New strategy for the synthesis of 4-amine-2-trifluoromethyl pyrroles *N*-substituted

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INTRODUCTION

Pyrroles are one the most important class of heterocyclic compounds that are frequently found in many natural products and bioactive molecules.[1] Furthermore, trifluoromethyl substituted pyrroles are rare compounds; however, they have been show to exhibit significant insecticidal and acaricidal activity.[2] The introduction of fluorine atoms and fluorinated groups into organic molecules often confers significant and useful changes in their chemical and physical properties.[3] Fluorinated enaminones are also very attractive synthons with high potential for the synthesis of fluorinated heterocycles.[4]

In this work, we present a versatile approach for the synthesis of a new series of 4-amine-3-trifluoromethyl pyrroles *N*-substituted from *β*-enaminones trifluoromethylate **2** with amines.

RESULTS AND DISCUSSION

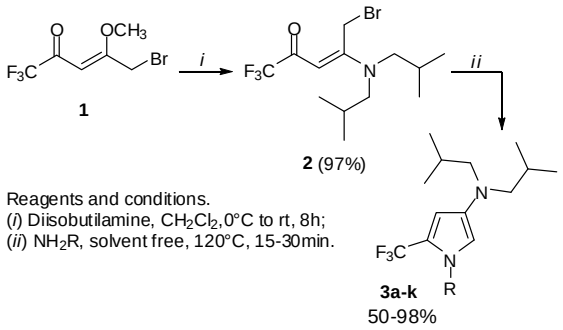
Scheme 1 presents the synthesis of pyrroles **3a-k**. Initially, diisobutilamine was added dropwise to enone **1** in CH_2Cl_2 at 0ºC to give an enaminone **2**. The primary amine is reacted with the enaminone **2** and then intramolecular cyclization occurs to form the desired pyrroles **3**. The reaction was performed with solvent free methodology using a sealed tube at 120 ° C for 15 min., only for the amine **j** the reaction time was 30 min. The reaction mixture was diluted with ethyl acetate and extracted with 3% hydrochloric acid solution (1x10 mL) and subsequently with water (2x10 mL). The organic phase was dried with anhydrous sodium sulfate and concentrated in a rotary evaporator.

In Table 1 are show the amines used and yields obtained for compounds **3a-k**.

Table 1. Optimized yields and amines used for the synthesis of compounds **3a-k**.

Product 3	Amine (NH_2R)	Yield (%)	Product 3	Amine (NH_2R)	Yield (%)
a	butylamine	93	**g**	3-fluoroaniline	90
b	allylamine	94	**h**	4-fluoroaniline	96
c	benzylamine	89	**i**	4-methoxyaniline	93
d	phenethylamine	95	**j**	4-nitroaniline	50
e	aniline	98	**k**	ethane-1,3-diamine	89
f	2-fluoroaniline	88			

Scheme 1. Synthesis of compounds **3a-k**



Reagents and conditions.
(*i*) Diisobutilamine, CH_2Cl_2,0°C to rt, 8h;
(*ii*) NH_2R, solvent free, 120°C, 15-30min.

The compounds were obtained as oil without purification. The pyrroles were analyzed by ^1H and ^{13}C NMR and GC-MS (EI).

CONCLUSION

In conclusion, we demonstrated a new method of synthesis the trifluoromethyl substituted pyrroles. The compounds were obtained in good yields through a simple procedure using a sealed tube and solvent-free.

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