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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.[1] 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.[2] The synthetic sex pheromone[3] 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**, *Z*11-16:Ac) and (*Z*)-13-octadecenyl acetate (**6**, *Z*13-18:Ac), were identified as the female sex pheromone of the rice leaffolder moth and field tested in India and Philippines (Figure 1).[4]

On the other hand, additional four compounds, (*Z*)-11-octadecen-1-ol (**2**, *Z*11-18:OH), (*Z*)-11-octadecenal (**3**, *Z*-11-18:Ald), (*Z*)-13-octadecen-1-ol (**4**, *Z*13-18:OH), and (*Z*)-13-octadecenal (**5**, *Z*13-18:Ald) were identified in Japan.[5]

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, *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).[6]

The diol **7** was monoprotected with dihydropyran (DHP)[7] 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[6a] and then, tosylation[8] 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

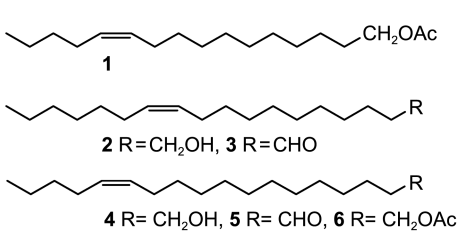
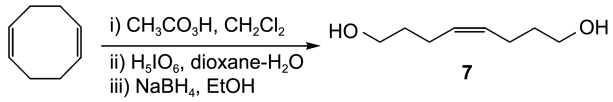
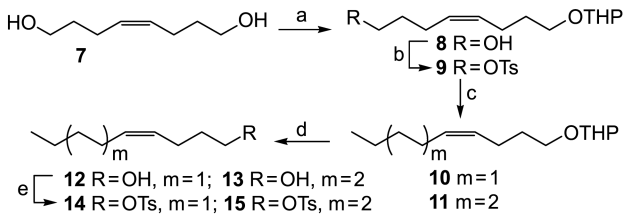


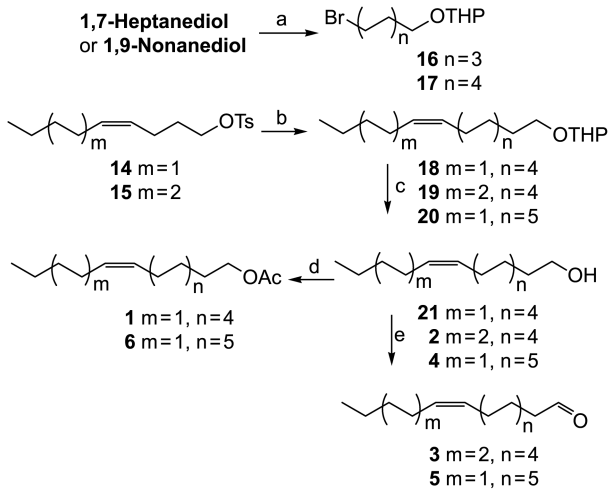
Figure 1. Six components of rice leaffolder moth sex pheromone.



Scheme 1. Synthesis of *cis*-1,8-oct-4-en-diol (**7**).



Scheme 2. Reagents and conditions: (a) DHP, PPTS, THF, 66% (b) *p*-TsCl, pyridine, 89% (c) CH_3MgCl, Li_2CuCl_4, THF, 88% for **10**; *n*-C_3H_7MgCl, 91% for **11** (d) PPTS, MeOH, 95% for **12**; 99% for **13** (e) *p*-TsCl, pyridine, 78% for **14**; 64% for **15**.



Scheme 3. Reagents and conditions: (a) HBr, benzene; DHP, PPTS, CH_2Cl_2, 77% for **16**; 74% for **17** (b) **16** or **17**, Mg, Li_2CuCl_4, THF, 93% for **18**; 71% for **19**; 73% for **20** (c) PPTS, EtOH, 92% for **21**; 88% for **2**; 85% for **4** (d) Ac_2O, pyridine, 97% for **1**; 96% for **6** (e) PCC, CH_2Cl_2, 69% for **3**; 75% for **5**.

