Ain Shams University
Faculty of Science
Department of Chemistry

Utilization of Compounds Bearing Carbonyl Group in Heterocyclic Synthesis

A Thesis Submitted for the Degree of Doctor of philosophy in Science (Organic Chemistry)

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Abstract

Abstract

The chemistry of 1,3-oxazolones had received great attention in the last decades. The importance of these compounds is due to facile opening of the oxazolone ring to give acyclic products which can recyclize again to afford varieties of heterocyclic systems of synthetic and biological importance.

The original work of this thesis can be classified into four parts:

Part 1: In this part, the 6-amino pyrazolo[1,2-a][1,2,4]triazines-4,8-diones derivative **3** was synthesized. Then it was reacted with several electrophiles to form novel pyrazolotriazine derivatives.

Part 2: In this part, some of the obtained compounds in part 1 were evaluated against their antitumor activity.

Part 3: In this part, the cyanoacetohydrazide derivative **16**, pyrazolone derivative **17** and pyridin-2-one derivative **25** were prepared and used as synthons for the construction of Schiff's bases, chromenone, tetrazolopyrazolone, pyrazol-one, pyran-2-one and triazolopyridine derivatives.

Part 4: In this part, some of the obtained compounds in part 3 were evaluated against their antimicrobial activity.

English Summary

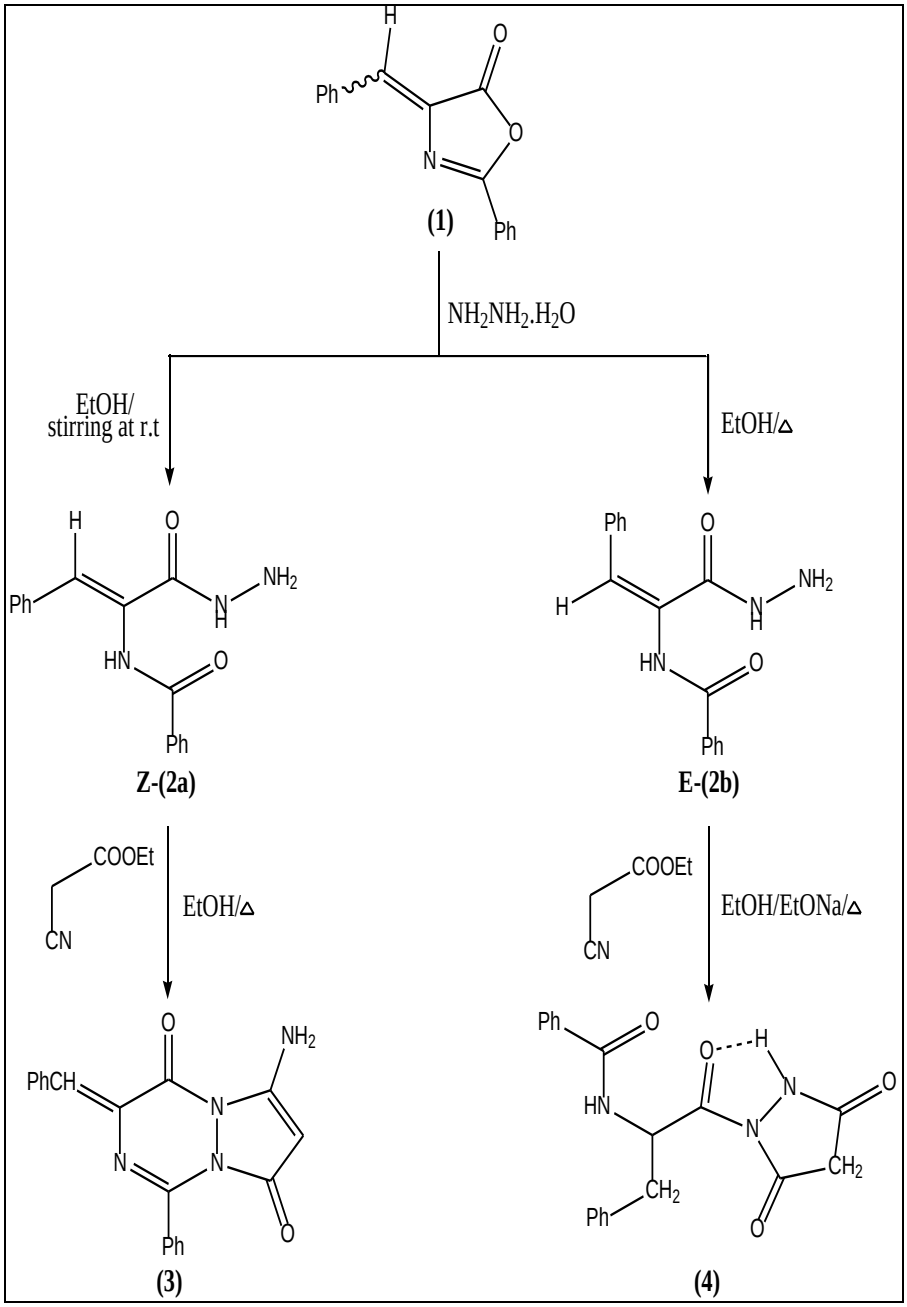
The 1,3-oxazolones, the pyrazole rings and their derivatives are classes of nitrogen containing heterocyclic compounds and used extensively as important synthons in organic synthesis. Also they have widespread potential biological activities in medicinal and pesticide chemistry.

