Synthesis of New 5-Trifluoromethyl-3-alkyl[aryl(heteroaryl)]-4-(2-benzyl-3-hydroxycyclohex-2-enone-2-yl)-1*H*-pyrazoles by a Ring-Opening Reaction

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Keywords: Fluorine-containing, Hidrazine, Pyrazoles

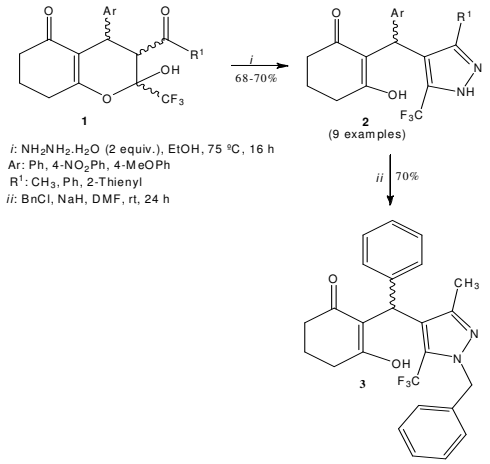
INTRODUCTION

Pyrazoles, including those containing fluorine, are a well-studied class of organic compounds that have found diverse uses in technology, medicine and agriculture.[1] Many pyrazole derivatives are known to exhibit a wide range of biological activity, of which can highlight arylpyrazoles, as Celecoxib, a cyclooxygenase-2 inhibitor.[2,3]

On the other hand, chromenones are important compounds with biological activity, as well components of natural products. Moreover, they can be use as valuable substrates for the synthesis of pharmacologically interesting compounds.[4] For instance, reaction of chromenones with 1,2-nucleophilic reagents, such as hydrazines would lead to the possible competition involving three different electrophlilic centers (acyl group at C-3, C-5 and C-8a). In the present study, we wish to report the results of the reactions of 2-hydroxy-2*H*-chromenones[5] with hydrazine.

RESULTS AND DISCUSSION

The reactions of chromenones **1** with hydrazine monohydrate (1:2) were performed under reflux of ethanol for 16 hours leading to the 5-trifluoromethyl-3-alkyl[aryl(heteroaryl)]-4-(2-benzyl-3-hydroxycyclo-hex-2-enone-2-yl)-1*H*-pyrazoles (**2**) as oil, in 68-80 % yields (Scheme 1). Subsequently, as an example of compounds **2** (Ar=Ph, R^1=CH_3), a *N*-alkylation reaction was performed using benzyl chloride as alkylating agent, in the presence of sodium hydride in DMF at room temperature for 24 hours. Compound **3** was obtained as oil in 70 % yield. All structures synthesized were characterized by NMR (^{1}H and ^{13}C) spectroscopy and GC/MS.



Sheme 1. Synthesis of new pyrazoles

CONCLUSION

In this work, the employed methodology proved to be a simple and efficient way to obtain exclusively and regioselectively new pyrazoles, despite the three distinct electrophlilic centers present in the trifluoromethylated chromenones precursor.

ACKNOWLEDGEMENTS

CNPq-CAPES-FATEC

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