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A chiron approach to (1*R*,2*R*,5*S*,7*R*)-2-hydroxy-*exo*-brevicomin, a component of the volatiles produced by the male mountain pine beetle, *Dendroctonus ponderosae*☆

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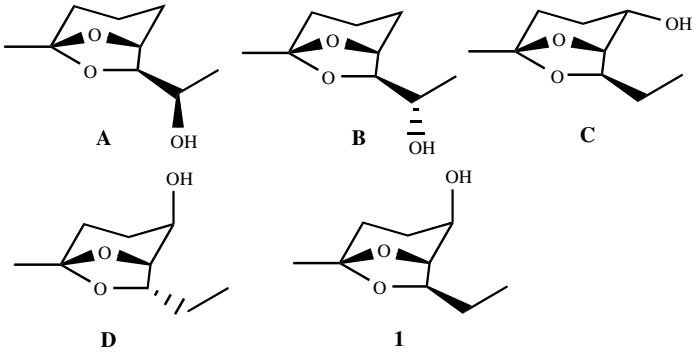
Abstract—A chiron approach to a synthesis of (1*R*,2*R*,5*S*,7*R*)-2-hydroxy-*exo*-brevicomin **1**, a component of the volatiles obtained from male mountain pine beetles, *Dendroctonus ponderosae* has been achieved. Our synthesis started with commercially available D-mannitol and involved Wittig olefination, acid catalysed one-pot hydrogenation and internal acetalization as key steps.

In 1996 Francke et al.[1] identified several new oxygenated derivatives of 6,8-dioxabicyclo[3.2.1]octane in the head space volatiles obtained from the male mountain pine beetle, *Dendroctonus ponderosae*, which are destructive pests causing damage to coniferous forests in the northern hemisphere. These compounds are mainly stereoisomers of 7-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-ol and 1-(5-methyl-6,8-dioxabicyclo- [3.2.1]octyl)-ethanol such as **A**–**D** and **1**.

Recently we reported an asymmetric synthesis of **A** and **B** and a formal synthesis of (+)-*exo*-brevicomin starting from α-picoline.[2] In continuation of our interest in synthesis of other members of the family, we report a chiron approach to the synthesis of **1**. This target has been synthesized twice since its discovery. The first synthesis by Francke et al.[1] was based on a kinetic resolution using a Sharpless asymmetric epoxidation. The second by Mori and co-workers[3] used a Sharpless asymmetric dihydroxylation as the key step. Our approach describes a synthesis of **1** starting from D-mannitol as depicted in Scheme 1.

1,2;3,4-Di-*O*-isopropylidene-D-mannitol **2** was prepared according to the literature procedure.[4] The vicinal diol **2** was converted into olefin **3** in 71% yield using triphenylphosphine, imidazole and iodine.[5] Selective hydrolysis of the terminal acetonide in **3** with 50% aq AcOH at 0 °C for 4 h gave **4** in 73% yield. Selective silylation of



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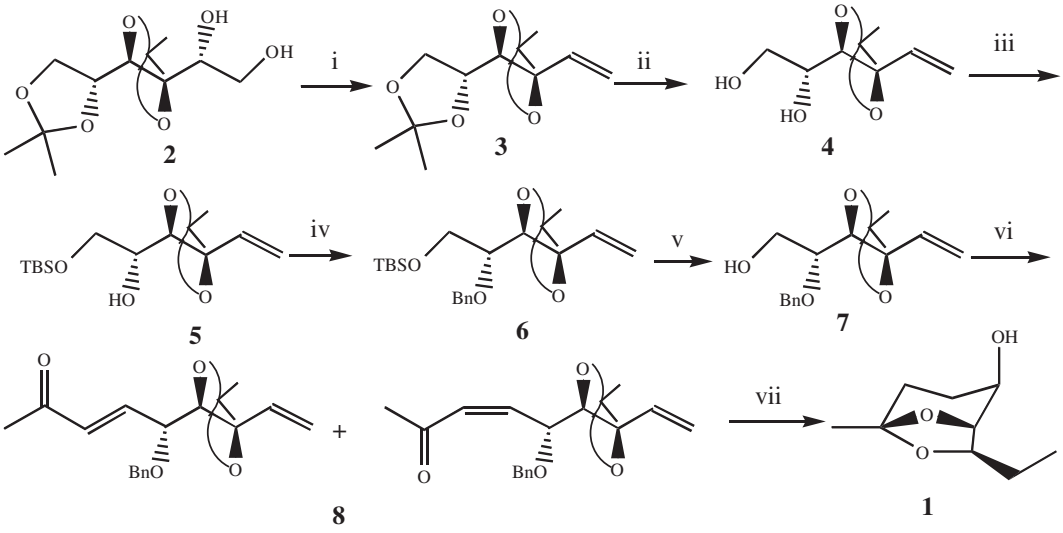

