STUDIES ON HETEROCYCLIC COMPOUNDS

A THESIS

In Partial Fulfilment of the requirements

of

Master of Science Degree

Submitted

By

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1973

STUDIES ON HETEROCYCLIC COMPOUNDS

The Action of Organomagnesium Compounds on 5-Aryl-indane-(2,1-*e*) pyridazin-3-(2H)-Ones.

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NOTE

Besides the work carried out in this thesis, the candidate has attended postgraduate courses for two years in organic chemistry including the following topics:

1) Reaction Mechanisms.
2) Electronic, Infrared, Raman, n.m.r. and Mass Spectroscopy of organic molecules.
3) Microanalysis of organic compounds.
4) Organic reactions.
5) Heterocyclic compounds.

He has successfully passed an examination in these topics.

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ACKNOWLEDGEMENT

The author wishes to express his deep thanks to Professor S.K. Tobia, Head of Chemistry Department, Faculty of Science Ain Shams University, for the facilities at his disposal.

The author wishes to express his sincere thanks and deep gratitude to Professor F.G. Baddar, D.Sc., Professor of Organic Chemistry, Kuwait University for suggesting the problem, valuable advice and criticism.

The author also wishes to express his deep thanks and gratitude to Dr. S.M.A. Omran, Professor assistant of Organic Chemistry, Faculty of Science, Ain Shams University for his interest and help and to Dr. M.T.Omar, Lecturer of Organic Chemistry, Faculty of Science, Ain Shams University, for his interest, suggestions, continuous advice and valuable help.

The author also acknouledge the assistance of Brunel and Salford Universities for carrying the N.M.R. spectra.

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SUMMARY

The study comprises the synthesis of 5-phenyl (LXIa) and 8-methoxy-5-(p-methoxyphenyl) (LXIb) indane (2,1-e)pyridazin-3(2H)ones by the action of hydrazine hydrate on either the corresponding 1-oxo-3-aryl-2-indenyl acetic acids LVIa and b or their ethyl esters IVIIa and b. It was observed that, the product of the reaction of LVIIIa and b depends on the experimental conditions. Thus, under mild and vigorous conditions, the corresponding hydrazones (LVIIIa and b) and pyridazin-3(2H)ones (LXIa and b), were obtained, respectively. The above hydrazones were found to be different from the acetohydrazides LIXa and b obtained by the action of hydrazine hydrate on the corresponding indenyl esters LVIIa and b.

The structure of the above products was based on i.r., u.v. and n.m.r. spectroscopy and also by a chemical evidence. It was proved also that the reaction between the indenyl acids and hydrazine hydrate proceeds via intermediate hydrazone formation.

The reaction of LXIa and b with Grignard reagents is another goal of our study. As a general, all the Grignard additions gave the corresponding 4-substituted pyridazin-3(2H)ones. This indicates that the initially

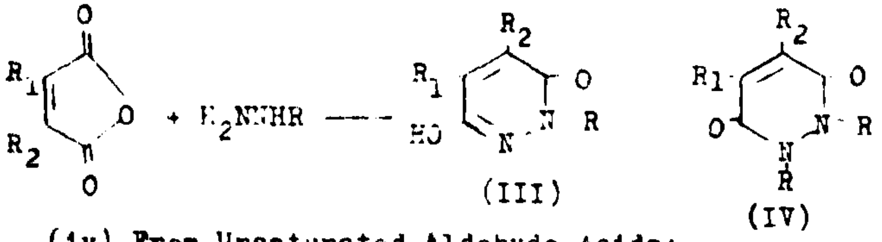
formed 4,5-dihydro derivatives which are obtained by 1,4-addition to the conjugated $-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=N$ system are dehydrogenated by the action of Grignard reagents to the corresponding pyridazin-3(2H)ones LXIX*a*-*l*. Thus, treating LXII*a* with phenyl, *p*-tolyl, *o*-methoxy, *p*-methoxy and α-naphthylmagnesium bromides and benzylmagnesium chloride give 4[phenyl (LXIX*a*), *p*-tolyl (LXIX*b*), *o*-methoxy (LXIX*c*), *p*-methoxy (LXIX*d*), α-naphthyl (LXIX*e*) and benzyl (LXIX*f*)] -5-phenylindane(2,1-*e*)pyridazin-3(2H) ones, respectively. Similar treatment of LXII*b* with Grignard reagents following the same cited order give 4-[phenyl (LXIX*g*), *p*-tolyl (LXIX*h*), *o*-methoxy (LXIX*i*), *p*-methoxy (LXIX*j*), α-naphthyl (LXIX*k*) and benzyl (LXIX*l*)] 8-methoxy-5-(*p*-methoxyphenyl)indane(2,1-*e*)pyridazin-3(2H)ones, respectively.

The structure of LXIX*a*-*l* was based exclusively on i.r., u.v. and n.m.r. spectroscopy. A chemical evidence is also reported.

CHAPTER 1

Synthesis of Pyridazin-3 (2H) ones And Pyridazines

derivatives with hydrazine. This method gives the pyridazin-3(2H)ones [illegible] (III) and (IV) in good yields[5].

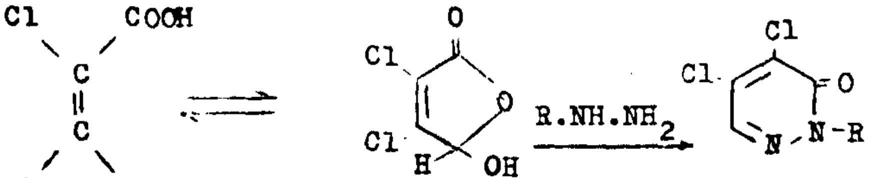


(III)

(IV)

(iv) From Unsaturated Aldehydo-Acids:

Mucochloric acid[6,7] and other halogenated β-formyl acrylic acids have been used recently to obtain 4,5-dihalo-pyridazin-3(2H)ones (V) by condensing with hydrazine derivatives.

