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Synthesis and chemical reactivity of some pyranoquinolinone derivatives

A Thesis Submitted
By

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Synthesis and chemical reactivity of some pyranoquinolinone derivatives

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بسم الله الرحمن الرحيم

قُلْ إِنَّ صَلاَتِي وَنُسُكِي وَمَحْيَايَ
وَمَمَاتِي لِلَّهِ رَبِّ الْعَالَمِينَ لاَ شَرِيكَ لَهُ
وَبِذَلِكَ أُمِرْتُ وَأَنَاْ أَوَّلُ الْمُسْلِمِينَ

صدق الله العظيم

سورة الانعام (الاية 162-163)

Dedication

To

my mother,

my father,

my wife,

and my children

Acknowledgement

First and foremost, praise and thanks be to Allah for enabling me to complete this research.

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Aim of the work

The present work aims to:

1. Synthesize the novel 6-methyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**4**).
2. Synthesize the novel 4-hydroxy-6-methyl-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**5**).
3. Utilize the two novel aldehydes as starting materials to prepare a variety of novel 4-hydroxyquinolin-2(1*H*)-ones and pyrano[3,2-*c*] quinoline-2,5(6*H*)-diones.
4. Investigate the chemical reactivity of aldehydes **4** and **5** towards different nucleophilic reagents.
5. Synthesize new heterocyclic compounds, containing both quinolinone and pyrano[3,2-*c*]quinolinone and other heterocycles in one molecular frame, of expected biological activity.
6. Study of spectral properties of different newly prepared quinolinones and pyrano[3,2-*c*]quinolinone products.
7. Evaluate the antimicrobial activity of the newly synthesized compounds.

Abstract

Synthesis and chemical reactivity of some pyranoquinolinone derivatives.

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Vilsmeier-Haack formylation of 3-acetyl-4-hydroxy-1-methylquinolin-2(1*H*)-one (**2**) and 3-(4-hydroxy-1-methy1-2-oxo-(1*H*)-quinolin-3-yl)-3-oxopropanoic acid (**3**) produced the novel 6-methyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**4**) and 4-hydroxy-6-methyl-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**5**). Reactions of carboxaldehyde **4** with a diversity of nucleophilic reagents were studied and a variety of products were obtained *via* ring-opening ring-closure (RORC) sequence. The Chemical reactivity of carboxaldehyde **5** with a diversity of nitrogen nucleophilic reagents were studied and a variety of products were obtained. Some 1,3,4-oxadiazolyl/1,3,4-thiadiazolyl/benzothiazolyl/chromeno[2,3-*b*]pyridyl linked pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione were efficiently synthesized. Structures of the new synthesized products were deduced on the basis of their analytical and spectral data. The newly synthesized compounds were screened for their antimicrobial activity.

Keywords: pyrano[3,2-*c*]quinoline, 4-hydroxyquinolin-2(1*H*)-one; Vilsmeier-Haack reaction, , ring-opening/ring-closure, nucleophilic reaction, heterocyclization.

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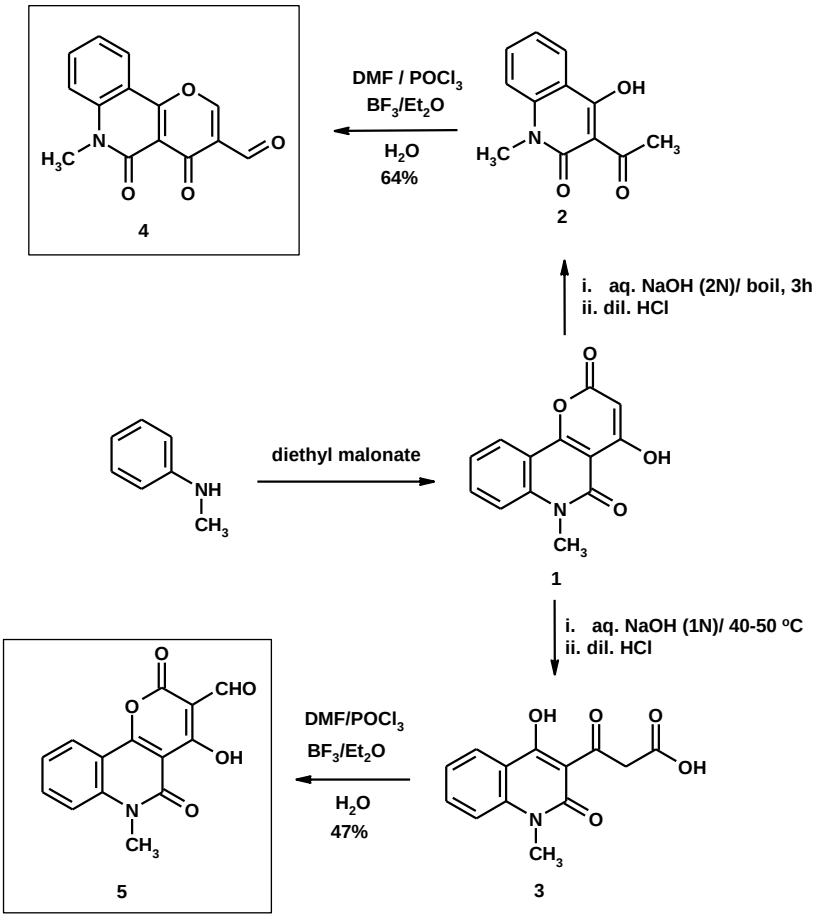
English Summary

Summary of the original work

Synthesis and chemical reactivity of some pyranoquinolinone derivatives.

