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Pheromone synthesis. Part 259: Synthesis of seven methyl-branched hydrocarbons as the pheromone candidates for female Korean apricot wasp, *Eurytoma maslovskii*☆

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ABSTRACT

Seven new methyl-branched hydrocarbons were synthesized, which were the pheromone candidates of the female Korean apricot wasp (*Eurytoma maslovskii*). They are (*Z*)-15-methyl-7-nonacosene (**1**), (*Z*)-17-methyl-7-hentriacontene (**2**), 3,7-dimethylheptacosane (**3**), 8,12-dimethyltriacontane (**4**), 8,18-dimethyltriacontane (**5**), 3,7,11-trimethylnonacosane (**6**), and 3,7,17-trimethylnonacosane (**7**). All of them were synthesized as stereoisomeric mixtures, employing short and simple routes. Hydrocarbon **7** was synthesized via 4,8-dimethyldecanal (**71**, tribolure), the red flour beetle pheromone. The hydrocarbons **1**,**2**,**3** and **6** were identified by GC–MS analysis as the components (with unknown stereochemistry) of the female-specific secretion of *E. maslovskii*.

1. Introduction

In 1959 when the first insect pheromone bombykol [(10*E*,12*Z*)-10,12-hexadecadien-1-ol] was discovered, its bioactivity against male silkworm moth was thought to be entirely due to that single compound.[2] At present it is generally believed that a pheromone is composed of plural components. A recent example of such multi-component pheromones is the male pheromone of the dried bean beetle, which is a mixture of six components.[3] In the cases of multi-component pheromones, identification of the each component is not always easy. All of the candidate components must be synthesized, and the synthetic components should be compared with the natural ones by GC–MS analysis as well as by bioassay. Usually, female- and male-secretions are compared, and the sex-specific components are found out, and they will be studied further. Accordingly, it is important to develop a quick and reliable synthetic methods for the components, even as stereoisomeric mixtures, to facilitate and speed up the identification of the bioactive components. Herein are described short and simple syntheses of various methyl-branched hydrocarbons as pheromone candidates.

The wasp *Eurytoma maslovskii* (Hymenoptera: Eurytomidae) is the most serious pest in Korean apricot orchards, causing up to 30% fruit damage in recent years. The cuticular extract of its females was shown to be pheromonally active and seven candidate structures **1**–**7** (Fig. 1) were proposed for the female pheromone components by GC–MS analysis (C.Y. Yang, manuscript in preparation), referring to Howard's paper on the identification of insect hydrocarbons by MS.[4] The present paper reports the synthesis of the stereoisomeric mixtures of **1**–**7**. Four of them (**1**, **2**, **3** and **6**) were identical with the natural components by GC–MS comparison. The synthesis of **1**–**7** must be of interest to those who are engaged in the study of methyl-branched hydrocarbons as semiochemicals.[5,6]

2. Results and discussion

The structures **1**–**7** of the target hydrocarbons indicate that they can be classified into four groups: (A) methyl-branched (*Z*)-alkenes (**1** and **2**), (B) dimethylated alkanes where the two methyl groups are separated by three methylene groups (**3** and **4**), (C) dimethylated alkanes whose methyl groups are separated by nine methylene groups (**5**), and (D) trimethylated alkanes (**6** and **7**). Details of the synthesis of **1**–**7** will be discussed in the order as shown above.

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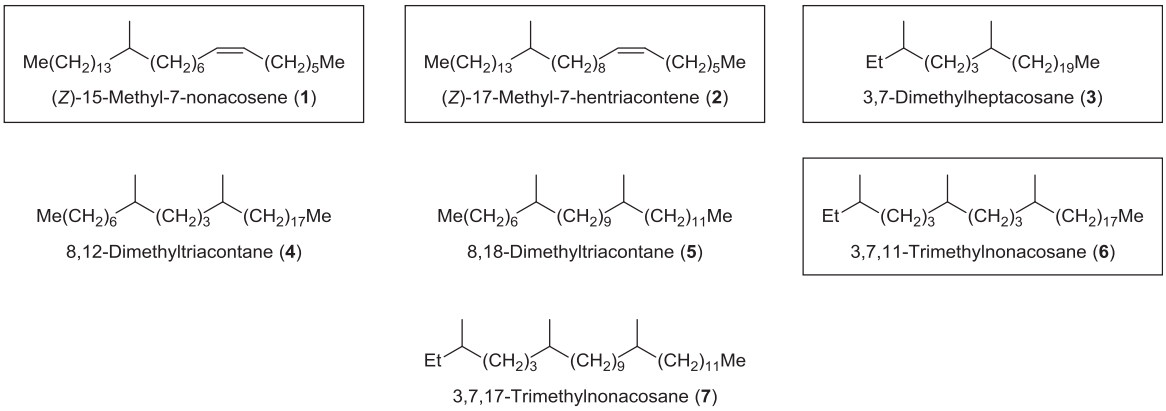

Fig. 1. Candidate structures **1**–**7** for the female-specific hydrocarbons of the Korean apricot wasp, *Eurytoma maslovskii*.

