Ain Shams University
Faculty of Science
Department of Chemistry

Utility of Oxo-Compounds as Synthons of Some Heterocycles

A Thesis Submitted for the Degree of Doctor of philosophy in

Chemistry (Organic Chemistry)

Presented by

Rabaa Mohamed Kamel Mohamed

B. Sc (Chemistry Department) 2009

M. Sc (Organic Chemistry) 2014

Department of Chemistry

Faculty of Science

Ain Shams University

Cairo, Egypt

(2017)

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Prof. of Organic Chemistry

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(M. Sc.)

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DEDICATION

To my distinguished parents:

I do appreciate my God for giving me such wonderfully parents for their continuous support, encouragement, and enlighting my life.

ACKNOWLEDGEMENT

The author wishes to refer her deep appreciation and gratitude

To

Prof. Dr. Ahmed Said Ahmed Youssef, *Professor of Organic Chemistry, Chemistry Department, Faculty of Science, Ain Shams University.*

Prof. Dr. Mohamed Emad Azab, *Professor of Organic Chemistry, Chemistry Department, Faculty of Science, Ain Shams University*

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For

Suggesting the subject, interpreting the results, their valuable scientific guidance, help, and encouragement during the work of this thesis.

QUALIFICATION

Name: Rabaa Mohamed Kamel Mohamed

Scientific Degree: M. D.

