SYNTHESIS OF SOME HETEROCYCLIC COMPOUNDS FOR COMBATING COTTON LEAF WORM"*SPODOPTERA LITTORALIS "*

Submitted By

Mohamed Sobhi Mohamed Ali

B.Sc. of science (Entomology/ Chemistry), Faculty of Science, Ain Shams University, 2010

A thesis submitted in partial fulfillment
Of
The Requirements for the Master's Degree
In
Environmental Sciences

Department of Environmental Basic Sciences

Institute of Environmental Studies and Research

Ain Shams University

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Mohammed Sobhi Mohammed Ali khamees

ABSTRACT

The crop plants are the major source of human nutrition, but insects and pests cause huge economic losses every year. The researcher was interested in developing novel insecticidal agents with low toxicity and an acceptable impact on the environment. Thus, 2-amino-5-(substituted)-1,3,4-thiadiazoles (**1a, b**) were used as versatile materials to synthesize novel compounds through reaction with different electrophiles. The insecticidal activity of the synthesized compounds was tested using 4th instar larvae of *spodoptera littoralis*. Most of the tested compounds showed good to excellent insecticidal activity. Thus, the synthesized compounds could be used in the field of pest control through using them in proper pesticide formulations.

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Introduction & Review of Literature

1. Chemistry of 1,3,4- thiadiazole

The chemistry of heterocyclic compounds has been an interesting field of study for a long time. 1,3,4-Thiadiazoles are important five-membered sulphur and nitrogen-containing heterocycles with a wide range of applications (**Hu, Y. *et al*. 2014**) in medicinal chemistry, material science, and organic synthesis. In particular, these thiadiazole structural motifs bearing an amino functionality in position 2 are valuable building blocks in drug design (**Matysiak, J.& Opolski A, 2006**).

It has been widely reported that compounds bearing thiadiazole rings exhibit anticancer, anti-inflammatory, antibacterial, antifungal, antiviral, anticonvulsant and antiparasitic activities.

Thiadiazole is a constrained pharmacophore with hydrogen binding domain and electron donor system, occurring in nature in four isomeric forms (1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole and 1,3,4-thiadiazole) where 1,3,4-thiadiazole isomer is the most investigated one (**Bhuva, H. *et al.*,2011**).

1,2,3-thiadiazole

1,2,4-thiadiazole

1,2,5-thiadiazole

1,3,4-thiadiazole

The 1,3,4- thiadiazole ring is a very weak base due to the inductive effect of the sulfur atom and possesses relatively high aromaticity (**Balaban, A. T., *et al*., 2004**). It is relatively stable in

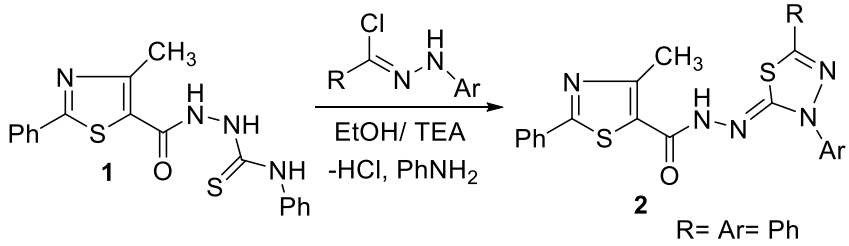
aqueous acid solutions but can undergo ring cleavage with aqueous base. Thus, possessing these properties, 1,3,4-thiadiazole derivatives are applied widely in pharmaceutical chemistry.

Thiadiazoles have become very important compounds in agriculture. A large number of 1,3,4-thiadiazoles have been patented in the agricultural field as herbicides and bactericides (**Wei, T-B. *et al*.,2006**). Also, 1,3,4-thiadiazole derivatives have been reported to be insecticidal agents (**Luo, Y-P., & Yang, J-F., 2007**).

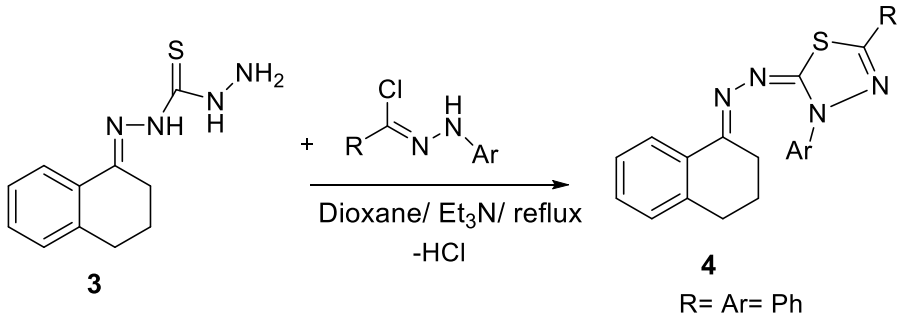
2. Synthesis of 1,3,4-thiadiazole

2.1.From Hydrazonoyl Halide

Treatment of 2-(4-methyl-2-phenylthiazole-5-carbonyl)-*N*-phenylhydrazinecarbothioamide **(1)** with hydrazonoyl chlorides (**Gomha, S. M.; Edrees, M. M., *et al.*, 2017**) led to the formation of 1,3,4-thiadiazoles **2**.



