Fayoum University
Faculty of Science
Chemistry Department

Synthesis of Some New Heterocyclic Compounds Containing Nitrogen Atom and Studies of Their Reactions and Biological Activities

By

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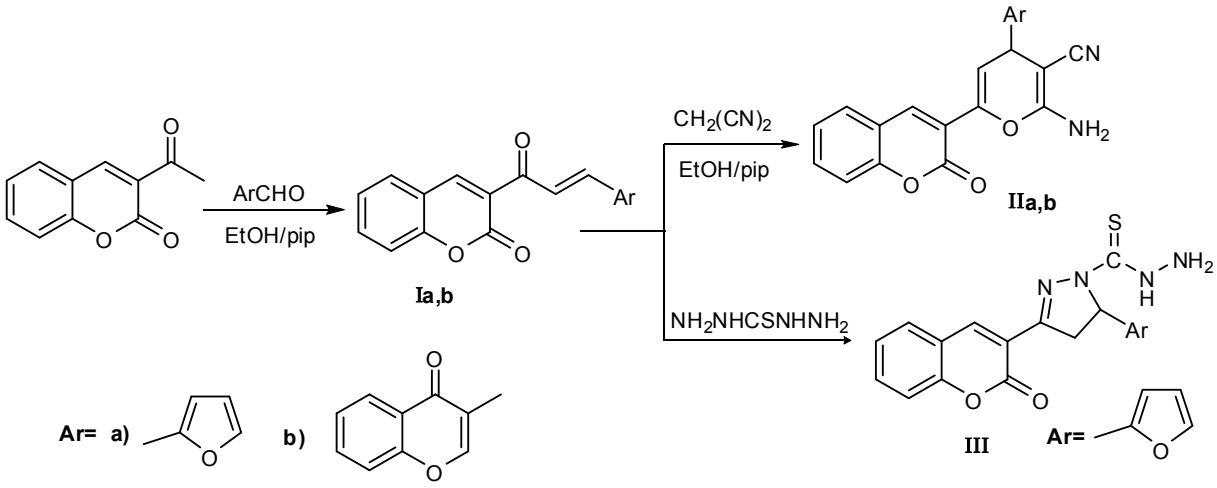
Synthesis of Some New Heterocyclic Compounds Containing Nitrogen Atom and Studies of Their Reactions and Biological Activities

This thesis describes the utility of 3-acetyl coumarin as a key starting material for the preparation of a novel series of coumarin derivatives and studies the antimicrobial activities of these compounds.

