SOME REACTIONS WITH PYRIDAZINE DERIVATIVES

A THESIS

PRESENTED BY

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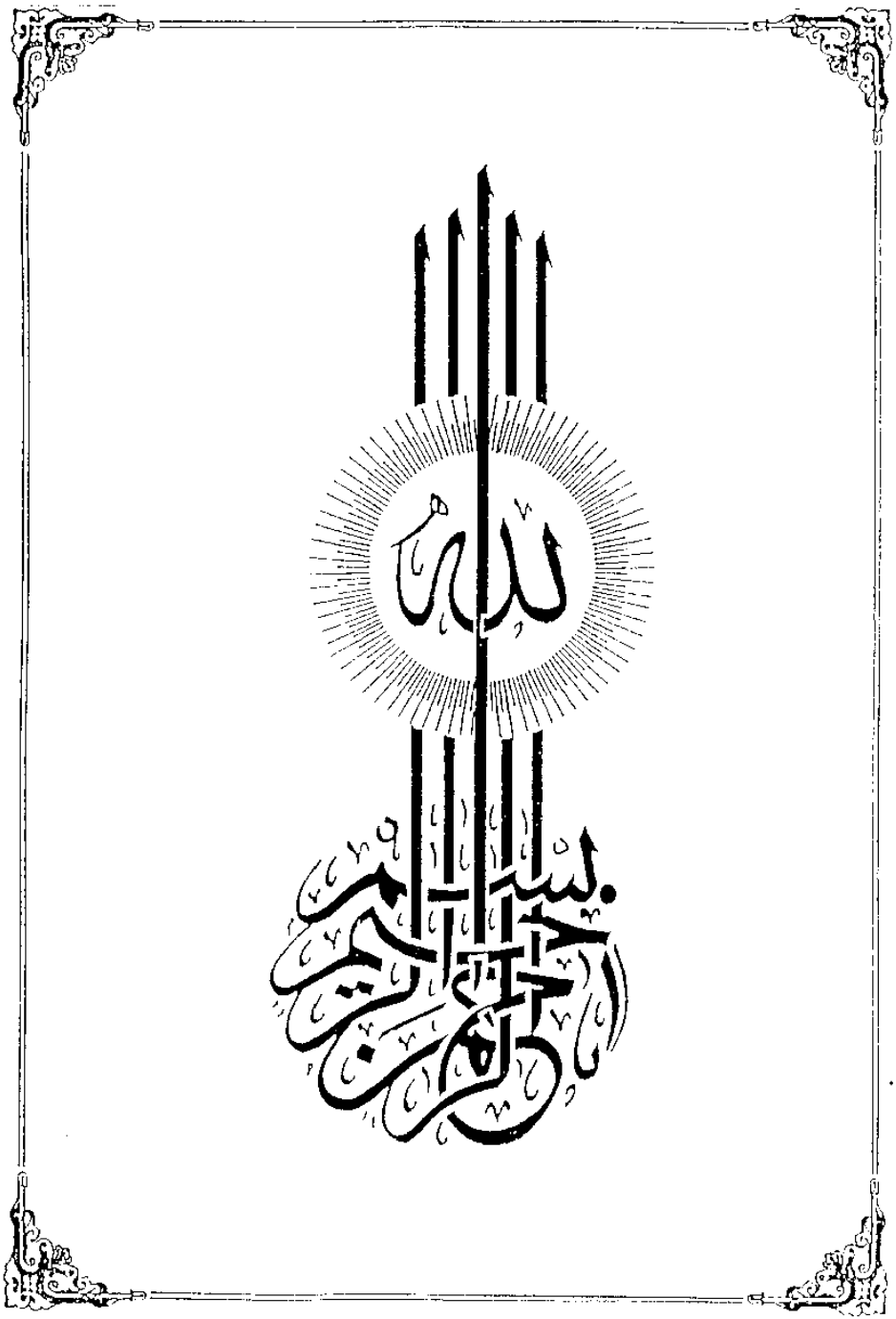

TO

MY PARANTS, MY WIFE

AND MY SON

ACKNOWLEDGEMENT

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VITAE

Mohamed Abd El-Megid Abd El-Hamid Mohamed was born in Dokki, Giza, Egypt on the nineteenth of November, 1958. He has attended the Orman Secondary School in 1973 and has got the secondary school certificate in 1976. He was then enrolled in the Faculty of Education, Ain Shams University, where he has received the degree of Bachelor of Science and Education in the year 1980. He has also received the degree of Bachelor of Science (Chemistry) from the Faculty of Science, Ain Shams University in 1984.

In 1986, he has registered for the degree of M.Sc. in Organic Chemistry under the supervision of Prof. Dr. H. Jahine, Dr. M. Seada, Ass. Prof. and Dr. M. Fawzy, Lecturer, Chemistry Department, Faculty of Education, Ain Shams University.

