

**SYNTHESIS OF 2,6-DIMETHYLHEPTA-1,5-DIEN-3-YL ACETATE,
THE PHEROMONE OF THE COMSTOCK MEALYBUG
*PSEUDOCOCCUS COMSTOCKI***

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The Comstock mealybug (CMB) *Pseudococcus comstocki* (Kuwana) (*Rhynchota Pseudo-coccidae*) is a highly polyphagous species widespread in Central Asia, Eastern Europe, USA and other regions.

It is one of the most serious pest of apple, pear and other agricultural crops. Scientific investigations and field tests demonstrated that 2,6-dimethyl-1,5-heptadien-3-yl acetate is the most attractive one for these species. According to literature, synthesis of this pheromone suffers from low overall yield (cca 9%), as well as increases the self-cost of this compound.

Hereby, we report an efficient synthetic route for obtaining of 2,6-dimethyl-1,5-heptadien-3-yl acetate with total yield more than 60%.

Keywords: attractant, field tests, agricultural crops, 1-Chloro-3-methylbut-2-ene, 2-Methylpropenal, 2,6-Dimethylhepta-1,5-dien-3-ol, 2,6-Dimethylhepta-1,5-dien-3-yl acetate, acetylation, optimization.

**SINTEZA 2,6-DIMETILHEPTA-1,5-DIEN-3-ILACETATULUI, FEROMONUL PENTRU
COMSTOCK MEALYBUG *PSEUDOCOCCUS COMSTOCKI***

Specia *Rhynchota Pseudococcidae* este o insectă (răspândită în Asia Centrală, Europa de Est, SUA și în alte regiuni), care distruge culturile agricole. Investigațiile și testările pe teren au demonstrat că cel mai eficient remediu în lupta cu acest dăunător este atractantul 2,6-dimetil-1,5-heptadien-3-acetat. Conform datelor din literatura, sinteza atractantului implică o serie de dificultăți însoțite de reducerea considerabilă a randamentului totalizant (cca 9%) și, respectiv, determină mărirea sinecostului acestui produs.

În studiul de față propunem o cale eficientă și economicoasă de obținere a 2,6-dimetil-1,5-heptadien-3-acetatului cu un randament general de peste 60%.

Cuvinte-cheie: attractant, testare pe teren, culturi agricole, 1-cloro-3-metilbut-2-enă, 2-metilpropenal, 2,6-dimetil-1,5-heptadien-3-ol, acetilare, optimizare.

Introduction

The Comstock mealybug (CMB) *Pseudococcus comstocki* (Kuwana) (*Rhynchota Pseudo-coccidae*) is a highly polyphagous species native to eastern Asia and widely distributed in that region. It was incidentally introduced in central Asia and Eastern Europe (Russia, Moldova, Ukraine, Georgia), in the USA, Canada, Brazil, and Argentina [1,2,3]. It is a notorious pest of *Morus* spp., *Catalpa* spp., fruit trees, and ornamentals in the countries where it was incidentally introduced.

Chemical and spectroscopic studies of the sex pheromone of the Comstock mealybug, *Pseudococcus comstocki* Kuwana, one of the most serious pests of apple, pear, and other agricultural crops, led to the isolation and identification of 2,6-dimethyl-1,5-heptadien-3-yl acetate (6), which was highly attractive in the laboratory test as well as in the field test [4,5]. In both cases the structure elucidation of the pheromone was verified by the synthesis. In the first case [4] yields were not mentioned, and in the other case [4b] the overall yield was ~9%. Analyzing other synthetic approaches that included cross-couplings, photooxidation [6], copper/lithium mediated couplings [4], instability of intermediates, formation of a byproducts that are hard to separate, high cost of reagents [7,8,9]. The goal of this work was to elaborate new efficient scientific approach to the synthesis of *Pseudococcus comstocki* sex pheromone.

Materials and methods

Reaction progress was monitored by Merck TLC, purity of products was proved by means of GC 5890A, column HP1701, L=30 m, carrier gas H₂.

1-Chloro-3-methylbut-2-ene (2). To a vigorously stirred mixture of 37% HCl (250 ml) and water (35 ml), 2-methylbut-3-en-2-ol (1 mol) was added at once. Reaction mixture was stirred for 15 min at room temperature (RT). Lower acidic layer was separated and organic layer was washed with 100 ml of water, saturated solution of NaHCO₃ and brine. Organic phase was dried over Na₂SO₄ and product was distilled giving 83,6 g (80% yield) of **2** with bp. 50-65°C/ 170 mm Hg.

