SHORT COMMUNICATION

SYNTHESIS OF 3,5-DISUBSTITUTED-2,6-DIARYLPIPERIDIN-4-ONE HYDROCHLORIDES

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ABSTRACT

A simple and efficient condensation reaction between aliphatic carbonyl compounds having active methylene protons with aromatic aldehydes and ammonium acetate yielded the corresponding 3-alkyl or 3,5-dialkyl-2,6-diarylpiperidin-4-one, which on treatment with hydroxylamine hydrochloride yielded the corresponding oximes. All the reactions are quantitative, involves very cheap chemicals and smooth reaction conditions. So we are reporting very simple synthetic methodology for the synthesis of 3,5-disubstituted-2,6-diarylpiperidin-4-ones and their corresponding oximes.

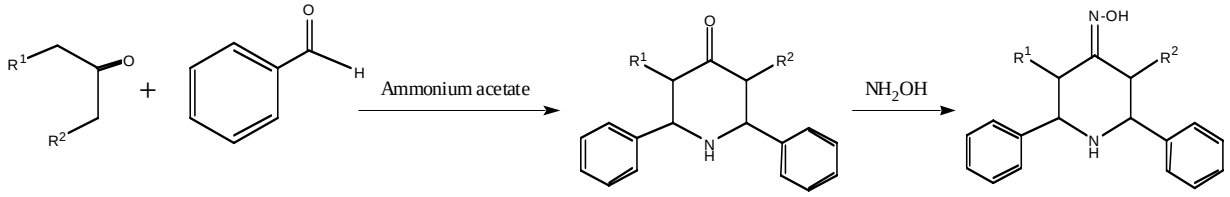
Keywords: *3,5-disubstituted-2,6-diarylpiperidin-4-ones, 3,5-dicarboxyethyl-2,6-dimethyl-4-(2-furyl)-1,4-dihydropyridine.*

INTRODUCTION

Several 2,6-disubstitutedpeperidine heterocyclic molecules have been found to possess useful biological activities such as herbicidal, insecticidal, fungicidal, bactericidal, anti-inflammatory, depressant and nerved activities[1,2,3,4]. And the alkaloid secodihydrocastoramine isolated from the roots of N.Japonicum has a furan substituent in the 2-position[5].

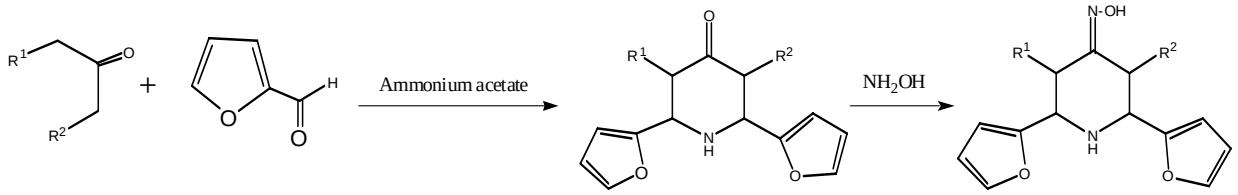
Scheme-1

Though several reports of using benzaldehyde as aromatic aldehyde in the synthesis of 2,6-diarylpiperidin-4-ones (Scheme-1) and their derivatives, very few studies[6,7] have been made on the preparation and stereochemistry of piperidinones with varying ring size at 2nd and 6th positions.(Scheme-2). The present investigation was focused on the synthesis of piperidinones in which five membered furan rings was incorporated at both 2 & 6th positions.



Scheme-2

Condensation reaction of 2-butanone with furfuraldehyde and ammonium acetate yielded 3-methyl-2,6-di-2'-furylpeperidin-4-one hydrochlorides **1,2,3** and when treated with hydroxylamine hydrochloride these piperidin-4-ones gave corresponding oximes **4, 5, 6**.(Scheme-3). However ethyl acetate yielded an unexpected product instead of 3-carboxyethyl-2,6-di-furylpiperidin-4-one **7**, we got 3,5-dicarboxyethyl-2,6-dimethyl-4-(2-furyl)-1,4-dihydropyridine **8**.



