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Desulfurization of Sultones with Simultaneous Methylenation

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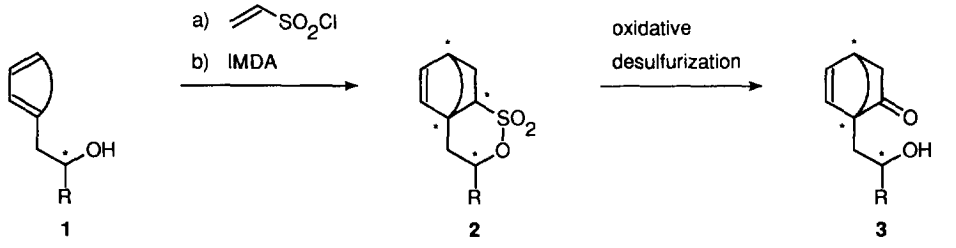
Abstract: Desulfurization of the δ-sultones **2** with simultaneous formation of an exocyclic olefin is achieved by alkylation of **2** with (iodomethyl)trimethylsilane and subsequent treatment of the resultant products **7** with tetra-*n*-butylammonium fluoride. Application of this two-step procedure to sultone **8** leads to 1,3-diene **10**, an intermediate for the synthesis of the highly oxygenated 1,10-*seco*-eudesmanolides eriolanin and eriolangin.

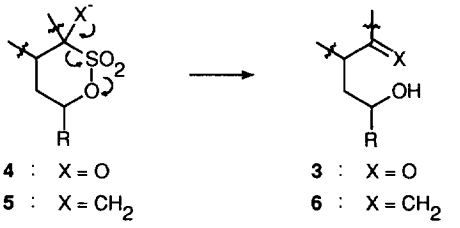
We recently reported a method for the desulfurization of sultones[1] to hydroxy ketones *via* borylation/peracid oxidation. Coupled with the preparation of δ-sultones **2** by intramolecular Diels-Alder reaction of the vinylsulfonates derived from hydroxyalkyl substituted cycloalka-1,3-dienes **1**, this procedure allows for a formal [4+2] cycloaddition of ketene to **1** in a completely regioselective and highly diastereoselective fashion (Scheme 1).[2]



Scheme 1. Formal [4+2] cycloaddition of ketene to cycloalka-1,3-dienes **1**

Since the α-oxygenated intermediates **4** involved in the oxidative cleavage smoothly decomposed in the depicted sense, we reasoned that the carbanions **5**[3] would similarly break down to give the bishomoallylic alcohols **6** *via* β-elimination (Scheme 2).

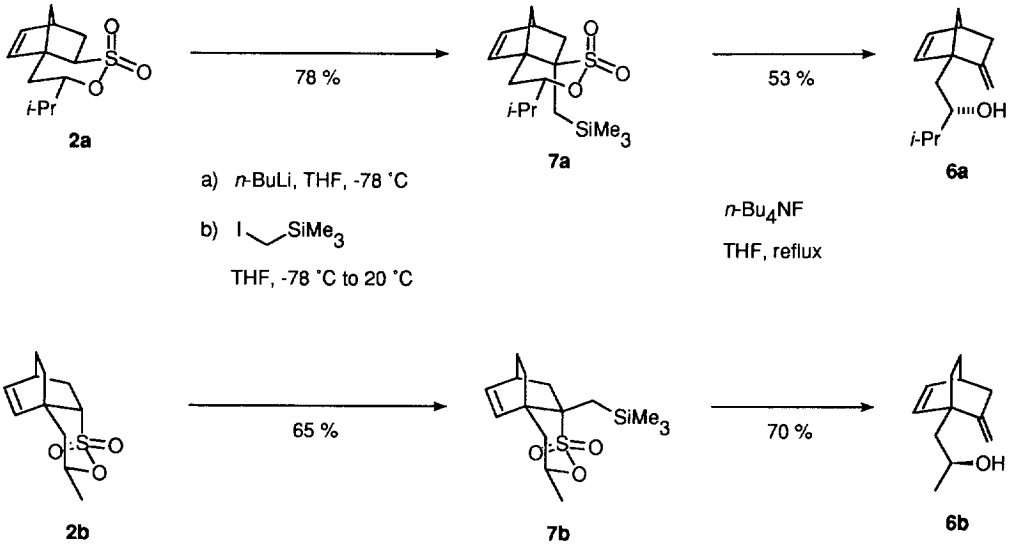
While a carbonyl methylenation of **3** to **6** would be a feasible alternative for simple substrates, a desulfurization with simultaneous formation of an olefin streamlines the route to **6** and, more importantly, such a process is even applicable if an oxidative sultone cleavage would lead to a base sensitive ketone, which might undergo side reactions during olefination.



