“Arylidene oxazolones as building blocks of some heterocycles of anticipated biological activity”

“A thesis submitted for the degree of master of science as a partial fulfillment for requirements of the master of science”

“David Shoukry Antoun”

Under supervision

“Prof. Dr. Ahmed Said Ahmed Youssef”

“Prof. Dr. Kamal Abdel Rahman Kandeel”

“Dr. Wael S. I. Abou El-Magd”

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A Thesis for M. Sc. Degree in Organic Chemistry

Presented by

David Shoukry Antoun

(B. Sc. 2011)

Department of Chemistry

Faculty of Science

Ain Shams University

Cairo, Egypt

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Thesis Advisors	**Thesis Approved**
Prof. Dr. Ahmed Said Ahmed Youssef Professor of Organic Chemistry, Faculty of Science, Ain Shams University.	……
Prof. Dr. Kamal Abdel Rahman Kandeel Professor of Organic Chemistry, Faculty of Science, Ain Shams University.	……
Dr. Wael S. I. Abou El-Magd Associated Professor of Organic Chemistry, Faculty of Science, Ain Shams University.	……

Head of Chemistry Department

Prof. Dr. Hamed A. Y. Derbala

Contents

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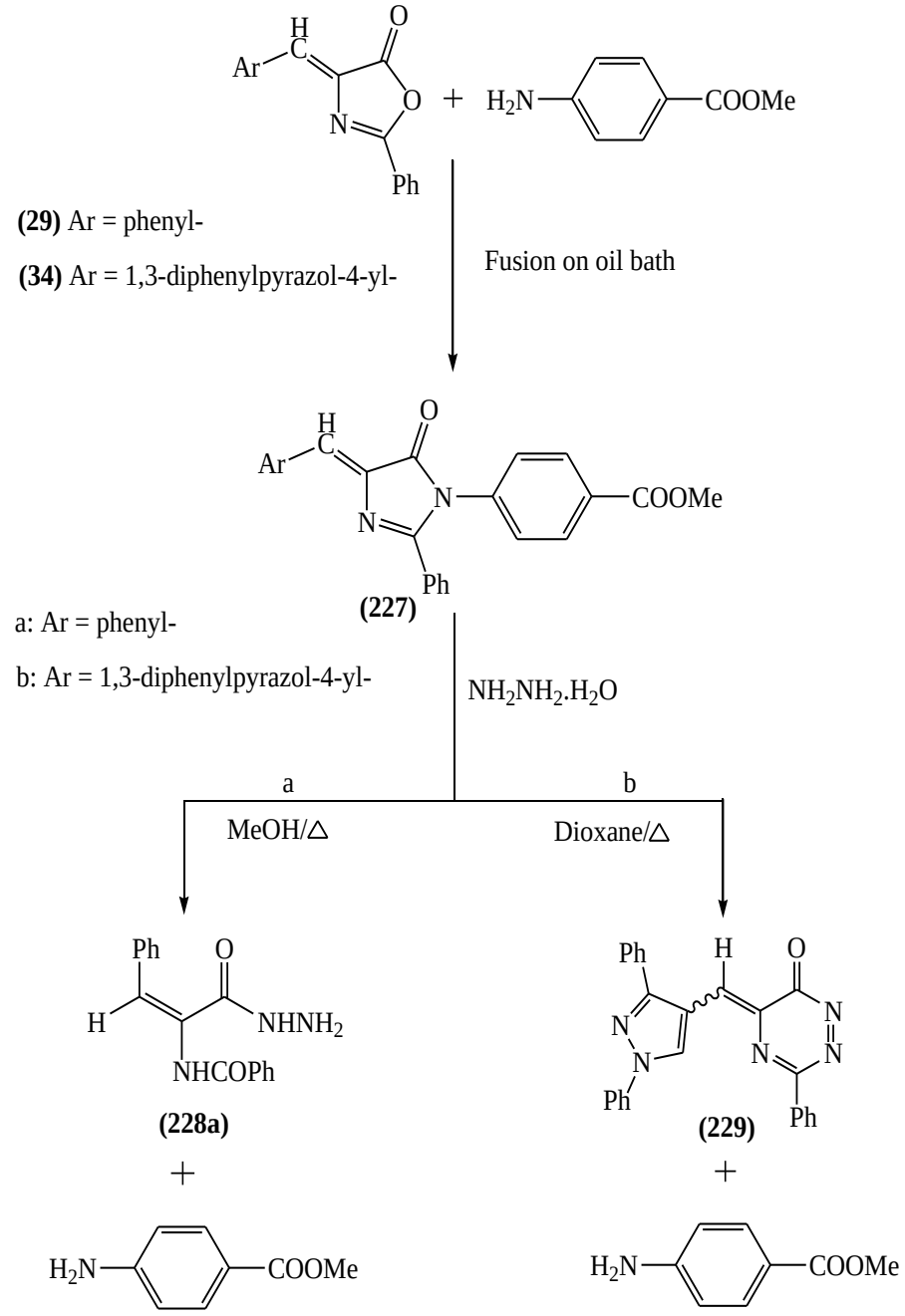
David Shoukry Antoun