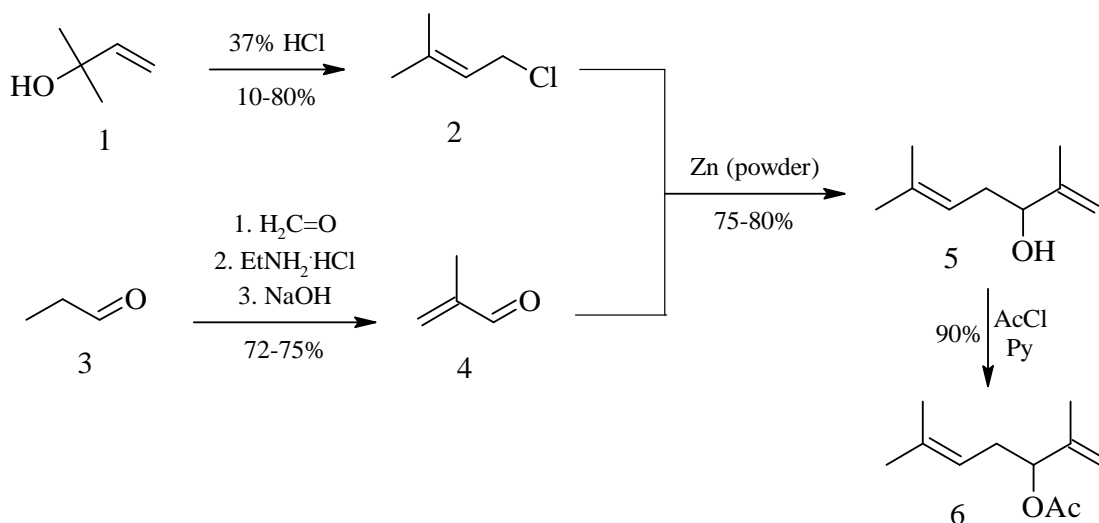
2-Methylpropenal (4). A mixture of propionaldehyde (0,2 mol), aqueous formaldehyde 37% (0,2 mol) and diethylamine hydrochloride (0,2 mol) was placed in a reaction flask. A solution of 4N NaOH (4 ml) was carefully added dropwise to a vigorously stirred reaction mixture. As soon as strong exothermic reaction took place (the temperature rises up to 70°C), reaction flask was cooled in an ice-bath to RT. Resulting mixture was placed in one-neck round-bottom flask and by simple distillation a heterogeneous mixture was distilled and collected up to 100 °C. The organic layer was separated and dried over Na₂SO₄ and fractionally distilled on a Vigreux column, giving 10,5 g (75% yield) of **4** with bp. 64-66°C (lit. 68-69°C).

2,6-Dimethylhepta-1,5-dien-3-ol (5). A mixture of 2-methylprop-2-enal (0,15 mol), 1-chloro-3-methylbut-2-ene (0,225 mol) and Zn powder (mesh 100 μm) (0,225 mol) in 100 ml of saturated NH₄Cl and 20 ml of THF was stirred until all Zn dust is consumed. Then organic layer was separated and water layer was extracted with diethyl ether twice. The combined organic phase was washed with brine and dried over Na₂SO₄. Solvent and volatile byproducts were evaporated under reduced pressure by rotary evaporation and residue was distilled to give 16.8 g (80% yield) of **5** with bp. 60-64°C/10-12 mm Hg.

2,6-Dimethylhepta-1,5-dien-3-yl acetate (6). To a solution of 2,6-dimethylhepta-1,5-dien-3-ol (0,12 mol) and dry pyridine (0,18 mol) in 150 ml of absolute diethyl ether was treated with acetyl chloride (0,18 mol) that was added dropwise and the reaction mixture was stirred overnight. Later it was quenched with water, and organic layer was separated. Water layer was extracted with diethyl ether twice and combined organic phase washed with saturated NaHCO₃ and brine. Organic extract was dried over Na₂SO₄ and concentrated *in vacuo*. Residue was distilled to give **6** with bp. 70-75°C and 80% yield.

Results and discussion

Our new synthetic route to Comstock mealybug attractant offers high purity and yields. It includes synthesis of 2-methylprop-2-enal and 1-chloro-3-methylbut-2-ene that participated in reaction with zinc dust that took place readily in aqueous NH₄Cl/THF (5:1). The acetylation of the corresponding alcohol gave the desired attractant of Comstock mealybug. We managed to avoid, Grignard reagent, copper- and lithium-organic intermediates (which need dry solvents and inert atmosphere) that are often plagued by low yield due to competing coupling side products and the use of very expensive reagents. Studying carefully the synthesis of 1-chloro-3-methylbut-2-ene, we have managed to determine the best conditions for this reaction in order to get the highest possible yield. After series of experiments, we came to a conclusion that best reaction time is 15 min at RT. Longer reaction duration dramatically reduces the yield.



Conclusions

We have developed a new cheap and effective synthetic route to Comstock mealybug attractant. The simplicity of its allylation reaction and its work up, makes this route highly recommended in the synthesis of the desired attractant. This stage refers to “green chemistry” methods, so we managed to reduce nonrewarding aspects of chemical production. Synthesis of 1-chloro-3-methylbut-2-ene was studied carefully, and the best conditions were developed. Our route excludes methods that are difficult in realization from the chemical point of view: absolute conditions, metal-organic intermediates that are unstable, difficult to obtain, and expensive. Also, we have managed to avoid formation of undesired byproducts which are hard to separate. Overall yield of this route is more than 60%, what places it at the highest place amongst any other known methods of synthesis of the Comstock mealybug attractant.

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