R^1	R^2		R^1	R^2
1. CH_3	H	4.	CH_3	H
2. C_2H_5	H	5.	C_2H_5	H
3. CH_3	CH_3	6.	CH_3	CH_3

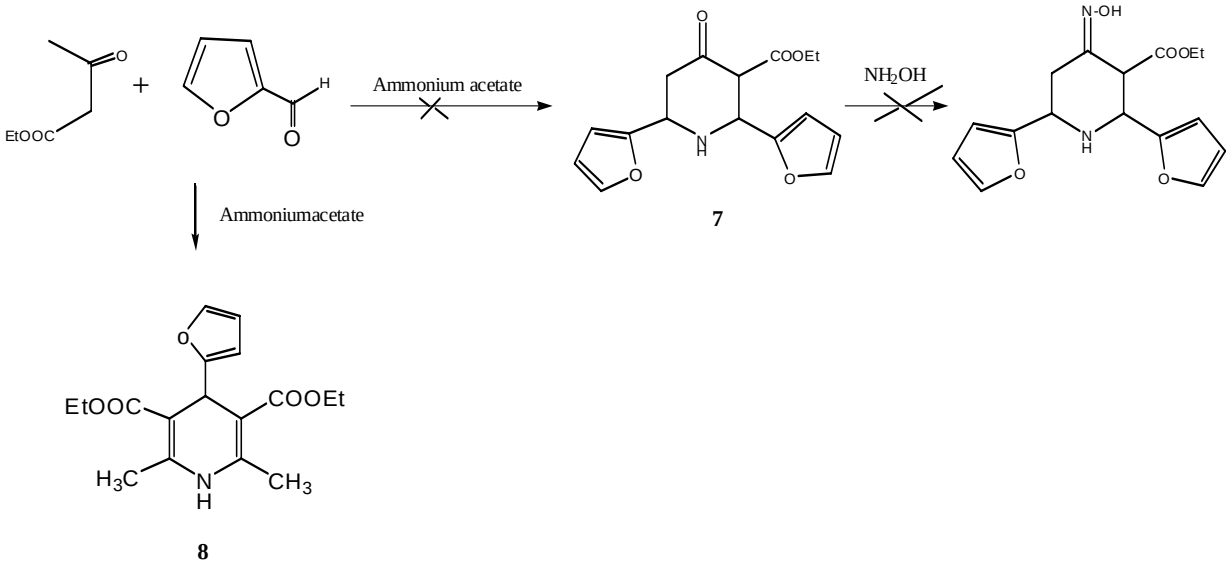
Scheme-3

RESULTS AND DISCUSSION

Synthesis of 2,6-diarylpiperidin-4-one was earlier reported by baliah[8] et al. A mixture of ammonium acetate (0.5 mol.), furfuraldehyde (1mol.) and butanone(0.5 mol.) in distilled ethanol was heated to boiling. After cooling, the viscous liquid obtained was dissolved in diethylether(200ml.) and shaken with 10ml. of conc. Hydrochloric acid. The precipitated hydrochloride of 3-methyl-2,6-di-2'-furylpiperidin-4-one hydrochloride was removed by filtration and washed with 40ml. mixture of ethanol and diethylether(1:1) , followed by diethylether to remove most of the impurities and then was crystallized from warm water yielded 82% of the required product. Which was decomposed above 221^{O}C (Scheme-4).

The condensation reaction of 2-butanone with benzaldehyde and ammonium acetate yielded the corresponding 3-methyl-2,6-diphenylpiperidin-4-one. Similar reaction with pent-2-one yielded the corresponding 3-ethyl-2,6-diphenylpiperidin-4-one in quantitative yield. Similar reaction of 3-pentanone with benzaldehyde and ammonium acetate yielded the corresponding 3,5-dimethyl-2,6-diphenylpiperidin-4-one[8]. The ketones thus obtained were treated with hydroxylamine hydrochloride yielded the corresponding oximes. Same reaction when did with furfuraldehyde, yielded 3-methyl-2,6-di-2'-furylpiperidin-4-one hydrochloride, which on reacting with hydroxylamine hydrochloride gave corresponding oxime. But when ethylacetoacetate was reacted with furfuraldhyde and ammoniumacetate did not yield the expected product 7, instead of 7 the product formed was assigned as 8 depending upon its spectral and analytical data. The

spectral and analytical data are in agreement with the reported in the literature[9].



Scheme - 4

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