

# STUDIES ON SOME FIVE AND SIX HETEROCYCLES

A Thesis in partial fulfillment of the requirements of  
master of Science degree (Chemistry)

by

**HATEM MOHAMED SAYED AHMED**

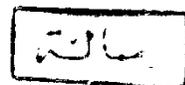
B.Sc. (Degree)

Supervisors

*Prof. Dr. A. A. M. HAMED*

*Prof. Dr. S. A. SHIBA*

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Faculty of Science  
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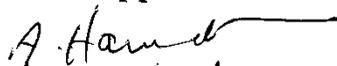
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# SUMMARY



### Summary

The present work is a continuation of our comparative studies on some newly prepared acrylonitrile derivatives.

The wide applications of 2-propenoyl derivatives as a precursors in the synthesis of biologically and pharmacologically active compounds, beside other interest in the synthesis of industrial products, like polymers, made them worthy to be synthesized hoping to obtain new structures with enhancing potency.

The thesis includes three parts:

#### Part 1:

#### Synthesis and reactions of 2-substituted-(4H)-3,1-benzoxazin-4-one and quinazolin-4-one derivatives.

This part deals with the synthesis of 2-[1'-cyano-2'-(4''-methoxyphenyl or 2''-thienyl)-ethen-1'-yl]-(4H)-3,1-benzoxazin-4-ones (**3 a-c**) via condensation of anthranilic acid and its 3,5-dibromo derivative with 2-propenoyl chloride derivatives (**1 a&b**) in presence of pyridine to give the acyl anilide derivatives (**2 a-c**) followed by cyclization with acetic anhydride.

The structures of **3** were elucidated with elemental analysis as well as spectral data (IR, <sup>1</sup>H-NMR and MS) and also a series of chemical reactions like:

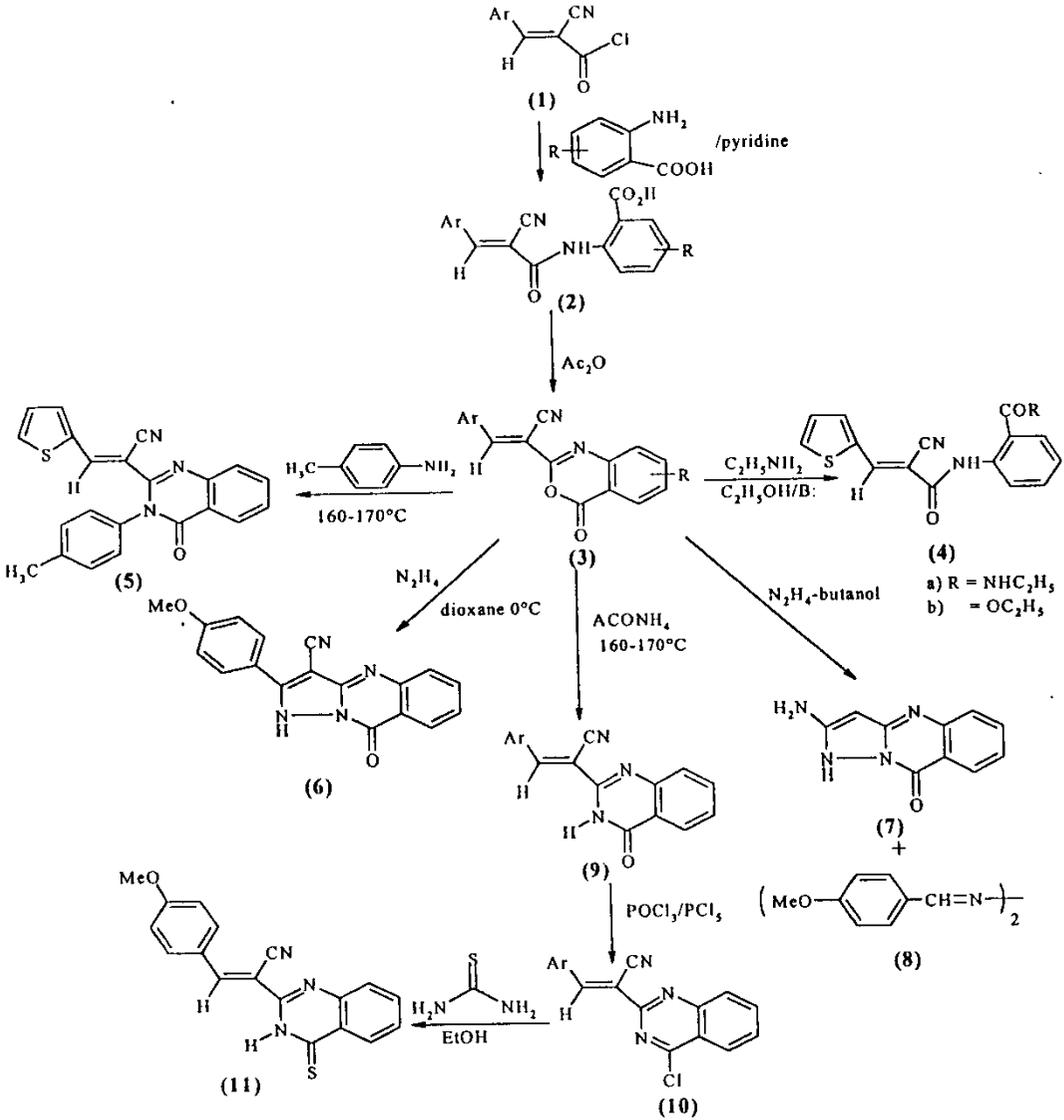
- i) Aminolysis of (**3b**) with ethyl amine to give the expected amides (**4a**).
- ii) Alcoholysis of (**3b**) with ethanol in presence of a base to give the ester (**4b**).
- iii) Condensation of (**3b**) with p-toluidine at 160-170°C yielded the expected 3-(4'-methylphenyl) quinazolinone (**5**).
- iv) Condensation of (**3a**) with hydrazine hydrate as strong nucleophile provides the unexpected products depending on