2.1. Synthesis of 1 and 2

Fig. 2 shows the retrosynthetic analysis of **1** and **2**, which differ only in the number of the methylene spacers between the methyl-branched position and the (*Z*)-double bond. Accordingly, they can be synthesized in a similar fashion, employing aldehyde **A** and bromide **B** or **C** as the building blocks, and connecting the two by Grignard reaction. Racemic aldehyde **A** can be prepared from commercially available (±)-citronellol (**8**). By using either (*R*)- or (*S*)-**8**, the enantiomers of **1** and **2** can be prepared readily. Citronellol enantiomers are versatile starting materials for natural products synthesis.[7]

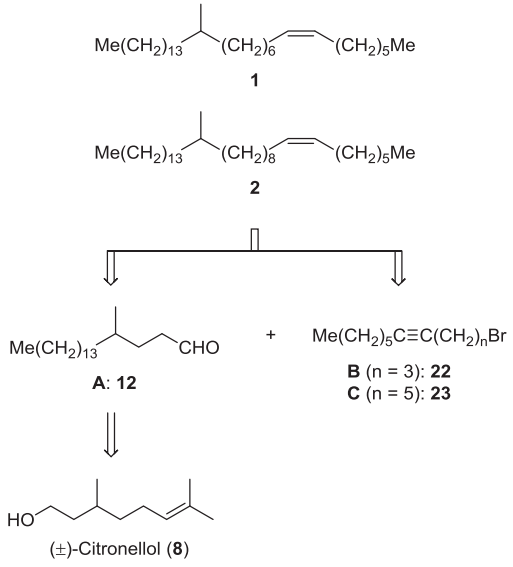

Fig. 2. Retrosynthetic analysis of **1** and **2**.

Scheme 1 summarizes the synthesis of (±)-**1** and (±)-**2**. (±)-Citronellol (**8**) was tosylated, and the resulting **9** was treated with *n*-$C_{12}H_{25}MgBr$ in the presence of Li_2CuCl_4 to give **10**. The crude **10** was dihydroxylated with OsO_4 and *N*-methylmorpholine-*N*-oxide (NMO). The product was purified by SiO_2 chromatography followed by recrystallization to give crystalline diol **11**. Cleavage of the diol **11** with HIO_4 in THF afforded oily **12** in 23% overall yield based on **8** (four steps).

Other two building blocks **22** (=**B**) and **23** (=**C**) were synthesized from 1-octyne (**13**). Alkylation of **13** with bromide **14** or **15** using *n*-BuLi as the base effected chain-elongation to give **16** or **17**. Then **16** or **17** was treated with TsOH in MeOH to give alcohol **18** or **19**. The corresponding tosylate **20** or **21** was converted to the desired bromide **22** or **23** by treatment with LiBr in DMF. The overall yield of **22** was 23% based on **13** (four steps), while that of **23** was 26% based on **13** (four steps).

The next stage was the coupling of the aldehyde **12** with the bromide **22** or **23** by means of the Grignard reaction. Accordingly, **12** was treated with the Grignard reagent prepared from **22** or **23** to give alkynol **24** or **25** as diastereomeric mixtures. Semi-hydrogenation of **24** or **25** with Lindlar's Pd catalyst gave (*Z*)-alkenol **26** or **27**. The corresponding mesylate **28** or **29** was reduced with $LiAlH_4$ to give the target hydrocarbon **1** or **2**. The yield of **1** was 48% based on **12** (four steps), while that of **2** was 28% based on **12** (four steps).

Racemic (*Z*)-15-methyl-7-nonacosene (**1**, 1.12 g) was obtained as a colorless oil. Its *Z*/*E* ratio was ca. 95:5, judging from its ^{13}C NMR spectrum (see 4.13). The overall yield of **1** was 11% based on (±)-citronellol (**8**, eight steps), or also 11% based on 1-octyne (**13**, eight steps). Racemic (*Z*)-17-methyl-7-hentriacontene (**2**, 653 mg) was also obtained as a colorless oil. Its *Z*/*E* ratio was ca. 94:6, judging from its ^{13}C NMR spectrum (see 4.14). The overall yield of **2** was 6% based on **8** (eight steps), or 7% based on **13** (eight steps). The synthetic **1** and **2** were identified with the naturally occurring **1** and **2** by GC–MS comparison. Details will be published later by Yang.

2.2. Synthesis of 3 and 4

Fig. 3 shows the retrosynthetic analysis of **3** and **4**, which possess in common the three-methylene spacer between the two methyl-branching positions. They can be synthesized by the Wittig reaction between **D** and **E** or **F** and **G**. The building blocks **E** and **G** can be synthesized from (±)-citronellal (**30**).

Scheme 2 summarizes the synthesis of **3** and **4** as stereoisomeric mixtures. Addition of *n*-$C_{18}H_{37}MgBr$ or *n*-$C_{16}H_{33}MgBr$ to (±)-citronellal (**30**) gave alcohol **31** or **32**. The hydroxy group of **31** or **32** was removed by reduction of the corresponding mesylate **33** or **34** with $LiAlH_4$ to give alkene **35** or **36**. Oxidation of the alkene **35** or **36** with SeO_2 in the presence of *t*-BuOOH gave aldehyde **37** or **38**. Treatment of **37** with $Ph_3P{=}CH_2$ afforded **39**, while that of **38** with *n*-$C_5H_{11}CH{=}PPh_3$ furnished **40**. Finally, the dienes **39** and **40** were hydrogenated over Pd–C to give the desired 3,7-dimethylheptacosane (**3**, 867 mg) and 8,12-dimethyltriacontane (**4**, 1.28 g), respectively, both as colorless oils. The overall yield of **3** was 10% based on (±)-citronellal (**30**, six steps), while that of **4** was 13%. 3,7-Dimethylheptacosane (**3**) was identified with the