NOTE

Besides the work carried out in this thesis, the candidate has attended post-graduate courses for one year in Organic Chemistry including the following topics:

(1) Physico-organic Chemistry.

(2) Infrared, U.V., N.M.R. and Mass Spectroscopy for Organic Molecules.

(3) Free Radical Reactions.

(4) Frontier Orbital Theory.

(5) Organic Reactions.

(6) Heterocyclic Chemistry.

(7) Quantum Mechanics.

(8) Conformational Analysis.

(9) Polymer Chemistry.

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CONTENTS

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SUMMARY OF

THE ORIGINAL WORK

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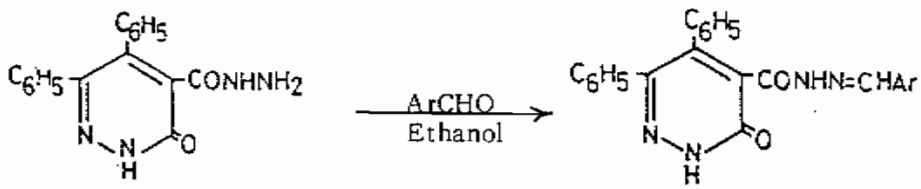
Thiazolidinone, pyrimidinedione and oxadiazoline derivatives are well known biological active compounds. In view of the varied physiological activities of these compounds, the present investigation deals with the synthesis of some pyridazine derivatives having thiazolidinone, pyrimidinedione and oxadiazoline nuclei and studying their antibacterial and antifungal activities.

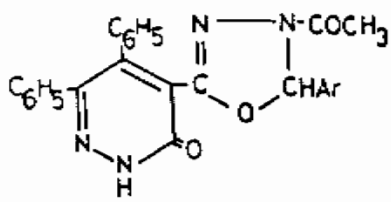
The condensation of 4-carboxyhydrazide-5,6-diphenyl-3(2H)-pyridazinone (I) with aromatic aldehydes gave the corresponding arylidenehydrazide (IIa-c).



(I) (II)

a, Ar = C_6H_5
b, Ar = C_6H_4Cl-p
c, Ar = $C_6H_4OCH_3$-p

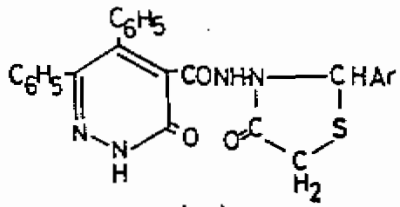
Arylidenehydrazides (IIa-c) underwent cyclization when refluxed with acetic anhydride yielding the respective oxadiazolines (IIIa-c).



(III)

a, Ar = C_6H_5
b, Ar = C_6H_4Cl-p
c, Ar = $C_6H_4OCH_3$-p

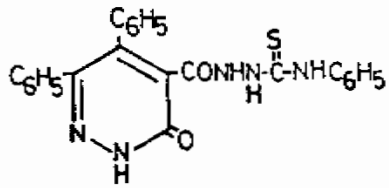
2-Phenyl-3-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-4-thiazolidinone (IVa) and 2-(p-chlorophenyl)-3-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-4-thiazolidinone (IVb) have been prepared by cycloaddition of thioglycollic acid with IIa and IIb, respectively.



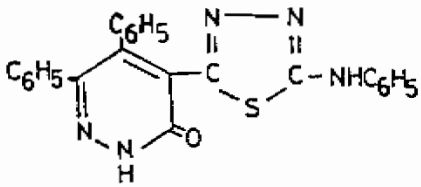
(IV)

a, Ar = C_6H_5
b, Ar = C_6H_4Cl-p

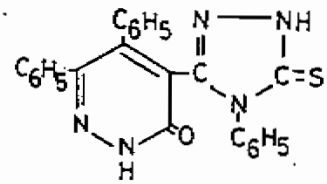
The condensation of I with phenyl isothiocyanate in absolute ethanol afforded 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-4-phenyl-3-thiosemicarbazide (V), which underwent cyclization in conc. H_2SO_4 giving 2-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-yl]-5-phenylamino-1,3,4-thiadiazole (VI), whereas, cyclization of V with alkali gave 4-phenyl-5-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-yl]-1,2,4-triazoline-3-thione (VII).



