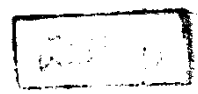
# SYNTHESES OF COMBINED HETEROCYCLIC COMPOUNDS FOR THEIR POSSIBLE BIOLOGICAL ACTIVITY

A THESIS SUBMITTED TO

FACULTY OF SCIENCE
AIN SHAMS UNIVERSITY



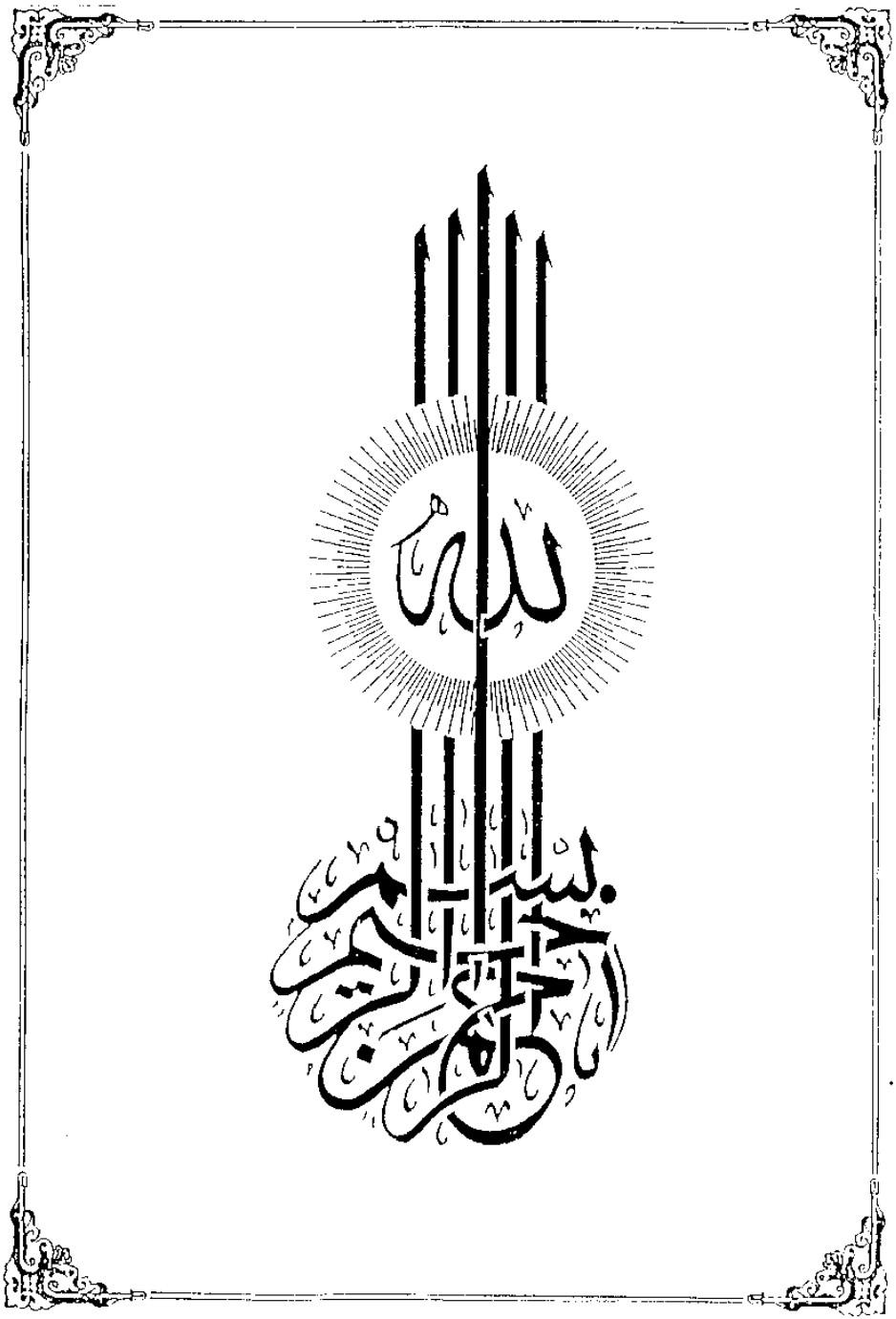
FOR
*PHILOSOPHY DOCTOR DEGREE*
*(Ph. Dr.)*
*IN CHEMISTRY*



BY
AFAF HUSSEIN ALI EL MASRY
(B.Sc., M.Sc.)

