STUDIES ON α - PYRONE DERIVATIVES

A THESIS

In Partial fulfilment of the requirements of

MASTER OF SCIENCE DEGREE

BY

MOHAMED MAGDY MOHAMED MOSTAFA

(B Sc.)

Supervised By

Prof Dr. M . K . EL-DEEK

Prof. Dr. M . Y . EL-KADY

Prof. Dr. M. EL- HASHASH

Ain Shams University

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الله

بسم الله الرحمن الرحيم

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STUDIES ON α -PYRONE DERIVATIVES

Thesis advisor	Thesis approved
Prof. Dr. M.K. El-Deek	M. EL-Deek
Prof. Dr. M. El-Kady	M. El Kady
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Head of Chemistry Department

CONTENTS

Statement and Objectives of the Problem

The multiple functionality of the coumarins offer a potential treasure of chemical reactivity. This prompted the author to Synthesis 3,4-dihydrocoumarin by Bechmann's condensation involving P-hydroxy biphenyl and P-bromobenzoylacrylic acid with the aim of investigation the behaviour of this compound toward many nitrogen and carbon nucleophiles .

The structures of the products were established by the following :

1) Correct analytical data .
2) Spectroscopic studies (infrared and nuclear magnetic resonance).
3) Some chemical reactions.

SUMMARY OF THE ORIGINAL WORK

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The condensation of B-(P-bromo)benzoylacrylicacid with p-hydroxybiphenyl gave 6-phenyl-3,4-dihydrocoumarin(I) and p-bromobenzoic acid. Compound I condensed with aldehydes to give 3-arylidine-6-phenyl 3,4-dihydrocoumarins (IIa-d)

The reaction of I with Grignard reagents gave 6-phenyl-2-alkyl(or aryl)-2-hydroxy chroman derivatives (III a-f) also the reaction of I with acrilonitrile gave B(6-phenyl-3,4-dihydrocoumarin-3yl) propionic acid (V).

The compound I reacted with bromine in boiling acetic acid to yield 6-phenyl-3-bromo-3,4-dihydrocoumarin (VI).

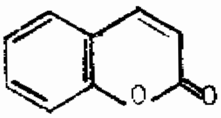
On the otherhand, I reacted with primary aromatic amines to give the corresponding 6-Phenyl-3,4-dihydro-2 (N-aryl) iminochromans (VIIa-e), while the reaction of I with p-aminoazobenzene of 2-amino pyridine gave 6-Phenyl-3,4 dihydro N(2-Pyridyl or 4-azo-benzenyl)-2-quinolinone (VIII a and b). The reaction of I with hydrazine-hydrate or semicarbazide yielded the corresponding 6-phenyl-3,4-dihydro-N (amino-or urido)-2-quinolinone (IX a and b).

In this study the author tends to compare the reactivity of 3-ethyl (4-carboxy-6-P-bromophenyl-3,4 dihydro 2-pyronoyl) acetate (x) which obtained via Michael condensation reactions of P-bromobenzoyl acrylic-acid with diethylsuccinate and 6-phenyl-3,4-dihydro-coumarin (I) towards the carbon and nitrogen nucleophiles. Thus he obtained pyrano-1(substituted)-pyridazinones (XIa and b) corresponding N-arylamides (XIII), 3-Vinyl-2-pyrano derivatives (XIVa-c), substituted alkyl or aryl butyl ketones (XV a-e); from the reactions of (X) with hydrazines, amines, aromatic aldehydes and/or Grignard reagents respectivelly .

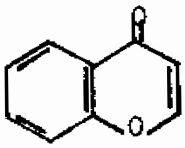
INTRODUCTION

Coumarins

Coumarins are a class of oxygen heterocyclic compounds which may be regarded as derivatives of 5,6-benzopyran-2-one (I) There are three possible isomers of benzopyranones these are chromone or 5,6-benzopyran-4-one(II) isocoumarin or 3,4-benzopyran-2-one (III) and 4,5 benzopyran-2-one(IV).



(I)



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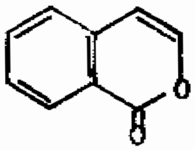
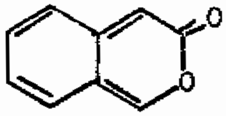


(III)

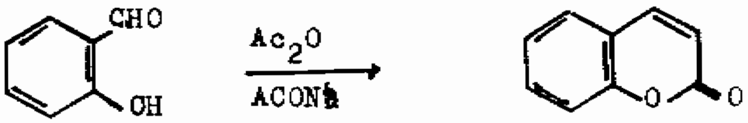


(IV)

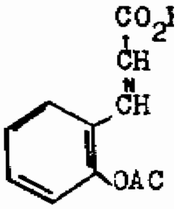
Synthesis of Coumarins

1. Perkin Synthesis :

This classic synthesis was discovered by Perkin[1] , who prepared coumarin(I) and acetyl coumaric acid (V) by heating salicylaldehyde with acetic anhydride and anhydrous sodium acetate.



(I)

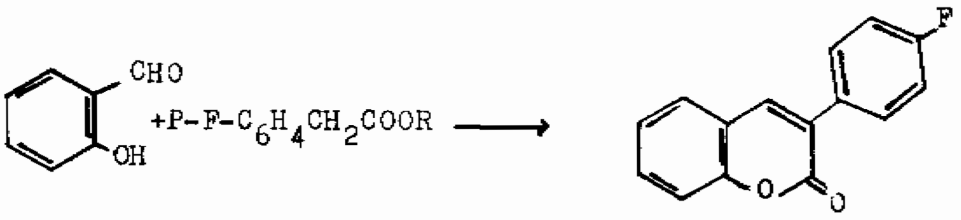


(V)

This method is especially advantageous in that there is no doubt about the orientation of the product, no opportunity for the formation of the isomeric chromones.