Department: Organic Chemistry

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M. D. Graduation Year: 2014

PhD. Sc. Graduation Year: 2017

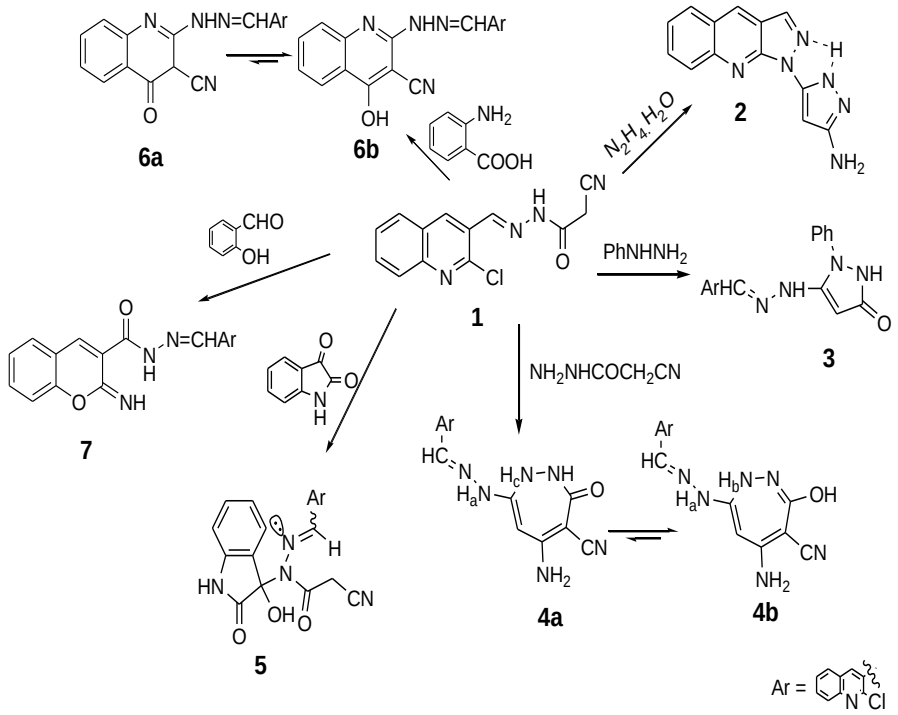
Contents

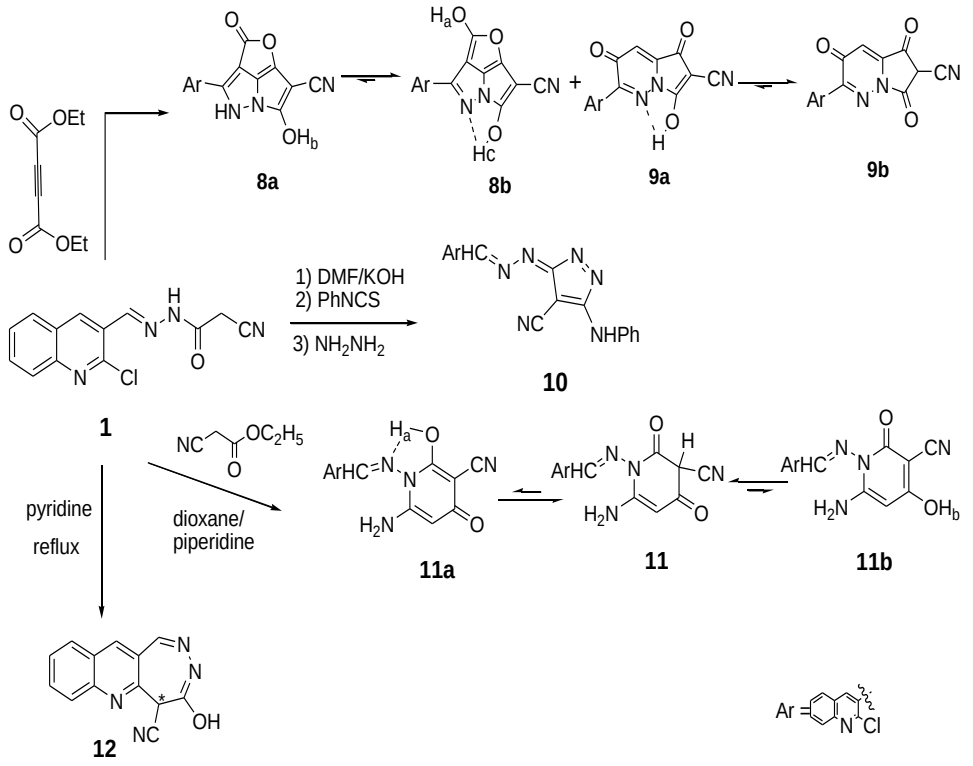
Summary

Part I: N'-((2-chloroquinolin-3-yl) methylene) 2-cyanoacetohydrazide (**1**) which was synthesized from 2-choloroquinolin-3-carbaldehyde was allowed to react with different nucleophilic and electrophilic reagents to construct new heterocycles which might have considerable potency as antimicrobial agents.

Thus, compound **1** was boiled with hydrazine hydrate and phenyl hydrazine to afford the pyrazolo derivatives **2** and **3**. On the other hand, its treatment with 2-cyanoacetohydrazide, it gave the diazepine derivative **4**. On treating compound **1** with isatin in boiling dioxane and few drops of piperidine as a base it yielded the adduct **5**. Refluxing of compound **1** with anthranilic acid gave quinoline derivative **6**. On the other hand, treatment of compound **1** with salicylaldehyde furnished chromene derivative **7** in a good yield. Heating a mixture of compound **1** and diethyl acetylenedicarboxylate in dioxane with few drops of piperidine afforded the furopyrrolodiazole derivative **8** and the pyrrolo-pyridazine derivative **9**. A solution of compound **1** in DMF and a

catalytic amount of potassium hydroxide was stirred for half an hour followed by adding an equivalent amount of phenyl isothiocyanate. Subsequent addition of hydrazine hydrate to the previous mixture, afforded the pyrazole derivative **10**. Compound **1** was refluxed with ethyl cyanoacetate and few drops of piperidine in dioxane to furnish pyridine derivative **11**. Finally, when compound **1** was treated with pyridine under reflux, it afforded the diazepinoquinoline derivative **12**.





