A New Method of Spiroketalization via Cascade Oxidative Dearomatization

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INTRODUCTION

Spiroketals have been isolated from an array of sources in Nature such as insects, bacteria and marine organisms.[1] The intriguing and often potent bioactivity of many spiroketal containing natural products, e.g. **1** & **2**, makes them frequent synthetic targets. Several high value pharmaceuticals, e.g. avermectin, contain a spiroketal motif.[2]

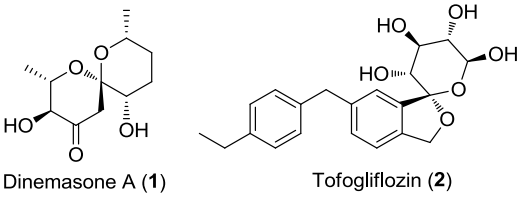


Figure 1. Example Spiroketal Natural Products

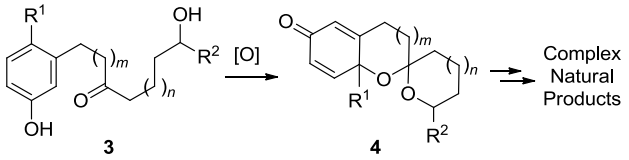
Many current methods for spiroketal formation do not lend themselves to the often architecturally challenging structures present in natural product targets. Thus the development of new methods for spiroketalization is of key importance for the synthesis of many biologically active natural products.

RESULTS AND DISCUSSION

A new method for the formation of spiroketals has been developed (Scheme 1). Treatment of phenolic hydroxy ketones e.g. **3** with hypervalent iodine reagents initiates a cascade oxidative dearomatizing cyclization to afford spiroketals **4**.[3]

Details of the conditions required for spirocyclization will be discussed, as will the nature of the diastereoselectivity of the process. A discussion of the elucidation of the structure of the products formed will also ensue.

This newly developed method assists a rapid increase in molecular complexity with the formation of two rings, two new stereocentres and two C−O bonds in one single synthetic step. A discussion of how this method can be elaborated towards synthetically challenging spiroketal natural products will be presented.



Scheme 1. Spiroketalization *via* Oxidative Cascade Dearomatization

CONCLUSION

A new method for spiroketalization has been developed assisting the rapid formation of synthetically challenging spiroketal ring systems. The development and further elaboration of this method will be discussed.

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