Summary

Comparison study between the reactivity of 1,3-oxazolones bearing phenylmethylene- and/or 1,3-diphenyl-pyrazolylmethylene- groups at position-4 towards methyl 4-aminobenzoate and hydrazine hydrate was studied.

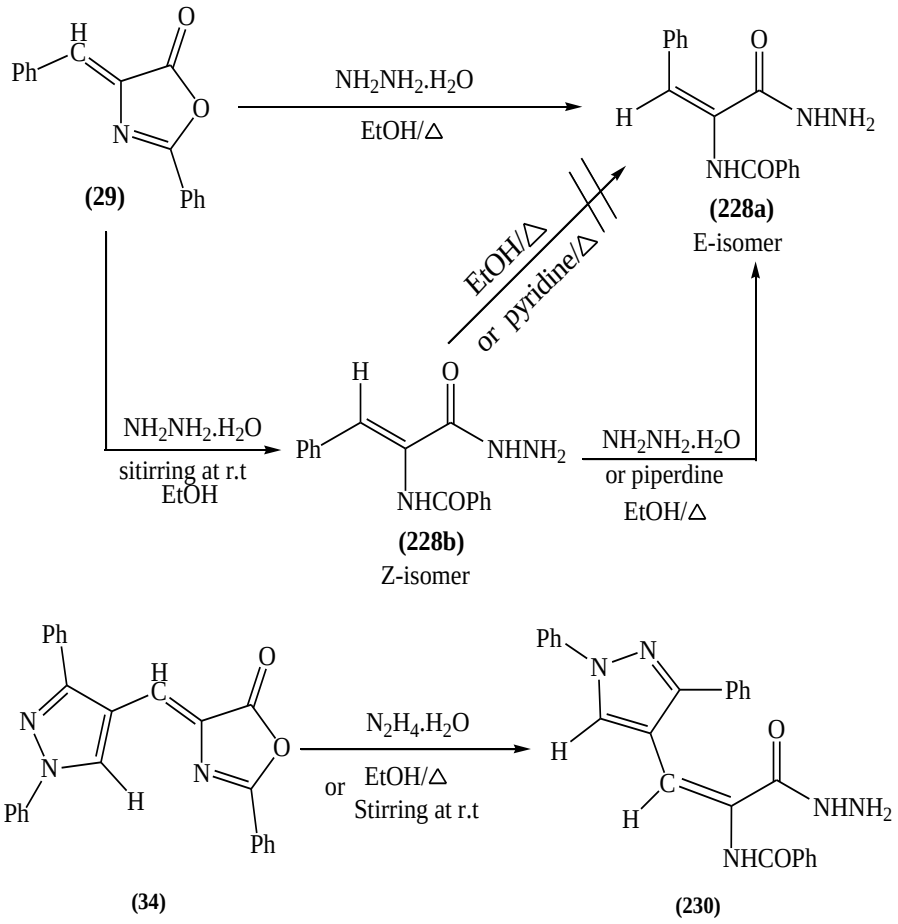
Fusion of oxazolones 4-phenylmethylene-2-phenyl-1,3-oxazole-5(4*H*)-one **29** and 4-((1,3-diphenyl-1*H*-pyrazol-4-yl) methylene) -2-phenyl-1, 3-oxazole-5(4*H*)-one **34** with methyl 4-aminobenzoate on an oil bath gave the imidazolone derivatives **227a** and **227b**, respectively**.** Refluxing **227a** with hydrazine hydrate in methanol for 3h, gave the acid hydrazide derivative **228a**; as E-configurated isomer with a better yield together with a compound which was identical in all respects (m.p., mm.p. and TLC) with methyl 4-aminobenzoate. While the treatment of the imidazolone **227b** with hydrazine hydrate in dioxane for 20h, gave the triazinone derivative **229 (Scheme 1)**.


