SOME STUDIES ON HETEROCYCLIC COMPOUNDS CONTAINING NITROGEN

A Thesis

Submitted in Partial Fulfilment of the Requirements

of M.Sc. Degree in Chemistry

Presented By

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B.Sc. (Excellent)

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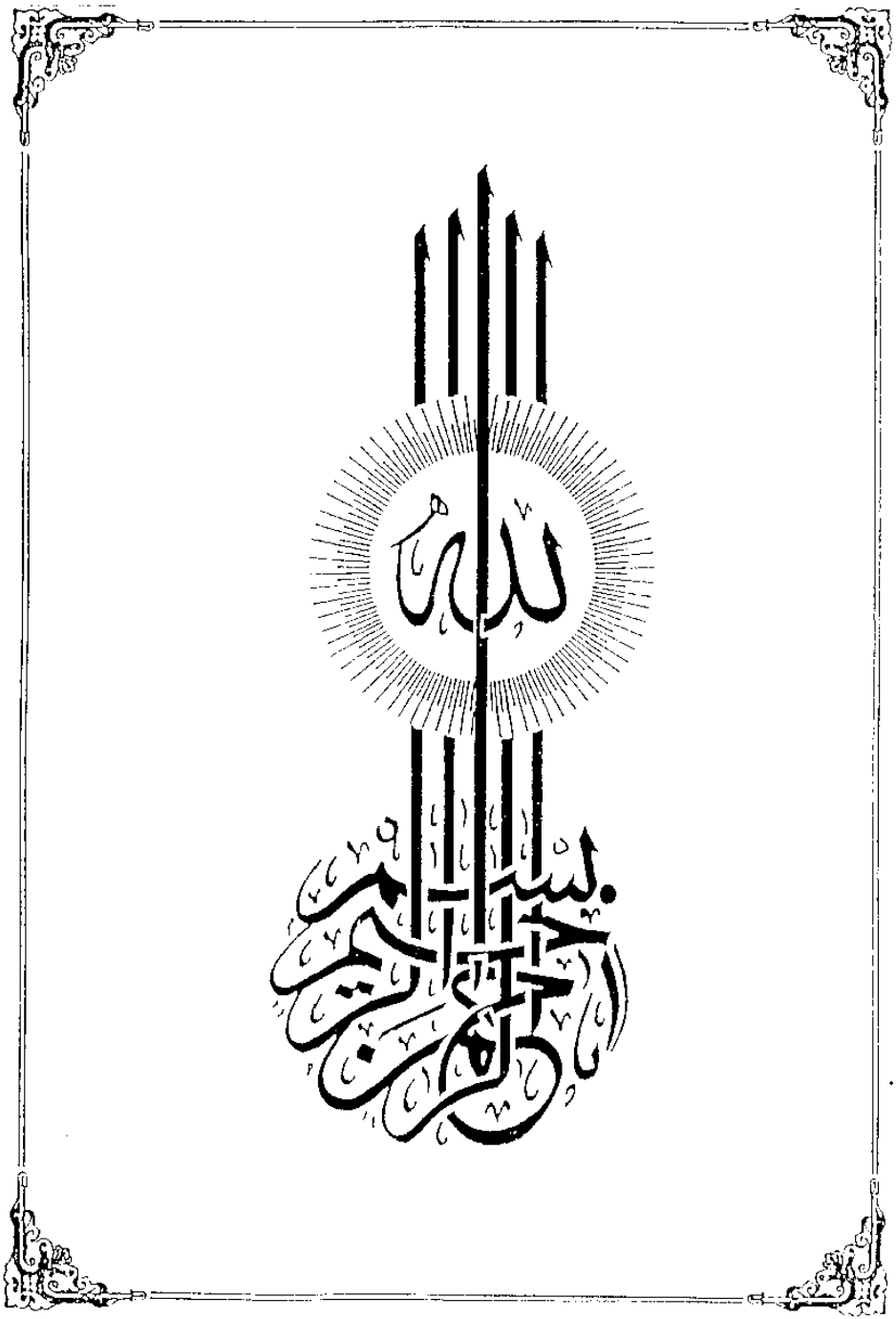
1992

بسم الله الرحمن الرحيم

وعلمك ما لم تكن تعلم

وكان فضل الله عليك عظيماً

" صدق الله العظيم "



وقل رب زدنى علما

صدق الله العظيم

SOME STUDIES ON HETEROCYCLIC COMPOUNDS CONTAINING NITROGEN

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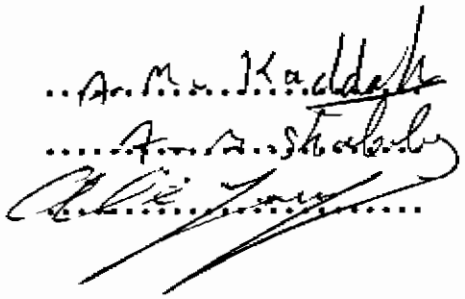

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AIN SHAMS UNIVERSITY
FACULTY OF SCIENCE
CHEMISTRY DEPARTMENT

POST GRADUATE STUDIES FOR M.Sc. STUDENT IN ORGANIC CHEMISTRY (89 - 90)

This is to certify that *Wael Abdel Fattah Youssef* has attended passed successfully the following postgraduate courses as partial fulfilment of the requirements for the Degree of Master of Science.

