SYNTHESIS AND SOME REACTIONS OF HETEROCYCLIC COMPOUNDS CONTAINING COUMARIN MOIETY

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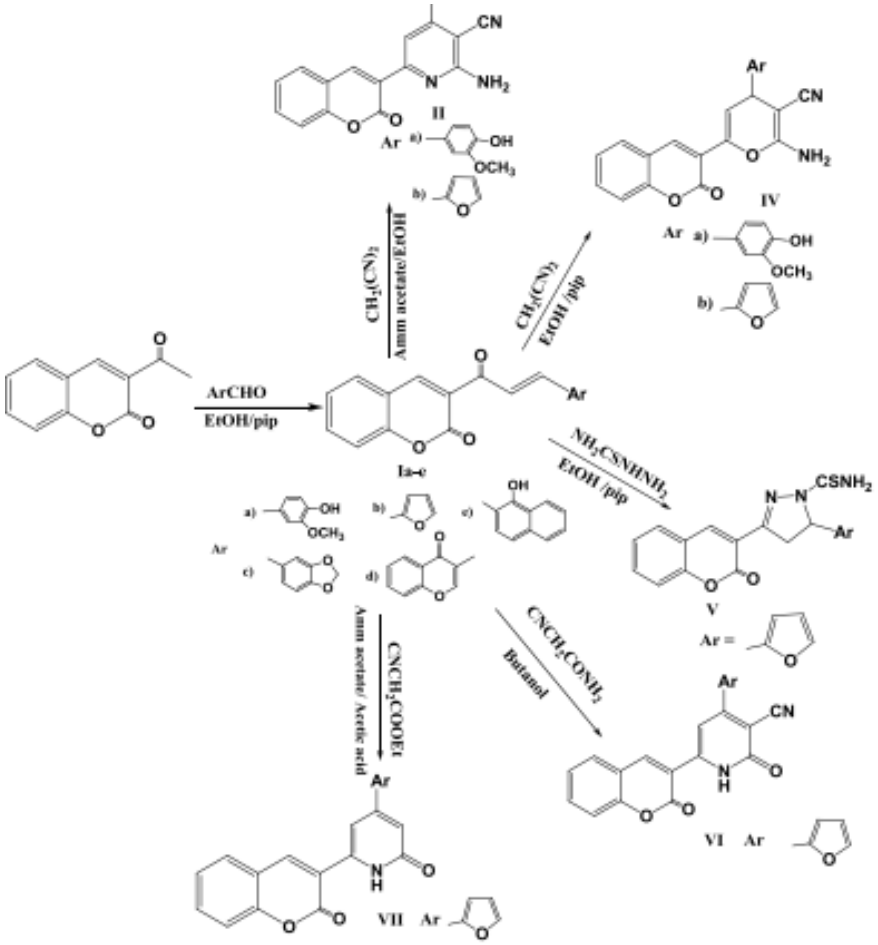
ABSTRACT

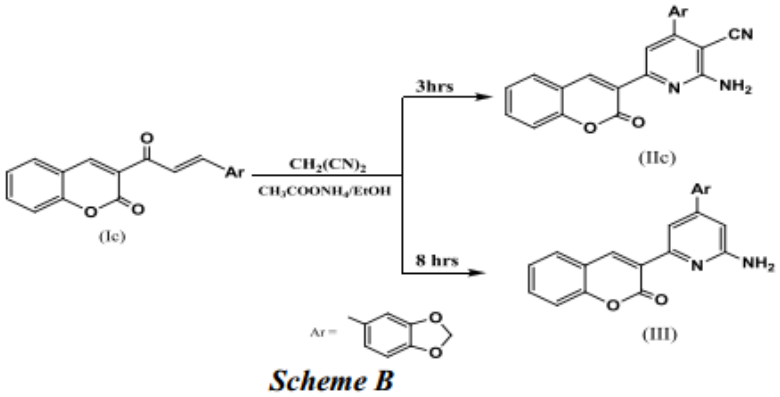
This thesis describes the utility of 3-acetyl coumarin as a key starting material for the preparation of a novel series of coumarin derivatives and studies the antimicrobial activities of these compounds.

SYNTHESIS OF 3- (3-ARYLACRYLOYL)-2H-CHROMEN-2-ONE DERIVATIVES Ia-e

Different chalcones **Ia-e** 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, thiosemicarbazide, cyano acetamide and ethyl cyanoacetate it gave the corresponding compounds **II, IV, V, VI and VII** (Scheme A). It was found that the reaction of chalcone **Ic** with malononitrile in presence of excess ammonium acetate gave compound **II**c when reaction was continued for 3 hrs, while when the reaction was continued for 8 hrs it gave compound **III** (Scheme B).



