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Tetrahedron: *Asymmetry* 18 (2007) 838–846
Tetrahedron: *Asymmetry*

Synthetic studies aimed at the elucidation of the stereostructure of the aggregation pheromone, 2-methyl-6-(4′-methylenebicyclo-[3.1.0]hexyl)hept-2-en-1-ol, produced by the male stink bug *Erysarcoris lewisi*☆

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Received 31 January 2007; accepted 20 March 2007
Available online 25 April 2007

Abstract—The male-produced aggregation pheromone of the stink bug *Erysarcoris lewisi* Distant was shown to be one of the two diastereomers of (2*Z*,6*R*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol by synthesizing and bioassaying (2*E*,6*R*)-, (2*E*,6*S*)-, (2*Z*,6*R*)-, and (2*Z*,6*S*)-isomers. These were synthesized from the enantiomers of citronellal by employing an intramolecular α-ketocarbene addition to a double bond and the *E*-selective or *Z*-selective olefination of a formyl group as the key steps. A reliable method was developed for the preparation of ethyl 2-(di-*o*-tolylphosphono)propanoate, Ando's reagent for *Z*-selective olefination.

1. Introduction

Erysarcoris lewisi Distant (Heteroptera: Pentatomidae) is a stink bug found in northern Japan, which damages rice grains. It usually lives in meadows and fields, and comes to the rice paddy fields where it attacks rice plants at the time of their grain formation. Its emergence can hardly be surveyed by conventional means, especially because it cannot be attracted by light traps. The possibility of using its pheromone for the purpose of monitoring its population was therefore examined by Takita et al. in 2000.[2] Takita then proposed the structure of the male-produced aggregation pheromone of *E. lewisi* as (*E*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol **1** (Fig. 1).[3]

Although the acetate of (*Z*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol **2** has been known since 1982 as a constituent of an African plant *Haplocarpha scaposa*,[4] there is no data about whether natural **2** possesses (2*Z*,6*R*)- or (2*Z*,6*S*)-stereochemistry. In fact, the synthesis of either **1** or **2** has not been reported. We became interested in achieving the synthesis of (2*E*,6*R*)-**1** and (2*E*,6*S*)-**1′** so as to supply the pheromone in an amount sufficient for evaluation of its practicality as a population monitoring agent.

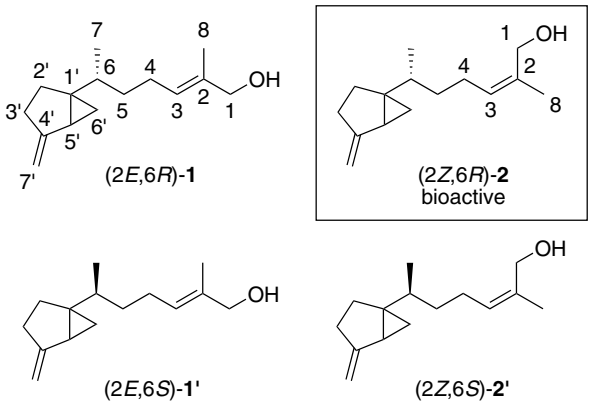

Figure 1. Structures of the pheromone candidates.

Scheme 1 summarizes our retrosynthetic analysis of **1**. Stork and Ficini were the first in 1961 to employ the intramolecular addition of α-ketocarbene to an olefin for the synthesis of bicyclo[4.1.0]heptan-2-one.[5] Their method was employed by us in 1970 to synthesize the racemic sabina ketone, as shown in Scheme 1.[6] Intramolecular α-ketocarbene-olefin addition (**D**→**C**) was therefore chosen as the key ring-forming reaction in the present synthesis.

☆ Pheromone synthesis, Part 233. For Part 232, see Ref. 1.