1- Advanced studies in physical organic chemistry:
   i) Polar reaction mechanism.
   ii) Pericyclic reaction mechanism.
2- Advnaced studies in heterocyclic chemistry.
3- Advanced studies in applied spectroscopic analysis.
   Electronic spectra, Infrared, N.M.R., ^{13}C and Mass spectroscopy of organic compounds.
4- Advanced studies in natural products.
5- Advanced studies in microanalysis.
6- Advanced studies in polymers chemistry.
7- Advanced studies in aromaticity.
8- Advanced studies in organic reagents.
9- Advanced studies in organometallic compounds.
10- Advanced studies in photochemistry.
11- Advanced studies in freeradical reaction mechanism.

12- Selected topics in organic reactions.

13- Courses English Language.

Prof. Dr. Nabila M. Guindy

Head of Chemistry Department
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CONTENTS

SUMMARY

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In the present work the follwoing subjects are investigated:

1- *Synthesis of 4-arylmethyl-6-phenyl (III a-b) and 6-p-phenoxyphenyl (III c-g) pyridazin -3(2H)-ones and their 3-chloro dervivatives (IV a-f)*

2- *Synthesis of 8-arylmethyl-3-phenyl-6-p-phenoxyphenyl-1,2,4-triazolo [4,3 - b] pyridazines (VII a & b)*

3- *Oxidation of 6-aryl-4-arylmethylpyridazin-3- (2H)-ones.*

4- *Synthesis of 4-aroyl-6-aryl-3-chloropyridazines (X a - g) and hydrazinolysis of 4-aroyl-3-chloro-6-phenylpyridazines.*

5- *Synthesis of aryl-4(6-P-phenoxyphenyl-2,3-dihydro-3-oxo) pyridazinyl oximes (XIV a-c) and silylation of the oximes (XIV b & c).*

1- Synthesis of 6-aryl-4-arylmethylpyridazin-3(2H)-ones (III a - g) and their 3-chloro derivatives (IV a - f):

Treating 4H, 5H-6-arylpyridazin-3(2H)-ones (II a & b) with aromatic aldehydes in basic medium gave the corresponding 4-arylmethylpyridazin-3 (2H)-ones (III a - g). The structure of the products was confirmed by elemental analysis and i.r. spectra. Reaction of (III a - g) with phosphorus oxychloride gave the corresponding 3-chloro derivatives (IV a - f). The structure of the products was exclusively confirmed by analytica data and i.r. spectra.

2- The action of benzoylhydrazine on compounds (IV c, d and e) for 48 hours afforded the triazolopyridazines (VII a & b) due to intramolecular cyclisation but for 12 hours the benzoylhydrazino derivatives (VIII a - c) were isolated. Prolonged heating of (VIII a - c) no triazolo derivative could be isolated in each case.

3- Oxidation of 6-aryl-4-arylmethylpyridazin-3 (2H)-ones (III a - g) with chromium trioxide in acetic acid gave 4-aroyl-6-arylpyridazin -3 (2H)-ones (IX a - g) in fairly good yields. The structure of these products was substantiated, other than elemental analysis by their i.r. spectra.

4- The reaction of 4-aroyl-6-arylpyridazin-3 (2H)-ones (IX a - g) with phosphorus oxychloride, yields 4-aroyl-6-aryl-3-chloropyridazines (X a - g). Hydrazinolysis of (X a - d) in excess hydrazine affords in each case one product, the structure of which was proved to be 1H-3-aryl-5-phenylpyrazolo [3,4-c] pyridazines (XIII a - d). The structure of compounds (X a - g) and (XIII a - d) was confirmed by elemental analysis and i.r. spectra.

