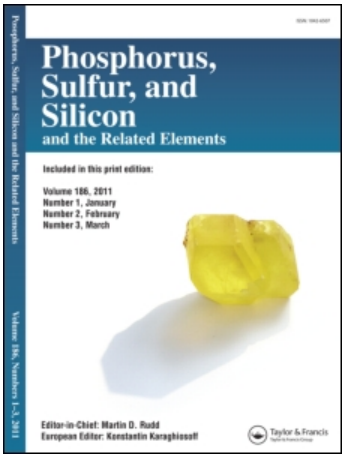


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# Recent Advances in the Synthesis of Pamamycin-607

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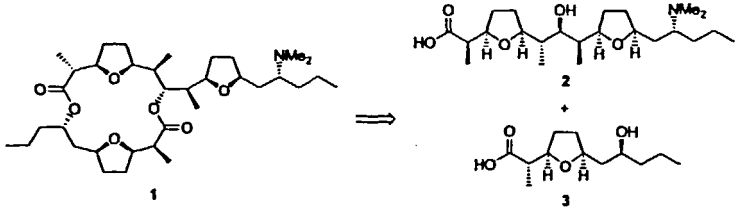
Using sultones as crucial intermediates, a short and highly stereoselective synthesis of a precursor of the larger fragment and the methyl ester of the smaller fragment of the macrodiolide pamamycin-607 was achieved.

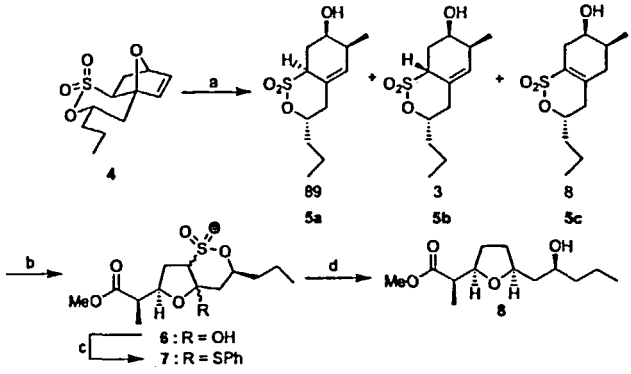
*Keywords:* sultones; pamamycin-607; stereoselective synthesis; tandem reactions

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**.



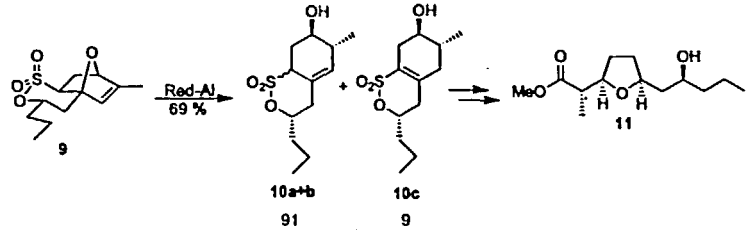

Sultones prepared *via* intramolecular Diels-Alder reaction of vinylsulfonates derived from hydroxyalkyl substituted 1,3-dienes have proven to be versatile intermediates for organic synthesis.[2]

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, $BF_3{\cdot}Et_2O$ (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 methyllithium to **4**, we applied a tandem elimination/1,6-hydride addition[3] to convert sultone **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**.

## *References*

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[2] P. Metz, *J. prakt. Chem.*, **340**, 1–10 (1998).
[3] P. Metz, E. Cramer, *Tetrahedron Lett.*, **34**, 6371–6374 (1993).