the reaction conditions, i.e. in dioxane at 0°C. The pyrazolo [5,1-b] quinazolin-9-one derivative (**6**) was obtained, while in polar solvent (n-butanol), the further addition of another molecule of N<sub>2</sub>H<sub>4</sub> at  $\alpha,\beta$ -unsaturated nitrile at position-2 with subsequent cleavage enhances the formation of azine (**8**) and 2-amino-pyrazolo [5,1-b] quinazolin-9-one (**7**).

v) Heating of (**3 a&b**) with ammonium acetate without solvent at 160-170°C afforded the quinazolin-4-ones (**9 a&b**).

The structure of (**9 a&b**) was established by spectral data and elemental analysis. Furthermore, quinazolinones (**9 a&b**) were subjected to the following reactions :

- i) Chlorination with POCl<sub>3</sub>/PCl<sub>5</sub> mixture gave 4-chloro quinazolines (**10 a&b**).
- ii) Conversion of (**10a**) to the quinazolin-4-thione (**11**) upon treatment with thiourea also was achieved.



## Part 2

### Amidation and esterification of 2-cyano-3-(4'-methoxyphenyl) 2-propenoyl chloride (1a)

The recent pharmaceutical applications of 2-propenoyl amide derivatives have stimulated the authors to synthesise some new derivatives of these classes of compounds of anticipated biological activities.

The reactions in this part include:

- 2.1) Reactions of (1a) with 2-aminopyridine in the presence of triethylamine afforded a mixture of N-(2'-pyridyl)-2-propenoyl amide derivative (12) and pyrido [1,2-a] pyrimidine derivative (13).
- 2.2) Condensation of (1a) with sulfanilic acid and sulfa drugs like, sulfmethoxazole and sulfamethazine in presence of base yielded the expected 2-propenoyl amide derivatives (14a -c).
- 2.3) Treatment of (1a) with hydrazine hydrate at 0°C in dry benzene gave a mixture of 3-aminopyrazol-5-one derivative (15), bis-N,N'-(2-propenoyl) hydrazine derivative (16) and azine (8), while with phenyl hydrazine, the expected 2-propenoyl phenyl hydrazine derivative (17a) was obtained. Furthermore with thiosemicarbazide, the acid chloride (1a) gave the expected condensed product (17b).
- 2.4) With hdyrazide derivatives, like, p-toulene sulfonyl hydrazide, (1a) reacts to give the expected product (17c), while upon treatment with benzoylhydrazine, the condensation with subsequent addition to the cyano group afforded the pyrazolone derivative (18).
- 2.5) Esterification of (1a) with different alcohols produces the corresponding new esters (19 a-d) in quantitative yield.
- 2.6) Condensation of (1a) with active bifunctional reagent, like, 2-aminothiophenol yielded a mixture of unexpected