

Aza-bicycles Synthesis Through Formal Aza [3+3], [3+2+1] and [3+1+1+1] Cycloadditions Between Enaminones, Aldehydes and Meldrum's Acid Derivatives.

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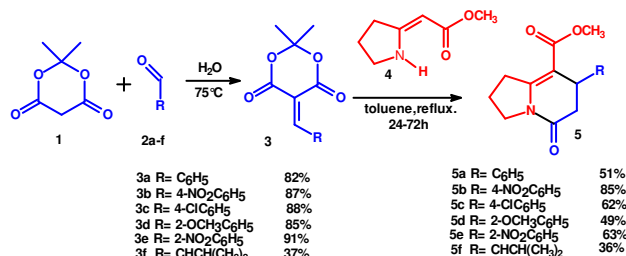
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INTRODUCTION

Aza-bicycles are an important scaffold because a great number of biological active alkaloids and synthetic analogous belong to this class.¹ Employing enaminones in order to obtain these compounds is strategic, once enaminones are obtained in good yields and can be used to prepare diverse heterocycles. This work evaluates the bicomponent aza-annulation [3+3] reaction between enaminones and Meldrum's acid derivatives, as well as the trimolecular [3+2+1] and the tetramolecular [3+1+1+1] multicomponent reactions.^{2,3}

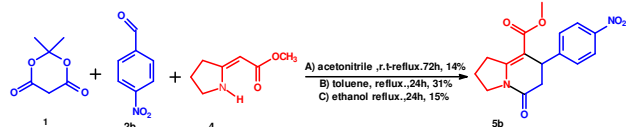
RESULTS AND DISCUSSION

The aza-annulation [3+3] reaction with previously synthesized Meldrum's acid alkylidenes^{4,5} and cyclic enaminone **4** led to several indolizidinones.



Scheme 1.

This kind of nucleous can also be accessed by a tricomponent [3+2+1] reaction, although with low yields, as shown on scheme 2.

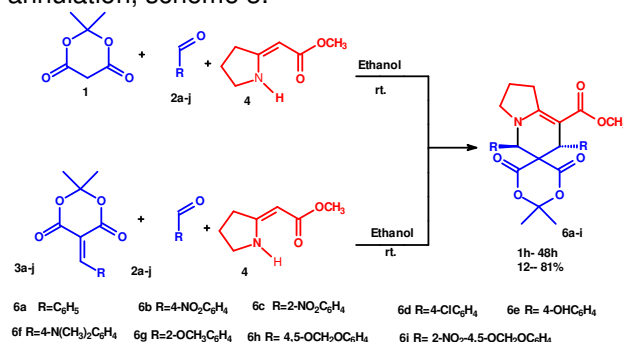


Scheme 2.

When the reaction was performed in ethanol, at room temperature, a tetramolecular [3+1+1+1] aza-annulation reaction occurred, leading to spirocompounds **6a-i**, following according to a Yonemitsu-like condensation and a single diastereomer was formed, scheme 3.

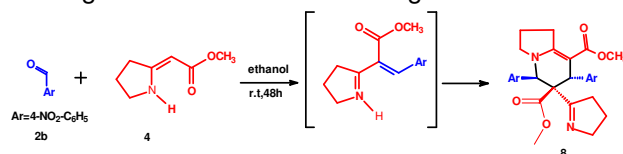
Presuming that Knoevenagel adducts are involved in the spirocompound formation, these arylidenes

were reacted in a tricomponent aza-[3+2+1] annulation, scheme 3.



Scheme 3.

The reaction between cyclic enaminone and 4-nitrobenzaldehyde were performed in order to evaluate the mechanism of this transformation. The result was compound **7**, as a single diastereomer, bearing three consecutive stereogenic centers.



Scheme 5.

CONCLUSION

Meldrum's acid derivatives and enaminones, depending on the conditions used, can react differently: by a [3+3] bicomponent aza-annulation reaction, by a [3+2+1] trimolecular pathway or by a [3+1+1+1] tetramolecular reaction.

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