Green Synthesis of some Pyrazoline-based Heterocycles and its Applications as Insecticides on Cotton Leafworm *Spodopetra littoralis* (Boisd)

BY

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A THESIS

FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN SCIENCE
CHEMISTRY (ORGANIC CHEMISTRY)

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2020

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SUMMARY

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The aim of the work described in this thesis is the synthesis ,reactions and spectral properties of some 3,5-pyrazolidine and 2-pyrazolin-5-one derivatives and study of its effects as an insecticide for cotton leafworm *Spodopetra littoralis* (Bosid.)

This thesis contains three chapters:

Chapter I: Introduction

This chapter is a continuation to the work done in our laboratory in the field of 3,5-pyrazolidinedione and 2-pyrazolin-5-one and is concerned with a concise survey on the work done in the last decade. 2-Pyrazolin-5-one and some 3,5-pyrazolidinedione derivatives are used in different fields and the most important field is the uses of these compounds as antioxidant in medicine for cancer, cardiovascular disorders, atherosclerosis and AlZheimer disease and these compounds are used in industry as color intermediates and recently are used as pesticide for cotton leafworm *Spodopetra littoralis* (Boisd).

Chapter II: Result and Discussion

This chapter is devoted to discussion of results obtained through the work of this thesis. As some derivatives of 1-phenyl-3,5-pyrazolidinedione and 3-methyl-1-phenyl-2-pyrazolin-5-one synthesized with a novel green synthetic approach and facile methods

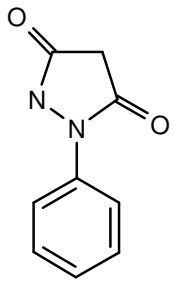
First: Synthesis of 3,5-pyrazolidinedione Derivatives

(A) 1-Phenyl-3,5-pyrazolidinedione:

The main features of green chemistry synthesis are simple methodology, fast, easy product isolation and purification. These

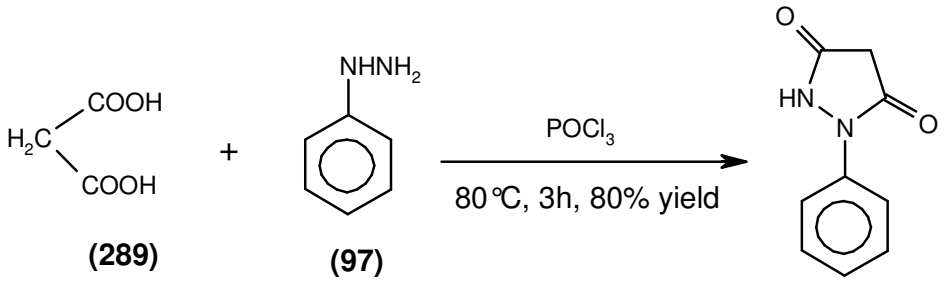
advantages prompted us to develop simple green method to synthesize 1-phenyl-3,5-pyrazolidinedione (1) and some of its derivatives and study

The effect of solvent on synthesis of (1)which give



(1)

Different yields (50%-60%) however, solvent-free
Reaction afforded higher yield (80%)



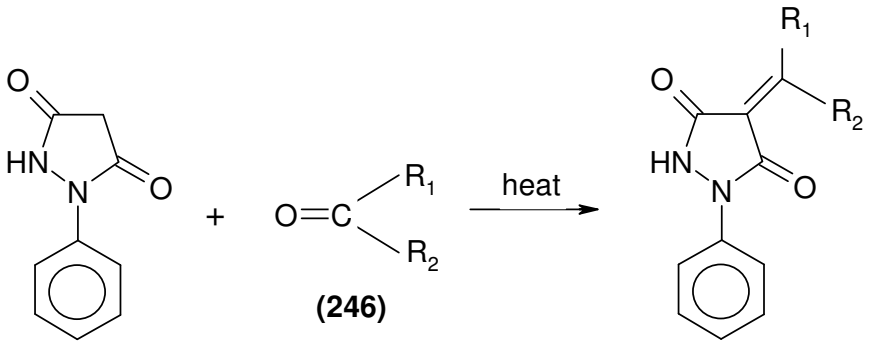
(289) **(97)** **(1)**

Scheme (1): Synthesis of 1-phenyl-3,5-pyrazolidinedione (**1**) under solvent-free condition.