The original work of this thesis can be classified into four parts:

Part (I): Synthesis of some novel pyrazolotriazine derivatives.

The geometrical isomers of the acid hydrazide derivatives Z-(**2a**) & E-(**2b**) were previously prepared by our research group upon hydrazinolysis of 4-benzylidene-2-phenyl-1,3-oxazole-5(4*H*)-one **1**.

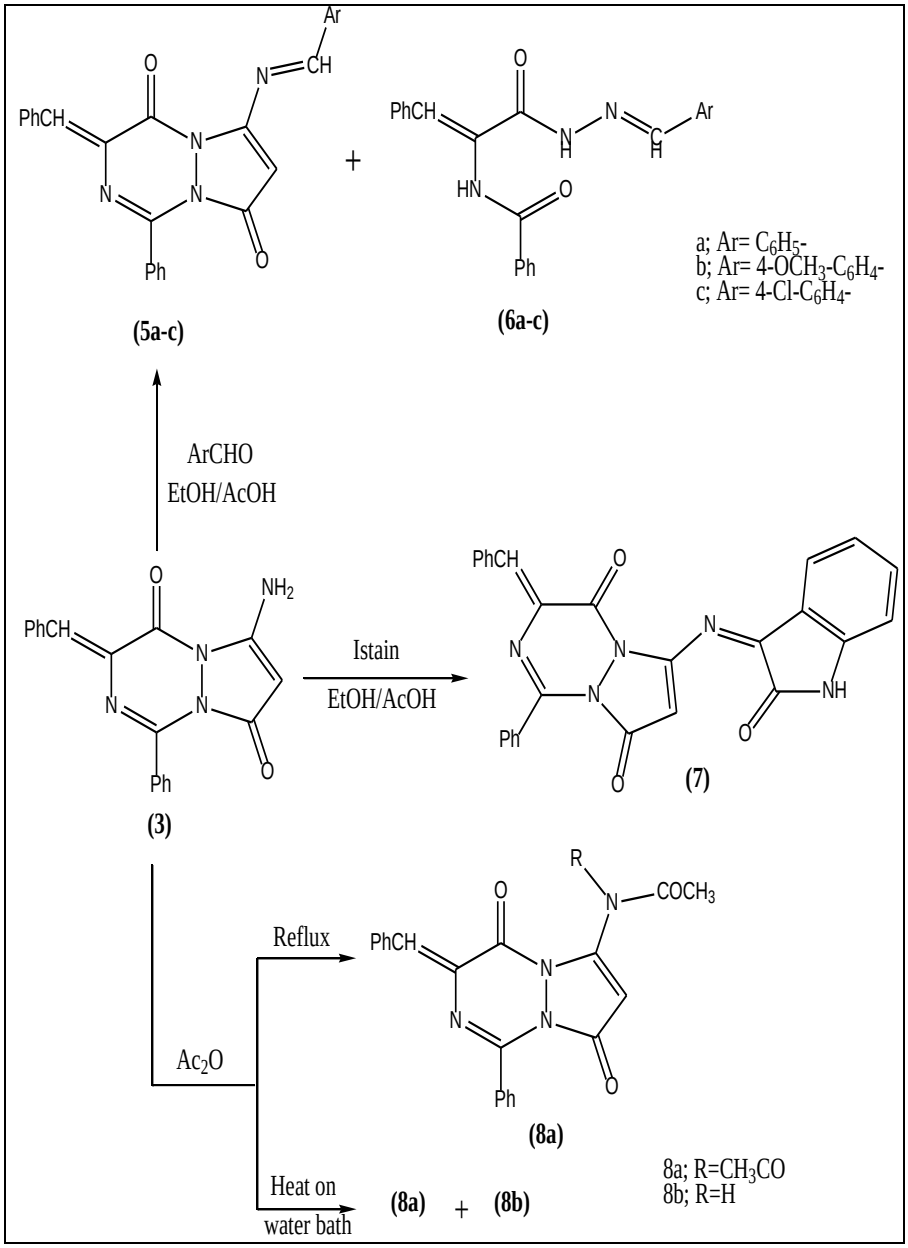
Treatment of the Z-(**2a**) with ethyl cyanoacetate in refluxing ethanol gives 6-amino pyrazolo[1,2-a][1,2,4]-triazines-4,8-diones derivative **3**. Similar treatment of the E-(**2b**) with ethyl cyanoacetate under the same conditions, gave E-(**2b**) recovered unchanged. However, its treatment with ethyl cyanoacetate in the presence of a catalytic amount of sodium ethoxide in refluxing ethanol affored the pyrazoline-3, 5-dione derivative **4 (Scheme 1)**.