Ar
H
C
O
O
N
Ph
+
H2N
COOMe
(29) Ar = phenyl-
(34) Ar = 1,3-diphenylpyrazol-4-yl-
Fusion on oil bath
(227)
a: Ar = phenyl-
b: Ar = 1,3-diphenylpyrazol-4-yl-
NH2NH2.H2O
a
b
MeOH/△
Dioxane/△
Ph
H
NHNH2
NHCOPh
(228a)
(229)

Scheme 1

The treatment of **29** with hydrazine hydrate in refluxing ethanol afforded the E-configurated isomer hydrazide derivative **228a** (low yield). However, on doing the same reaction by stirring at room temperature, gave the Z- configurated isomer hydrazide derivative **228b** in a good yield. When Z-isomer **228b** was heated under reflux in ethanol or in pyridine, the isomeisation didn't occur. However, the isomerisation was happened upon heating an ethanolic solution of **228b** with prototype nucleophiles as, hydrazine hydrate or piperidine **(Scheme 2)**.

On the other hand, when the pyrazol-3-yl-methylene oxazolone derivative **34** was treated with the hydrazine hydrate in refluxing ethanol, it afforded one isomer of the hydrazide derivative **230** in low yield. However, on doing the same reaction by stirring at room temperature, the same isomer was isolated but in a good yield **(Scheme 2)**.

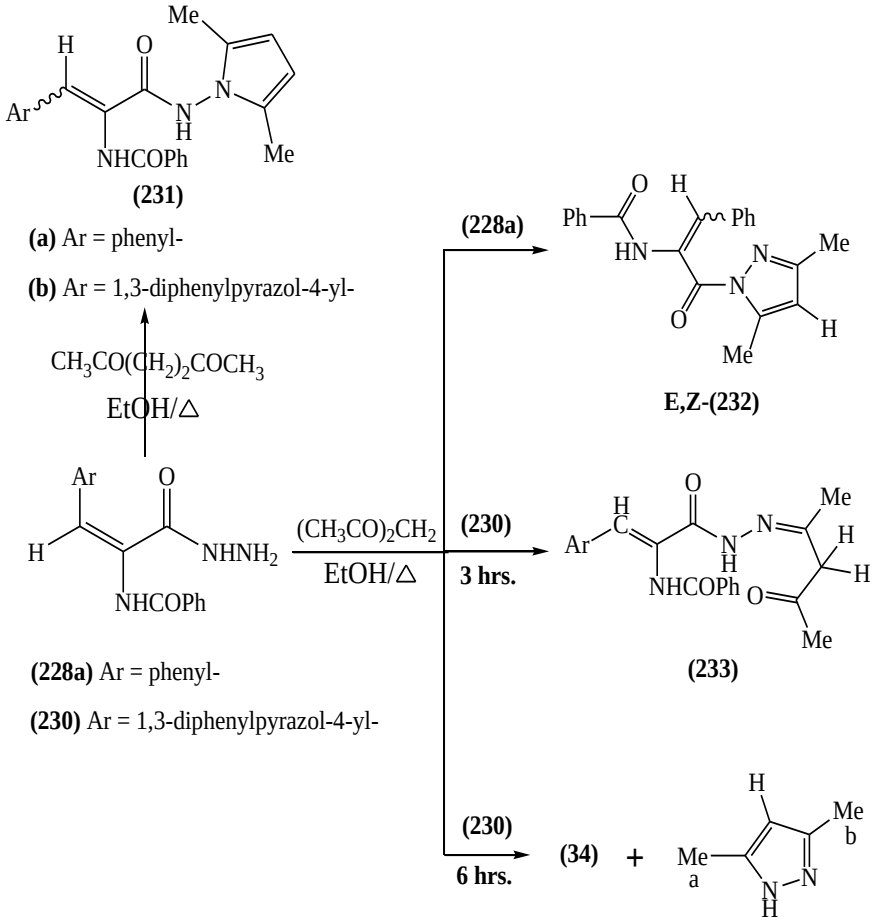


Scheme 2

Reactions of the acid hydrazide dervitatives **228a** and **230** with carbon nucleophiles such as: acetonylacetone, acetylacetone, ethyl acetoacetate and diethyl malonate were investigated.

N-pyrrolo derivatives **231a,b** were obtained upon treatment of the acid hydrazide derivatives **228a** & **230** with acetonylacetone in refluxing ethanol **(Scheme 3)**.