Synthesis of 3-(3-arylacryloyl)-2*H*-chromen-2-onederivatives Ia-b

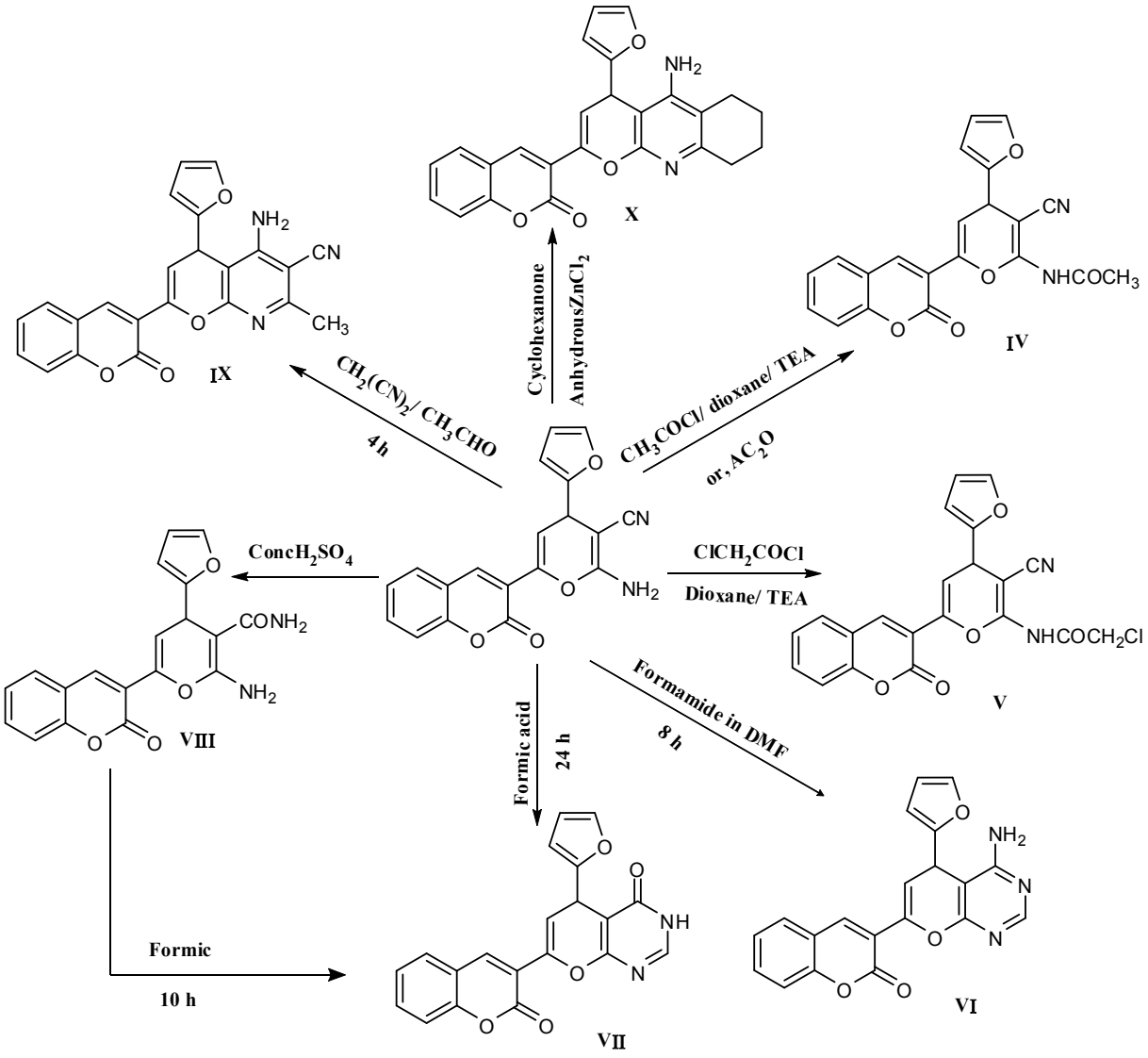
Different chalcones**Ia**,**b**were synthesized to be used as a starting material for synthesizing some new heterocyclic compounds containing coumarin moiety. When compounds **Ia**,**b**reacted with malononitrile, it gave**IIa**,**b** and when**Ia**reacted *chemeA).S*with aminothiosemicarbazide, it gave **III** *(*



