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Synthesis of Biologically Active and Environmental Friendly Insect Pesticides: Pheromones

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There is a continuous fight with insects and herbs by utilizing pesticides in agricultural productions. Besides their insect killing benefits, these chemicals are extremely harmful for other living things. Recently, pheromones are being suggested as an alternative to these harmful chemicals, especially for the preservation of air, water and soil. These are the secretion of insects used for the comunicating each other by perceiving that secretion. The most important problem with such an application is the synthesis of these substances. Pheromones have ability to select the harmful insects and provide opporunity to kill them. Therefore, in this study, synthesis of two pheromones are studied for the harmful insects cotton- and apple-worms. Under laboratory conditions, synthesis method was developed for biologically active substance *trans-trans*-8,10-dodecadien-1-ol. Then its suitable aldehyde and ester derivatives were also synthesized.

Key Words: Pheromones, Synthesis, Biologically active.

INTRODUCTION

Pesticides and insecticides are the chemicals extensively used in agricultural productions for insect killing purposes. It is well known that besides their insect killing benefits, these are extremely harmful for other living things. They accumulate in the body and reach lethal doses. Despite their harmful effects they are still being widely used in agriculture since there is no alternating insect killing chemicals. There are many types of insects extremely harmful for plants. 25-30 % of annual agricultural products were lost because of these harmful insects. Therefore new effective, economical and environmentally friendly insect pests are strongly required for a healthy agriculture.

Recently, as an alternative to these harmful chemicals, pheromones are being suggested especially for the preservation of air, water and soil. Pheromones are the secretion of insects used for the comunicating purposes between each other. There are limited studies to the synthesis and utilization of pheromones, although a great economical and environmental benefits are being expected from them. They can be

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used with great success as components of insect pest management strategies. However, difficulties in achieving cheap and efficient synthesis starting from fine chemicals have obstructed commercial production[1].

Generally pheromones are divided into several groups such as signalling and priming. Signalling pheromones are substances that cause an immediate behavioural response, invoking a classical stimulus-response paradigm mediated by the central nervous system. Pheromones may also have dual signalling and priming effects and identified in insects. For example, 9-oxodecenoic acid, a pheromone produced by the queen honey bee, has two priming functions *i.e.*, inhibition of queen rearing and suppression of oogenesis in workers and in addition, 9-oxodecenoic acid attracts drones during the nuptial flight, a releasing function[2].

Pheromones are synthesized by various insects. Actually insects have a very sensitive analyzers which are much more sensitive to smells that cannot be analyzed by any of the most sensitive laboratory systems. By this property these insects have been still alive for thousands of years. Pheromone systems of insects have proved to be some of the richest intellectual sources for the nascent science of chemical ecology[3].

Another advantage of pheromones are their economical benefits such that, pesticides are used about 1-3 kg per hectar while about 1-3 g pheromone is enough per hectar. Therefore, by the use of pheromones, huge quantities of harmful chemicals could be decreased to small quantities and there will be no more accumulation of pesticides from soil through food chain.

Studies on pheromones have started since 1965 and in 1972 totally 37 types of pheromones have identified by Jackobson[4]. These 37 pheromones were extracted from insects, their structures were defined and studies have started to describe their methods of synthesis. Over the past 4 decades, extensive research on insect pheromones has resulted in the chemical and/or behavioural elucidation of pheromone components from over 1500 of the estimated 875,000 described species of insects. In a number of cases, the application of knowledge of insect pheromones in integrated pest management tactics is well underway[5-8].

Bütendart[9] synthesized 20 mg L^{-1} of the compound *trans*-*cis*-10,12-hegzade-kadien-1-ol named "bombycol" (compound (1) below) from more than 500000 insects by the method of extraction.

In the pheromone structures of some insects, epoxide group was determined. Donald[10] have synthesized 21 *cis*- and *trans*-epoxides containing epoxide groups in their structures and in field applications he observed that, only *cis*-9,10-epoxyocta-decan-1-ol (2) is effective.

It is possible to get information about the existence of any insects in the environment such as fields, forests. Identification of existing insects is of vital importance especially in fighting with them. Without preliminary assessment, it is difficult to determine the reproduction period of harmful insects to be killed. In some cases, female insects secret their pheromones under certain temperatures and in certain times of the day.

