Stereocontrolled Synthesis of (±)-Acorenone B Based on New Ring Conversion

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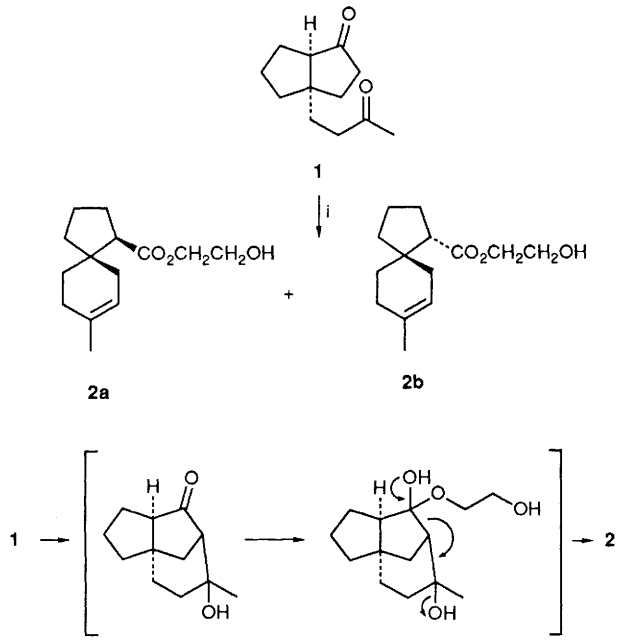
On the basis of a new ring conversion reaction from the bicyclo[3.3.0]octane ring to the spiro[4.5]decane ring, (±)-acorenone B was synthesized in a stereocontrolled fashion.

The characteristic framework of spiro[4.5]decanes such as β-vetivone, acorenone and hinesol is an attractive target for synthetic chemists. In the synthesis of spirocyclic compounds, the key step is the creation of the pivotal quaternary carbon centre.

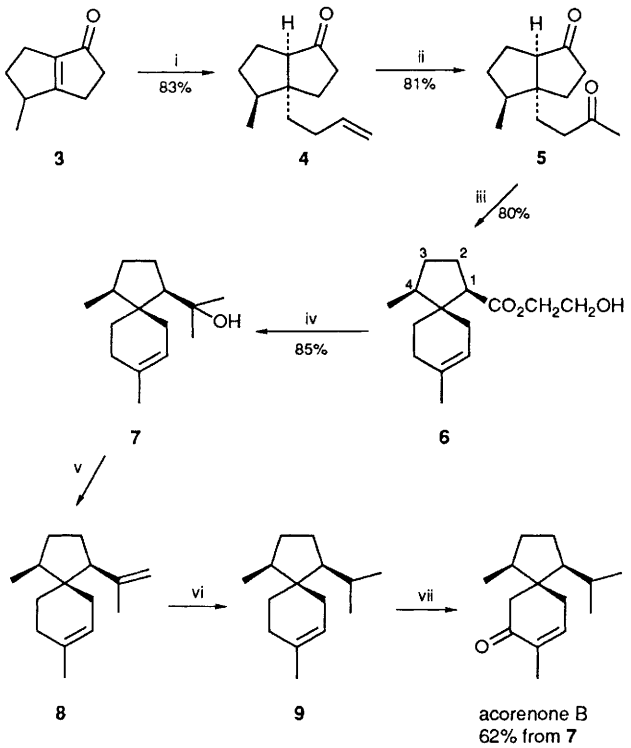
In this paper, we describe the synthesis of (±)-acorenone B with the spiro[4.5]decane skeleton based upon a new ring conversion reaction[1] developed in this laboratory. The sesquiterpene, acorenone B,[2] was isolated from *Bothriochloa intermedia*, and has been synthesized by several research groups.[3] In these syntheses, the common strategy is to build up from the first of the five or six membered rings in order to construct the second ring. Our strategy involved construction of the spiro[4.5]decane skeleton in one reaction. In a preliminary experiment for one-pot ring conversion, treatment with ethylene glycol (5 equiv.) and BF_3–Et_2O (7 equiv.) in CH_2Cl_2 at room temperature[1] converted compound **1**† successfully to the spiro-ring **2** in 83% yield (Scheme 1). A reaction mechanism involving aldol condensation, hemiacetalization, and Grob type fragmentation is proposed in Scheme 1.

