FIRST TOTAL SYNTHESIS OF VARIOXIRANOL A

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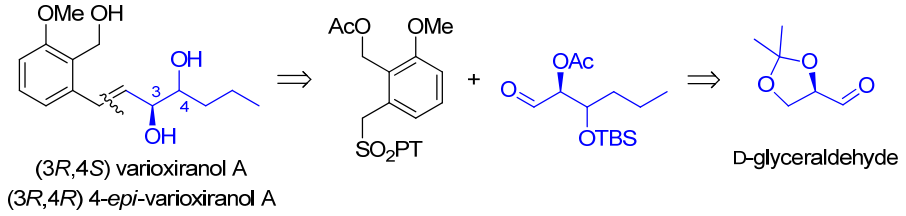
During past several decades the fungus *Emericella variecolor* [1] has proven itself as a promising source of the large number of natural products with diversiform biological activities [2-3]. Chemical investigation of a sponge (*Cinachyrella* sp.)-associated *Emericella variecolor* fungus provided new polyketide derivatives bearing benzyl alcohol motif as a part of their structure. Such derivatives were tested as inhibitors against lipid accumulation in HepG2 liver cells. Varioxiranol A, among other isolated metabolites, exerted high biological activity and showed no toxicity [4]. We accomplished the first total synthesis of varioxiranol A using chiral pool approach. Using 1,2-O-isopropylidene-D-glyceraldehyde as an initial chiral source and exploitation of its prochiral centre allowed us to simultaneously prepare not only natural varioxiranol A but also 4-*epi*-varioxiranol A. Both varioxiranol A as well as its diastereoisomer were obtained after ten steps using a synthetic strategy based on the Julia-Kocienski coupling reaction between aromatic sulfone and corresponding aliphatic chiral derivative (**Scheme 1**) in an overall yield of 10% and 6%. Absolute configuration of final enantiomerically pure products was confirmed by single-crystal X-ray analysis [5]. Proposed synthetic strategy has significant potential in preparing other interesting structurally similar polyketide derivatives.



Scheme 1: Retrosynthetic analysis of varioxiranol A and its 4-epimer.

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