In the experimental studies performed in U.S.A., the effects of pheromone "grandlur", which is a component synthesized by glycerol, water, polyethyleneglycol and methanol is found as important as the determination of the formation of alive male insect in the field. Pheromones were secreted only by alive insects.

In another study, extremely dilute solution of pure phenol is found as effective on the insect seizing It was observed that, by using this solution in a trap, 222 male insect *Costelystra zealandica* were captured in a night. About 1500 male and female insects were collected around a trap prepared by 2 L solution of diluted phenol[2].

In order to determine the activity of any synthetic pheromone, it can be compared with the attractiveness of the insects put in a trap. For example, in a study performed by Staten *et al.*[8], an extracted pheromone obtained from 10 *Molesta* insects was put in a trap which is placed 30 cm distance from an apple tree. A number of insects of the same type were gathered around the trap. Although there was another trap including another type of chemical, insects were not interested with the smell in it.

In a cotton field, a trap was prepared with 4 female insects in the July-August season, about 238 male and 43 female insects were gathered to the smell of pheromone secreted by these 4 insects. In the control trap, the dead insects of the same type were utilized and it was observed that no insects were gathered.

Therefore, literature indicated that synthetic pheromones have been utilized in struggling with harmful insects in agriculture.

In this study, pheromone named as "*trans*-8-*trans*-10-dodecadien-1-ol"and its ester and aldehyde derivatives, which are biologically active and can be used for the struggling with apple and cotton worms are synthesized. In this paper, the method of synthesis and the effects of the synthesized pheromone were explained. The further step of this study will include the applications of the sythesized pheromones in apple gardens in the local area Konya/Turkey.

EXPERIMENTAL

1,6-Hexanediol, toluene, 3,4-dihydropyrene, dichloromethane (DCM), *p*-toluenesulfonic acid (*p*-TsOH), 3,4-dihydro-2*H*-pyran, methanol, acetic anhydride (AA), benzene, tetrahydrofuran (THF), 2,4-hexadien-1-ol, pyridinium chlorochromate (PCC) and dimethylformamide (DMF) were purchased from Fluka

Synthesis of 6-bromo-hexane-1-ol (Scheme-I, I): A reactor composed of mixer and thermometer was used in the experiments. 6 g (0.06 mol) H_2SO_4 was added to the 20 g (0.17 mol) 1,6-hexanediol and 21 g (0.25 mol) HBr in 100 mL toluene drop-by-drop. Reaction was ended in 17 h at the temperature of 95 ºC. After the reaction, the 6-bromo-hegzane-1-ol was separated by extraction with toluene and dried with $MgSO_4$ and purified in the distillation process under vacuum. The values obtained for 6-bromo-hexane-1-ol were $d^{20} = 1.3628$; $n^{20} = 1.4820$.

Synthesis of 2-pyran ether of 6-bromo-hexane-1-ol (Scheme-I, III): 1.27 g (15 mmol) 3,4-dihydro-2*H*-pyran solution in 4 mL DCM was added to the 1.4 g

(0.08 mol) 6-bromo-hexane-1-ol solution in 20 mL DCM and 0.01 g catalyst *p*-TsOH at the room temperature. Reaction mixture was stired for 5 h, waited for 12 h and then organic phase separated. The values obtained for 2-pyran ether of 6-bromo-hexane-1-ol were $d^{20} = 1.2082$; $n^{20} = 1.4764$.

Synthesis of Grignard reactant from III (Scheme-I, IV): 15.4 g 2-pyran ether of 6-bromo-hexane-1-ol solution in 15 mL THF was added to the 1.14 g Mg and 25 mL THF drop-by-drop at the room temperature for 3 h. Reaction mixure was cooled to the -78 °C and was added 6.4 mL catalyst Li_2CuCl_4.

Synthesis of methyl ester of *trans*,*trans* 2,4-hexadien-1-ol (Scheme-II, V): A reactor composed of mixer and thermometer was used in the experiments. 15 g (0.153 mol) 2,4-hexadien-1-ol was added to the 15.6 g (0.153 mol) acetic anhydride and 14 mL DMF drop-by-drop at the room temperature for 3 h. Reaction mixure was boiled in the water bath, then added to the ice water and organic phase was separated. The values obtained for methyl ester of *trans*,*trans*-2,4-hexadien-1-ol were $d^{20} = 0.9462$; $n^{20} = 1.4690$.