B) Chemical Reactivity of 1-Phenyl-3,5-pyrazolidinedion:

i) Reaction of with Different Carbonyl Compounds:

1-Phenyl-3,5-pyrazolidinedione (**1**) reacts readily with aldehydes or ketones either aliphatic or aromatic under solvent-free condition to give excellent yield of 4-alkylidene (**290a** and **290b**) or 4-arylidene derivatives (**290c-h**) (chalcone derivatives) (Scheme 3) compared with reported literature[247-261].



(1) **(246)** **(290a-h)**

a, $R_1 = R_2 = CH_3$, 90%

b, $R_1 = R_2 = (CH_2)_5$, 92%

c, $R_1 = H$, $R_2 = C_6H_5$, 90%

d, $R_1 = H$, $R_2 = 4\text{-}CH_3C_6H_4$, 88%

e, $R_1 = H$, $R_2 = 2\text{-}CH_3OC_6H_4$, 95%

f, $R_1 = H$, $R_2 = 2\text{-}ClC_6H_4$, 94%

g, $R_1 = H$, $R_2 = 2\text{-}NO_2C_6H_4$, 85%

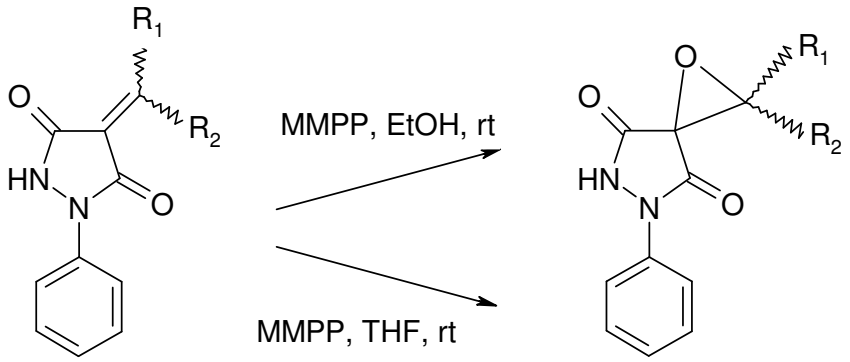
h, $R_1 = H$, $R_2 = 4\text{-}NO_2C_6H_4$, 87%

Scheme (3): Synthesis of chalcone derivatives **(290a-h)**

The structure of each derivative from the series **(290a-h)** was confirmed via elemental and spectral analysis

ii) Epoxidation of 4-Alkylidene or 4-Arylidene Derivatives (Chalcone Derivatives):

The green chemistry approach was employed to investigate the effect of solvent polarity in the epoxidation of chalcone derivatives **(290a-h)** by using magnesium monoperoxyphophate hexahydrate (MMPP) as a versatile oxidizing agent.



(290a-h) **(293a-h)**

a, $R_1 = R_2 = CH_3$ (94%, EtOH; 54%, THF)

b, $R_1 = R_2 = (CH_2)_5$ (92%, EtOH; 50%, THF)

c, $R_1 = H$, $R_2 = C_6H_5$ (89%, EtOH; 52%, THF)

d, $R_1 = H$, $R_2 = 4\text{-}CH_3C_6H_4$ (88%, EtOH; 48%, THF)

e, $R_1 = H$, $R_2 = 2\text{-}CH_3OC_6H_4$ (85%, EtOH; 45%, THF)

f, $R_1 = H$, $R_2 = 2\text{-}ClC_6H_4$ (82%, EtOH; 46%, THF)

g, $R_1 = H$, $R_2 = 2\text{-}NO_2C_6H_4$ (85%, EtOH; 54%, THF)

h, $R_1 = H$, $R_2 = 4\text{-}NO_2C_6H_4$ (87%, EtOH; 52%, THF)

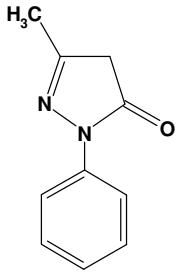
Scheme (13): Synthesis of 1-phenyl-3,5-dioxo-1,2,3,5-tetrahydrospiro-pyrazole-4,3'-oxirane derivatives (**293a-h**).