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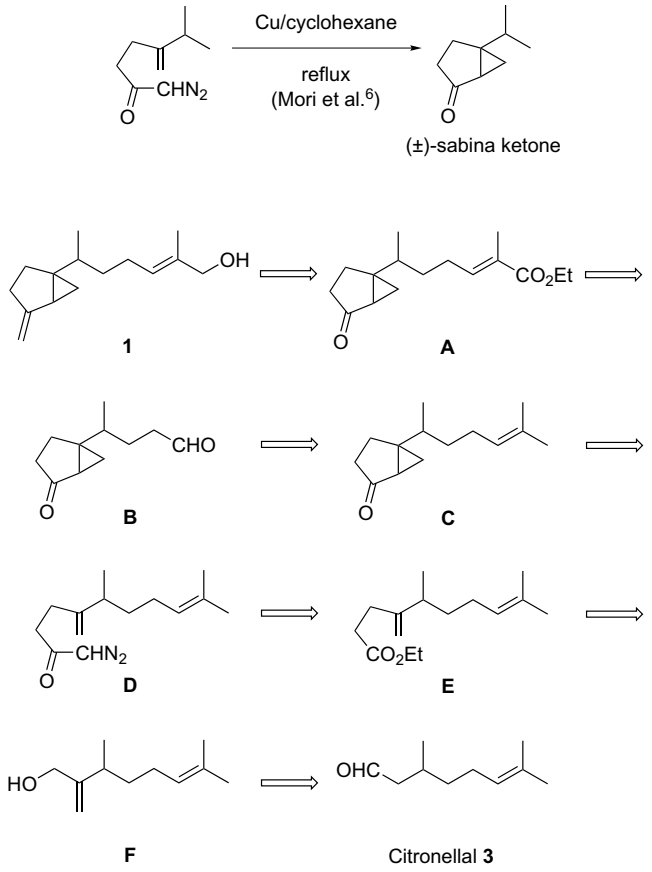
doi:10.1016/j.tetasy.2007.03.019



Scheme 1. Retrosynthetic analysis of **1**.

Pheromone candidate **1** can be prepared from keto ester **A**, while *E*-selective Wittig reaction converts **B** to **A**. Aldehyde **B** is secured by oxidation of **C**. Bicyclo[3.1.0]hexane **C** was prepared by the intramolecular addition to a double bond of an α-ketocarbene generated from diazoketone **D**, which was synthesized from ester **E**. The orthoester Claisen rearrangement when applied to **F**, affords **E**. Finally, the commercially available enantiomers of citronellal **3** were envisaged as the starting materials. At the step **D** to **C**, the stereochemistry of the ring junction cannot be controlled, meaning that **C** is obtained as a diastereomeric mixture.

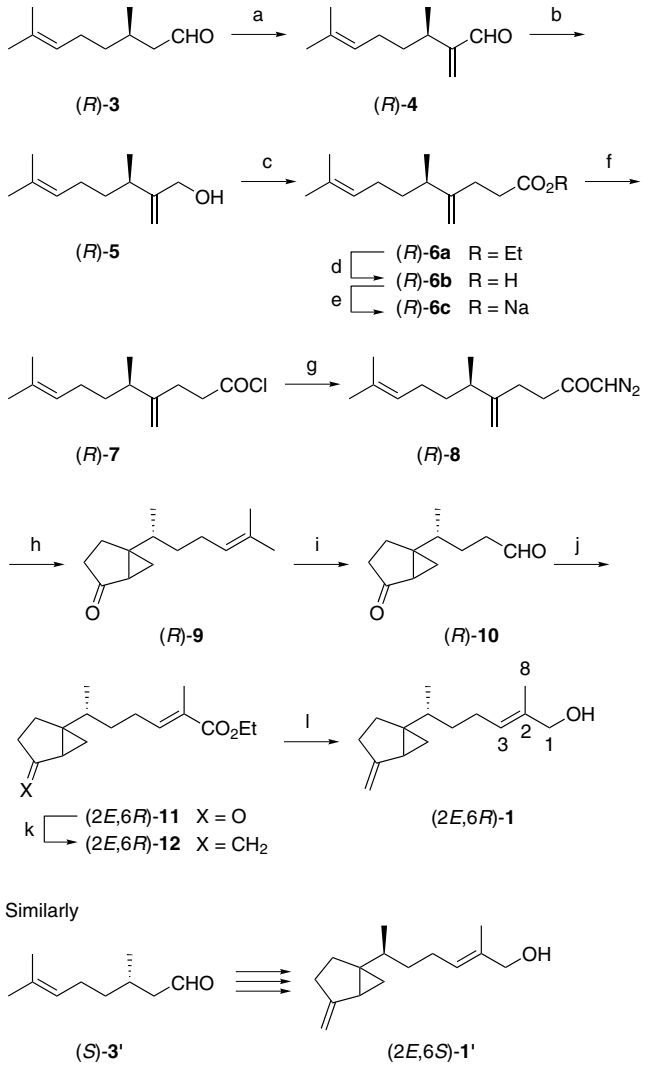
The ^{1}H and ^{13}C NMR comparison of (2*E*,6*R*)-**1** or (2*E*,6*S*)-**1′** with the natural pheromone indicated the latter to be **2** or **2′** with a *Z*-double bond. We therefore synthesized (2*Z*,6*R*)-**2** and (2*Z*,6*S*)-**2′** by employing a *Z*-selective olefination at the step of **B** to **A**. Bioassay of our synthetic **1**, **1′**, **2**, and **2′** against *E. lewisi* revealed (2*Z*,6*R*)-**2** as pheromonally active. Herein, we report in detail the above mentioned studies.

