

Microwave-Assisted Synthesis of Nitroketene *N,O*-aminoacetals and Nitroketene *N,N*-aminals

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INTRODUCTION

Association of biological activity with heterocyclic motifs is well known and is an important strategy in drug discovery programs. Thus, the development of the fast strategies to formation of these compounds is very important.¹

Polarized ketene dithioacetals **1** have been recognized as useful building blocks in many synthetic operations. They can further be converted into the corresponding *S,N*- and *N,N*-ketals, **2** and **3** respectively, making them important as precursors for a large variety of functionalized ketals.² As part of our studies on ketene dithioacetal for the synthesis of heterocyclics, we found that microwave irradiation accelerates the vinylic substitution of the anilines and amines in nitroketene *S,S*-acetals³. In this work, we report the annulation reaction of hydroxylamines and diamines to the formation of the heterocyclic compounds.

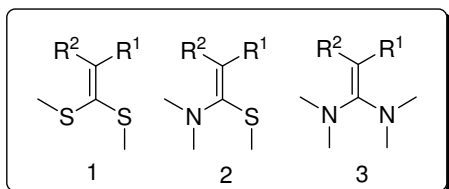
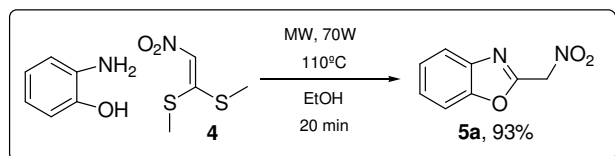


Figure 1

RESULTS AND DISCUSSION

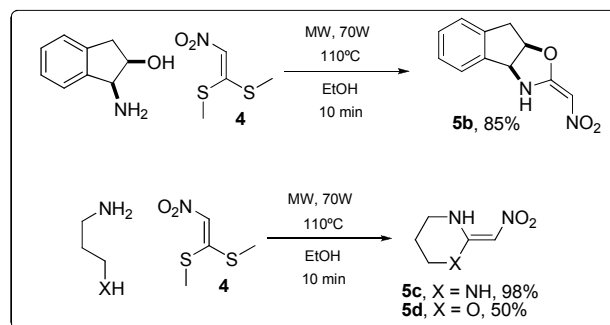
Using a reactor Discover-CEM, we irradiated the suspension formed by 1,1-bis(thiomethyl)-2-nitroethylene **4** and 2-aminophenol in ethanol obtaining the **5a** with 93% of yield.

Scheme 1



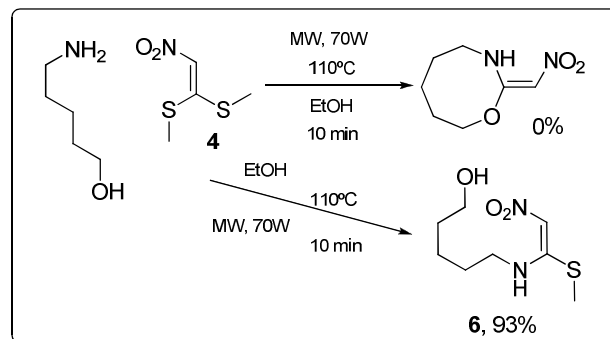
After obtaining this result, we also investigated the scope of this methodology with aliphatic amines (Scheme 2) and good results were obtained.

Scheme 2



However, when we tested this methodology to the formation of an 8-membered ring, the second substitution has not occurred (Scheme 3), furnishing only the *N,S*-acetal **6**.

Scheme 3



CONCLUSION

In summary, we have shown that the double nucleophilic substitution, between hydroxylamines and diamines with 1,1-bis(thiomethyl)-2-nitroethylene employing microwave heating furnished the corresponding nitroketene *N,O*-aminoacetals and *N,N*-aminals with moderate to good yields, in very short reaction time.

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