Treatment of **228a** with acetylacetone in refluxing ethanol for 6h. gave the pyrazolyl derivative **232**. Similarly treatment of **230** with acetylacetone in refluxing ethanol gave a product which was proved by IR and ^{1}H-NMR spectra to be a mixture of oxazolone **34** and 3,5-dimethyl-pyrazole. While the reaction of **230** with acetylacetone for 3 h. gave the open chain compound **233 (Scheme 3)**.

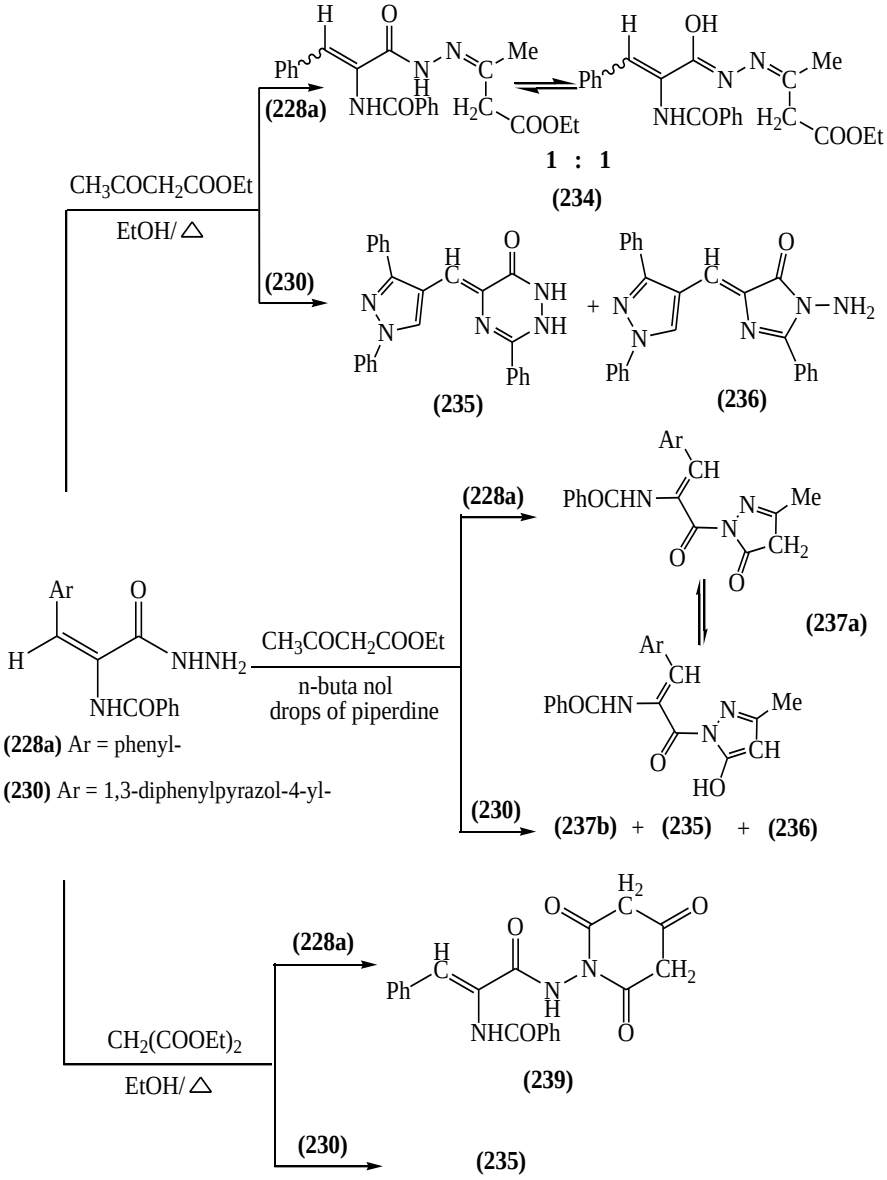


Scheme 3

Heating of an ethanolic solution of **228a** with ethyl acetoacetate afforded the open chain adduct butanoate derivative **234**. On the other hand, ring closure of **230** occurred upon treatment **230** with ethyl acetoacetate. The six and five membered closed forms **235** and **236** were obtained, respectively **(Scheme 4)**. Compound **235** found in two forms and it exists in solution in the lactim form.

Refluxing **228a** with ethyl acetoacetate in n-butanol solution in presence of drops of piperidine afforded the pyrazolone derivative **237a**. Similar treatment of **230** with ethyl acetoacetate under the same condition afforded a mixture of pyrazolidinone derivative **237b**, triazinone and imidazolone derivatives **235** and **236**, respectively **(Scheme 4)**.