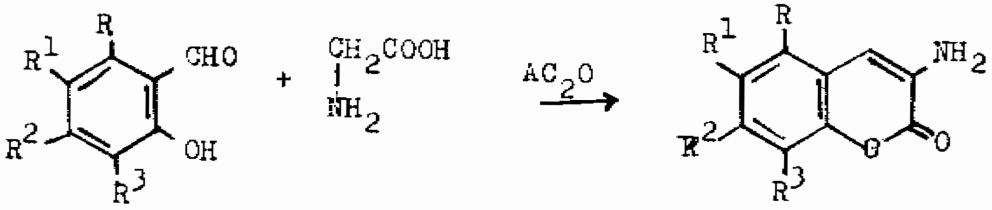
The perkin method has been widely[2] used but there are some limitations, the required *o*-hydroxyaldehydes are not always easily obtained and the yields of coumerins are generally low, although it is claimed that they are improved by the addition of iodine[3].

3-(*p*-Fluorophenyl) coumarin(VI)[4,5] were prepared by condensation *p*-fluorophenylacetic acid and/or its ester with salicylaldehyde.



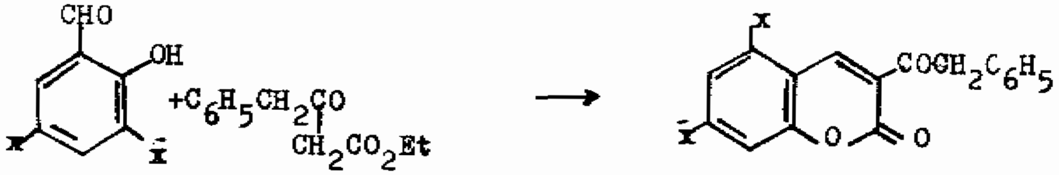
(VI)

3-Aminocoumarin derivatives (VII)[6-9] were prepared by heating O-hydroxybenzaldehyde derivatives with glycine and acetic anhydride.



(VII)

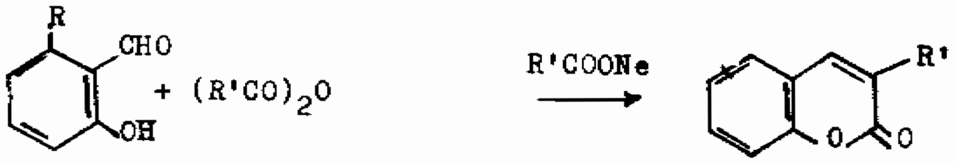
Perkin synthesis of 3,5-dihalo-2-hydroxybenzaldehyde with ethyl phenylacetoacetate gave the corresponding 5,7-dihalo-3-substituted coumarin(VIII)[10].



$X = \bar{X}$ = Cl , Br

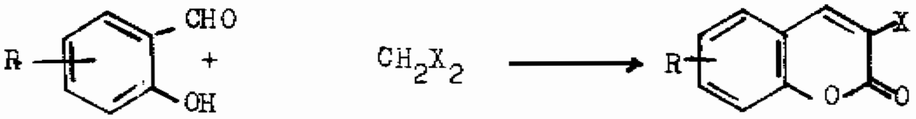
(VIII)

Other fatty aliphatic acid anhydrides and salts may be substituted for the acetic acid derivatives to give-3-substituted coumarin (IX)[11,12]



(IX)

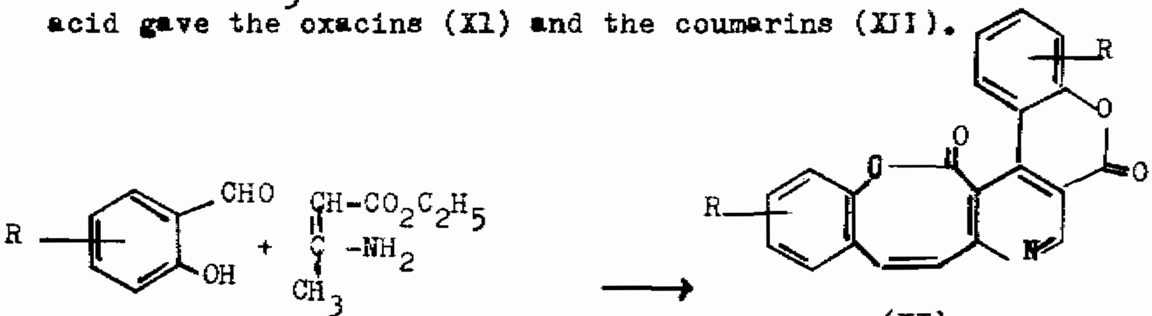
By somewhat similar reaction of Knoevenagel[13-16] o-hydroxyaldehyde derivatives condense with compounds containing active methylene groups such as malonic acid, diethyl malonate, and malononitrile in presence of organic base to yield 3-substituted coumarins (X).



(X)

$X = CO_2H, -CO_2C_2H_5, -CN$

Recently[17], it was found that on refluxing equimolar amount of o-hydroxybenzaldehyde derivatives with $C_2H_5O_2CCH=\underset{CH_3}{C}-NH_2$ in the presence of traces of acetic acid gave the oxacins (XI) and the coumarins (XII).



(XI)