Synthesis of C7–C31 fragment of (–)-cryptocaryol A

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INTRODUCTION

The natural product (+)-cryptocaryol A is an α-pyrone containing a 1,3-polyol moiety that was isolated in 2011 from the trees of *Cryptocarya* sp. (Figure 1).[1,2] This compound is able to stabilize Pdcd4 (programmed cell death 4), a tumor suppressor protein that inhibits transformation, migration, and invasion of cancer cells *in vitro*.[3]

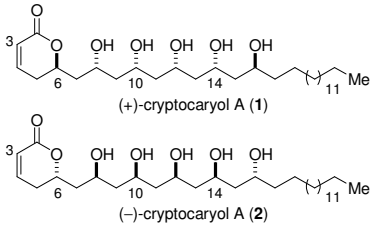
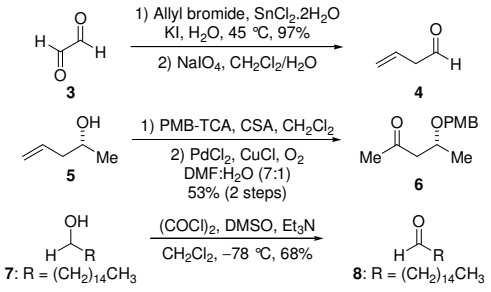


Figure 1. (+) and (–) Cryptocaryol A structure.

This work aims the synthesis of C7–C31 fragment of (–)-cryptocaryol A.

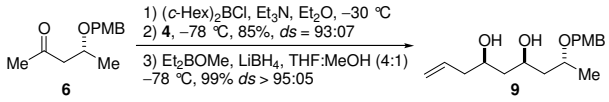
RESULTS AND DISCUSSION

The aqueous Barbier reaction between glyoxal (**3**) and allyl bromide (97%), followed by an oxidative cleavage by $NaIO_4$, provided aldehyde **4** (Scheme 1). The protection of alcohol **5** with PMB-trichloroacetimidate (PMB-TCA), followed by a Wacker oxidation, led to the formation of methylketone **6** in 53% yield for 2 steps. The aldehyde **8** was prepared under Swern oxidation conditions in 68% yield from alcohol **7**.



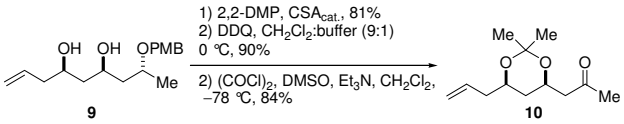
Scheme 1. Preparation of aldehyde **4**, methylketone **6** and aldehyde **8**.

The aldol reaction between the boron enolate of methylketone **6** and aldehyde **4** provided the 1,5-*anti* aldol adduct in 85% yield (*ds* = 93:07) (Scheme 2).[4] The corresponding aldol adduct was reduced with Et_2BOMe and $LiBH_4$ leading to the formation of 1,3-*syn* diol **9** (*ds* > 95:05).



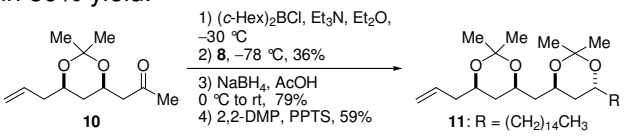
Scheme 2. Preparation of diol **9**.

The diol **9** was treated with 2,2-dimethoxypropane (2,2-DMP), providing the corresponding acetonide in 81% yield (Scheme 3). Then, the methylketone **10** was prepared by treating the acetonide with DDQ in 90% yield, followed by a Swern oxidation (84%).



Scheme 3. Preparation of methylketone **10**.

The aldol reaction between the boron enolate of methylketone **10** and aldehyde **8** provided the corresponding 1,5-*anti* aldol adduct in 36% yield (Scheme 4). The corresponding aldol adduct was treated with $NaBH_4$ in AcOH providing the corresponding 1,3-*anti* diol (79%), that was used in a protection reaction with 2,2-DMP, leading to the formation of C7–C31 fragment of cryptocaryol A (**11**) in 59% yield.



Scheme 4. Preparation of C7-C31 fragment of (–)-cryptocaryol A (**11**).

CONCLUSION

The synthesis of C7–C31 fragment of (–)-cryptocaryol A was concluded in 10 steps in 5% yield.

ACKNOWLEDGEMENTS

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