The structure of each derivative from the series **(293a-h)** was confirmed via elemental and spectral analysis

Second: Synthesis of 3-Methyl-1-phenyl-2-pyrazolin-5-one:

A) 3-Methyl-1-phenyl-2-pyrazolin-5-one:

Which was prepared from more than 130 yeas and came back in the last decade starting from 2001 under the name Edaravone which is used as free radical scavenger. This compound was prepared by the German chemist Ludwig Knorr in 1883.



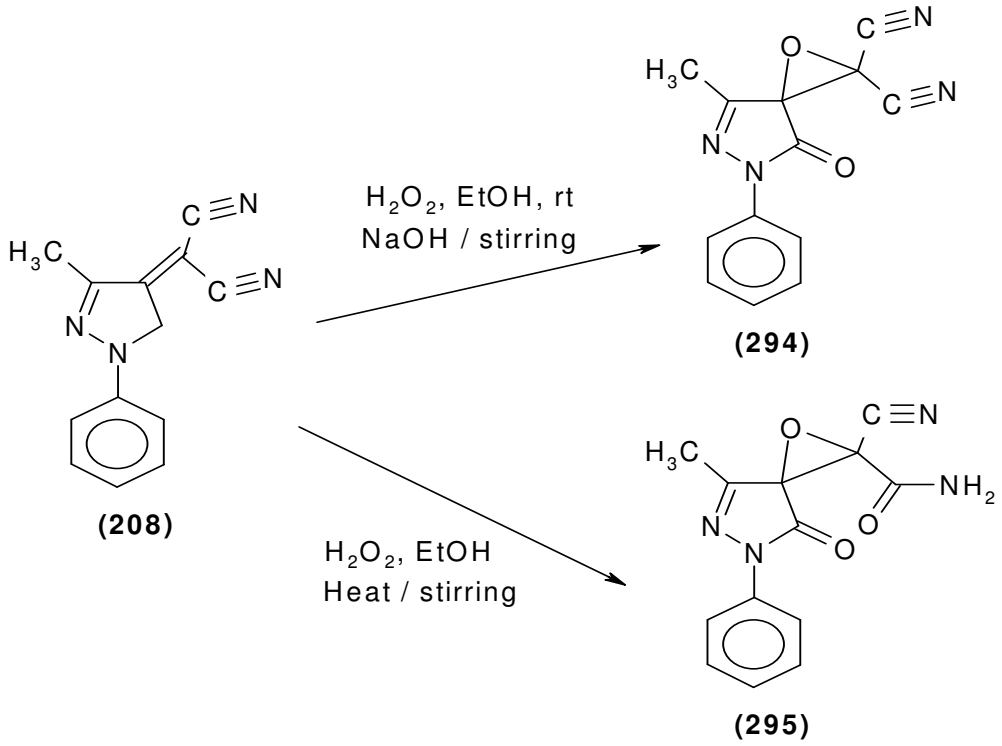
(2)

B) Epoxidation of 4-Dicyanomethylene-3-methyl-1-phenyl-2-pyrazolin-5-one (208):

2',2'-Dicyano-3-methyl-1-phenyl-5-oxo-1,5-dihydrospiropyrazole-4,3'-oxirane **(294)** was prepared by two Routers

Route1: Using Hydrogen Peroxide as Oxidizing Agent:

By addition of hydrogen peroxide[317-323] to a stirred alkaline solution of 4-dicyanomethylene-3-methyl-1-phenyl-2-pyrazolin-5-one (**10**).