Synthesis of *trans*-*trans*-8,10- dodecadien-1-ol (Scheme-II, VII): Reaction product **V** was added to the **IV** and reaction temperature was raised from -78 ºC to the room temperature for 3 h. Then to the reaction mixture was added H_2SO_4 solution and organic phase 2-pyran ether derivative (**Scheme-II**, **VI**) was separated. 1.5 g **VI**, 0.1 g *p*-TsOH and 30 mL methanol were stired at 50 ºC for 3.5 h. Reaction mixture was neutralized with $NaHCO_3$ and *trans*-*trans*-8,10-dodecadien-1-ol (**Scheme-II**, **VII**) was extracted with ether. Reaction efficiency was 42 %.

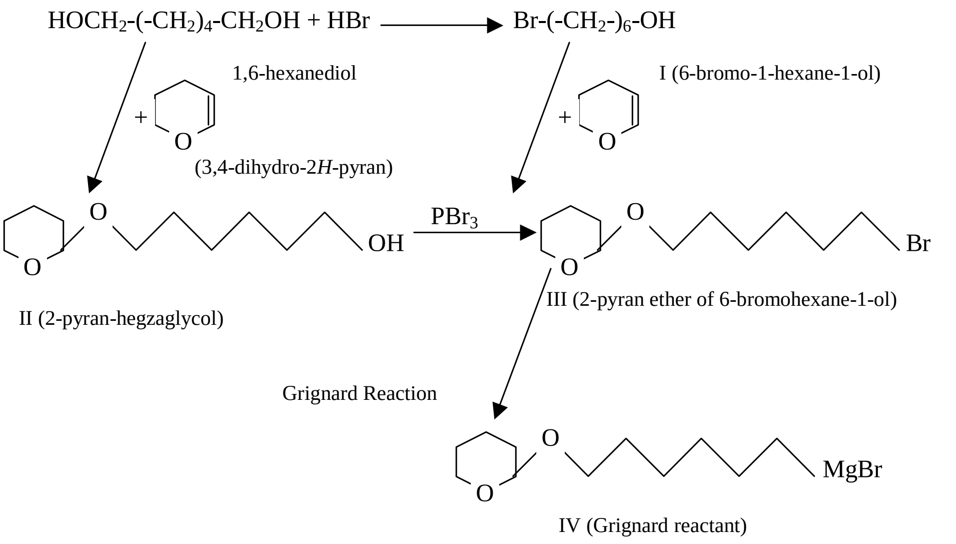
Synthesis of methyl ester and aldehyde derivatives of VII: Methyl ester of *trans*-*trans*-8,10-dodecadien-1-ol was synthesized from **VII** with acetic anhydride in DMF. *Trans*,*trans*-8,10-dodekadien-1-al was synthesized from **VII** by oxidation with PCC in DCM.

RESULTS AND DISCUSSION

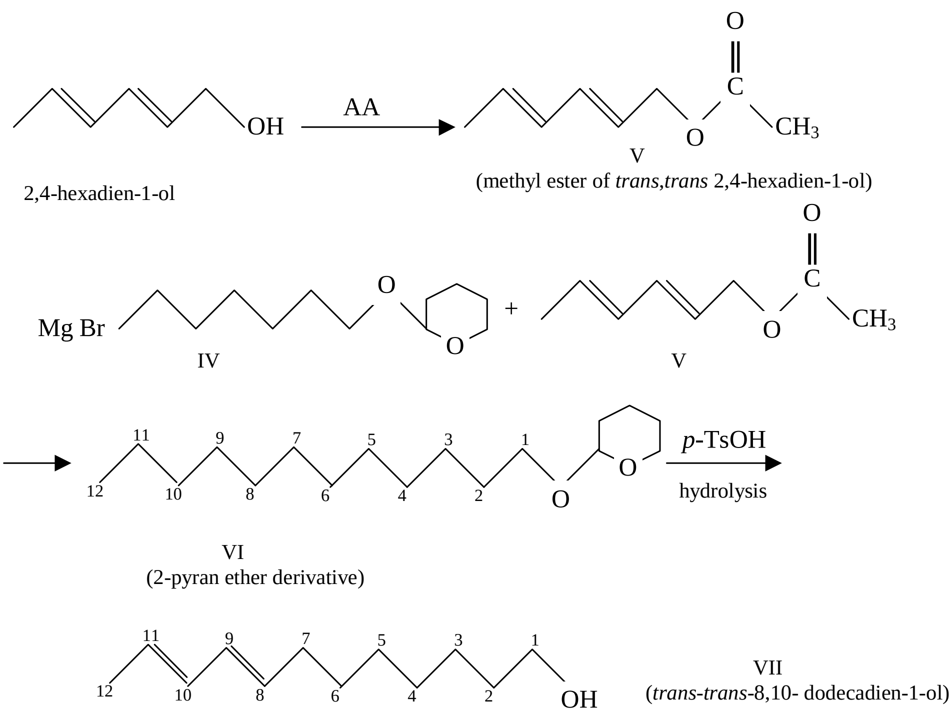
Insects, as in all animals, communicate information concerning reproduction to conspecifics in order to coordinate reproductive activities. The term pheromone refers to air-borne chemical substances, that are secreted externally by an animal in urine, feces or secreted by cutaneous glands and cause a specific reaction in a receiving individual of the same species; the reaction involves either the release of a specific behaviour or physiological change in the recipients endocrine or reproductive system.

