The Stereospecific Synthesis of the Rice Leaffolder Moth Sex Pheromone Components from 1,5-Cyclooctadiene†

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The rice leaffolder moth, *Cnaphalocrocis medinalis*, is widely distributed in humid tropical to temperate countries of Asia, Oceania, and Africa. It is an important leaf feeding pest of rice. It's known that one leaf folder consumes 6 to 7 leaves during larval stage. Recently, it has become widespread throughout the major rice growing regions of Asia and become serious pests. The synthetic sex pheromone may not only be an effective monitoring tool for timing insecticide application, but also a possible control agent. Previously, two compounds, \((Z)-11\)-hexadecenyl acetate (1, Z11-16:Ac) and \((Z)-13\)-octadecenyl acetate (6, Z13-18:Ac), were identified as the female sex pheromone of the rice leaffolder moth and field tested in India and Philippines (Figure 1).

On the other hand, additional four compounds, \((Z)-11\)-octadecen-1-ol (2, Z11-18:OH), \((Z)-11\)-octadecenal (3, Z11-18:Ald), \((Z)-13\)-octadecen-1-ol (4, Z13-18:OH), and \((Z)-13\)-octadecenal (5, Z13-18:Ald) were identified in Japan. In order to control the pest eco-friendly the obtention of each pheromone component is essential. A new method is described for the stereospecific syntheses of six sex pheromone components 1 to 6 for the rice leaffolder moth. The crucial synthetic step for the compounds is the introduction of pure \((Z)\)-double bond in the molecules. The starting material, \( \text{cis}-1,8\)-oct-4-en-diol (7) consisting of 100% \((Z)\)-configuration was stereospecifically prepared from readily available 1,5-cyclooctadiene by known synthetic method (Scheme 1).

The diol 7 was monoprotected with dihydropyran (DHP) and then, tosylated to give compound 9. The Grignard reaction to the tosylate with methylmagnesium chloride or \(n\)-propylmagnesium chloride gave each coupling products 10 or 11 in high yields (Scheme 2). Continuously, deprotection and then, tosylation of the THP ethers produced the intermediates 14 and 15.

On the other hand, bromides 16 and 17 were easily prepared from the corresponding diols by monobromination and then, tosylation of the THP ethers produced the intermediates 14 and 15.

Scheme 1. Synthesis of \( \text{cis}-1,8\)-oct-4-en-diol (7).

Scheme 2. Reagents and conditions: (a) HBr, benzene; DHP, PPTS, CH2Cl2, 77% for 16; 74% for 17 (b) 16 or 17, Mg, Li2CuCl2, THF, 93% for 18, 71% for 19; 73% for 20 (c) PPTS, EtOH, 92% for 21; 88% for 2; 85% for 4 (d) Ac2O, pyridine, 97% for 1; 96% for 6 (e) PCC, CH2Cl2, 69% for 3; 75% for 5.

Figure 1. Six components of rice leaffolder moth sex pheromone.

†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.
then, protection (Scheme 3). The second Grignard coupling reaction of the tosylates 14 or 15 with 16 or 17 gave the corresponding intermediates 18, 19, or 20 (Scheme 3). Deprotection and then, acetylation of 18 led to pheromone component Z11-16:Ac (1). Deprotection of 19 gave Z11-18:OH (2), which led to Z11-18:Ald (3) by oxidation. On the other hand, deprotection of 20 produced pheromone component Z13-18:OH (4). Continuously, oxidation or acetylation of the alcohol 4 led each to pheromone components Z13-18:Ald (5) or Z13-18:Ac (6).

In conclusion, the synthetic sex pheromone may not only be an effective monitoring tool for timing insecticide application, but also a possible control agent. In order to control the pest economically, the obtention of each pheromone component is essential. Stereospecifically pure six sex pheromone components for the rice leafhopper moth were synthesized from readily available 1,5-cyclooctadiene.