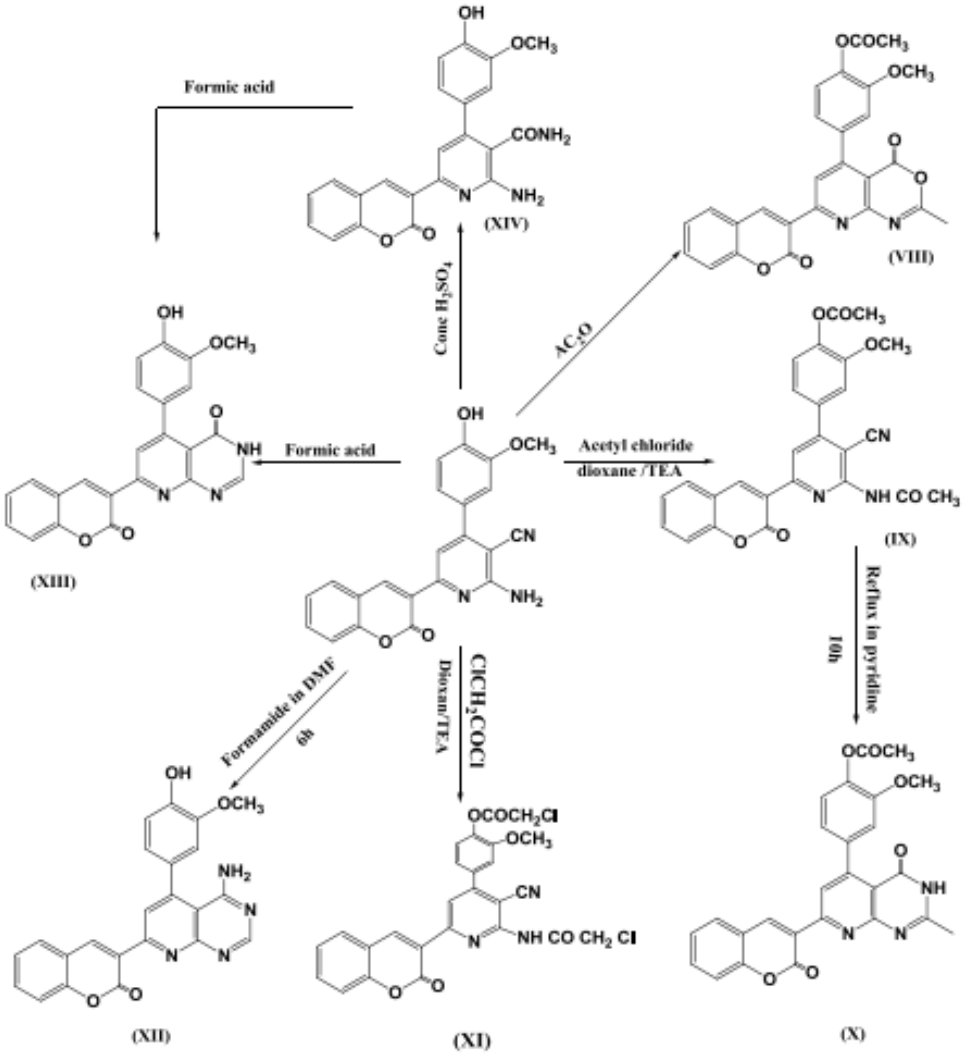
Scheme A



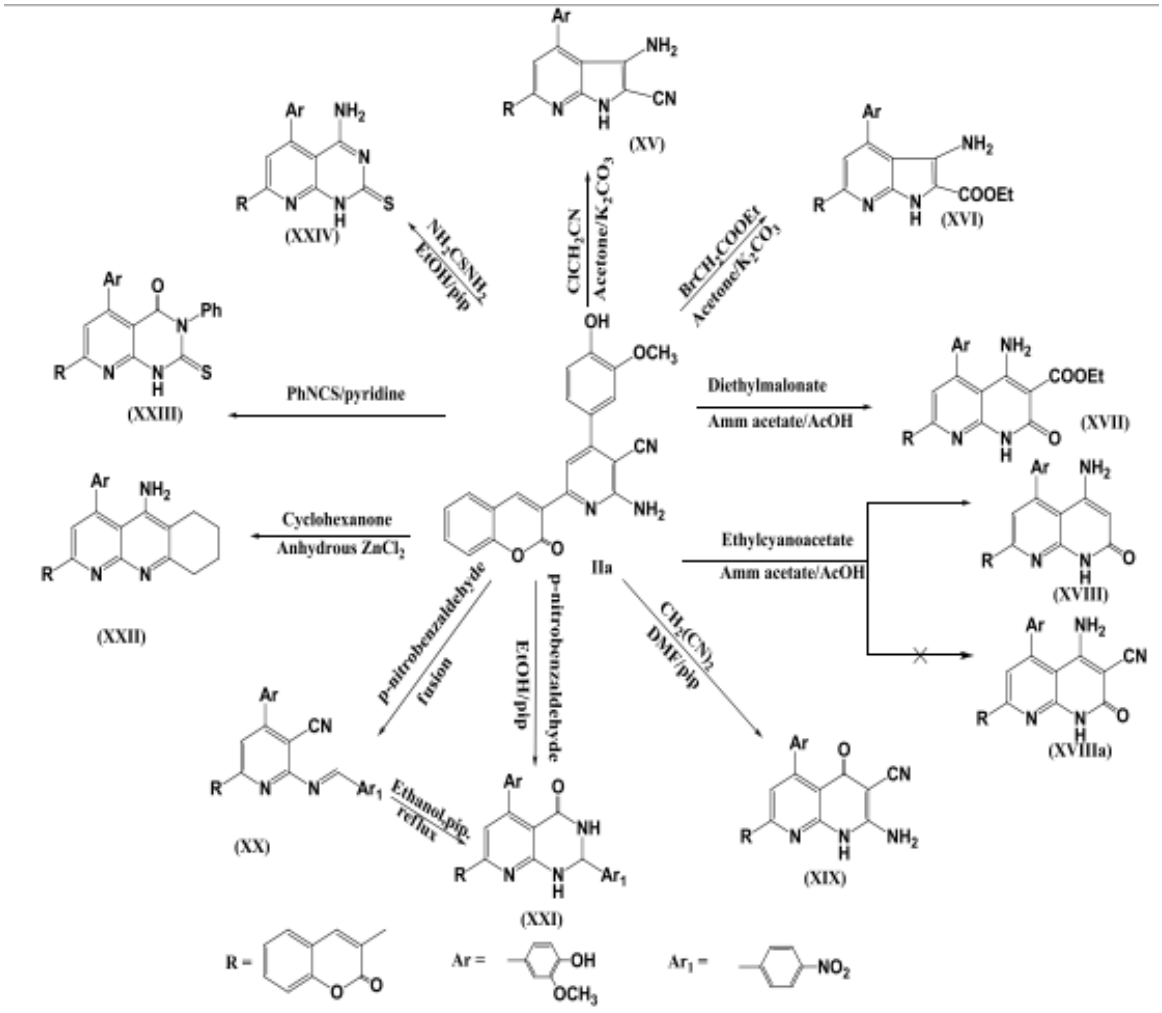
Scheme B

STUDIES ON 3-(2\-AMINO-3\-CYANO-4\-(4-HYDROXY-3-METHOXYPHENYL) PYRID-6\-YL) COUMARINE

The compound **IIa** reacted with acetic anhydride and afforded pyrido[2,3-d][1,3]oxazinone derivative **VIII**, while acetylation with acetyl chloride afforded the compound **IX** which on cyclization by refluxing in pyridine for 10 hrs gave 3,4- dihydropyrido[2,3-d]pyrimidin-4-one derivative **X**, chloroacetylation of compound **IIa** afforded the compound **XI,** the reaction of the compound **IIa** with formamide in refluxing DMF and formic acid gave the compounds **XII** and **XIII** respectively**,** the acid hydrolysis of nitriles to amides afforded the compound **XIV** which was cyclized into the compound **XIII** by boiling in formic acid (Scheme C). The alkylation of compound **IIa** with α-halo acetic acid derivatives (chloroacetonitrile and ethyl bromoacetate) was achieved in dry acetone containing anhydrous potassium carbonate and afforded the compounds **XV** and **XVI** respectively, the reaction of compound **IIa** with active methylene compounds such as diethyl malonate, ethyl cyanoacetate and malononitrile afforded the compounds **XVII-XIX** respectively. The reaction of compound IIa with p-nitro benzaldehyde in ethanol afforded the compound **XXI**, while on fusion it gave the compound **XX** which cyclized into **XXI**. The reaction of compound **IIa** with cyclohexanone in presence of anhydrous zinc chloride afforded Tacrine analogue **XXII**, while the reaction of **IIa** with phenyl isothiocyanate and thiourea afforded pyrimidinethione derivatives **XXIII** and **XXIV** respectively (Scheme D).