Biological activity

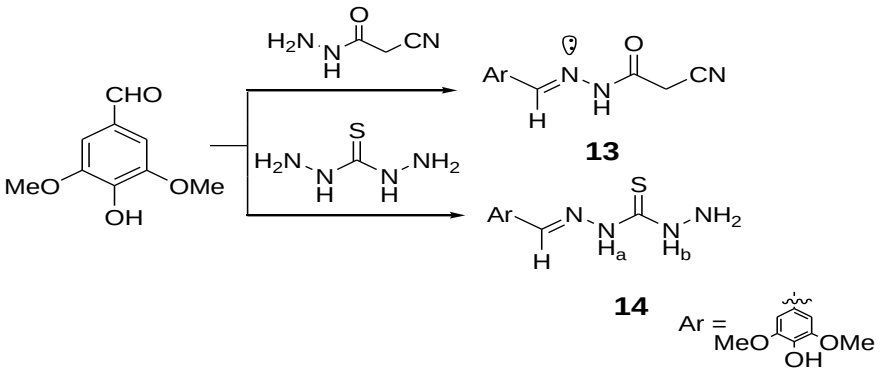
The possible antimicrobial activities of the synthesized heterocyclic compounds **2, 3, 7, 10** and **12** were investigated against six reference microbial isolates including; Fungi: (RCMB 02568) (Af) and Candida albicans (RCMB 05036) (Ca); gram-positive bacteria:, Streptococcus pneumoniae (RCMB 010010) (Sp) and Staphylococcus aureus (RCMB 010028) (Sa); gram-

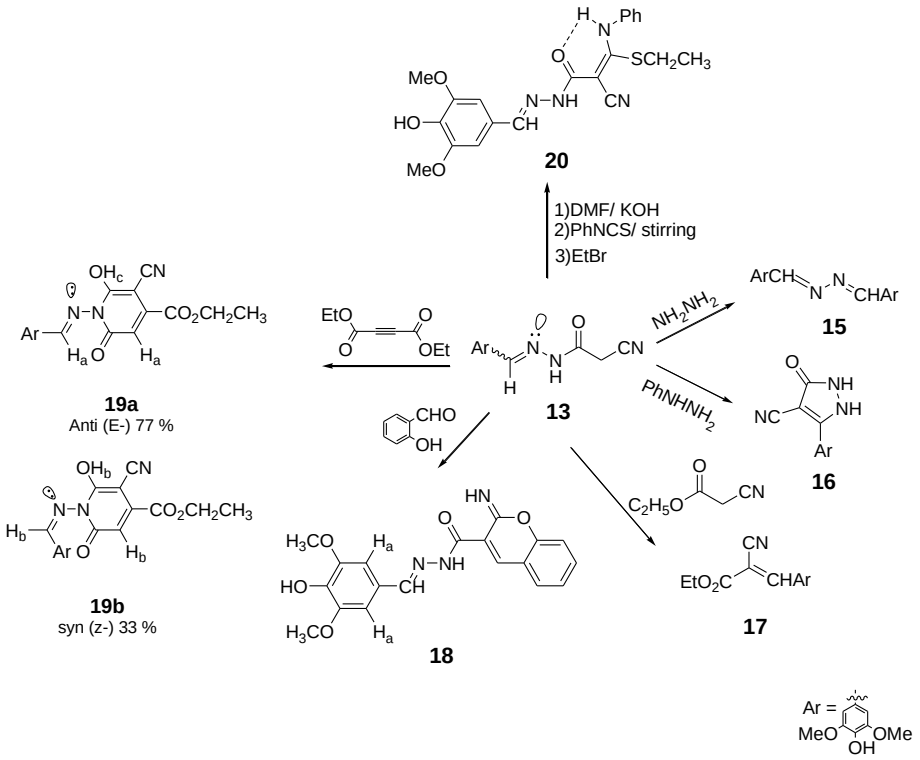
negative bacteria: Pseudomonas aeruginosa (RCMB 010043) (Pa) and Escherichia coli (RCMB 010052) (Ec). Mean zone of inhibition in mm ± Standard deviation beyond Aspergillus fumigatus well diameter (6 mm) produced on a range of environmental and clinically pathogenic microorganisms using (5mg/ml) concentration of tested samples.

