STUDIES ON SOME HETEROCYCLIC COMPOUNDS

A Thesis

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M.Sc. Degree in Chemistry

Presented By

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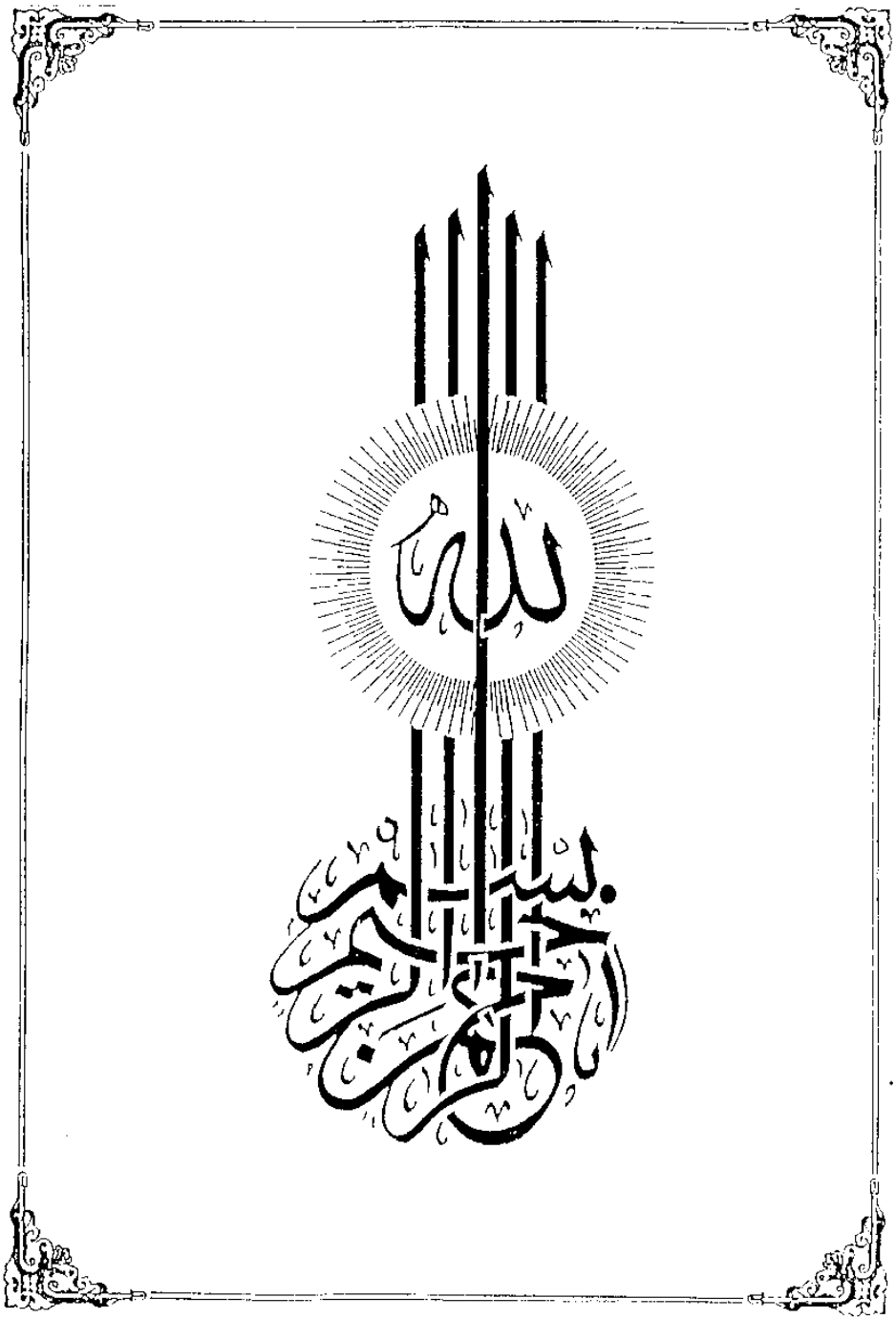

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POST GRADUATE STUDIES FOR M.Sc.STUDENT IN ORGANIC CHEMISTRY (87-88)

This is to certify that ***Sayed Manssour Ahmed Farahat*** *has attended passed successfully the following postgraduate courses as partial fulfilment for the Degree of Master of Science.*

1- Advanced studies in physical organic chemistry :

i) Polar reaction mechanism

ii) Pericyclic reaction mechanism

2 - Advanced studies in heterocyclic chemistry

3- Advanced studies in applied spectroscopy analysis.

Electronic spectra, Infrared, H^1NMR, C^{13}-NMR and mass spectroscopy of organic chemistry.

4- Advanced studies in natural products.

