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Recent Advances in the Synthesis of Pamamycin-607

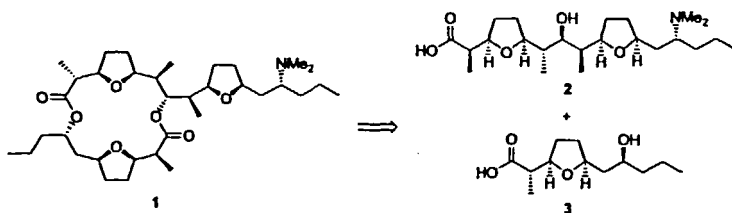
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Germany*

Using sultones as crucial intermediates, a short and highly stereoselective synthesis of a precursor of the larger fragment and the methyl ester of the smaller fragment of the macrodiolide pamamycin-607 was achieved.

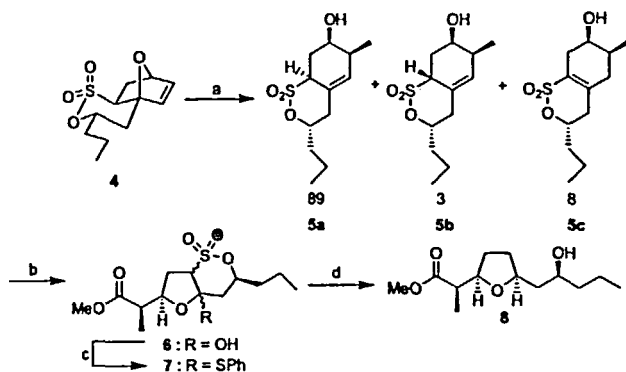
Keywords: sultones; pamamycin-607; stereoselective synthesis; tandem reactions

Pamamycin-607 (**1**) exhibits antibiotic activities against Gram positive bacteria and pathogenic fungi.¹ The retrosynthetic analysis of **1** leads to a larger fragment **2** and a smaller fragment **3**.



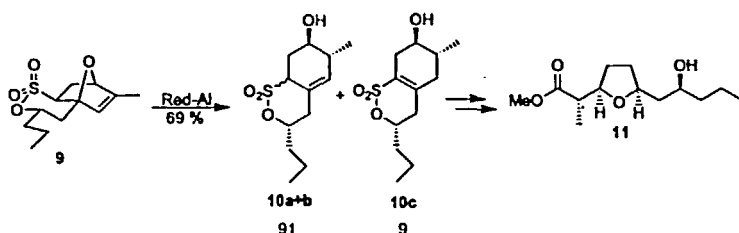
Sultones prepared via intramolecular Diels-Alder reaction of vinylsulfonates derived from hydroxyalkyl substituted 1,3-dienes have proven to be versatile intermediates for organic synthesis.²

Treatment of furan adduct **4** with 2 equivalents of methyllithium induces a tandem elimination/1,6-addition to yield the bicyclic compounds **5**. Ozonolysis of this mixture, followed by eliminative work-up affords two diastereomeric hemi-acetals **6**. A Lewis acid catalyzed exchange of the hydroxyl group in **6** against a phenylsulfanyl group in **7** sets the stage for a tandem reductive elimination/hydrogenation with Raney nickel to give **8**.



a: 2 MeLi (66 %). b: O_3 , MeOH; Ac_2O , pyridine (61 %).
 c: PhSH, $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (82 %). d: Raney Ni (35 %).

Using a similar strategy, we have also succeeded in installing the unusual relative configuration at C-2 in the epimeric smaller fragment 3. Instead of adding methyl lithium to 4, we applied a tandem elimination/1,6-hydride addition³ to convert sulfone 9 to the bicyclic compounds 10.



Further elaboration of 10 analogous to the conversion of 5 leads to 11, the methyl ester of the smaller fragment 3.

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