2. Results and discussion

2.1. Synthesis of (2*E*,6*R*)- and (2*E*,6*S*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol 1 and 1′

Commercially available enantiomers of citronellal **3** (Takasago, 97% ee) were employed as the starting materials. Methylenation of (*R*)-**3** with formalin, pyrrolidine, and propanoic acid was carried out according to Erkkilä and Pihko[7] to give α,β-unsaturated aldehyde (*R*)-**4** (Scheme 2). Reduction of (*R*)-**4** with lithium aluminum hydride furnished allylic alcohol (*R*)-**5**, which was subjected to a Johnson orthoester Claisen rearrangement[8] by heating with triethyl orthoacetate in the presence of propanoic acid to afford ethyl ester (*R*)-**6a** in 78% overall yield, based on citronellal (*R*)-**3**.

Alkaline hydrolysis of (*R*)-**6a** yielded the corresponding acid (*R*)-**6b**. After converting (*R*)-**6b** into its sodium salt (*R*)-**6c** by adding sodium ethoxide in ethanol, the concentrated and dried (*R*)-**6c** was treated with oxalyl chloride



Scheme 2. Synthesis of (2*E*,6*R*)-**1** and (2*E*,6*S*)-**1′**. Reagents and conditions: (a) 37% CH_2O, $EtCO_2H$, pyrrolidine, *i*-PrOH, 45 °C, 4 h, 90%; (b) $LiAlH_4$, Et_2O, 91%; (c) $MeC(OEt)_3$, $EtCO_2H$, 140 °C, 1 h, 95%; (d) KOH, EtOH, H_2O, reflux, 2 h, 83%; (e) NaOEt, EtOH; (f) $(COCl)_2$, C_5H_5N hexane, quant. (2 steps); (g) CH_2N_2, Et_2O, quant.; (h) Cu, $CuSO_4$, cyclohexane, reflux, 1 h, 58%; (i) OsO_4, $NaIO_4$, *t*-BuOH, THF, H_2O, quant. (85% in the presence of 2,6-lutidine); (j) $Ph_3P{=}C(Me)CO_2Et$, THF, CH_2Cl_2, 57%; (k) $Ph_3P(Me)Br$, *n*-BuLi, THF (96%); (l) $(i\text{-}Bu)_2AlH$, toluene, 55%.

in hexane in the presence of a small amount of pyridine as the reaction promotor. The resulting acyl chloride (*R*)-**7** in hexane was added to an excess amount of diazomethane in diethyl ether to give diazoketone (*R*)-**8** as a yellow oil. Subsequently, (*R*)-**8** in cyclohexane was added dropwise to a stirred and refluxing suspension of powdered copper and copper(II) sulfate in cyclohexane. The product was purified by silica gel chromatography followed by distillation to give bicyclic ketone (*R*)-**9**, $\nu_{max} = 1728\ cm^{-1}$, in 48% overall yield based on ester (*R*)-**6a**. Ketone (*R*)-**9** was obtained as a diastereomeric mixture of two isomers with regards to the newly formed cyclopropane ring with either the α- or β-orientation. The ratio of the diastereomers was analyzed by GC–MS, and shown to be 51.9:46.5 with 1.6% of unidentified impurities. The (*R*)-configured methyl group of (*R*)-**8** did not exert a significant steric effect over the course of the intramolecular addition of α-ketocarbene to the double bond.

