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بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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بالرسالة صفحات لم ترد بالاصل

A Thesis Entitled

Synthesis and chemical reactivity of polyfunctionally substituted pyridazines and pyridazines containing hydroxy substituents

Submitted for Ph.D. Degree
(Organic Chemistry)
By

Miead Adel Nasra

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2009

Abstract

Name: Miead Adel Nasra

Title of thesis: Synthesis and chemical reactivity of polyfunctionally substituted pyridazines and pyridazines containing hydroxy substituents.

Degree (Ph.D.) thesis, Faculty of Science, Cairo University, 2009.

Abstract

In the first part of this thesis, 2-Arylhydrazonals were used as aldehyde components in Baylis-Hillman reaction. 2-Arylhydrazonals reacted with acrylonitrile to yield 1,6-dihydropyridazine-4-carbonitrile derivatives and with cyclohexenone to yield tetrahydrocinnoline derivatives.

In the second part of this thesis novel azaenamines incorporated tetrahyderothiophene were prepared. Michael addition reaction of azaenamine with α, β-unsaturated nitriles, took place and led to thia-triaza-benzo[*a*]fluorine derivatives. The condensation with malononitrile resulted in the formation of 11-thia-1,5,11b-triaza-benzo[a]fluorene-4-carbonitrile. Azaenamines reacted also with aldehydes and piperidine to give Mannich products.

In the appendix (third part), a novel route to the three-component Biginelli-like cyclocondensation reaction of enamines, urea and aldehydes in dioxan-acetic acid efficiently afforded the corresponding 4-unsubstituted 3,4-dihydropyrimidin-2-(1H)-ones in moderate yields. The reaction of azaenamines with aldehydes and urea afforded 6-acetyl-1,2,4-triazin-3-one in moderate yields.

Keywords: 2-Arylhydrazonals, Baylis-Hillman, dihydropyridazine, tetrahydrocinnoline, azaenamine, Michael addition, Mannich adduct, enamines Biginelli-like reaction, 5-Aroyl pyrimidine-2-ones.

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Contents

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List of abbreviations

- DMFDMA — Dimethylformamide dimethylacetal
- DMF — Dimethylformamide
- DABCO — diazabicyclo[2.2.2]octane
- DHPMs — 3,4-dihydropyrimidin-2-(1H)-ones
- IR — Infrared Spectroscopy
- MS — Mass Spectroscopy
- MW — Microwave
- NMR — Nuclear Magnetic Resonance Spectroscopy
- DMSO — Dimethylsulphoxide

Aim of the work

Derivatives of arylhydrazonal, pyridazine and dihydropyrimidinones have attracted considerable interest due to their wide spectrum of pharmacological and therapeutic activities.

In view of the biological importance of such classes of compounds we aimed to investigate chaper and simpler routs, in addition to the synthesis of new related compounds as shown in the following:

I) - Investigate the possible utility of 2-arylhydrazonals as aldehyde components in Baylis-Hillman reaction

II- a) Synthesize new azaenamines and studying their utility for preparation of new heterocycles by thermal and / or microwave heating.

b) Comparing the percent yield of conventional and microwave heating.

c) Investigate the possible Michael addition reaction of the synthesized azaenamines with α,β-unsaturated nitriles.

d) Study the reactivity of azaenamines towards active methylenes and Mannich reaction.

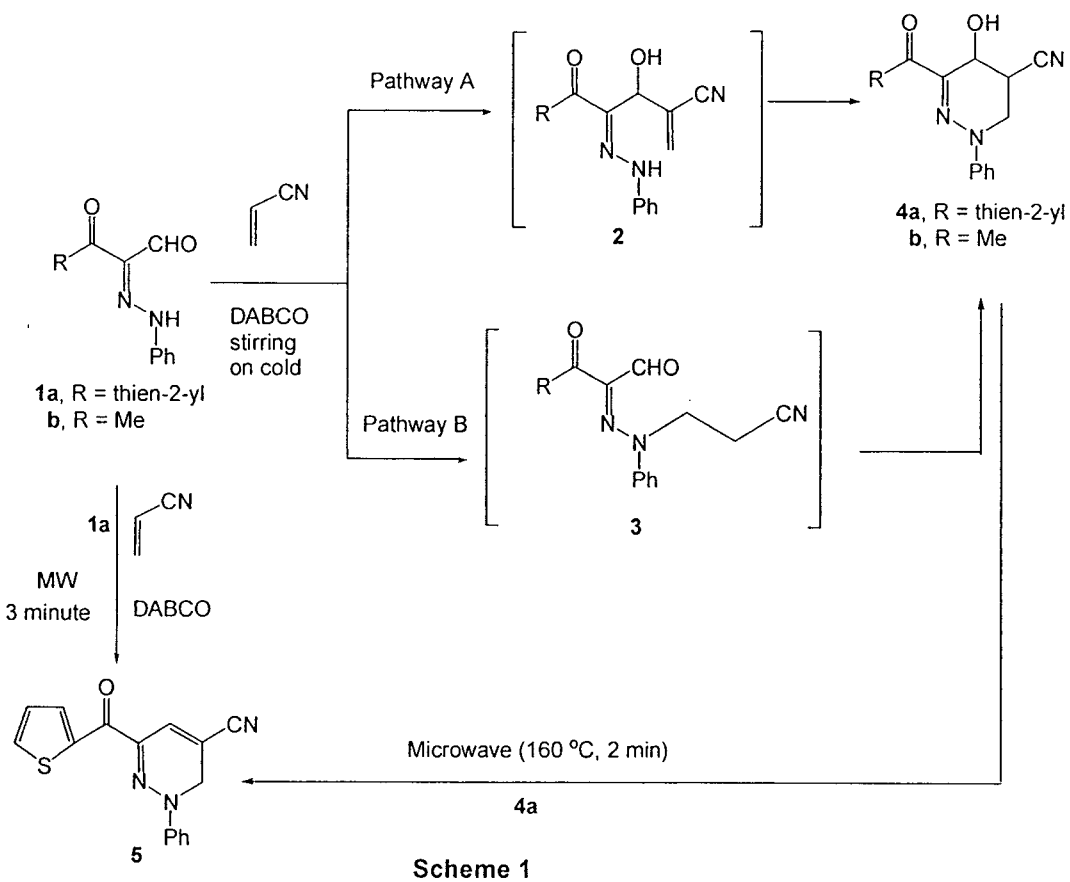
III) - Examine the utility of enamines as substitutes to β-ketoesters in the Biginelli-like three-component cyclocondensation reactions.

Summary of the original Work

Summary of the first part

Arylhydrazonals as aldehyde components in Baylis-Hillman reaction: Synthesis of 5-hydroxy-2, 3, 4, 5-tetrahydropyridazine-4-carbonitrile and 6, 7, 8, 8a-tetrahydrocinnolin-5(1*H*)-one

The reaction of 3-oxo-2-phenylhydrazono-2-yl-propionaldehydes **1a,b** with acrylonitrile in presence of DABCO (1,4-diazabicyclo[2.2.2] octane) as a catalyst and dioxane as a solvent, resulted in the formation of compound **4** which could be formed through the Baylis-Hillman intermediate **2** (*Pathway A*) (cf. scheme 1). Compound **4** can be also formed *via* intermediate **3** that results most likely *via* initial addition of the hydrazone NH to the electrophilic double bond in acrylonitrile followed by normal aldol condensation (*Pathway B*) (cf. scheme 1).



Scheme 1