†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 *Z*11-16:Ac (**1**). Deprotection of **19** gave *Z*11-18:OH (**2**), which led to *Z*11-18:Ald (**3**) by oxidation. On the other hand, deprotection of **20** produced pheromone component *Z*13-18:OH (**4**). Continuously, oxidation or acetylation of the alcohol **4** led each to pheromone components *Z*13-18:Ald (**5**) or *Z*13-18: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 eco-friendly the obtention of each pheromone component is essential. Stereospecifically pure six sex pheromone components for the rice leaffolder moth were synthesized from readily available 1,5-cyclooctadiene.

Experimental Section

Genenral Techniques. IR spectra were recorded on a Jasco FT/IR 460 Plus, and NMR spectra were recorded on a 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-yloxy)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_2SO_4) and evaporated *in vacuo*. The residue was purified by column chromatography (silica gel, 33% ethyl acetate in hexane) to provide **9** (1.50 g, 89%). IR (KBr) 3005, 2941, 2868, 1599, 1454, 1361, 1176 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 5.42-5.35 (m, 1H), 5.28-5.21 m, 1H), 4.55 (dd, *J* = 4.4, 2.8 Hz, 1H), 4.01 (t, *J* = 6.4 Hz, 2H), 3.88-3.83 (m, 1H), 3.74-3.68 (m, 1H), 3.52-3.46 (m, 1H), 3.38-3.32 (m, 1H), 2.44 (s, 3H), 2.09-2.01 (m, 4H), 1.85-1.48 (m, 10H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.7, 133.1, 130.8, 129.8, 127.9, 127.8, 98.9, 70.0, 66.8, 62.4, 30.7, 29.6, 28.8, 25.4, 23.8, 23.0, 21.6, 19.7.

(*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_3MgCl (13.6 mL of 3 M, 40.8 mmol) at –40 °C in the presence of Li_2CuCl_4 (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 NH_4Cl solution, the reaction mixture was diluted with H_2O and extracted with ethyl ether. The organic layer was dried (Na_2SO_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 °C in MeOH to give alcohol **12** (1.80g, 95%) after purification. IR (KBr) 3334, 3005, 2928, 2860 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43-5.33 (m, 2H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.17-2.10 (m, 2H), 2.06-2.01 (m, 2H), 1.66-1.59 (m, 2H), 1.35-1.26 (m, 4H), 0.89 (t, *J* = 8.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.8, 128.8, 62.6, 32.6, 31.9, 26.9, 23.6, 22.3, 14.0.

(*Z*)-Undec-4-en-1-ol (13). Prepared in 90% yield (two step) in same method as that described for **12** except using *n*-C_3H_7MgCl instead of CH_3MgCl. IR (KBr) 3328, 3005, 2926, 2856 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43-5.32 (m, 2H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.14-2.09 (m, 2H), 2.06-2.00 (m, 2H), 1.66-1.59 (m, 2H), 1.35-1.28 (m, 8H), 0.87 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.8, 128.8, 62.6, 32.6, 31.7, 29.6, 29.0, 27.2, 23.6, 22.6, 14.1.

(*Z*)-Hexadec-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 °C in the presence of Li_2CuCl_4 (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 NH_4Cl, the reaction mixture was diluted with H_2O and extracted with ethyl ether. The organic layer was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to give the THP ether **18** (1.83 g, 93%). Continuously, ether **18** (1.97 g, 6.1 mmol) was deprotected with PPTS at 80 °C in EtOH to give the alcohol **21** (1.34g, 92%) after purification. IR (KBr) 3332, 3004, 2926, 2854 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.38-5.30 (m, 2H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.04-1.98 (m, 4H), 1.59-1.52 (m, 2H), 1.36-1.25 (m, 18H), 0.89 (t, *J* = 8.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.9, 129.8, 63.0, 32.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 27.2, 26.9, 25.7, 22.3, 14.0.