**Experimental Section**

**General Techniques.** IR spectra were recorded on a Jasco FT/IR 460 Plus, and NMR spectra were recorded on an Avance Digital 400 MHz Spectrometer. All reactions were monitored by thin layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) under UV light. All new compounds were identified by spectroscopic methods.

(Z)-8-(Tetrahydro-2H-pyran-2-yl)oct-4-enyl 4-methylbenzensulfonate (9). To a solution of compound 8 (1.00 g, 4.4 mmol) in pyridine (30 mL) was added p-toluenesulfonyl chloride (1.25 g, 6.6 mmol) and stirred at room temperature for 4 h. The reaction mixture was diluted with ethyl acetate and washed with cold 6 N HCl. The organic layer was dried (Na$_2$SO$_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to give alcohol 9 (1.80 g, 95%) after purification. IR (KBr) 3334, 3005, 2926, 2854 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.4 Hz, 3H); $^1$C NMR (100 MHz, CDCl$_3$) $\delta$ 130.9, 129.8, 63.1, 32.8, 32.0, 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 27.5, 22.7, 14.1.

(Z)-Non-4-en-1-ol (12). To a solution of 9 (6.00 g, 15.7 mmol) in dry THF (12 mL) was added CH$_3$MgCl (13.6 mL of 3 M, 40.8 mmol) at $-40^\circ$C in the presence of Li$_2$CuCl$_2$ (0.1 M in THF, 1.6 mL, 0.16 mmol). The reaction mixture was stirred at room temperature for 3 h. After quenching the reaction with aqueous NaHCO$_3$ solution, the reaction mixture was diluted with H$_2$O and extracted with ethyl ether. The organic layer was dried (Na$_2$SO$_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to give the THP ether 10 (3.14 g, 88%). Continuously, ether 10 (3.00 g, 13.2 mmol) was deprotected with PPTS at 80 $^\circ$C in MeOH to give alcohol 12 (1.80 g, 95%) after purification. IR (KBr) 3334, 3005, 2928, 2860 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.4 Hz, 3H); $^1$C NMR (100 MHz, CDCl$_3$) $\delta$ 130.9, 129.8, 63.1, 32.8, 32.0, 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 27.5, 22.7, 14.1.

(Z)-Octadec-11-en-1-ol (21). To a solution of the tosylate 14 (1.80 g, 6.1 mmol) in dry THF (10 mL) was added Grignard reagent prepared from Mg (0.56 g, 23.0 mmol) and bromide 16 (5.37 g, 10.2 mmol) in THF (5 mL) at $-40^\circ$C in the presence of Li$_2$CuCl$_2$ (0.1 M in THF, 0.64 mL, 0.064 mmol). The reaction mixture was stirred at room temperature for 1.5 h. After quenching the reaction with aqueous NaHCO$_3$ solution, the reaction mixture was diluted with H$_2$O and extracted with ethyl ether. The organic layer was dried (Na$_2$SO$_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to give the THP ether 21 (1.34 g, 92%). Continuously, ether 19 (1.97 g, 6.1 mmol) was deprotected with PPTS at 80 $^\circ$C in EtOH to give the alcohol 21 (1.34 g, 92%) after purification. IR (KBr) 3332, 3004, 2926, 2854 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.4 Hz, 3H); $^1$C NMR (100 MHz, CDCl$_3$) $\delta$ 129.9, 129.8, 63.0, 32.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 27.5, 22.7, 14.0.