Scheme 2. Sultone cleavage *via* elimination

Using **2b**[2] as a model substrate, we first attempted a one-pot conversion to dienol **6b** by alkylation of the lithiated[2] sultone with chloromethylmagnesium chloride.[4] However, in contrast to the clean olefination of lithiated sulfones with electrophilic monohalogenocarbenoids,[5] only a complex product mixture was obtained from **2b**.

Gratifyingly, the desired transformation of **2a,b** to **6a,b**[6] was achieved in good yield by alkylation of the sultones with (iodomethyl)trimethylsilane[7,8] followed by fluoride-induced elimination[9,10] of the resultant silanes **7a,b**[11] using tetra-*n*-butylammonium fluoride (Scheme 3). Since the dienols **6a,b** are formal [4+2] adducts of allene with the hydroxyalkyl dienes from which the sultones **2a,b** were prepared,[2] vinylsulfonyl chloride[12] can serve as a regio- and stereoselectively reacting allene equivalent for the intramolecular Diels-Alder cycloaddition, too.

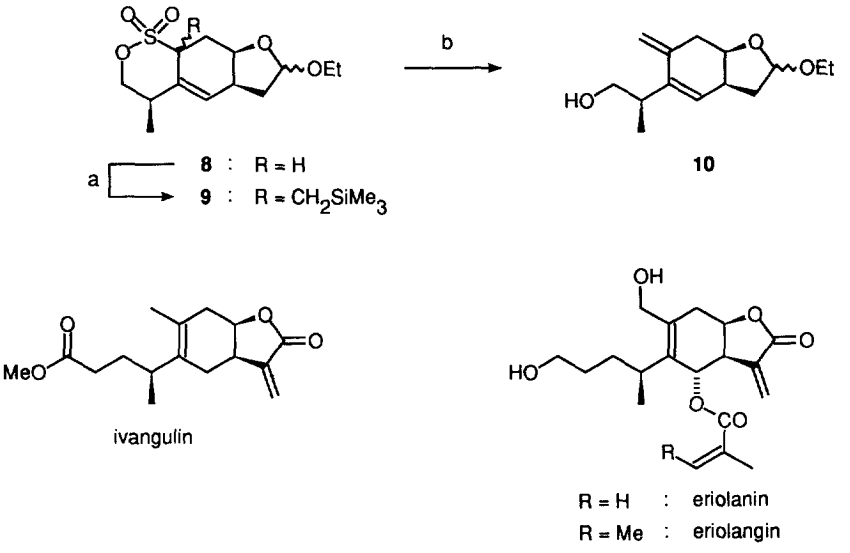


Scheme 3. Desulfurization of sultones **2** to dienols **6**

After some minor modifications, the two-step procedure described above was successfully applied to sultone **8**[13,14] as well (Scheme 4). As we already noted during our synthesis of the 1,10-*seco*-eudesmanolide ivangulin *via* methylation of **8**,[14] the use of methyllithium is essential for complete lithiation. Moreover, efficient alkylation of the resultant allyllithium species required addition of (iodomethyl)trimethylsilane at

room temperature and subsequent warming to 40 °C for 30 min. Fluoride-induced elimination of silane **9** proceeded uneventfully within 1 h to give the acid sensitive dienol **10** as a mixture of two acetal epimers.

Both termini of the 1,3-diene unit in **10** are activated towards an oxygenation[15] and thus, this compound represents a promising intermediate for the total synthesis of the highly oxygenated, antileukemic[16] 1,10-*seco*-eudesmanolides eriolanin[17-19] and eriolangin[17] by a route similar to the one that led to ivangulin.[14]



Scheme 4. Preparation of 1,3-diene **10**, an intermediate for the synthesis of eriolanin and eriolangin. a: (i) MeLi, THF, -78 °C to 20 °C, (ii) ICH_2SiMe_3, 20 °C to 40 °C, 71 %; b: *n*-Bu_4NF, THF, reflux, 65 %

In summary, a novel method for the desulfurization of sultones has been established that complements our procedures for oxidative[2] and reductive[20] sultone cleavage. Elaboration of the epimeric acetals **10** to eriolanin and eriolangin is currently under investigation in our laboratories.

Acknowledgment

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