(*Z*)-Octadec-11-en-1-ol (2). Prepared in 62% yield (two steps) in same method as that described for **21** except using the tolylate **15** instead of **14**. IR (KBr) 3327, 3004, 2926, 2854 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.38-5.32 (m, 2H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.03-1.98 (m, 2H), 1.60-1.53 (m, 2H), 1.37-1.23 (m, 24H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.9, 129.8, 63.1, 32.8, 31.8, 31.7, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 29.0, 27.2, 25.7, 22.6, 14.1.

(*Z*)-Octadec-13-en-1-ol (4). Prepared in 62% yield (two steps) in same method as that described for **21** except using the bromide **17** instead of **16**. IR (KBr) 3327, 3004, 2926, 2854 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.38-5.31 (m, 2H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.04-1.99 (m, 4H), 1.59-1.52 (m, 2H), 1.38-1.24 (m, 22H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.9, 129.8, 63.1, 32.8, 32.0, 31.9, 29.8, 29.6(3), 29.5, 29.4, 29.3, 27.2, 26.9, 25.7, 22.3, 14.0.

(*Z*)-Hexadec-11-enyl acetate (1). 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 °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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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), 0.83 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32-5.24 (m, 2H), 3.98 (t, J = 6.8 Hz, 2H), 1.98 (s, 3H), 1.99-1.92 (m, 4H), 1.58-1.51 (m, 2H), 1.28-1.18 (m, 22H), 0.83 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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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References

1. Sakai, K.; Ikeda, Y.; Sumeshima, J. *Appl. Ent.* **1942**, *4*, 1.
2. (a) Khan, Z. R.; Barrion, A. T.; Litsinger, J. A.; Castilla, N. P.; Joshi, R. C. *Insect Science and its Application* **1988**, *9*, 129. (b) Rani, W. B.; Amutha, R.; Muthulakshmi, M.; Indira, K.; Mareeswari, P. *Res. J. Agric. & Biol. Sci.* **2007**, *3*, 394.
3. Kang, S.-K.; Moon, B.-H.; Lee, J.-O.; Goh, H.-G. *Bull. Kor. Chem. Soc.* **1985**, *6*, 228.
4. (a) Ganeswara, R.; Krishnaiah, K.; Hall, D. R.; Cork, A.; Reddy, D. R. *Indian Journal of Plant Protection* **1993**, *21*, 228. (b) Ganeswara, R. A.; Reddy, D. D. R.; Krishnaiah, K.; Beever, P. S.; Cork, A.; Hall, D. R. *Entomologia Experimentalis et Applicata* **1995**, *74*, 195. (c) Ramachandran, R.; Caballero, P.; Khan, Z. R. *Japanese Journal of Applied Entomology and Zoology* **1990**, *25*, 26.
5. Kawazu, K.; Hasegawa, J.; Honda, H.; Ishikawa, Y.; Wakamura, S.; Sugie, H.; Kamiwada, H.; Kamimura, T.; Yoshiyasa, Y.; Tatsuki, S. *Entomologia Experimentalis et Applicata* **2000**, *96*, 103.
6. (a) Raederstorff, D. A.; Shu, Y. L.; Thompson, J. E.; Djerassi, C. *J. Org. Chem*. **1987**, *52*, 2337. (b) Nagarkatti, J. P.; Ashley, K. R. *Tetrahedron Lett*. **1973**, *14*, 4599. (c) Tolstikov, G. A.; Odinokov, V. N.; Galeeva, R. I.; Bakeeva, R. S. *Tetrahedron Lett.* **1978**, *19*, 1857.
7. Khan, A. T.; Choudhury, L. H.; Ghosh, S. *Tetrahedron Lett.* **2004**, *45*, 7891.
8. Johnson, W. S.; Collins, J. C.; Pappo, R.; Rubin, M. B.; Kropp, P. J.; Johns, W. F.; Pike, J. E.; Bartmann, W. *J. Am. Chem. Soc.* **1963**, *85*, 1409.