Scheme A

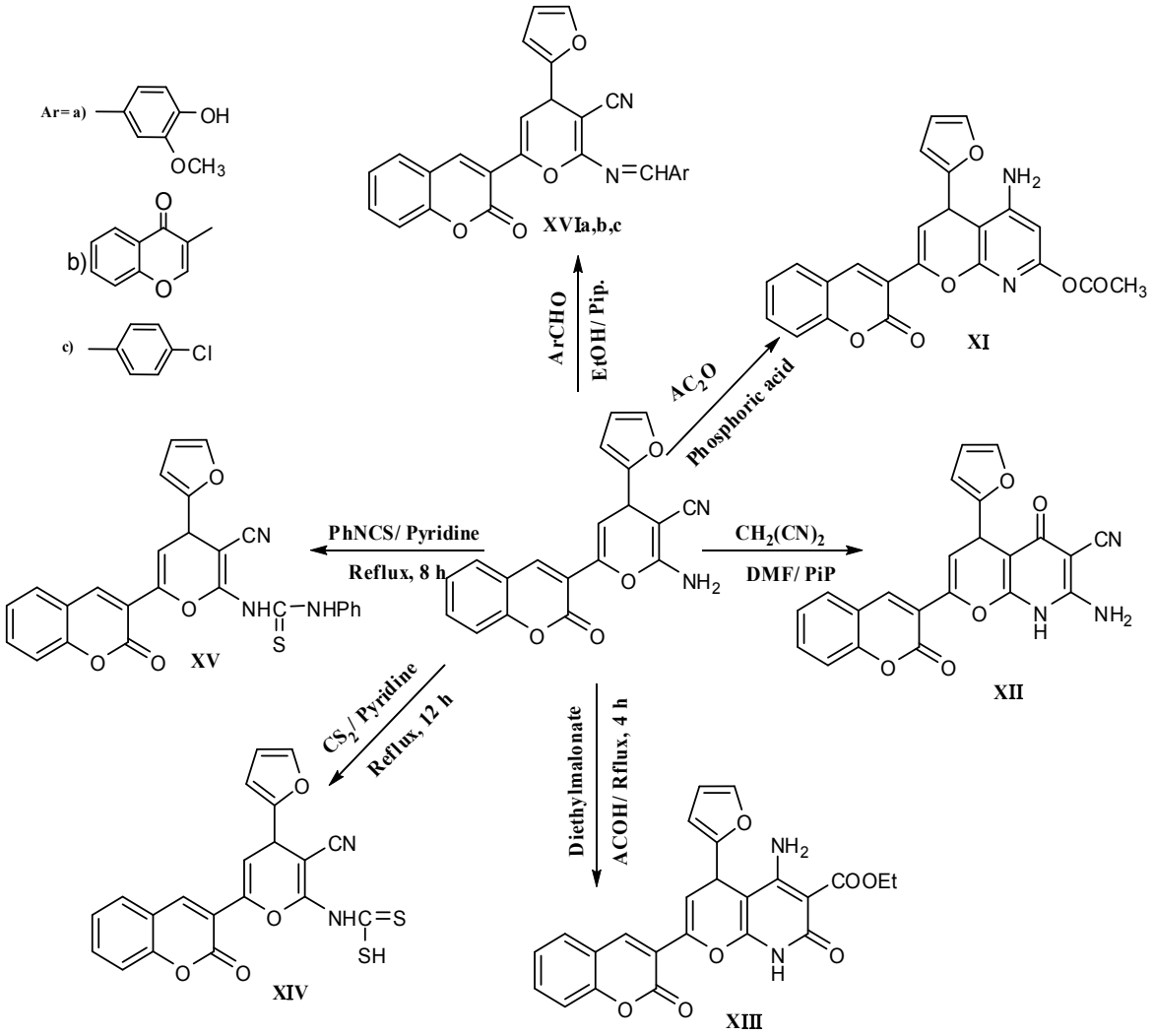
Studieson2-amino-4-(furan-2-yl)-6-(2-oxo-2*H*-chromen-3-yl)-4*H*-pyran-3-carbonitrile IIa

The acetylation of compound **IIa**with acetyl chloride or acetic anhydride afforded compound **IV**, chloroacetylation of compound**IIa**afforded the compound **V**,the reaction of compound **IIa**with formamide in refluxing DMF and formic acid gave compounds **VI** and **VII**,respectively,the acid hydrolysis of nitriles to amides afforded compound **VIII** which was cyclized into compound **VII** by boiling in formic acid. Also, the reactionof compound **IIa**withmalononitrile in acetaldehyde *chemeB).S*afforded **IX** and with cyclohexanone submitted **X**(


X
Cyclohexanone
Anhydrous$ZnCl_2$
IX
$CH_2(CN)_2$/ CH_3CHO
4 h
IV
CH_3COCl/ dioxane/ TEA
or, AC_2O
VIII
ConcH_2SO_4
V
$ClCH_2COCl$
Dioxane/ TEA
Formic acid
24 h
Formamide in DMF
8 h
Formic
10 h
VII
VI