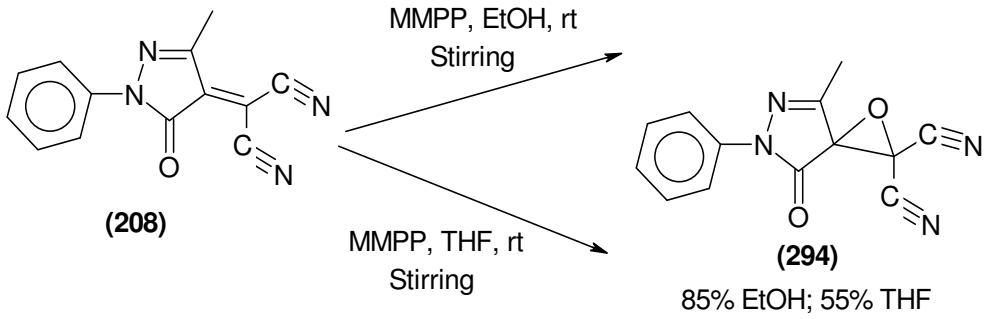


(208) **(294)** **(295)**

Scheme (25): Synthesis of 2',2'-dicyano-3-methyl-1-phenyl-5-oxo-1,5-dihydrospiropyrazole-4,3'-oxirane (**294**)

The corresponding monoamide[324] product (**295**) was obtained by conducing the reaction at higher temperature.

Route 2: Using Magnesium Monoperoxyphethalate Hexahydrate (MMPP)



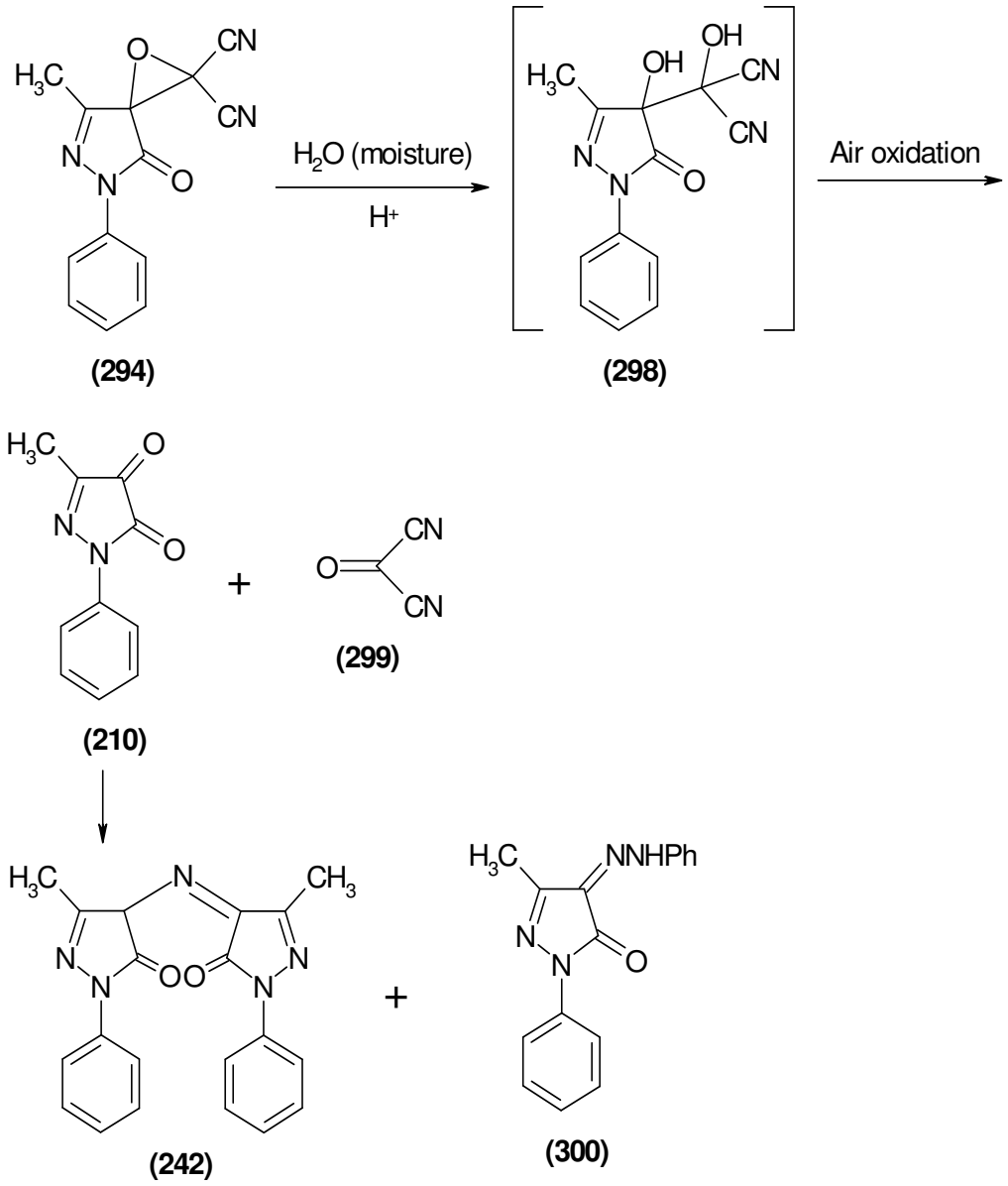
Scheme (27)