5- Advanced studies in microanalysis.

6- Advanced studies in organometallic compounds.

7- Advanced studies in photochemistry.

8- Advanced studies in thermodynamics.

9- Advanced studies in kinetics.

10- Advanced studies in quantum chemistry.

11- German language course.

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بسم الله الرحمن الرحيم

وَقُل رَّبِّ زِدْنِي عِلْماً

(سورة طه آية ١١٤)

SUMMARY

Summary

The present investigation deals with the synthesis of some new benzoxazinone and quinazolinone derivatives bearing a bulky moiety at position - 2 , in order to find out a role for the heterocyclic 2 - moiety, on the stability of benzoxazinone nucleus and its reactivity towards some nucleophilic and electrophilic reagents .

The hitherto unknown 2- (β - benzamido - 3′,4′,5′- trimethoxy styryl) - 3,1- benzoxazin - 4 (H) - one (3) was prepared by reaction of oxazolone derivative (1) with anthranilic acid in the presence of acetic acid to afford N- (α - benzamido - 3′,4′,5′- trimethoxy cinnamoyl) anthranilic acid (2) which cyclized under the influence of acetic anhydride to give (3) .

Reaction of 3 (in presence of n-butanol or pyridine) with hydrazine hydrate and/or hydroxylamine hydrochloride afforded 4- (3′,4′,5′- trimethoxy benzylidene) - 1,4- dihydro -2- phenyl - 1,2,4 -triazino [3,2-b] quinazolin - 10 (H) - one (4) and 2 - (β - benzamido 3′,4′,5′- trimethoxy styryl) -3- hydroxyquinazolin - 4 (H) - one (5) which recyclized in acetic anhydride to yield 4- (3′,4′,5′- trimethoxy benzylidene) - 2 - phenyl - 1,2,5 oxadiazino [3,2-b] quinazolin - 10 (H)-one (6), respectively.

Treatment of 3 with semicarbazide hydrochloride in presence of fused sod. acetate/ acetone gave 2 - (β - benzamido- 3′,4′,5′- trimethoxy styryl) -3- urido - quinazolin -4 (H)- one (7) and 8,9- benzo-6H - 6 - arylidene - 4- phenyl - 1,3,5,7 tetrazacyclazine - 2 (H) - one (8), while reaction of 3 with thiosemicarbazide, guanidine hydrochloride, formamide, benzidine, o-phenylene diamine and/or N- (α - naphthyl) ethylene diamine hydrochlorid (in presence of boiling alcohol or pyridine or on fusion) yielded (9) , 2 - (β - benzamido - 3′,4′,5′- trimethoxy styryl) - quinazolin - 4 (H) - one

(10), 1H-1- (3',4',5'- trimethoxy benzylidene) -3- phenylimidazolo [4,3-b] quinazolin - 5 (H) - one (11) , 2 - [N - (α-benzamido-3',4',5'- trimethoxy cinnamoyl) amino -N- (p -aminophenyl) benzamide (12 , 13) , 2 - (β - benzamido - 3',4',5'- trimethoxy styryl) -benzimidazolo [3,2 - c] quinazoline (14) and 2- (β - benzamido - 3',4',5'- trimethoxy styryl) - 3 - β - (naphthylaminoethyl) - quinazolin - 4(H) - one (15), respectively .

On the other hand, fusion of 3 with sulphamidie compounds, namely, sulphanilamide, sulphathiazole, sulphaguanidine, sulphamezathine and / or sulphamethoxazole, furnished. 2- (β - benzamido - 3',4',5'- trimethoxy styryl) - 3 - (p- N - alkylamino sulphonylphenyl) - quinazolin - 4 (H) - ones (16 a - e), respectively.

Ring opening of 3 with hydrazoic acid, gave the tetrazole derivative (17), whereas, under Friedel - Craft's conditions , (3) afforded 2 - [N- (α - benzamido - 3',4',5'- trimethoxy cinnamoyl] - aminoarylophenone (18 a - b), upon treatment with benzene and / or toluene, respectively .

Action of $P_2 S_5$ upon (3) in boiling dry xylene was also studied and found to yield 2- (β-benzamido - 3',4',5'- trimethoxy styryl] - 3,1- benzothiazin - 4 (H)- thione (19).

By studing the reaction of 3 with active methylene compounds, namely diethyl malonate, and / or ethyl cyanoacetate (in presenc of a base), it was found that the product was [N - (α - benzamido - 3',4',5'- trimethoxy cinnamoyl] - amino - benzoyl acetate (20) .

Structural assignment of the products was substantiated from their analytical data as well as their IR and H^1- NMR spectroscopy .