Scheme B

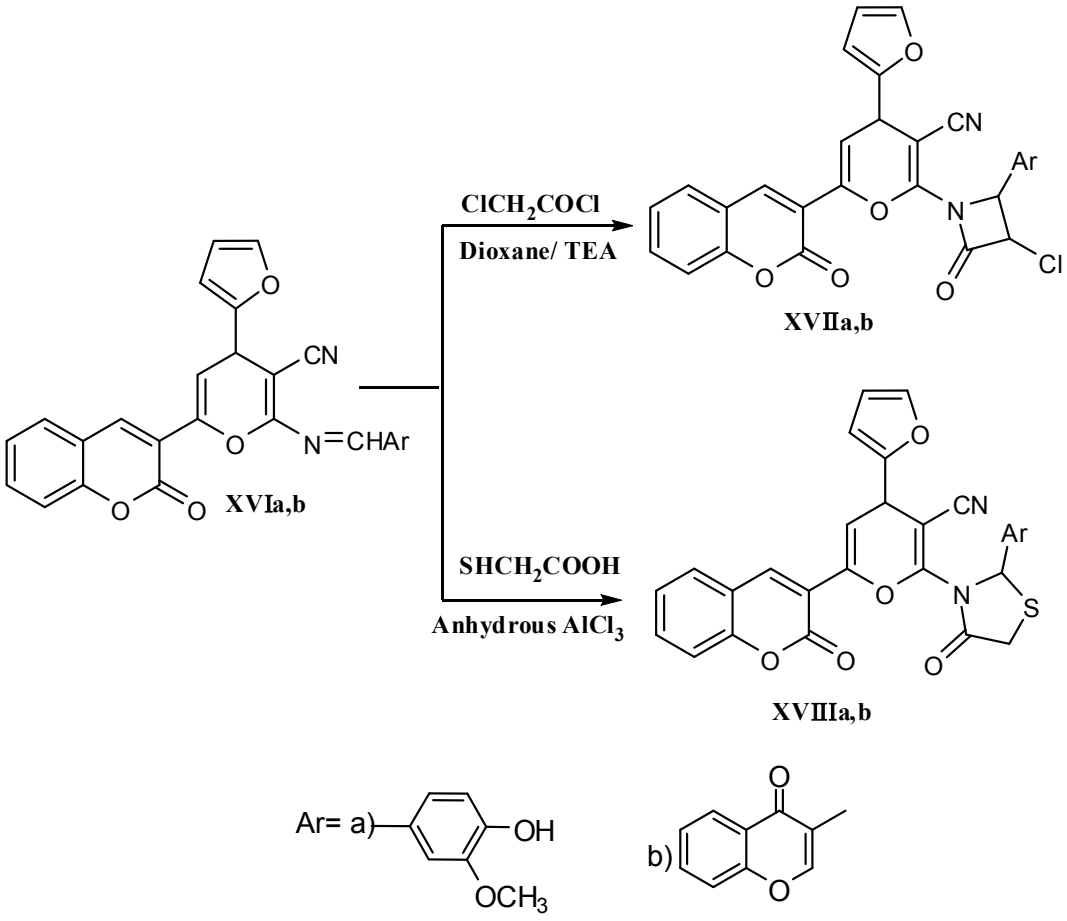
Additionally, the reaction of **IIa**with acetic anhydride in phosphoric acid gave **XI**,the reaction of**IIa** with active methylene compounds such as malononitrile and diethylmalonate afforded **XII**and **XIII**,respectively, the reaction of **IIa**with carbon disulfide in pyridine and phenyl isothiocyanate afforded**XIV**and**XV**,respectively,



Scheme C

while the reaction of **IIa** with different aldehydes (vanillin, formylchromone,*p-chemeC).S*chlorobenzaldehyde) submitted **XVIa**,**b**,**c**(

Furthermore, the interaction between compounds**XVIa**,**b** with chloroacetylchloride gave azetidine**XVIIa**,**b** and with thioglycolic acid submitted *chemeD). S*thiazolidinone**XVIIIa**,**b**(