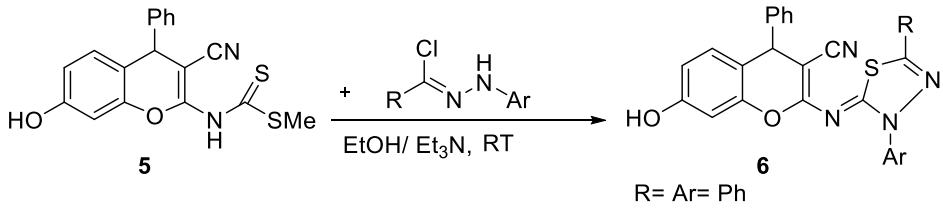
Reaction of compound **3** with hydrazonoyl chlorides in dioxane in the presence of triethylamine under reflux afforded thiadiazoles **4** (**El-Hag, F. A. A., *et al*., 2017**).



3 **4**

R= Ar= Ph

The methylthio derivative **5** underwent nucleophilic substitution when reacted with hydrazonoyl halides in presence of triethylamine at room temperature to afford the thiadiazoles **6** (**Badrey, M. G.,*et al.*, 2017**).

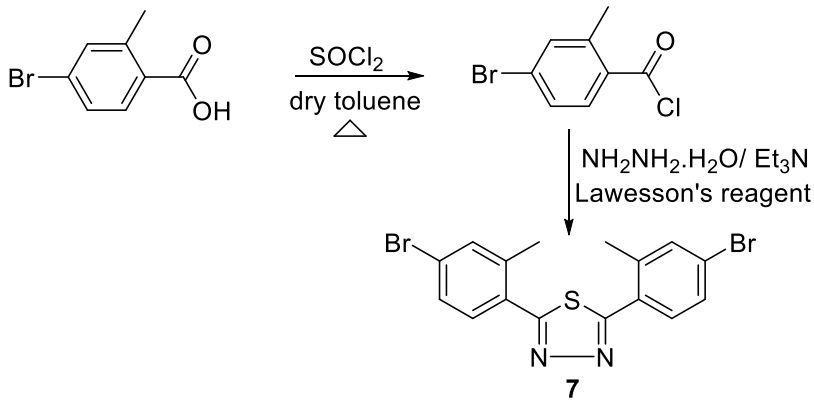


5 **6**

R= Ar= Ph

2.2. From Hydrazine Hydrate

4-bromo-2-methylbenzoic acid was heated in the presence of thionyl chloride in dry toluene giving the corresponding acid chloride, which was treated with hydrazine hydrate in the presence of triethylamine and Lawesson's reagent to afford the thiadiazole **7** in excellent yields (**Wróblowska, M., *et al.*, 2017**).

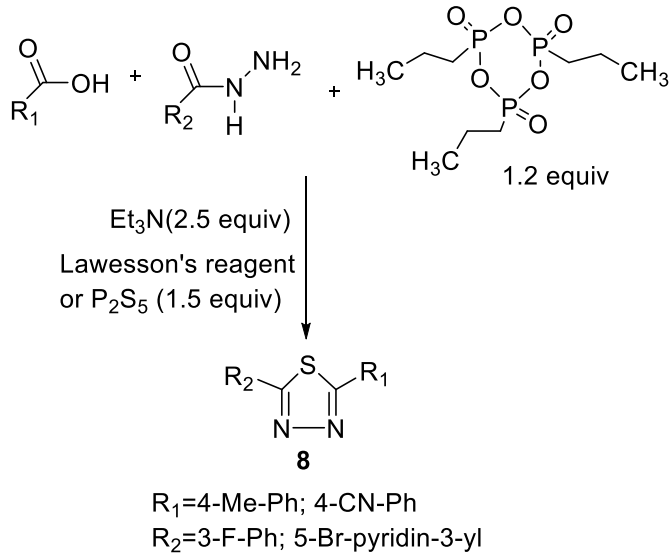


2.3. From Acylhydrazines

1,3,4-Thiadiazoles can be prepared *via* sulfuration of the corresponding 1,4 dicarbonyl or acyl precursors using phosphorus sulfide reagent P_2S_5 and / or Lawesson's reagent **(Kuo, H-M., *et al.*, 2012**).

2.3.1. From Acid Hydrazides

Augustine *et al.* (**2009**) reported a one-pot synthesis of the 1,3,4-thiadiazoles **8** directly from carboxylic acids with acid hydrazide using propylphosphonic anhydride (T3P) in which it acts as both a coupling and a cyclodehydration reagent.



R_1=4-Me-Ph; 4-CN-Ph
R_2=3-F-Ph; 5-Br-pyridin-3-yl