Acknowledgement

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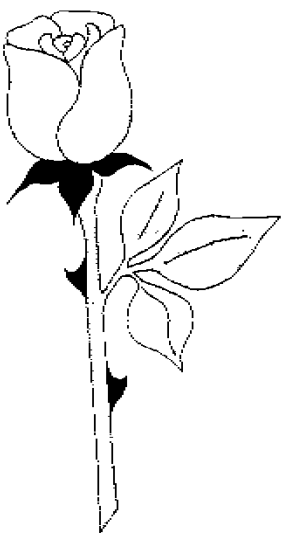
TO MY FAMILY



CONTENTS

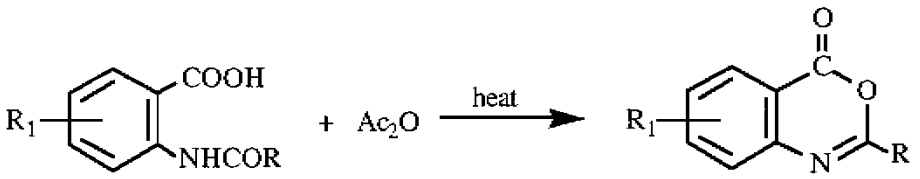
INTRODUCTION

BENZOXAZINONES

Synthesis of 3,1-Benzoxazin-4-ones :

(i) Via cyclization of N-acylanthranilic acids :

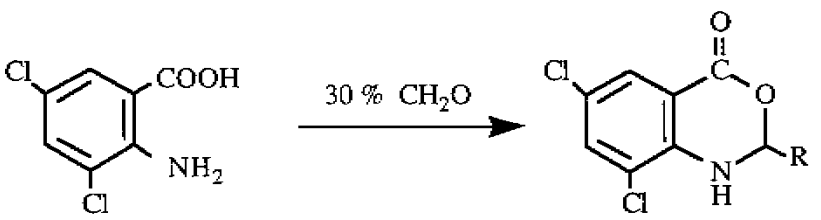
2-Substituted-3,1(4H)-benzoxazinones (I) have been obtained by heating the corresponding N-acylanthranilic acid with acetic anhydride[1-25]



(I)

(ii) Via condensation of anthranilic acid derivatives with formaldehyde :

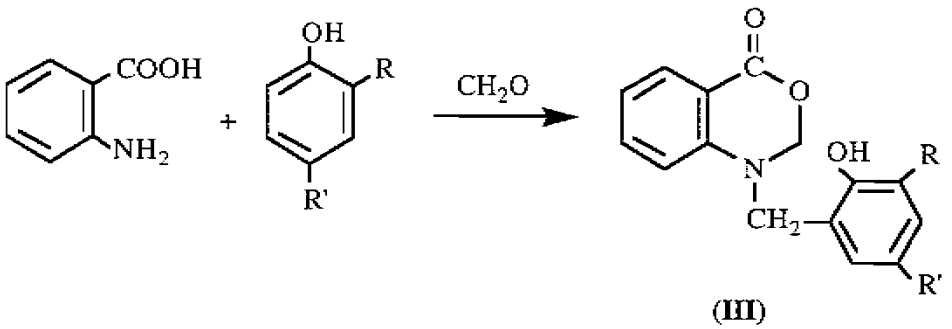
Villiger [26] *condensed a number of chloro-derivatives of anthranilic acid with formaldehyde to obtain 1,2 -dihydro - 3,1 - benzoxazin -4- ones (II)* [27].



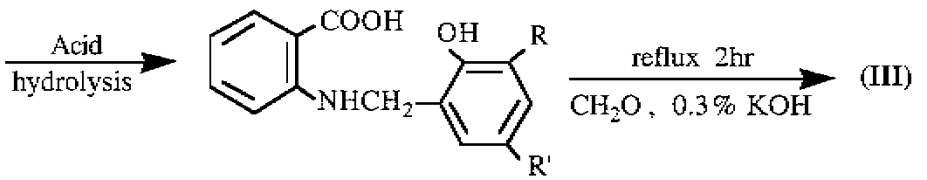
(II)

Mannich reaction of 2,4-disubstituted phenols with HCHO and anthranilic acid gave the corresponding benzoxazinones (III) which on acid hydrolysis gave Mannich type products.

The reaction mechanism discussed in terms of electrophilic addition [28] as the following :



(III)



Mannich product

(iii) Via the action of alcoholic potassium hydroxide solution on 2 - alkyl - 3,1 - benzothiazin - 4 - thiones :

A number of 2-substituted benzoxazinones were prepared from 2-alkyl -3,1-benzothiazine -4- thiones (IV) on boiling with alcoholic potassium hydroxide solution and heating the unstable (V) with acetic acid [29].