Scheme 1. Reagents and conditions: (i) PPh_3, imidazole, I_2, toluene, reflux, 4 h, 71%; (ii) 50% aq AcOH, 0 °C, 4 h, 73%; (iii) TBSCI, imidazole, DCM, rt, 3 h, 90%; (iv) NaH, benzyl bromide, THF, 77%; (v) 1 M TABAF in THF, THF, 80%; (vi) a. TEMPO, NaOCl, toluene, ethyl acetate, water; b. $Ph_3PCHCOCH_3$, DCM, 76% (for two steps); (vii) H_2–Pd/C and catalytic aq HCl, 62%.

the primary hydroxyl of **4** gave **5** in 90% yield. Compound **5** was subjected to benzylation using NaH, benzyl bromide to give compound **6** in 77% yield. Desilylation of compound **6** using 1 M TBAF solutions in THF gave compound **7**. The primary alcohol was oxidized to the aldehyde using TEMPO and the aldehyde subsequently treated with $Ph_3PCHCOCH_3$ to give **8** in 76% yield as a 0.9:1.1 *cis*,*trans*-diastereomeric mixture (by NMR). Hydrogenation of **8** in the presence of catalytic aq HCl using Pd/C, MeOH gave directly the target **1** in 62% yield in the form of a colourless oil. The physical and spectral data of compound **1** were in good agreement with the reported values.[6] In the final step, debenzylation, hydrogenation of the double bonds, hydrolysis of acetonide and internal acetalization were successfully carried out in one pot by adding a catalytic amount of aq HCl.

In conclusion we have demonstrated a chiron approach for the synthesis of **1** starting from D-mannitol.

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References and notes

1. Francke, W.; Schroder, F.; Philipp, P.; Meyer, H.; Sinnwell, V.; Gries, G. *Bioorg. Med. Chem.* **1996**, *4*, 363–374.
2. Naveen Kumar, D.; Rao, B. V. *Tetrahedron Lett.* **2004**, *44*, 2227–2229.
3. Takikawa, H.; Shimbo, K.-i.; Mori, K. *Liebigs Ann./Recueil* **1997**, 821–824.
4. Wiggins, L. *J. Chem. Soc.* **1946**, 13–14.
5. Garegg, P. J.; Samuelsson, B. *Synthesis* **1979**, 469–470.
6. Spectral data for compound **1**: colourless oil; $[\alpha]_D^{29.2}$ −79.38 (*c* 1, $CHCl_3$), {lit.[1] $[\alpha]_D^{19}$ −18 (*c* 1.91, $CHCl_3$) and lit.[3] $[\alpha]_D^{24}$ −79.5 (*c* 1.94, $CHCl_3$)}; IR (film cm^{-1}): 3440, 2965, 2936, 1450, 1384, 1240, 1200, 1180, 1044, 1028, 967, 875 and 850; ^1H NMR (300 MHz, C_6D_6): δ 0.77 (t, 3H, J = 7.32 Hz), 1.37 (s, 3H), 1.17–1.77 (m, 6H), 2.10 (br, 1H, OH), 3.22 (br s, 1H), 3.42 (t, 1H, J = 6.46 Hz), 3.82 (br s, 1H); ^{13}C NMR (75 MHz, C_6D_6): δ 9.67, 24.95, 25.51, 28.68, 31.61, 66.00, 79.36, 82.53, 107.85; EI-MS *m*/*z*: 143 [M^+−29], 129, 115, 114, 113, 112, 101, 99, 97, 85, 84, 83, 81, 73, 71, 70, 69, 61, 59, 58, 57, 56, 55, 43.