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LETTERS

# A new and expeditious entry to 7-oxabicyclo[3.2.1]octan-8-ol and 2-oxabicyclo[3.3.1]nonan-9-ol skeletons via intramolecular Michael addition–S<sub>N</sub>2' ring opening of 7-oxabicyclic sulfones

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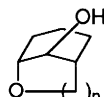
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## Abstract

A new intramolecular ring opening of 7-oxabicyclic sulfones allows the synthesis of the title compounds. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords:* intramolecular Michael addition; ring opening; 7-oxabicyclo[2.2.1]heptane; natural products.

The 7-oxabicyclo[3.2.1]octan-8-ol **1** and 2-oxabicyclo[3.3.1]nonan-9-ol **2** systems (Scheme 1) are present in different families of natural products.<sup>1</sup> However, to the best of our knowledge no systematic study concerning their synthesis has been previously considered.



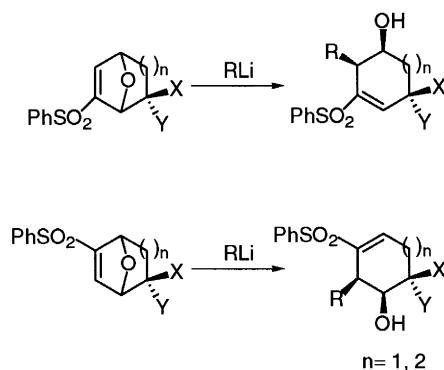
**1**, n= 1  
**2**, n= 2

Scheme 1.

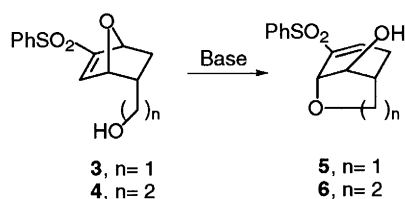
In previous papers we have reported that the alkylative ring opening of 7-oxanorbornenic sulfones constitutes an appropriate tool for the synthesis of functionalised cyclohexene derivatives<sup>2</sup> (Scheme 2). Application of this methodology for the preparation of natural products or their fragments has also been previously considered.<sup>3</sup>

At this point we speculated that the intramolecular version of this reaction,<sup>4</sup> using an alkoxide as internal nucleophilic reagent, could be an interesting possibility for the synthesis of conveniently functionalised systems<sup>5</sup> with the general structures **1** and **2** (Scheme 3).

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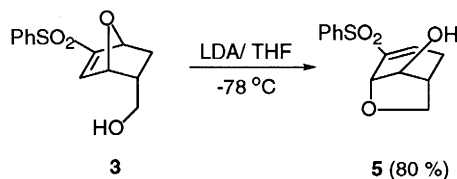


Scheme 2.



Scheme 3.

Confirmation of this hypothesis was obtained when sulfone **3**,<sup>2</sup> by reaction with LDA at  $-78^\circ\text{C}$ , afforded compound **5**<sup>†</sup> (80% isolated yield) (Scheme 4).



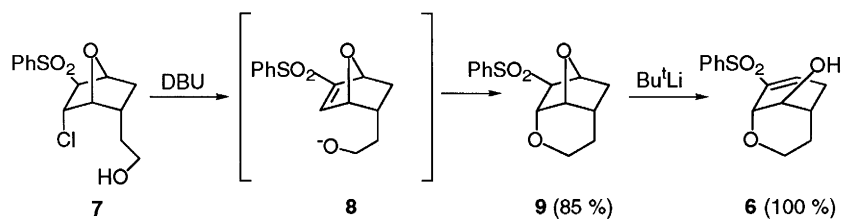
Scheme 4.

The behaviour of chlorosulfone **7**<sup>‡</sup> towards basic reagents is especially interesting (Scheme 5). Thus, reaction of **7** with DBU ( $\text{CH}_2\text{Cl}_2$ ,  $0^\circ\text{C}$  to rt, 4 h, as in the case of the chlorosulfone precursor of **3**), afforded the tricyclic system **9** (85%) via spontaneous Michael addition of the hydroxyl functionality to the produced (and not observed) vinyl sulfone **8**. Treatment of compound **9** with  $\text{Bu}^t\text{Li}$  (THF,  $-78^\circ\text{C}$ , 1 min) gave rise to the desired bicyclic system **6** in a quantitative yield (Scheme 5). Although this sequence has been carried out using racemic compounds, it is also possible to obtain the final products in enantiomerically pure forms since both enantiomers of 7-oxanorbornene derivatives are readily available.<sup>6</sup>

In summary, the intramolecular Michael addition–ring opening reaction of oxanorbornenic vinylsulfones constitutes an appealing method for the synthesis of functionalised 7-oxabicyclo[3.2.1]octan-8-ol and 2-oxabicyclo[3.3.1]nonan-9-ol systems.

<sup>†</sup> All described compounds gave satisfactory analytical and spectroscopical data according to the indicated structures. Spectroscopic data ( $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR) for compounds **5** and **6** and detailed experimental procedures are available upon request to the authors.

<sup>‡</sup> Chlorosulfone **7** was prepared in five steps (96% overall yield) from 7-oxabicyclo[2.2.1]hept-2-en-5-one. Full details are available upon request to the authors.



Scheme 5.

## Acknowledgements

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## References

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