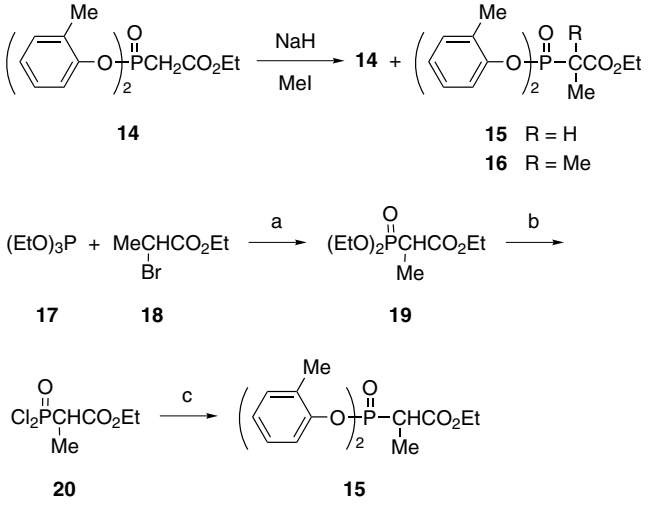
Lemieux-Johnson oxidation of (*R*)-**9** with osmium tetroxide and sodium periodate in aqueous THF was carried out under the modified conditions reported by Jin et al.[9] in the presence of 2,6-lutidine to give keto aldehyde (*R*)-**10**. In this particular case, the yield of (*R*)-**10** was slightly better when the reaction was done in the absence of 2,6-lutidine. Treatment of (*R*)-**10** with (carbethoxymethylidene)triphenylphosphorane afforded (2*E*,6*R*)-**11** as the major product. Keto ester (2*E*,6*R*)-**11** was subjected to the Wittig reaction with 1.1 equiv of methylenetriphenylphosphorane in THF at −78 °C to give (2*E*,6*R*)-**12**. Finally, reduction of (2*E*,6*R*)-**12** with diisobutylaluminum hydride afforded (2*E*,6*R*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]-hexyl)hept-2-en-1-ol **1** as a colorless oil. The overall yield of (2*E*,6*R*)-**1** was 30% based on (*R*)-**9** or 11% based on (*R*)-**3** (11 steps). In a similar manner, (2*E*,6*S*)-**1′** was synthesized by starting from (*S*)-citronellal **3′**.

GC–MS analysis of (2*E*,6*R*)-**1** and (2*E*,6*S*)-**1′** revealed them to be 1.06–1.09:1 mixtures of each two diastereomers, both of which showed identical MS with a molecular ion peak at $m/z = 220$ ($C_{15}H_{24}O$). Their NMR spectra were then measured in C_6D_6 to compare them with the data of the natural pheromone (Table 1). Distinct differences were observed as follows: in the ^1H NMR spectrum, synthetic **1** showed signals at $\delta = 1.59$ (8-Me), 3.80 (1-C*H*$_2$OH), and 5.34 (3-CH=C), while the natural pheromone absorbed at $\delta = 1.75$, 3.96, and 5.17. In the ^{13}C NMR spectrum, synthetic **1** exhibited signals at $\delta = 26.0$ (C-8), 68.6 (C-1), 125.6 (C-3), and 135.0 (C-2), while the natural pheromone showed them at 21.3, 61.5, 128.1 and 135.4. These differences were due to the *cis*/*trans*-isomerism of the double bond. By comparing these δ-values of **1** and the natural pheromone with the literature data,[10–12] the latter was thought to be **2** with a *Z*-double bond. We, therefore, turned our attention to the synthesis of **2**.

2.2. Synthesis of ethyl 2-(di-*o*-tolylphosphono)propanoate 15

In order to synthesize the desired pheromone with a *Z*-double bond, there was a need to select a suitable *Z*-selective olefination method. We chose Ando's method for this purpose. Ando reported that methylation of ethyl (di-*o*-tolylphosphono)acetate **14**[13] gave a very useful *Z*-selective olefination reagent, ethyl 2-(di-*o*-tolylphosphono)propanoate **15**.[14] By employing **15**, (*Z*)-olefinic esters were obtained in 78–100% yield with a *Z*-selectivity of 92–99%.[14] For the methylation of **14**, sodium hydride and methyl iodide in DMSO were employed by Ando.[14] When we methylated commercially available **14** according to Ando,[14] the product was impure **15**, contaminated with small amounts (about 10% each) of non-methylated **14** and dimethylated **16** (Scheme 3). This result seems natural, because it is well known that methylation of diethyl malonate gives a mixture of the starting material, the monomethylated, and dimethylated malonates. The use of this impure olefination reagent **15** would cause problems for the preparation of pure **2**.

Therefore, we made an effort to achieve a reliable synthesis of pure **15**, and prepared **15** in three steps from triethyl



Scheme 3. Synthesis of ethyl 2-(di-*o*-tolylphosphono)propanoate (**15**). Reagents and conditions: (a) 160 °C, 2 h, 60%; (b) PCl_5, 75–80 °C, 14 h, 67%; (c) *o*-cresol, Et_3N, CH_2Cl_2, 0–5 °C, 30 min, room temperature, 1 h, 60%.

