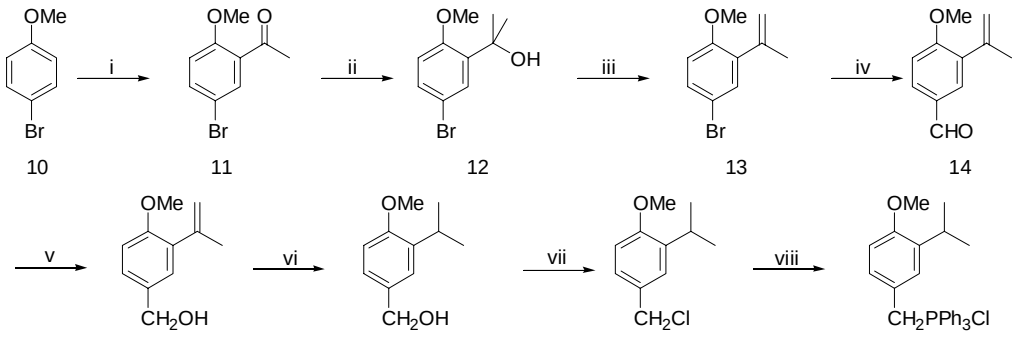
Abstract: A stereoselective synthetic route to (+)-Δ^5-dehydrosugiyl methyl ether was developed from (S)-(-)-α-cyclocitral, DDQ as a better oxidant for enone was used.

Keywords: synthesis, diterpenoids,geranic, (+)-Δ^5-dehydrosugiyl methyl ether.

Most diterpenoids exhibit significant bioactivities[1-4]. Δ^5-Dehydrosugiyl methyl ether was separated from *Taxodium distichum* Rich which showed significant bioactivity against KB[5], and assigned the structure **1**. This compound was obtained by Takashi MATSUMOTO from (+)-dehydroabietic acid with a known procedure[6], but the synthetic route is too long. In order to study the relationship between the structure and bioactivities. The certain diterpene synthesis has been extended in our laboratory[7,8], it is desirable to improve our synthetic route, proposed before to obtain the (+)-Δ^5-dehydrosugiyl methyl ether **1**[9]. Our spectrum data agree with Takashi's[6].

As shown in **scheme 1** and **2**, our synthetic strategy is AC→ABC. (S)-(-)-α-cyclocitral **9** which was prepared from geranic acid *via* five steps according to Charles'method[10] was used as A ring starting material. In this new route, we used readily available *p*-bromoanisole **10** as C ring starting material. Compared with our early work[8], we introduced iso-propyl before intramolecular cyclization, it is more rational in synthetic strategy.

Scheme 1



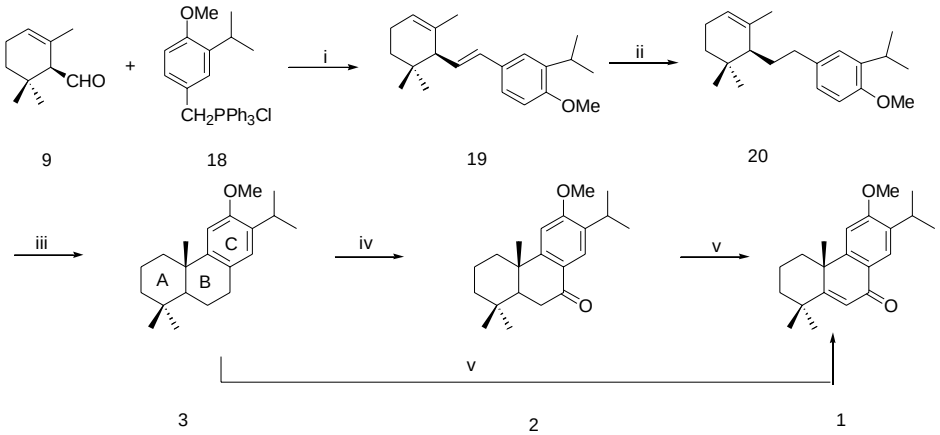
10 11 12 13 14 15 16 17 18

Reagents and conditions: (i) $AlCl_3$, CH_3COCl, CH_2Cl_2; (ii) CH_3MgI, Et_2O; (iii) TosOH, Ben.; (iv)

BuLi, DMF, -78°C; (v) $NaBH_4$, CH_3OH; (vi) Raney Ni, H_2, EtOH; (vii) $SOCl_2$, Benzene, pydine; (viii) PPh_3, Benzene.

As shown in **scheme 2**, in the intramolecular cyclization step, we found that $BF_3 \cdot Et_2O$ in CH_2Cl_2 is the best condition, after the mixture stood overnight at room temperature, sole *trans* isomer was obtained. Compound **1** can be obtained by oxidation with DDQ in methanol at room temperature from **2** and **3** respectively.

Scheme 2



Reagents and conditions: (i) BuLi, hexane; (ii) Pd/c, EtOH; (iii) BF_3 Et_2O; (iv) CrO_3/HOAc; (v) DDQ, CH_2Cl_2

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9. m.p. 156-157°C. $([\alpha]_D^{25}$ +18 (c 0.05, $CHCl_3$), ^1H NMR δ 1.22 and 1.25 (each 3H, d, J=6.8Hz), 1.27 (s,3H), 1.36 (s, 3H), 1.54 (s, 3H), 3.25 (sept, 1H), 3.90 (s, 3H), 6.46 (s, 1H), 6.86 (s, 1H), 7.99 (s, 1H). ^{13}C NMR 16.65, 22.40, 22.50, 26.65, 29.16, 32.50, 32.63, 37.44, 37.80, 40.30, 41.33, 55.39, 105.55, 123.56, 124.08, 124.61, 135.99, 153.80, 160.78, 172.62, 185.12. MS (EI): 312, 297, 282, 269, 243, 201, 165, 115, 77. IR 1640, 1605, 1560, 1500.
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