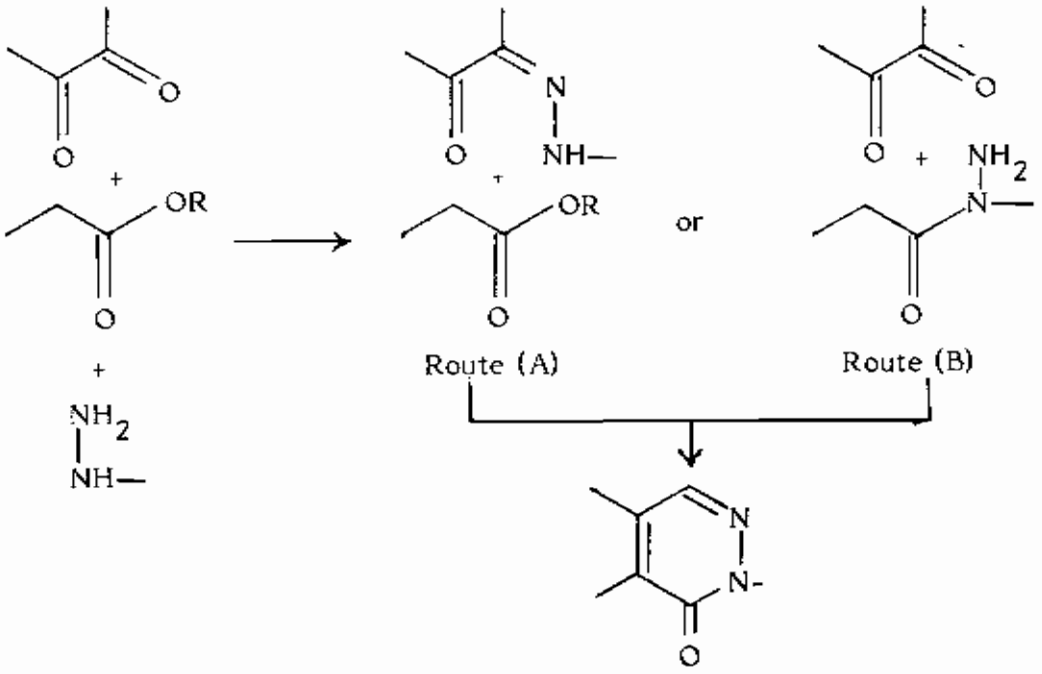
5- Treating of 4-aroyl-6-p-phenoxyphenylpyridazin -3 (2H)-ones (IX e, f and g) with hydroxylamine hydrochloride in aquous-ethanol mixture gave aryl-4 (6-p-phenoxyphenyl-2,3-dihydro-3-oxo) pyridazinyl oximes (XIV a - c). Silylation of (XIV b and c) with dimethyldichlorosilane in pyridine gave the corresponding dimethylsilyl dervatives (XVI a & b). The structure of the products (XIV) and (XVI) was substantiated from elemental analysis and their i.r. spectra.

CHEMISTRY OF PYRIDAZIN-3(2H)-ONES AND HALOPYRIDAZINES

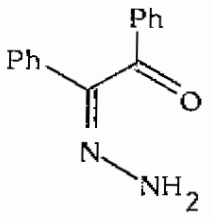
SYNTHETIC METHODS OF PYRIDAZIN-3(2H)-ONES

I- From α-dicarbonyl monohydrazones (azaenaminones) and active methylene containing compounds or from acid hydrazides and α-dicarbonyl compounds :-

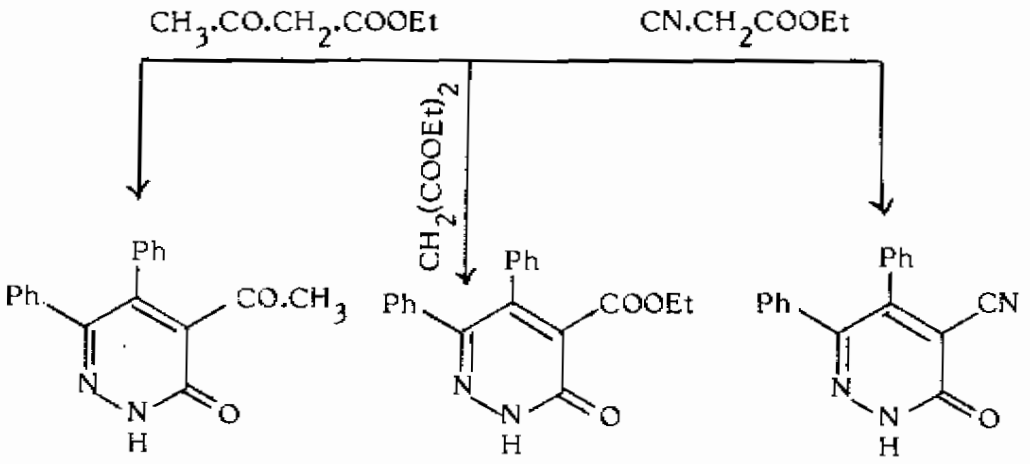
This standard synthesis of pyridazin-3(2H)-ones has been applied to the preparation of many derivatives[1-3]. The synthesis could be represented simply by the following scheme :



The most important example for route (A) is the reaction of benzil monohydrazone (1) with either ethyl acetoacetate, diethyl malonate or ethyl cyanoacetate to give 5,6-diphenyl-4-acetyl (2), 4-carbethoxy (3) and 4-cyano-(4)-pyridazin-3(2H)-one, respectively.