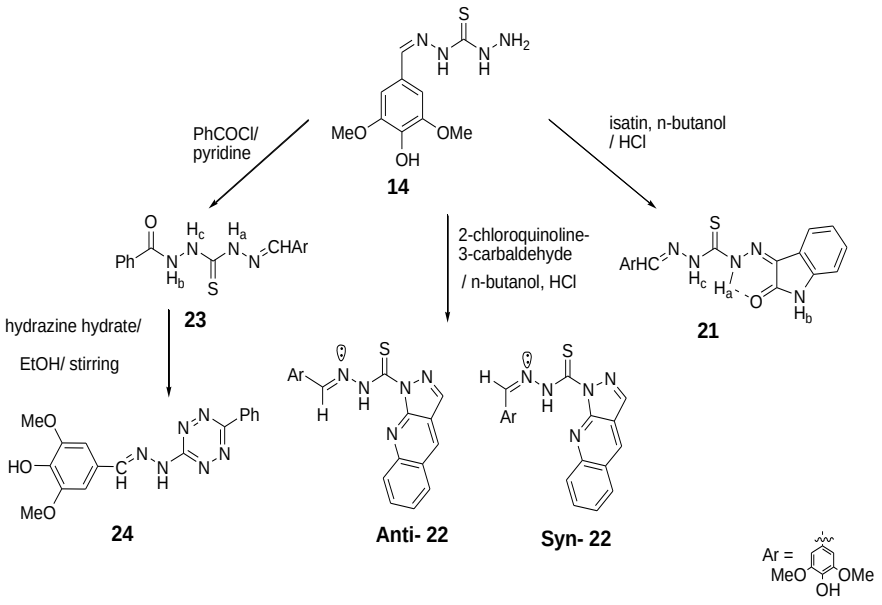
Part II. Reaction of syringaldehyde with cyanoacetohydrazide and thiocarbohy-drazide:

Heating of syringaldehyde with cyanoacetohydrazide in ethanol yielded an adduct **13** in a good yield. On the other hand, its reaction with thiocarbohydrazide gave derivative **14**. The behavior of **13** towards different reagents was investigated. Initially, compound **13** was reacted with hydrazine derivatives such as hydrazine hydrate and phenyl hydrazine producing the diarylidene hydrazine **15** and the pyrazolone deravative **16a,b**. Also, compound **13** was refluxed with ethyl cyanoacetate in dioxane in the presence of piperidine giving the arylidine derivative **17**. Reaction of compound **13** with salicyaladehyde in dioxane and few drops of piperidine furnished benzopyrane

derivative **18** in a good yield**.** Boiling of compound **13** with diethyl acetylene dicarboxylate furnished pyridine derivative **19**. A solution of compound **13** in dimethyl formamide and a catalytic amount of potassium hydroxide was stirred for half an hour followed by adding an equivalent amount of phenyl isothiocyanate. Subsequent addition of ethyl bromide to the previous mixture afforded the adduct **20**. Reaction of compound **14** with isatin and 2-chloroquinoline-3-carbaldehyde in n-butanol and few drops of HCl afforded the condensation products **21** and **22**, respectively. On the other hand, stirring of compound **14** with benzoyl chloride in pyridine at room temperature gave the thiocarbohydrazone derivative **23**. Stirring of compound **23** with hydrazine in ethanol furnished the tetrazine derivative **24** in a good yield.




20
1)DMF/ KOH
2)PhNCS/ stirring
3)EtBr
19a
Anti (E-) 77 %
19b
syn (z-) 33 %
13
15
16
17
18
Ar =


14
PhCOCl/
pyridine
isatin, n-butanol
/ HCl
23
2-chloroquinoline-
3-carbaldehyde
/ n-butanol, HCl
21
hydrazine hydrate/
EtOH/ stirring
24
Anti- 22
Syn- 22
Ar =