(1)
NH2NH2.H2O
EtOH/
stirring at r.t
EtOH/Δ
Z-(2a)
E-(2b)
COOEt
CN
EtOH/Δ
EtOH/EtONa/Δ
(3)
(4)

Scheme 1

The treatment of an ethanolic solution of compound **3** with different aromatic aldehydes such as benzaldehyde, *p*-methoxybenzaldehyde and *p*-chlorobenzaldehyde in the presence of a catalytic amount of acetic acid, afforded the expected Schiff's bases **5a-c** beside small amounts of the unexpected product **6a-c**, respectively. On the other hand, when compound **3** is treated with istain in refluxing ethanol and a catalytic amount of acetic acid, it afforded the Schiff's base derivative **7 (Scheme 2)**.

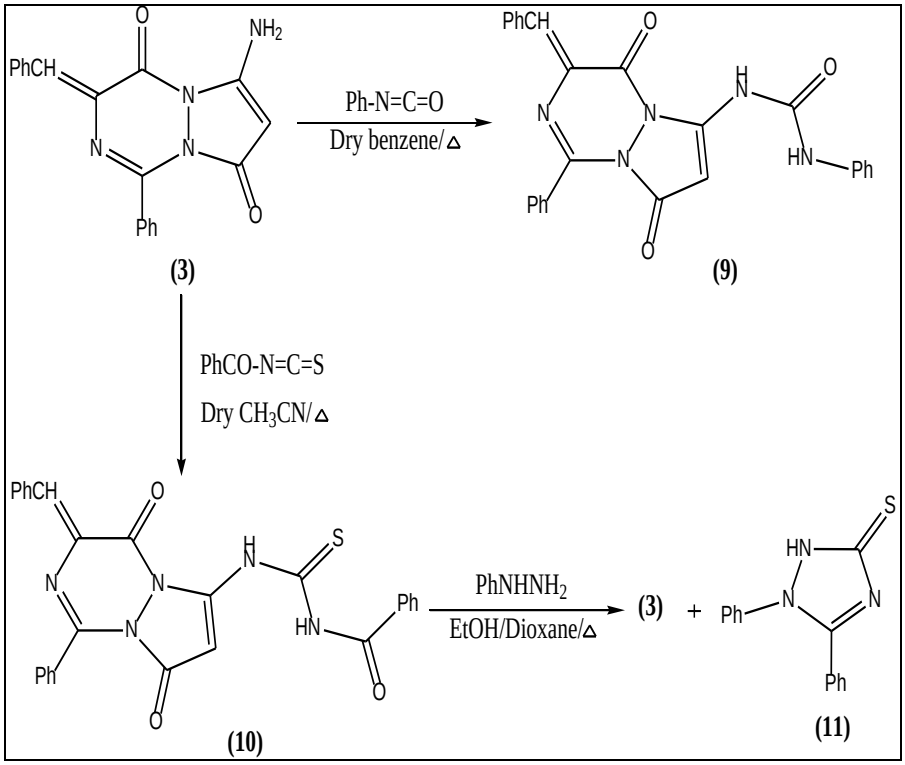
Refluxing of compound **3** in acetic anhydride afforded the diacetyl derivative **8a**. However, its heating on water bath with acetic anhydride yielded a mixture of diacetyl and monoacetyl derivatives **8a** & **8b**, respectively **(Scheme 2)**.



Scheme 2

Treatment of compound **3** with phenyl isocyanate in dry benzene gives the urea derivative **9**. However, its refluxing with benzoyl isothiocyanate in dry acetonitrile

yielded the thiourea derivative **10**. Heating of the thiourea derivative **10** with phenylhydrazine in ethanol/dioxane (1:1) mixture in the presence of a catalytic amount of acetic acid afforded a mixture of two compounds one of them is identical in all respects (m.p., mixed m.p., TLC) with compound **3** and the other was proved to be the 1,2,4-triazole derivative **11 (Scheme 3)**.



Scheme 3

Refluxing compound **3** with *p*-toluenesulphonyl chloride in dry benzene afforded *p*-toluene sulfonamide derivative **12**. Treatment of a solution of compound **3** in