Toward the Total Synthesis of a Sesquiterpene

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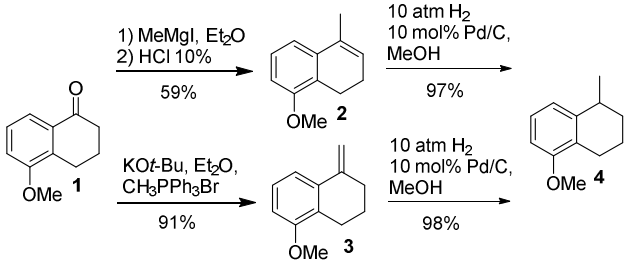
Introduction

The sesquiterpene jungianol was isolated by Bohlmann and his group from *Jungia malvaefolia*.[1] The total synthesis of jungianol was investigated by Hashmi and his group, as an application of gold catalysts, yielding *epi*-jungianol as major isomer.[2] Recently, Dethe and Murhade attempted this synthesis, also obtaining *epi*-jungianol.[3] This project aims the total synthesis of (±)-jungianol as main product from 5-methoxy-1-tetralone (**1**) using a ring contraction reaction promoted by iodine(III) as key step. Similar to this project are the racemic[4] and asymmetric[5] total synthesis of the isomer mutisianthol.

Results and Discussion

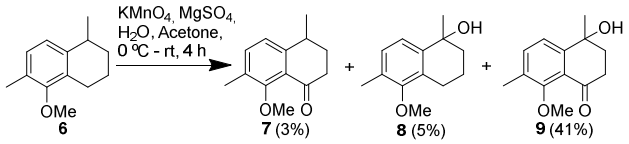
The initial plan for the synthesis was to transform 5-methoxy-1-tetralone (**1**) using classic reactions (Grignard, *in situ* dehydration and hydrogenation) to obtain tetralin **4**. However, the hydrogenation step showed problems with reproducibility, and a new route was developed (**Scheme 1**).



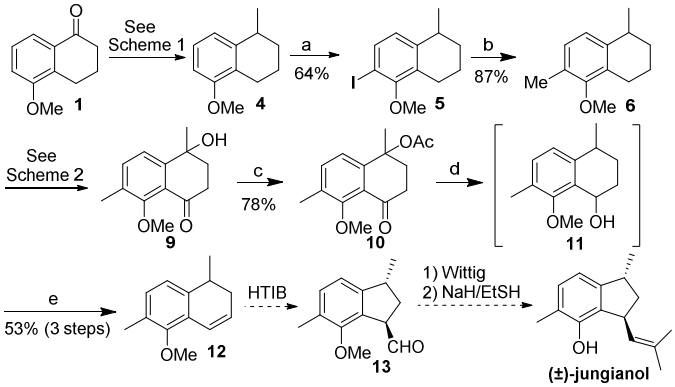
Scheme 1. Preparation of tetralin **4**

Iodination of **4** gave iodoarene **5**. Stille coupling of **5** with $SnMe_4$ yielded tetralin **6** (**Scheme 3**). The next challenge of the synthesis was a benzylic oxidation. Several conditions were tested, however it was not possible to isolate the desired tetralone **7**, as a major product (**Scheme 2**). Thus, we decided to continue the synthesis using **9**.

Scheme 2. Benzylic oxidation of tetralin **6**



The dioxidated compound **9** was submitted to several hydrogenolysis conditions. Eventually, a freshly prepared complex of ethylenediamine (en) with Pd/C allowed the chemoselective hydrogenation of **10**,[6] yielding a mixture of alcohol **11** and tetralone **7**, which was reduced to alcohol **11**. After dehydration, the dihydronaphthalene **12** was obtained (**Scheme 3**).



Scheme 3. Synthesis of jungianol

a. i) *t*-BuLi, TMEDA, rt., 6 h; ii) ICH_2CH_2I, 0 ºC – rt., 2 h; **b.** $SnMe_4$, $Pd(PPh_3)_2Cl_2$, PPh_3, LiCl, DMF, 160 ºC, 10 min.; **c.** DMAP, Ac_2O, AcOEt, 2 h; **d.** i) H_2 (balloon), Pd/C(en), MeOH, 18 h; ii) $NaBH_4$, MeOH, 0 ºC – rt., 2 h; **e.** H_3PO_4 (85%), THF, 95 ºC, 1 h.

Conclusions

Dihydronaphthalene **12** was synthesized from 5-methoxy-1-tetralone (**1**) in nine steps. After ring contraction, affording aldehyde **13**, followed by a Wittig and a deprotection step, the target molecule will be obtained.

Acknowledgements

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