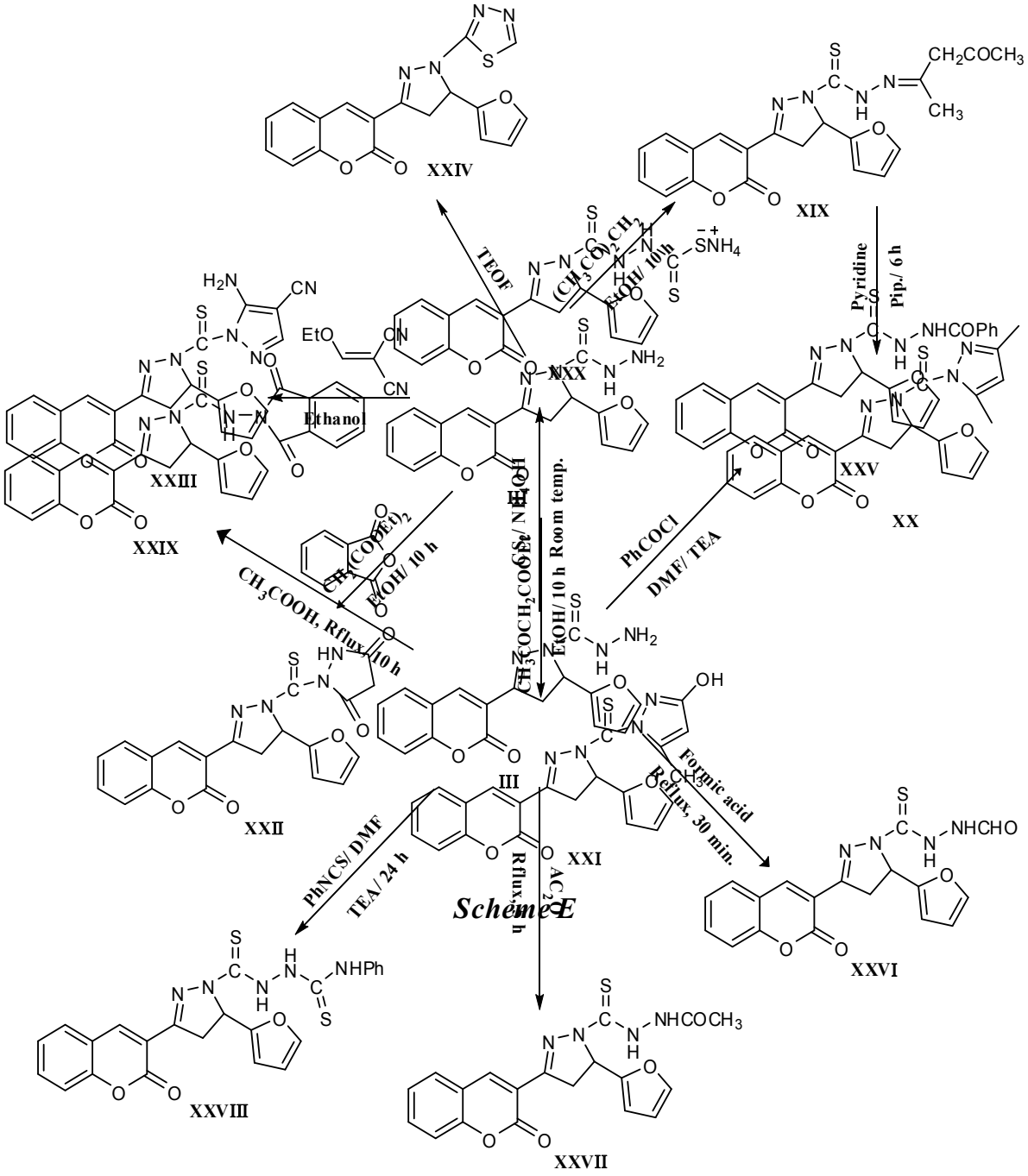


Scheme D

Studieson5-(furan-2-yl)-3-(2-oxo-2*H*-chromen-3-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide III

The compound **III** used as a starting material for the synthesis of several heterocyclic derivatives through the interaction with a variety of activated reagents.The interaction of compound **III** with acetyl acetone then refluxed in pyridine, ethylacetoacetate, and diethylmalonate afforded **XX**, **XXI**, and **XXII**, respectively. The interaction of**III** with ethoxymethylenemalononitrile submitted *chemeE).S***XXIII**,the interaction of **III** with triethylorthoformate afforded **XXIV**(

As well, the interaction of **III** with benzoyl chloride, formic acid, acetic anhydride,

