

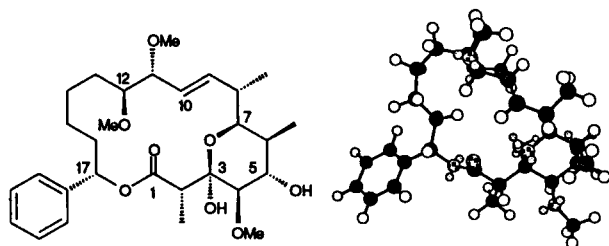
## Synthesis of C10-C17 Fragment of Soraphen A

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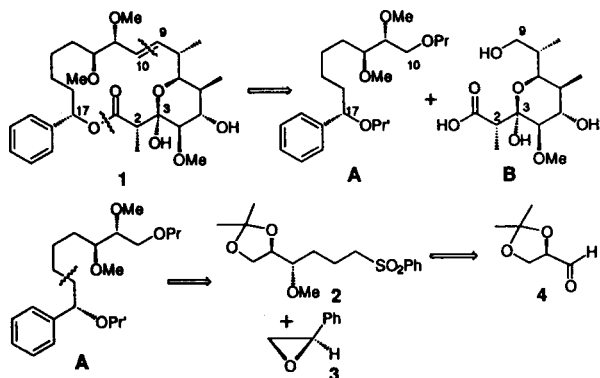
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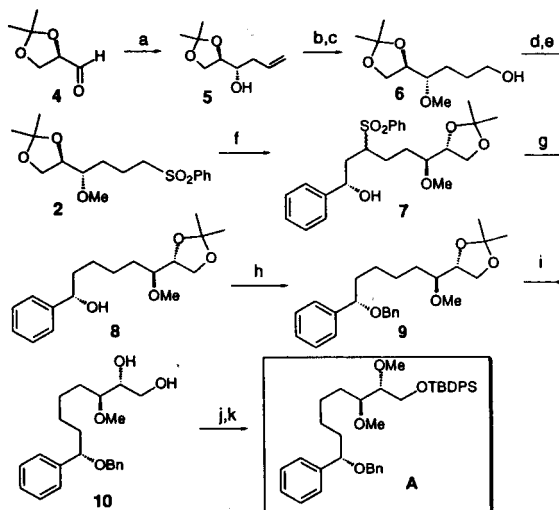
Soraphen A (1) is a macrolide isolated from the myxobacterium *Sorangium cellulosum*.<sup>1</sup> Soraphen A has potent fungicidal activity against various plant pathogenic fungi. So far the synthesis of soraphen A reported in the literature has been mainly about the fragment of C1-C9.<sup>2</sup> Herewith we would like to report synthesis of C10-C17 fragment of soraphen A.



Retrosynthetic analysis of soraphen A straightforwardly reveals two major fragments A and B, resulted from the disconnection at a pair of bonds at C9-C10 and C-O of lactone (Scheme 1). Further retrosynthetic analysis of fragment A suggests use of (*R*)-glyceraldehyde (4) as a starting material to introduce the stereochemistry at C11 and C12. Accordingly in our synthetic route toward the fragment A, reaction of (*R*)-glyceraldehyde with organometallic allylic reagent was carried out in the first place (Scheme 2). In general, reaction between organometallic allylic compound and (*R*)-glyceraldehyde usually gives a mixture of product. In our case, the desired product is chelated Cram's product 5. Although reactions of glyceraldehyde with allylic boronic esters with chiral auxiliary such as one derived from *L*-(+)-diisopropyl tartrate have been reported to give predominantly 5,<sup>3</sup> we have found the utilization of an allylindium reagent to be more advanta-



Scheme 1.



Scheme 2.

geous not only because of its simplicity but also because of its appropriateness for large scale reactions.<sup>4</sup> After the chromatographic separation, 5 was subjected to methylation with NaH and CH<sub>3</sub>I and subsequent hydroboration with BH<sub>3</sub>·Me<sub>2</sub>S to obtain 6 in 82% yield for two steps. The treatment of hydroxyl group of 6 with diphenyl disulfide and tributyl phosphine provided a phenyl sulfide derivative<sup>5</sup> and following oxidation of the sulfide with mcpba and NaHCO<sub>3</sub> gave 2 in 92% yield. The next step along the sequence was the coupling of sulfone with epoxide to provide the necessary stereogenic hydroxyl group at C-17. The reaction of dicarbonyl of 2, generated by two equivalents of *n*-BuLi, with commercially available (*R*)-styrene oxide (3) gave coupled sulfonyl products 7 as a diastereoisomeric mixture in 86% yield. <sup>1</sup>H NMR spectrum of this mixture showed two distinctive peaks of CH<sub>3</sub>O<sup>-</sup> at δ 3.23 and δ 3.33. Without separation of isomers, reductive removal of sulfonyl group of 7 was performed by employing sodium amalgam in a buffered methanolic solution to furnish 8 in 82% yield. <sup>1</sup>H NMR spectrum of 8 exhibited only one singlet peak at δ 3.37. Furthermore, (*R*)-MTPA ester derivative of 8 showed the presence of single isomeric product. Consequently we achieved all the required stereochemistry for fragment A. The hydroxyl group of 8 was transformed to benzyl ether by treatment with NaH and benzyl bromide in DMF to obtain 9 in 93% yield. The acidic treatment of acetonide group of 9 in 70% aqueous acetic acid afforded diol 10 in 98% yield. The methylation of the secondary hydroxyl group of 10 needs the protection of a primary hydroxyl group. Compound 10 was selectively protected as TBDPS ether at a primary hydroxyl group by treating with TBDPSCl and imidazole in the presence of catalytic amount of dimethylaminopyridine. The consecutive methylation at the remaining secondary hydroxyl group of 10 provided the desired product A in 65% for two steps and thus this formally completed the synthesis of C10-C17 moiety of soraphen A.

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