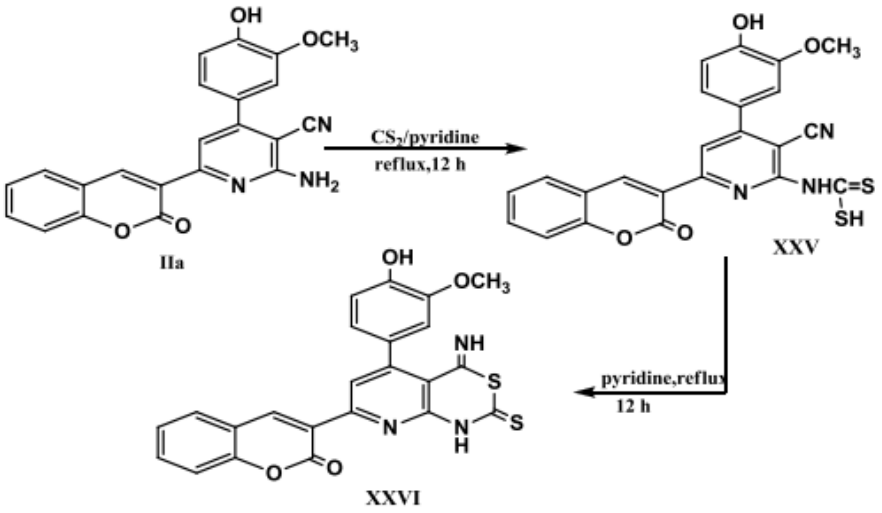

Formic acid
Conc H_2SO_4
AC_2O
Formic acid
Acetyl chloride
dioxane /TEA
Reflux in pyridine
10h
Formamide in DMF
6h
$ClCH_2COCl$
Dioxan/TEA
(XIV)
(VIII)
(XIII)
(IX)
(XII)
(XI)
(X)

Scheme C



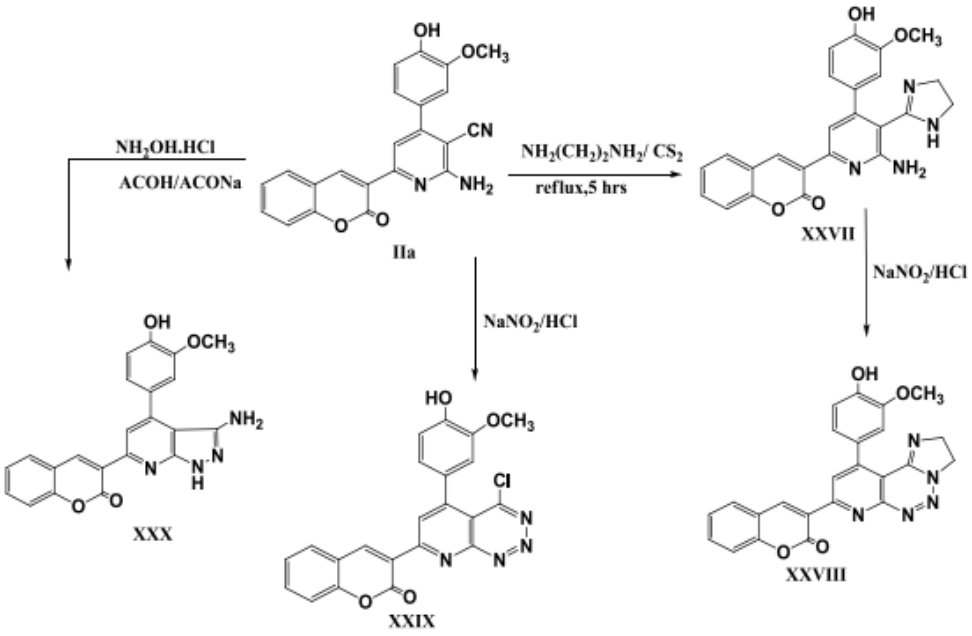
Scheme D

The reaction of compound **IIa** with carbon disulfide in refluxing pyridine; firstly afforded carbamodithioic acid derivative **XXV** which then undergo cyclization with further reflux and gave pyrido[2,3-d][1,3]thiazine derivative **XXVI** (Scheme E).



Scheme E

The compound **IIa** reacted with ethylenediamine in the presence of a catalytic amount of carbon disulfide and gave the compound **XXVII** which on diazotization afforded 2,3-dihydroimidazo[1,2-c]pyrido[3,2-e][1,2,3]triazine derivative **XXVIII**, in the other hand diazotization of compound **IIa** afforded pyrido[2,3-d][1,2,3]triazine derivative **XXIX**. The refluxing of compound **IIa** with hydroxylamine hydrochloride in glacial acetic acid containing a catalytic amount of anhydrous sodium acetate gave pyrazolo[3,4-b]pyridine derivative **XXX** (Scheme F).



Scheme F

All of the newly synthesized compounds were

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