*NATIONAL RESEARCH CENTRE*
*DOKKI, CAIRO, EGYPT*
*1991*

بسم الله الرحمن الرحيم



بسم الله الرحمن الرحيم

وعلمك ما لم تكن تعلم وكان فضل الله عليك عظيما

« صدق الله العظيم »

SYNTHESES OF COMBINED HETEROCYCLIC

COMPOUNDS FOR THEIR POSSIBLE

BIOLOGICAL ACTIVITY

Advisors

Prof. Dr. A.A. Sammour (D. Sc.)

Prof. Dr. I.M. Nabih

Thesis Approved

TO MY FAMILY

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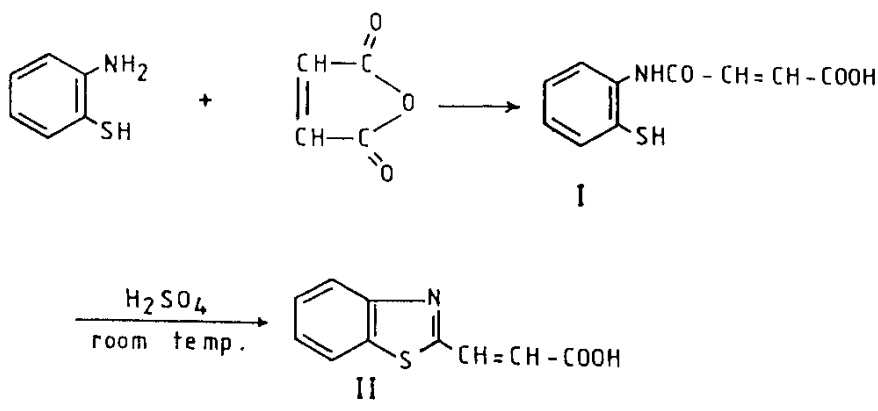
# AIM AND SUMMARY OF THE WORK

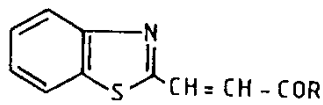
## Aim and Summary of the Work

In view of the fact that several benzothiazole-2-acrylic acid and their derivatives have been found to exhibit pharmacological activity, and the fact that the different heterocyclic compounds have been showed a significance biological activity. So, it was of interest to introduce a newly group of compounds structurally containing the benzothiazole-2-acrylic acid moiety incorporated with different biologically active heterocycles moieties as a trial to obtain biologically new active compounds that can be of more pharmacological activity.

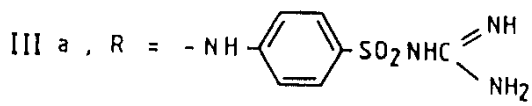
The parent compound in this group is benzothiazole-2-acrylic acid (II) which was prepared by condensation of O-aminothiophenol with maleic anhydride.

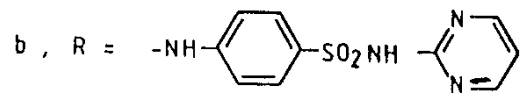


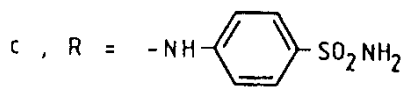
Compound (II) reacted with different sulpha drugs, namely, sulphaguanidine, sulphadiazine, sulphanilamide and / or sulphadimidine, sodium salt to give the corresponding 4-[1-(diaminomethyl)-sulphamoyl]-(IIIa), 4-[2-(pyrimidinyl) sulphamoyl]-(IIIb), 4-(sulphamoyl)-(IIIc)-2-benzothiazoleacrylanilide and / or 4-[(4,6-dimethyl-2-pyrimidinyl)-sulphamoyl]-2-benzothiazole acrylanilide, mono sodium salt (IIId) respectively.

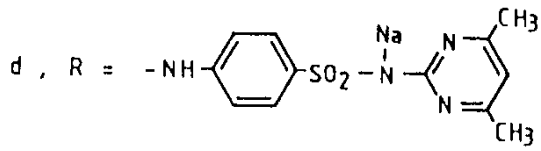



III (a - d)