(Z)-Octadec-13-en-1-ol (4). To a solution of alcohol 21 (0.79 g, 3.3 mmol) in pyridine (3.0 mL) was added acetic anhydride (0.62 mL, 6.6 mmol) and stirred at 0 $^\circ$C for 3 h. The reaction mixture was diluted with ice water and extracted with ethyl ether. The organic layer was washed with saturated NaHCO$_3$ solution, water, saline, and then evaporated in vacuo. The residue was purified by column chromatography (silica gel, 25% ethyl ether in hexane) to provide acetate 1 (0.90 g, 97%). IR (KBr) 3004, 2926, 2855, 1743, 1238, 1038.
cm$^{-1}$; $^{1}H$ NMR (400 MHz, CDCl$_3$) $\delta$ 5.32-5.24 (m, 2H), 3.98 (t, $J = 6.8$ Hz, 2H), 1.98 (s, 3H), 1.98-1.92 (m, 4H), 1.56-1.51 (m, 2H), 1.29-1.18 (m, 18H), 0.88 (t, $J = 7.0$ Hz, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$) $\delta$ 171.2, 129.8 (2), 64.6, 31.9, 29.7, 29.5 (2), 29.3, 29.2, 29.1, 28.6, 27.2, 26.9, 25.7, 22.3, 21.0, 14.0.

(Z)-Octadec-13-enyl acetate (6): Prepared in 96% yield in the same method as that described for 1 except using the alcohol 4 instead of 21. IR (KBr) 3005, 2925, 2854, 1743, 1239, 1039 cm$^{-1}$; $^{1}H$ NMR (400 MHz, CDCl$_3$) $\delta$ 5.32-5.24 (m, 2H), 3.98 (t, $J = 6.8$ Hz, 2H), 1.98 (s, 3H), 1.99-1.92 (m, 4H), 1.56-1.51 (m, 2H), 1.29-1.18 (m, 18H), 0.83 (t, $J = 7.0$ Hz, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$) $\delta$ 171.3, 129.9, 129.8, 64.7, 31.9, 30.9, 29.8, 29.6 (2), 29.5 (2), 29.3, 29.2, 28.6, 27.2, 26.9, 25.9, 22.3, 21.0, 14.0.

(Z)-Octadec-11-enal (3): To a solution of alcohol 2 (0.50 g, 1.9 mmol) in dry dichloromethane (8 mL) was added PCC (0.60 g, 2.8 mmol) at room temperature. After 3 h stirring, the reaction was quenched with a few drop of EtOH, and the reaction mixture was filtered with celite. After evaporating solvent, the residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to give aldehyde 3 (0.34 g, 69%). IR (KBr) 3005, 2925, 2854, 2713, 1729 cm$^{-1}$; $^{1}H$ NMR (400 MHz, CDCl$_3$) $\delta$ 9.76 (t, $J = 2.0$ Hz, 1H), 5.38-5.30 (m, 2H), 2.42 (td, $J = 7.6$, 2.0 Hz, 2H), 2.03-1.98 (m, 4H), 1.66-1.59 (m, 2H), 1.32-1.18 (m, 20H), 0.88 (t, $J = 7.2$ Hz, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$) $\delta$ 203.1, 129.9, 129.8, 43.9, 31.8, 29.7, 29.5, 29.4, 29.3 (2), 29.2, 29.1, 29.0, 27.2 (2), 22.7, 22.1, 14.1.

(Z)-Octadec-13-enal (5): Prepared in 75% yield in the same method as that described for 3 except using the alcohol 4 instead of 2. IR (KBr) 3004, 2925, 2854, 2713, 1730 cm$^{-1}$; $^{1}H$ NMR (400 MHz, CDCl$_3$) $\delta$ 9.76 (t, $J = 2.0$ Hz, 1H), 5.38-5.30 (m, 2H), 2.41 (td, $J = 7.6$, 2.0 Hz, 2H), 2.01-1.96 (m, 4H), 1.66-1.58 (m, 2H), 1.35-1.23 (m, 20H), 0.88 (t, $J = 7.2$ Hz, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$) $\delta$ 203.1, 129.9, 129.8, 43.9, 31.9, 29.7, 29.6 (2), 29.5, 29.4, 29.3 (2), 29.1, 27.2, 26.9, 22.3, 22.1, 14.0.

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