In the present thesis, applying *Vilsmeier-Haack* formylation on 3-acetyl-4-hydroxy-1-methylquinolin-2(1*H*)-one (**2**) and 3-(4-hydroxy-1-methy1-2-oxo-(1*H*)-quinolin-3-yl)-3-oxopropanoic acid (**3**) produced the novel 6-methyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**4**) and 4-hydroxy-6-methyl-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**5**), respectively (Scheme i).

The present work aimed to study the chemical reactivity of the novel aldehydes **4** and **5** towards a diversity of nucleophilic reagents hoping to construct a novel series substituted quinolin-2(1*H*)-ones and substituted pyrano[3,2-*c*]quinoline-2,5(6*H*)-diones of potential biological activity.

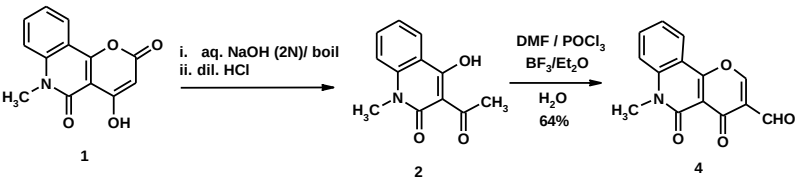


Scheme i. Synthesis of the novel pyrano[3,2-*c*]quinoline-3-carboxaldehydes **4** and **5**.

Part I

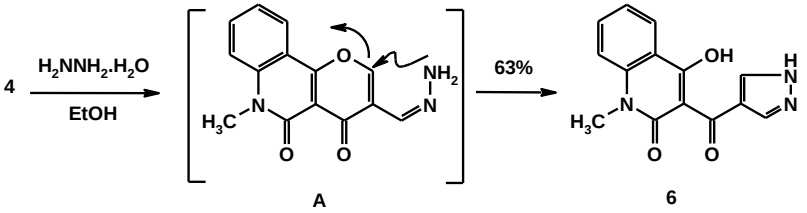
Synthesis, characterization and antimicrobial evaluation of some novel 4-hydroxyquinolin-2(1*H*)-ones

Vilsmeier-Haack formylation of 3-acetyl-4-hydroxy-1-methylquinolin- 2(1*H*)-one (**2**), using dimethylformamide and phosphoryl chloride, led to the novel 6-methyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**4**) (Scheme 1).



Scheme 1. Synthesis of the novel pyrano[3,2-*c*]quinoline-3-carboxaldehyde **4**.

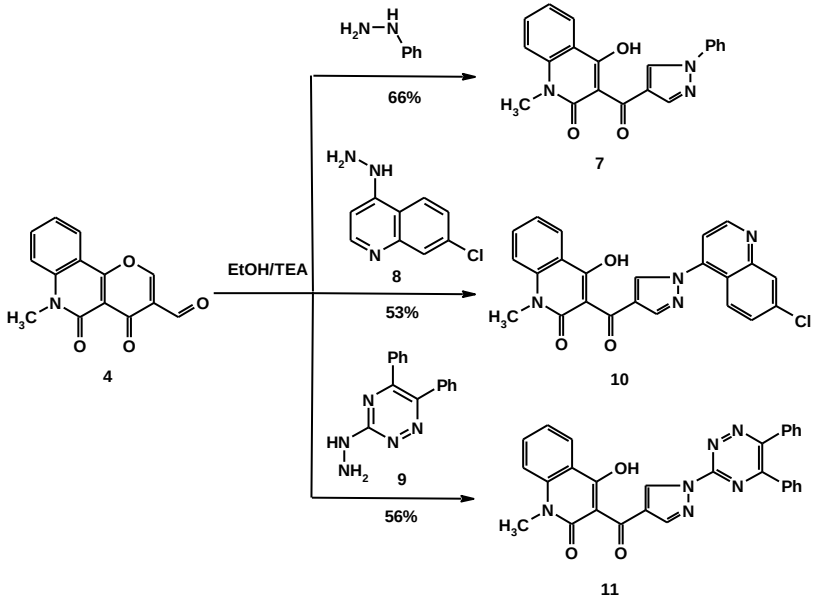
The present work aimed to study the chemical reactivity of carboxaldehyde **4** towards a variety of nitrogen and carbon nucleophiles hoping to construct some novel 4-hydroxyquinolinones bearing a diversity of heterocyclic systems of expected biological activity. Thus, treatment of carboxaldehyde **4** with hydrazine hydrate in boiling ethanol afforded 4-hydroxy-1-methyl-3-(1*H*-pyrazol-4-ylcarbonyl)quinolin-2(1*H*)-one (**6**), *via* the non isolable hydrazone intermediate **A** which underwent, *in situ*, intramolecular nucleophilic attack of N^2H at C-2 position with concomitant γ-pyrone ring opening (Scheme 2).



Scheme 2. Reaction of carboxaldehyde **4** with hydrazine hydrate.

Also, condensation of carboxaldehyde **4** with phenyl hydrazine in absolute ethanol containing few drops of triethylamine (TEA) gave phenylpyrazole derivative **7**.

Similarly, condensation of carboxaldehyde **4** with 7-chloro-4-hydrazinoquinoline (**8**) and 3-hydrazino-5,6-diphenyl-1,2,4-triazine (**9**) under the same reaction conditions produced the quinolinylpyrazolylcarbonyl- quinolinone **10** and triazinylpyrazolylcarbonylquinolinone **11**, respectively (Scheme 3).



Scheme 3: Condensation of carboxaldehyde **4** with some hydrazine derivatives.

On the other hand, carboxaldehyde **4** was allowed to react with some 1,3-*N*,*N*-binucleophiles. Treatment of carboxaldehyde **4** with guanidine hydrochloride, cyanoguanidine and thiourea in ethanolic potassium hydroxide solution gave the corresponding pyrimidine derivatives **12**-**14**, respectively (Scheme 4).