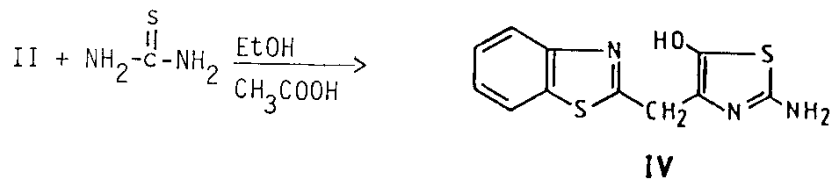
III a , R = 


b , R = 

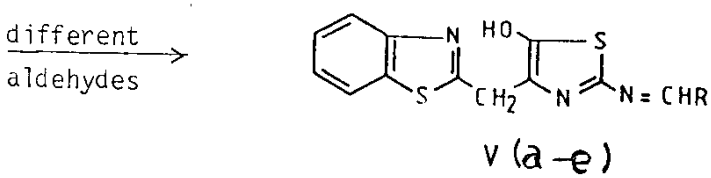

c , R = 


d , R = 

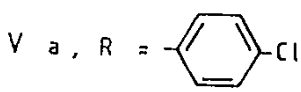
Upon treatment of compound (II) with thiourea in acidic medium to form 2-amino-4-(2-benzothiazolylmethyl-5-thiazolol (IV) which condensed with different aldehydes such as p-chlorobenzaldehyde, p-methylbenzaldehyde, anisaldehyde, p-dimethylaminobenzaldehyde and / or 3,4,5-trimethoxybenzaldehyde to give the 4-[2-benzothiazolyl[-methyl-(substituted)-benzylidene]amino]-5-thiazolol (Va - c).

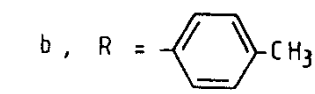


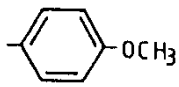
IV

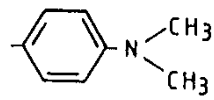


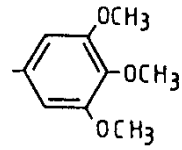
V (a-e)





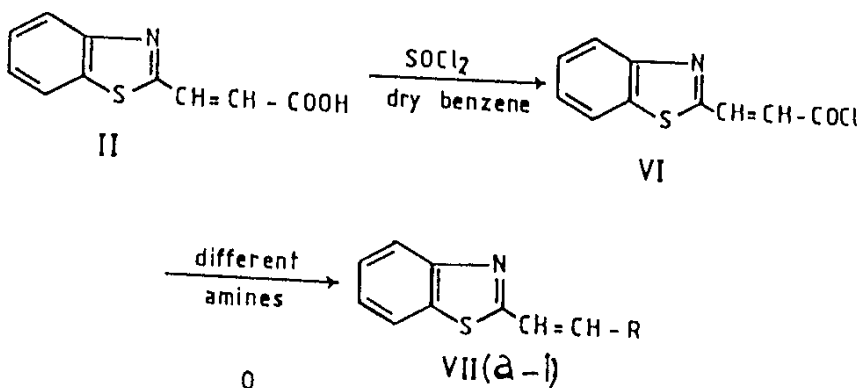
c , R = 

d , R 

e , R 

Upon treatment of compound ( II) with thionyl chloride, to give the acid chloride (VI) which condensed with diethylamine, piperidine, morpholine, 3-amino-1-phenyl-5-pyrazolone and / or cyclohexylamine to give the respective acrylamides (VIIa - e). Furthermore, acid chloride (VI) fused with ethylene diamine, O-phenylene diamine, O-aminophenol and /

or O-aminothiophenol in presence of sulphuric acid to give imidazoline (VIIf), benzimidazole (VIIg), benzoxazole (VIIh) and / or benzothiazole (VIIi).




II VI VII(a-i)

VII , a , R = $-\overset{O}{\overset{\|}{C}}-N(C_2H_5)_2$ b , R = $-\overset{O}{\overset{\|}{C}}-N$

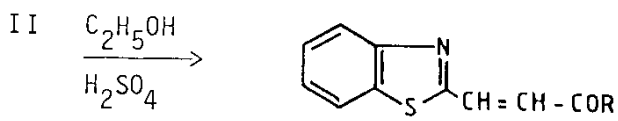
c , R = $-\overset{O}{\overset{\|}{C}}-N\,O$ d , R = $-\overset{O}{\overset{\|}{C}}-NH$

e , R = $-\overset{O}{\overset{\|}{C}}-NH$ f , R =

g , R = h , R =

i , R =

Esterification of compound ( II) with absolute ethanol afforded the ethyl ester ( VIII) which allowed to condense with hydrazine hydrate to give benzothiazole-2-acrylic acid, hydrazide (IX).




VIII, R = $-OC_2H_5$

IX, R = $-NH\ NH_2$

The hydrazide ( IX) reacted with different aromatic and heterocyclic aldehydes, namely, anisaldehyde, p-nitrobenzaldehyde, p-chlorobenzaldehyde, p-dimethylaminobenzaldehyde, 4-pyridinealdehyde and / or 2-thiophenealdehyde to give the corresponding Schiff's bases (Xa- f) respectively.

Cyclocondensation of thioglycolic acid with Schiff bases (Xa - f) gave (XIa - f) respectively.