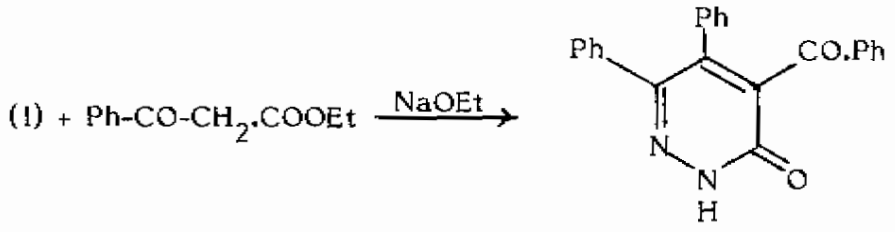


(1)



(2) (3) (4)

Recently, N. Shams et al[4] reported that the reaction of benzil monohydrazone (1) with benzoyl ethylacetate yields 4-benzoyl-5,6-diphenylpyridazin-3(2H)-one (5).

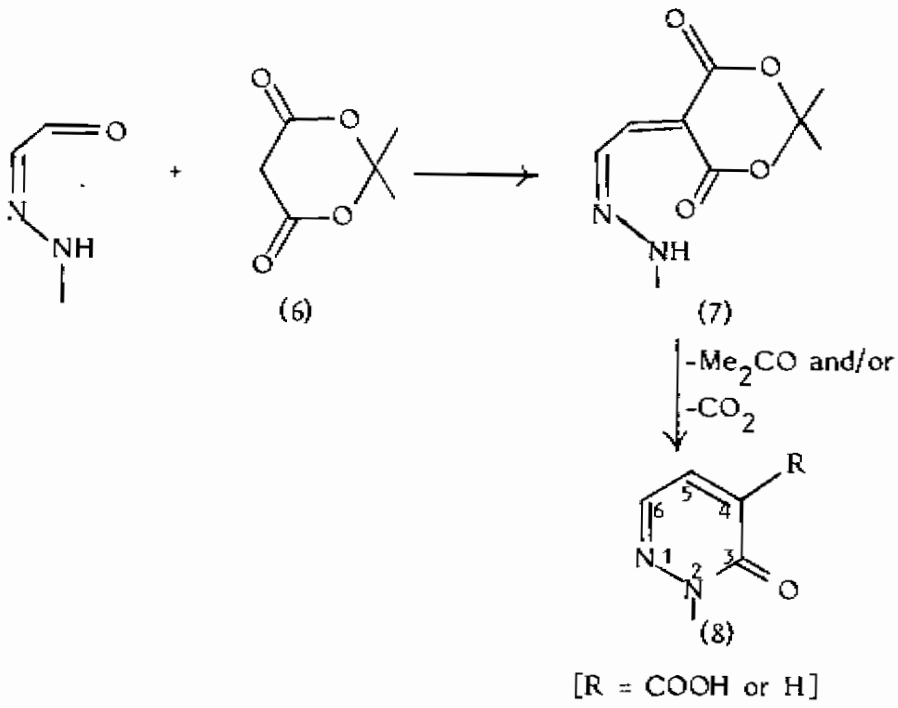


(5)

Among the α-dicarbonyl monohydrazones used in this synthesis are the monohydrazone of diacetyl, benzoylacetyl, cyclohexane dione, glyoxal, methyl glyoxal and phenanthraquinone. The active methylene containing compounds participating in the synthesis are

ethyl phenylacetate, ethyl hippurate etc.

Recently, Meldrum's acid (6)[5] which is 2,2-dimethyl-1,3-dioxan-4,6-dione was used as an active methylene containing compound. Thus, treatment of azaenaminones with Meldrum's acid gave the condensation product of general formula (7), cyclisation of these products to the corresponding pyridazin-3(2H)-ones (8) can be effected under basic conditions[6].



[R = COOH or H]

H. Mc Nab et al[6] suggest that the six ring atoms of the heterocycle derive from Meldrum's acid (6) [C (3) and C (4)] and from azaenaminones [N (1), N (2), C (5) and C (6)]. The C (4) —C (5) bond is formed by Knoevenagel condensation of the two components, while cyclisation of the resulting products generates the lactam function of the pyridazin-3(2H)-one. This method represents