Synthetic Application of New Enaminodiketone: Regioespecific Synthesis of Aza-Heterocycles

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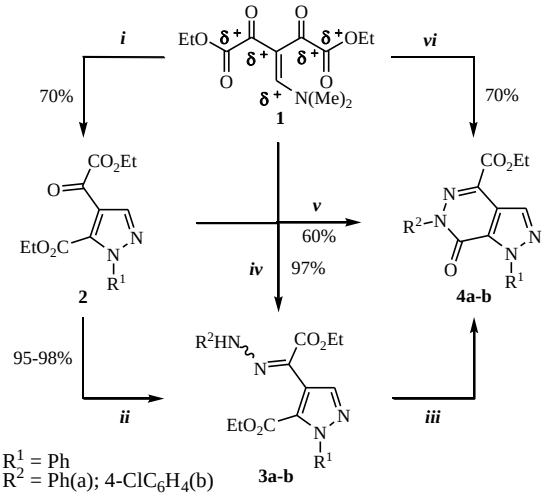
INTRODUCTION

Aza-heterocyclic compounds, such as pyrazoles[1] and pyridazinones[2], have become increasingly important because they have proven to be extremely bioactive moieties. The synthesis of nitrogen-containing heterocyclic compounds has been well explored by reacting of blocks precursors enaminodiketones with N-$(C)_n$-N dinucleophiles. Data from the literature have demonstrated an efficient method for obtaining a series of enaminodiketones from *C*-acylation of enaminoketones with ethyl oxalyl chloride[3–5]. The reaction of these precursors with N-N dinucleophiles was shown to be highly attractive for the synthesis of multifunctionalized pyrazoles[4] and other aza-heterocyclic.[5] Thus, considering the importance of nitrogen-containing heterocyclic compounds, the aim of this work, is to report synthetic application to obtain pyrazole multifunctionalized and pyrazolopyridazinones from cyclocondensation reaction of enaminodiketone (**1**) block precursor with hydrazines.

RESULTS AND DISCUSSION

The synthesis of the new precursor β-enaminodiketone (**1**) was performed from *C*-acylation of ethyl 3-[(dimethylamino)methylidene]pyruvate[6] with ethyl oxalyl chloride in dichloromethane and pyridine[3]. Synthetic application and study on the different electrophilic centers present in the enaminodiketone system was evaluated from cyclocondensation reaction with hydrazines (**scheme 1**). Surprisingly, the reaction of compound **1** with phenylhydrazine was regioespecific affording pyrazole **2**. The reaction of pyrazole **2** with an additional equivalent of hydrazine leading pyrazolopyridazinone **4** (condiction *v*) and when employed reaction condiction ***ii*** the intermediate hydrazonylpyrazole **3** was isolated in the form of stereoisomers ***E*** (75%) *and* ***Z*** (25%). In addition, the compounds **3** and **4** were also obtained from the enaminodiketone **1** with two equivalent of hydrazine (condiction ***iv*** and ***vi***). Thus, was possible to obtain three differents compounds varying only the reaction condiction. The compounds were characterized by MS, ^{1}H and ^{13}C NMR Spectroscopy, HSQC and NOESY.



i) EtOH, NH_2NHR^1, r.t.; ***ii***) CH_2Cl_2, NH_2NHR^2, $BF_3.OEt_2$, r.t.; ***iii***) EtOH, AcOH, reflux; ***iv***) CH_2Cl_2, NH_2NHR^2(2 eq.), $BF_3.OEt_2$, r.t. (**4a**); ***y***) EtOH, NH_2NHR^2(2. eq.), AcOH, reflux; ***vi***) EtOH, NH_2NHR^2(2 eq.), reflux (**5a**).

Scheme 1.

CONCLUSION

In summary, the reaction of enaminodiketone **1** with phenylhydrazine was regiospecific and shown to be highly attractive for the synthesis of multifunctionalized pyrazole. Furthermore, the enaminodiketone **1** was shown to be powerful precursor for the construction of new aza-heterocyclic derivatives.

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