(V)

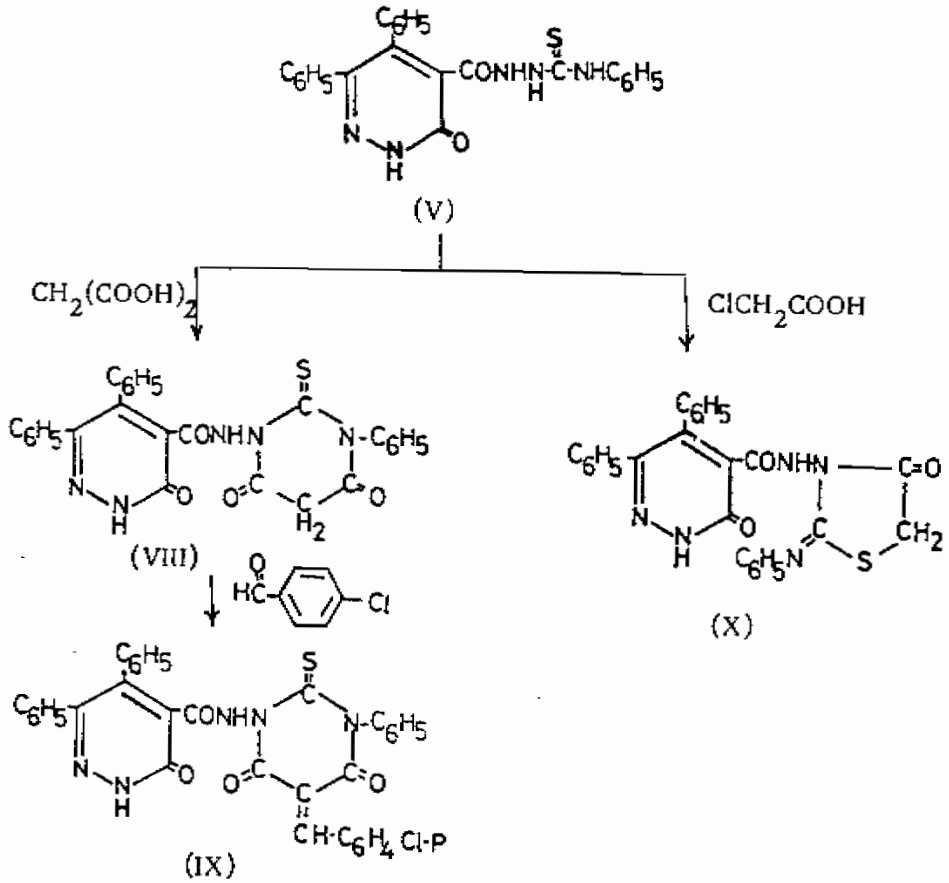


(VI)



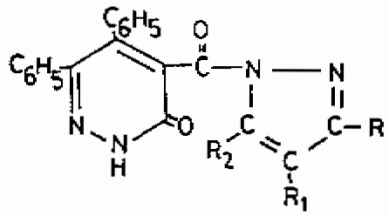
(VII)

Treatment of 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-4-phenyl-3-thiosemicarbazide (V) with malonic acid and acetyl chloride gave 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-3-phenyl-2,3-dihydro-2-thioxo-4,6 (1H,5H)-pyrimidinedione (VIII), which underwent condensation with p-chlorobenzaldehyde in the presence of sodium acetate and acetic acid yielding 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-3-phenyl-5-(p-chlorobenzylidene)-2,3-dihydro-2-thioxo-4,6 (1H,5H)-pyrimidinedione (IX). X was synthesized from V by the action of monochloroacetic acid and sodium acetate.



Condensation of I with β-dicarbonyl compounds, namely acetylacetone and benzoylacetone gave 1-[5',6'-diphenyl-3'(2H)oxopyridazin-4-ylcarbonyl]-3,5-dimethylpyrazole (XIa) and 1-(5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-5-methyl-3-phenylpyrazole (XIb), respectively.

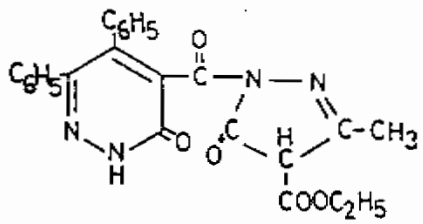
On the other hand, I reacted with ethoxymethylenecyanoacetate in ethanol to give 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-5-amino-4-carbethoxypyrazole (XIc).



(XI)

a, R = R_2 = CH_3; R_1 = H
b, R = C_6H_5; R_1 = H; R_2 = CH_3
c, R = H; R_1 = $COOC_2H_5$; R_2 = NH_2

I on refluxing with a mixture of acetic anhydride and ethyl cyanoacetate afforded 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-4-carbethoxy-3-methylpyrazole-5(4H)-one (XII).



(XII)

Acylation of 4-carboxyhydrazide-5,6-diphenyl-3(2H)-pyridazinone (I) with different acylating agents, namely acetic anhydride, phthalic anhydride and benzoyl chloride gave the acyl derivatives XIII, XIV and XV respectively.