Treatment of the acid hydrazide **228a** with diethyl malonate gave the trioxopiperidine **239**. However, similar treatment of the hydrazide **230** with diethyl malonate, yielded a compound that was identical in all respects (m.p., mm.p. and TLC) with the imidazolone derivative **236 (Scheme 4)**.

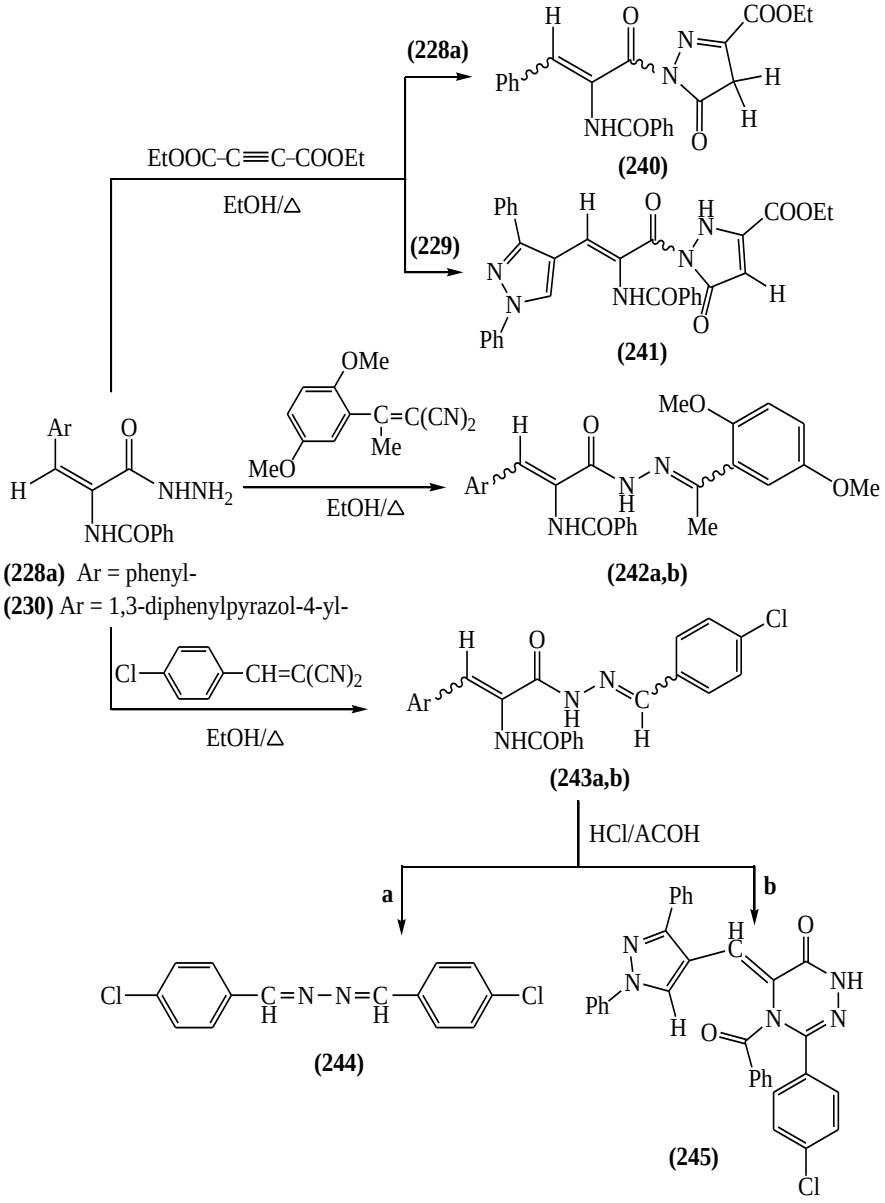


Scheme 4

Treatment of **228a & 230** with diethyl acetylene-dicarboxylate gave the pyrazolone derivatives **240** and **241(Scheme 5)**. When **228a & 230** were treated with the arylidenemalononitriles in refluxing ethanol, they afforded

the N-substituted hydrazone derivatives **242** and **243 (Scheme 5).**

Refluxing of **243a, b** with HCl/AcOH mixture afforded bis-(arylidene) hydrazine **244** in case of **243a** and triazinone derivatives **245** in case of **243b**, respectively **(Scheme 5)**.



Scheme 5

The hydrazide **230** is easily condensed with aromatic aldehydes such as p-anisaldehyde in refluxing ethanol to give the Schiff base product **246 (Scheme 6)** which exists as a mixture of two stereoisomers.