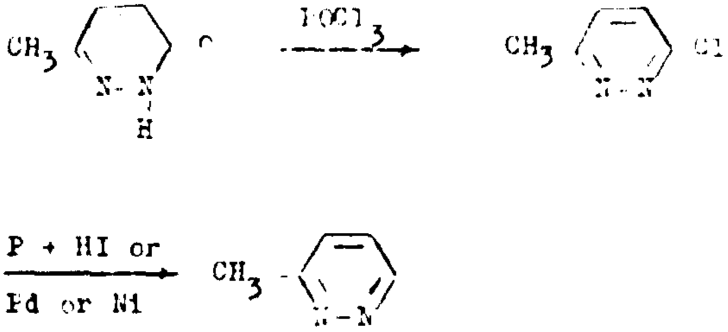


(V)

(B) SYNTHESIS OF PYRIDAZINES:

(i) From Pyridazin-3(2H)ones:

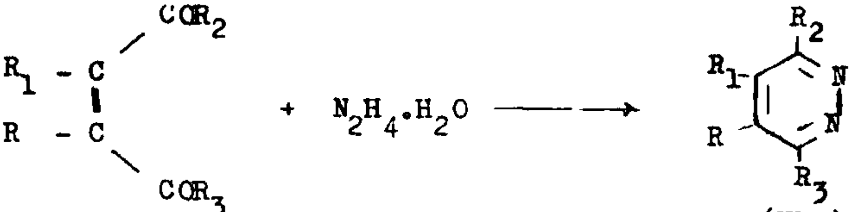
The formation of pyridazines from pyridazin-3(2H)ones is carried out by treating the latter compounds with $POCl_3$ followed by reduction as illustrated below.



(VI)

(ii) From 1,4-Diketones:

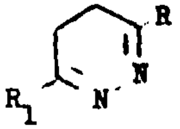
Many alkyl-or aryl-substituted pyridazines (VII) have been prepared by a direct one step cyclisation from unsaturated 1,4-diketones and hydrazine[8].



(VII)

From saturated 1,4-diketones two types of dihydropyridazines may be obtained. 4,5-Dihydropyridazines (VIII) are formed in the reaction between hydrazine and di- or poly-substituted saturated 1,4-diketones bearing aliphatic[9] or aryl[10] groups.

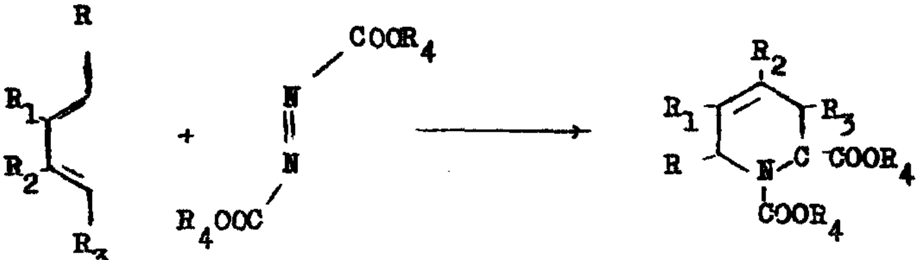
Some 4,5-dihydropyridazines (VIII) are not particularly stable and are dehydrogenated in the presence of air or during distillation into the more stable pyridazine[11].



(VIII)

(iii) By Application of Diels-Alder Reaction:

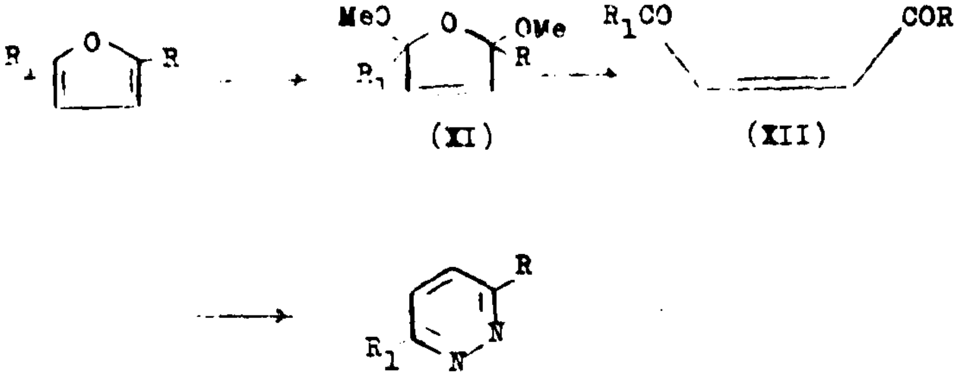
1,2,3,6-Tetrahydropyridazines (X) can be successfully prepared via the Diels-Alder reaction. The most used dienophile is the dialkyl azodicarboxylate (IX), and inspite of its most likely trans-configuration, it reacts easily with simple conjugated dienes in 1,4-addition to give (X)[12].



(IX) (X)

(iv) From Furans:

Pyridazines have been prepared from furans and their reduced analogues. Furans treated with bromine in an methanolic solution gave derivatives of 2,5-dihydrofuran (XI)[13]. These are then submitted to acid hydrolysis and the intermediate (XII) reacts with hydrazine to form the corresponding pyridazines (XIII)[14].



(XI)

(XII)

(XIII)

CHAPTER II

Action of Grignard Reagents on Pyridazin-3 (2H) ones And 4,5-Dihydropyridazin 3 (2H) ones.