Compounds **(294)**,**(295)** were confirmed via elemental and spectral analysis.

C) Chemical Reactivity of 2',2'-Dicyano-3-methyl-1-phenyl-5-oxo-1,5-dihydrospiropyrazole-4,3'-oxirane (294):

i) Aging:

The colorless freshly prepared 2',2'-dicyano-3-methyl-1-phenyl-5-oxo-1,5-dihydrospiropyrazole-4,3'-oxirane (**294**) turns red by aging in presence of light and moisture. Thin layer chromatography indicates the presence of two main products beside the starting material (**294**) which were identified as 3-methyl-4-((3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazole-4-ylidene)amino)-1-phenyl-2-pyrazoline-5-one (**242**) and the hydrazone derivatives (**300**)

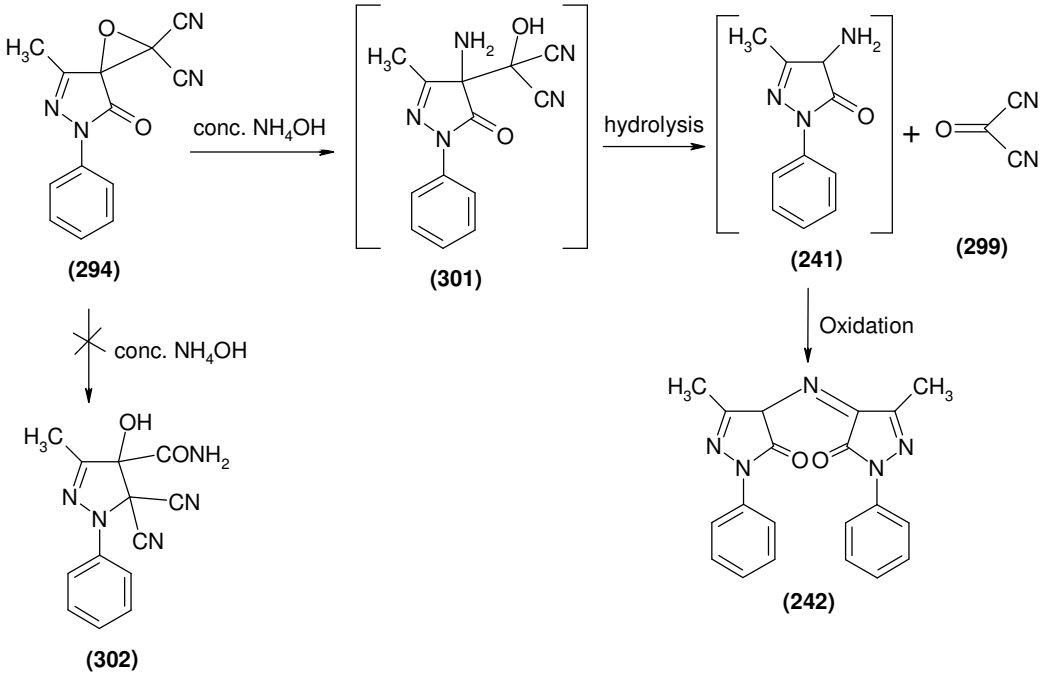


Scheme (31)

ii) Reactions of (294) with Nucleophiles:

a) Reaction of (294) with Ammonia:

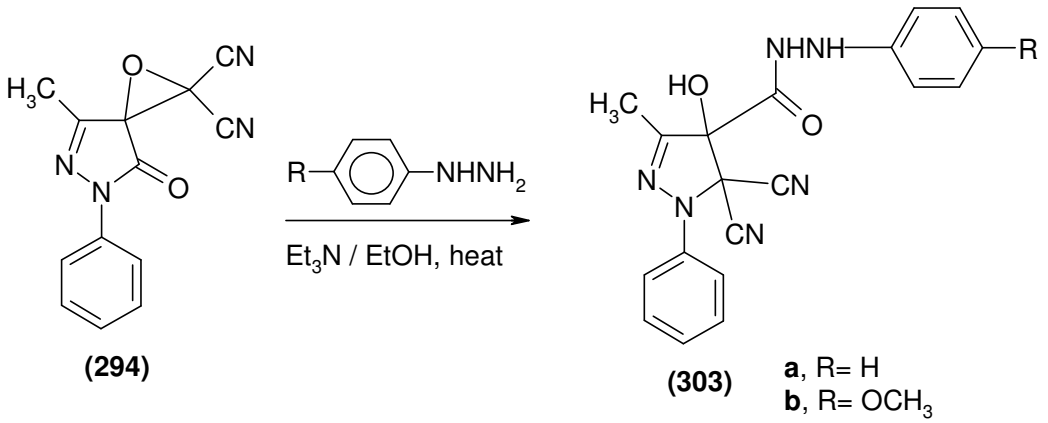
Ammonium hydroxide reacts rapidly with (**294**) with the formation of 3-methyl-4-((3-methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazole-4-ylidene)amino)-1-phenyl-2-pyrazoline-5-one (**242**) All traies to get 4,5-dihydro-4-hydroxy-1H-pyrazole-4-carbohydrazide (**302**) failed.



Scheme (32)

b) Reaction of (294) with Phenylhydrazine:

2',2'-Dicyano-3-methyl-1-phenyl-5-oxo-1,5-dihydrospiropyrazole-4,3'-oxirane (**294**) reacted with phenylhydrazine and/or 4-methoxyphenyl-hydrazine in absolute ethanol as a solvent in presence of few drops of triethylamine and gave the corresponding 5,5-dicyano-4,5-dihydro-4-hydroxy-3-methyl-1-phenyl-1H-pyrazole-4-carboxylic acid derivatives (**303a,b**).



Scheme (33)

Compounds (**303a,b**) were identified via elemental and spectral analysis.

Application part

Four 3,5-pyrazolidinedione derivatives namely, 4-(4'-chlorobenzylidene)-1-phenylpyrazolidine- 3,5-dione (**290f**), 4-(4'-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione (**290h**), 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (**293f**) and 2'-(4-nitrophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (**293h**) were prepared in pure state and bioassayed against 2nd and 4th instars larvae of cotton leaf worm, Spodoptera littoralis (Boised) (Lepidoptera: Noctuidae) using feeding and dipping bioassay. The results of bioassays indicated that title compounds exhibit satisfactory insecticidal activities. Among those, compound (**290f**) exhibit the highest insecticidal activities against 2nd instar larvae, with LC_{50}s 3.23 and 0.619 mgL-1 for feeding, and 36.04 and 28.69 mgL-1 for dipping, after 48 and 72 h treatment. According to the toxicity index the compound (**290f**) showed the highest larvicidal activity against 4th instar larvae with LC_{50}s 141.33 and 76.12 mgL-1 for feeding larvae, and 26.94 and 12.29 mgL-1 for dipping larvae after 48 and 72 h treatment. These results showed that, the 2nd larvae was more susceptible than 4th instars larvae to these compounds. In addition, the insecticidal activity of these compounds was more effective on cotton leaf worm larvae in feeding bioassay as compared with the dipping treatment. The rest of the tested compounds possessed moderate to strong larvicidal activities against cotton leaf worm. In general, the results indicate the possible use of 3,5-pyrazolidinedione derivatives as components in integrated pest management program against Cotton Leafworm ,Spodopetra littoralis.