The structure of **2** was determined by spectroscopic analysis. The ^1H NMR spectrum showed the alkenic proton at

† Compound **1** was prepared *via* 1,4-addition of CH_2 = CH–CH_2CH_2MgBr–CuI to bicyclo[3.3.0]oct-1(5)-en-2-one followed by Wacker oxidation.



Scheme 1 *Reagents*: i, BF_3–Et_2O (7 equiv.), $HOCH_2CH_2OH$ (5 equiv.)



Scheme 2 *Reagents and conditions*: i, CH_2=$CHCH_2CH_2MgBr$, CuI, BF_3–Et_2O, tetrahydrofuran, −78 °C; ii, $PdCl_2$, CuCl, H_2O, O_2 *N,N'*-dimethylformamide, 20 °C; iii, BF_3–Et_2O (7 equiv.), $HOCH_2CH_2OH$ (5 equiv.), CH_2Cl_2, 20 °C; iv, LiMe (2 equiv.), ether, 20 °C; v, Al_2O_3, pyridine, 200 °C; vi, Li, $EtNH_2$, Bu^tOH, tetrahydrofuran, 20 °C; vii, SeO_2, EtOH, reflux

δ 5.28 (1 H, m), the ethylene glycol half ester at δ 3.78–3.84 (CH_2O, 2 H, m) and 4.11–4.24 (CO_2CH_2, 2 H, m), and vinyl methyl at δ 1.63 (=CMe, 3 H, br s) respectively. The IR spectrum also supported this structure by the presence of absorption bands at ν 3400(OH) and 1730(CO) cm^{-1}. However, examination using GC–EIMS indicated **2** to be a stereoisomeric mixture of **2a** and **2b** in almost the same amounts. In addition, in the ^1H NMR spectrum of the corresponding methyl ester, two methyl signals were observed at δ 3.63 and 3.65, respectively. The formation of a stereoisomeric mixture suggests that the ester function was epimerized by BF_3–Et_2O (room temp., 1 h) under the reaction conditions employed. However, in the 8-oxo-spiro[4.5]deca-6,9-diene **6**, possessing a CO_2Me moiety at C-1 and Me at C-4, it is known that the 1,4-*cis*-isomer is more stable than the *trans*-isomer.[4] This stability of the *cis*-isomer indicated that the undesired epimerization of the ester function could be suppressed in this case. 1,4-Addition[5] of CH_2=$CHCH_2CH_2$-MgBr–CuI–BF_3 to the enone **3**[6] proceeded in an *anti*-fashion to the Me substituent to afford **4** (83%),‡ which was subjected to Wacker oxidation. The diketone **5** has the functional groups required for a one-spot ring conversion. In accord with our expectation, **5** was converted to the spiro-ring product **6**, in 80% yield, by similar treatment to that employed for **1**. The structure of **6** was determined by spectroscopic analysis. The ^{13}C NMR spectrum of **6** indicated the presence of ester carbonyl (δ 176.7), two alkene carbons (δ 133.2, 120.6), and one quaternary carbon (δ 46.8), and the ^1H NMR spectrum showed the vinyl proton at δ 5.28 (1 H, m), the ethylene glycol half ester at δ 3.78–3.80 (2 H, m) and 4.00–4.19 (2 H, m), the vinyl methyl at δ 1.61 (3 H, s), and methyl at δ 0.90 (3 H, d, *J* 7.1 Hz). The stereoisomer of **6** was not detectable by GC-EIMS or ^{13}C NMR spectroscopy. By treatment[7] with LiMe followed by dehydration, **6** was converted to the diene **8**. Selective reduction of the exomethylene moiety in **8** with Li–ethylamine and subsequent oxidation with SeO_2 afforded (±)-acorenone B,[3] whose spectroscopic data were in good agreement with those reported.

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‡ All compounds obtained in Scheme 2 gave satisfactory spectroscopic data.