The first step of the study was the synthesis of the initial raw material '6-bromo-hexane-1-ol' which was synthesized as follows: 1,6-hexandiol was reacted with the HBr in a solvent medium (toluene) under the catalysing effect of H_2SO_4 (**Scheme-I**, **I**).

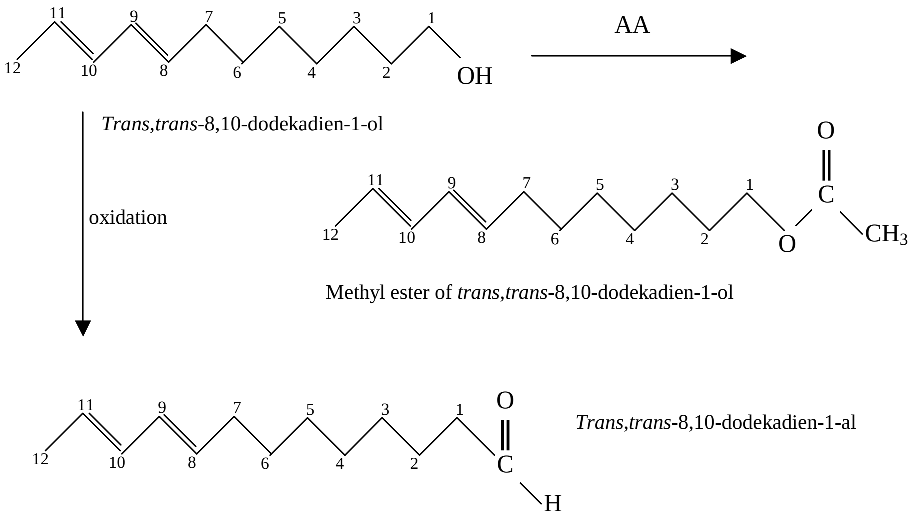
The obtained 6-bromo-hexane-1-ol was reacted with 3,4-dihydro-2*H*-pyran in DCM solvent medium under the catalysing effect of *p*-TsOH. The product of this reaction was 2-pyran ether of 6-bromohexane-1-ol (**Scheme-I**, **III**).



Scheme-I: First step in pheromone synthesis



Scheme-II: Second step in pheromone synthesis



Scheme-III: Synthesis of ester and aldehyde derivatives of pheromone

Purity of the obtained product was controlled by chromatographical method. In the next part of the synthesis, pheromone was synthesized according to the steps indicated in **Schemes I** and **II** below. The ester and aldehyde derivatives of the synthesized *trans-trans*-8,10-dodecadien-1-ol are biologically active compounds and they can be used as pheromones. Their synthesis is indicated in **Scheme-III** below.

Conclusion

In the present study, biologically active pheromones that can be used instead of insect pests were surveyed and under laboratory conditions, synthesis methods were developed for biologically active substances *trans-trans*-8,10- dodecadien-1-ol. The first step of synthesis was the synthesis of initial raw material 6-brom-hexane-1-ol and final product was the ester and aldehyde derivatives of the synthesized *trans-trans*-8,10-dodecadien-1-ol which are biologically active compounds and they can also be used as pheromones. As the further step of the study, it is recommended that the synthesized pheromones will be applied for apple trees for the determination of effectiveness as insect pests.

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