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 IIc when reaction was continued for 3 hrs, while when the reaction was continued for 8 hrs it gave compound III (Scheme B).
STUDIES ON 3-(2\(^{\text{I}}\)-AMINO-3\(^{\text{I}}\)-CYANO-4\(^{\text{I}}\)-(4-HYDROXY-3-METHOXYPHENYL) PYRID-6\(^{\text{I}}\)-YL) COUMARINE

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