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 Pdc4 (programmed cell death 4), a tumor suppressor protein that inhibits transformation, migration, and invasion of cancer cells in vitro.3

RESULTS AND DISCUSSION

The aqueous Barbier reaction between glyoxal (3) and allyl bromide (97%), followed by an oxidative cleavage by NaIO4, 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.

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 Et3BOMe and LiBH4 to leading to the formation of 1,3-syn diol 9 (ds = 95:05).

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%).

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 NaBH4 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.

CONCLUSION

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

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REFERENCES


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