Efficient Three-Step Method for 1*H*-Pyrazolinyl-*N*-Phenylglicine Derivatives

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INTRODUCTION

Secondary amines bearing a heteroaryl scaffold are well known for their applications in the chemical industry as basic intermediates to prepare fine chemicals, pharmaceuticals and agrochemicals. In addition, their remarkable biological properties confer to them an import role in the chemotherapy of a variety of diseases.[1] Pyrazole and its derivatives are compounds whose synthesis, reactivity and bioactivity as anti-inflammatory, analgesic and anesthetic have been well explored.[2] On the other hand the presence of the trifluoromethyl group (CF_3) attached to heterocycles, has provided significant changes in their chemical, physical, spectroscopic[3] and especially biological[4] properties.

Thus, the aim of this work is to report a facile and regioselective method to efficiently incorporate a *N*-phenylglicine substituent into a new series of 1,3,5,5-tetrasubstituted 4,5-dihydro-1*H*-pyrazoles **4**.

RESULTS AND DISCUSSION

Initially, aniline (**1**), anhydrous K_2CO_3 and ethyl bromoacetate were refluxed in anhydrous acetone for 6 h. The resulting ester and hydrazine were refluxed in ethanol for 8 h to obtain *N*-phenylglycine hydrazide as described in literature.[5] The cyclocondensation reactions of β-alkoxyvinil trifluoromethyl ketones **3** and **2**, in equimolar ratio, were stirred in methanol as solvent, under reflux for 16 h. The products **4** were isolated as stable brown solids in 73 – 86 % yields (**Scheme 1**). The compounds were characterized by GC – MS, ^{1}H and ^{13}C NMR spectroscopy and their purity was verified by Elemental Analyses data.

CONCLUSION

We showed a method to obtain a new series of 1,3,5,5-tetrasubstituted 4,5-dihydro-1*H*-pyrazoles **4** with introduction of a *N*-phenylglicine moiety in a three step reaction. This method regioselectively furnished **4**, as air-stable brown solid products in very good yields and high purity.

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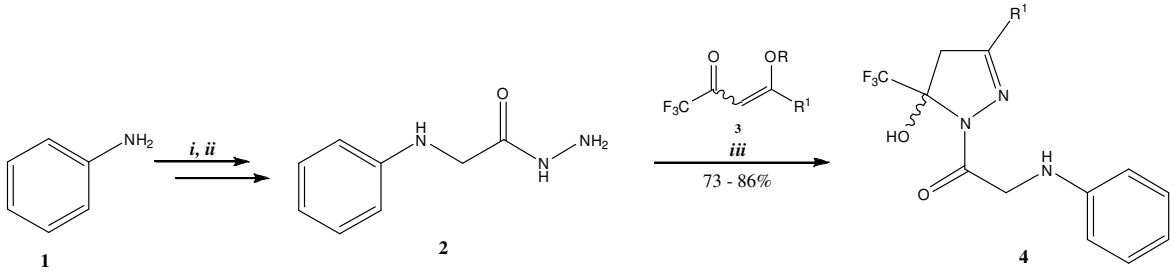

i = K_2CO_3, $BrCH_2COOC_2H_5$, anhydrous acetone, reflux, 6 h
ii = $NH_2NH_2.H_2O$, EtOH, reflux, 8 h.
iii = MeOH, reflux, 16 h; R = Me, Et; R^1 = alkyl, aryl, heteroaryl

5 Examples

Scheme 1. Synthesis of 3-Alkyl[aryl(heteroaryl)]-5-hydroxy-5-trifluoromethyl-4,5-dihydro-1*H*-1-phenylamino pyrazoles