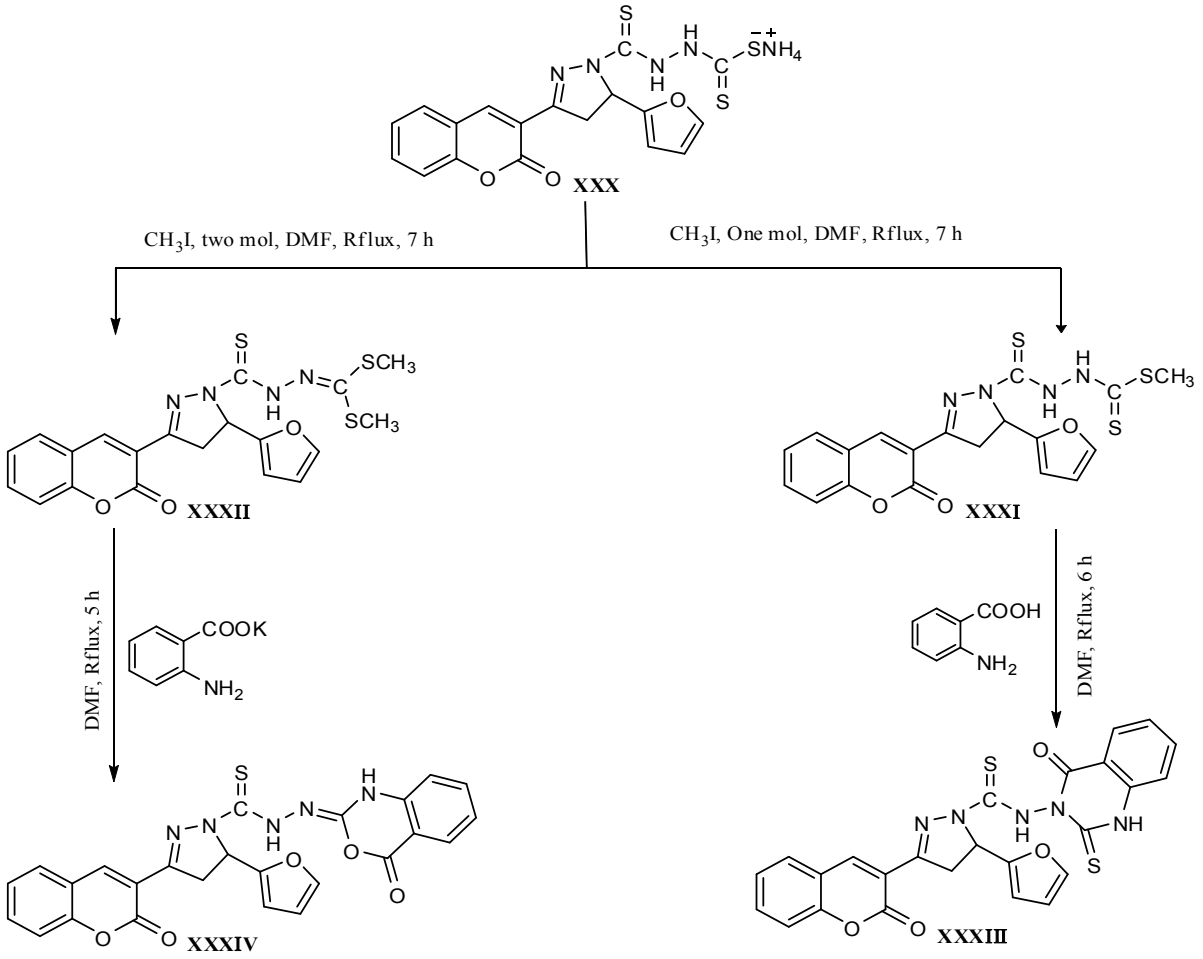


Scheme E

and phenyl isothiocyanate produced **XXV**, **XXVI**, **XXVII**,and **XXVIII**, respectively. Also,the interaction of **III** withphthalic anhydride as adicarbonyl compound in cyclic structure resulted **XXIX**,the interaction of **III** with carbon *chemeF). S*disulfide and ammonium hydroxide afforded **XXX**(

Otherwise, the compound **XXX** was reacted with alkylating agents such as 1 mol and 2mol of methyl iodide to prepare **XXXI** and**XXXII**, respectively. Then, monomethylated compound **XXXI** refluxed with anthranillic acid to give **XXXIII**. On the other hand, dimethylated compound **XXXII** reacted with potassium salt of *cheme G). S*anthranillic acid to afford **XXXIV**(

All of the newly synthesized compounds were:



Scheme G

- Confirmed from elemental analysis and spectral data.
- Tested *in vitro* against a variety of bacteria to study their anti-bacterial activity.