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Kinetics of Acid Catalysed Cyclisation of some Hydrazones

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

TO

MY PARENTS

MY HUSBAND

MY BROTHERS

&

MY SON "MOHAMED"

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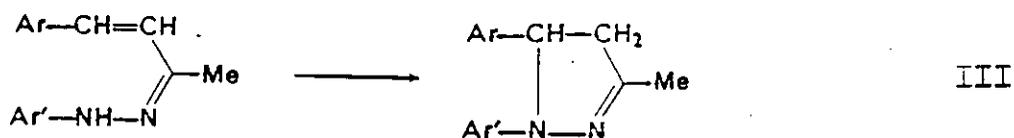
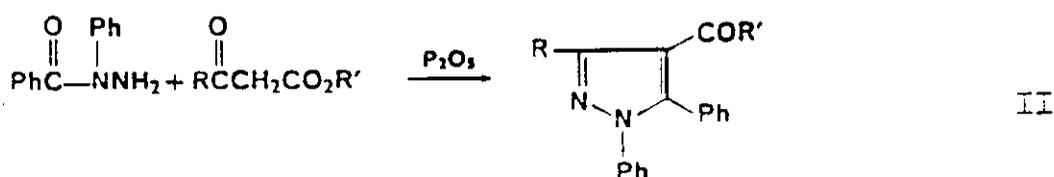
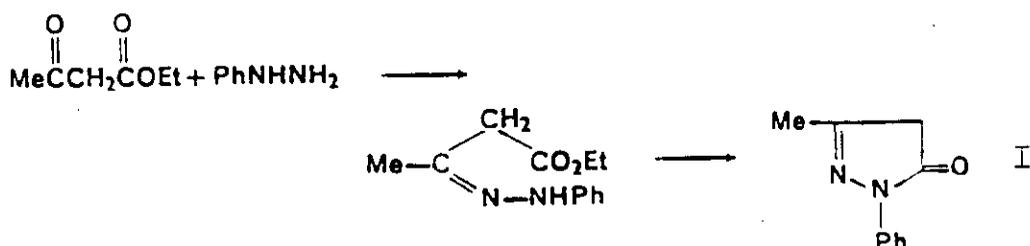
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Chapter 1

INTRODUCTION

Arylhydrazones have a rich chemistry of their own and may be converted to many derivatives which serve as substrates undergoing cycloaddition, internal cyclisation and displacement reactions.

When the hydrazine or the carbonyl substrate has more than one reactive site then the hydrazone which is formed may cyclize; several examples are given in equations I-III. Cyclization is normally acid catalysed,



but oxidising agents such as lead tetra-acetate or bromine have also been widely used^(1,2).

1.1. Cyclisation of Hydrazones to Pyrazolines

Pyrazolines are an important class of nitrogen heterocycles which can be obtained from the cyclisation of hydrazones. They are chemical subunits of pyrazoles. The 2-pyrazolines being for the most common, have been synthesized most frequently by condensation of hydrazines with aldehydes or ketones having either potential or actual α, β -unsaturated double bond. This reaction appears to involve the subsequent addition of N-H across the carbon-carbon double bond and is generally regarded as proceeding through a hydrazone intermediate, which in some instances is stable enough to be isolated. The initial report of a pyrazoline synthesis occurred in 1885 when Knorr and Blank⁽³⁾ described the slow reduction of 1,3-diphenyl-5-methyl pyrazole with sodium and ethanol. The product melted at 109°C was analyzed as $C_{16}H_{16}N_2$ and when reacted with nitrous acid in heated hydrochloric acid produced a blue-green colour. The nitrous acid reaction was later used as the basis for the Knorr⁽³⁾ pyrazoline test which has been used diagnostically. Pyrazoline itself was first synthesized by Curtius and Wirsing⁽⁴⁾, who obtained it in less than 50% yield from the "spontaneous" reaction of acrolein with hydrazine.

1.1.1. Condensations with α , β -unsaturated carbonyl compounds:

Aromatic hydrazines condense with α,β -unsaturated carbonyl compounds to yield pyrazolines under a wide variety of experimental conditions. Among these are reaction in methanol at room temperature⁽⁵⁾, diethyl ether cold⁽⁶⁾ and at room temperature⁽⁷⁾, refluxing ethanol using reaction times⁽⁸⁻¹¹⁾ varying from 10 minutes⁽⁹⁾ to 3 hours⁽¹²⁾, ethanol at room temperature⁽¹³⁾ alone and in combination with acetic acid⁽¹⁴⁾, ethanol and acetic acid at reflux for various periods of time^(15,16), and aqueous ethanol and sodium⁽¹⁷⁾ or potassium acetate⁽¹⁸⁾ and glacial acetic acid at many temperatures and reaction times^(14, 19-24). The reaction will take place in refluxing 3% sodium hydroxide⁽²⁷⁾, sulphuric acid⁽²⁸⁾, refluxing benzene and xylene⁽²⁹⁾. By contrast, aldehydes with terminal unsaturation do not undergo hydrazone cyclisation with any great facility.

Ketones such as dibenzalacetone, which may form pyrazolines by cyclisation in either of two directions have not been studied extensively.

A reported mechanism for the pyrazoline formation reaction as applied to Mannich bases and acidic conditions has been evolved by Nesbit⁽³⁰⁾. It postulates the formation of a phenylhydrazone intermediate, followed by β -elimination and subsequent addition to the newly