



## A preparation of bicyclo[2.2.2]octan-2-one by sequential Michael reactions.

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## INTRODUCTION

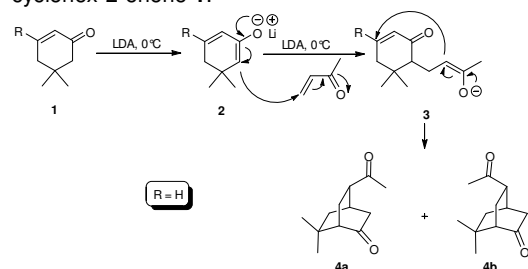
Bicyclo[2.2.2]octan-2-ones are efficient starting materials for the synthesis of natural products. Bicyclic compounds are traditionally synthesized through Diels Alder reactions; these bicyclo[2.2.2]octan-2-ones have been synthesized using cross-conjugate dienes derived from cyclohexenones.<sup>2</sup>

We report here some experimental results in which the bicyclic system was obtained by reaction of an enolate with methyl vinyl ketone, indicating that it could be the result of two sequential Michael additions.

## RESULTS AND DISCUSSION

As part of an ongoing synthetic study, we directed our attention to the reaction between the cross-conjugated enolate (**2**) and methyl vinyl ketone as a Michael acceptor (Scheme 1) for the preparation of the intermediate **3**. However, under these reaction conditions we obtained only the bicyclo[2.2.2]octan-2-one **4**, as a mixture of diastereoisomers (Scheme 1), resulting from two sequential Michael additions.

**Scheme 1:** Sequential Michael additions of cyclohex-2-enone **1**.



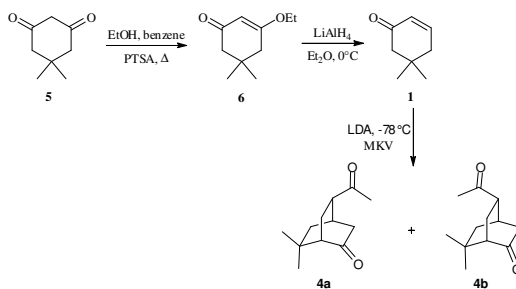
Comparing this result with others described in the literature<sup>3</sup> we can conclude what the cyclization is favored either by the absence of a strong steric hindrance ( $R=H$ ) (Scheme 1) and by increase in bond energy that accompanies the transformation of a  $\pi$ -bond to a  $\sigma$ -bond.

This opens the possibility to convert 1,3-diketones into bicyclo[2.2.2]octan-2-ones through two sequential Michael additions, because 1,3-diketones can be easily converted to enones without  $\beta$ -substituents.

According to scheme 2 the intermediate **1** can be easily obtained from 5,5-dimethylcyclohexane-1,3-dione (**5**), a readily available starting material.

For this purpose dimedone (**5**) was converted to intermediate **6** by esterification<sup>4</sup> followed by reduction<sup>5</sup> with  $\text{LiAlH}_4$ , furnishing the enone **1**. Treatment of enone **1** with LDA and MVK provides the bicyclo[2.2.2]octan-2-one (**4a** and **4b** (1:1)).

**Scheme 2:** Synthesis of bicyclo[2.2.2]octan-2-one (**4**) from the dimedone (**5**).



## CONCLUSION

The sequential Michael addition of MVK to cross-conjugate enolates is a convenient and rapid alternative to Diels-Alder reactions for the preparation of bicyclo[2.2.2]octan-2-ones.

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