Table 1. Comparison of the NMR data of the natural pheromone with synthetic (2*E*,6*R*)-**1** and (2*Z*,6*R*)-**2**

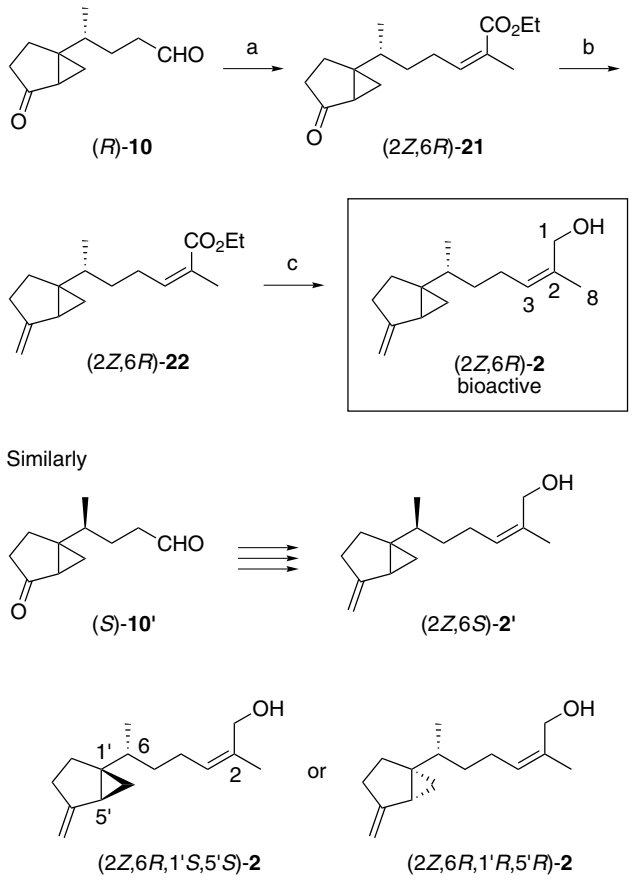
	^1H NMR (δ, in C_6D_6)			^{13}C NMR (δ, in C_6D_6)			
	8-C*H*$_3$	1-C*H*$_2$OH	3-C*H*=C	C-8	C-1	C-3	C-2
Natural pheromone[a]	1.75	3.96	5.17	21.3	61.5	128.1	135.4
(2*E*,6*R*)-**1**[b]	1.59	3.80	5.34	26.0	68.6	125.6	135.0
(2*Z*,6*R*)-**1**[b]	1.75	3.97	5.18	21.3	61.3	128.1	134.5

[a] 600 MHz for ^1H NMR; 125 MHz for ^{13}C NMR.
[b] 400 MHz for ^1H NMR; 100 MHz for ^{13}C NMR.

phosphite **17** and ethyl 2-bromopropanoate **18**. The Arbuzov reaction between **17** and **18** gave the known phosphonate **19**.[15] Treatment of **19** with phosphorus pentachloride at 75–80 °C overnight afforded phosphoryl chloride **20.** *o*-Cresol was esterified with **20** in the presence of triethylamine to give the desired **15** in 18.6% overall yield based on bromo ester **18**. In its ^{1}H NMR spectrum, **15** showed a 3H signal at $\delta = 1.69$ as dd ($J_{HH} = 7$, $J_{PH} = 19$ Hz), indicating the presence of a single methyl group at C-2.

2.3. Synthesis of (2*Z*,6*R*)- and (2*Z*,6*S*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol 2 and 2′

Olefination of (*R*)-**10** with ethyl 2-(di-*o*-tolylphosphono)-propanoate **15** was achieved by using sodium hydride in THF as a base at −78 °C. The resulting diastereomeric mixture of ester (2*Z*,6*R*)-**21** (Scheme 4) showed ^{1}H NMR signals at $\delta = 1.89$ and 1.90 (total 3H, 13-Me) and also at $\delta = 5.88$ (1H, 10-CH=C). On the other hand, (2*E*,6*R*)-**11** exhibited signals at $\delta = 1.80$ and 1.82 (total 3H) and also at 6.70 (1H). Ethyl (*E*)-2-methyl-5-phenyl-2-pentenoate was reported to show signals at $\delta = 1.78$ (3H) and 6.80 (1H), while its (*Z*)-isomer exhibited signals at $\delta = 1.89$ (3H) and 5.96 (1H).[16] It was therefore thought that **21** possessed a *Z*-double bond. Methylenation of (2*Z*,6*R*)-**21** with methylenetriphenylphosphorane furnished (2*Z*,6*R*)-**22**. This ester was reduced with diisobutylaluminum hydride to give (2*Z*,6*R*)-2-methyl-6-(4′-methylenebicyclo[3.1.0]-hexyl)hept-2-en-1-ol **2** in 22% overall yield based on (*R*)-**10** or 8% overall yield based on (*R*)-**3**: (11 steps). Similarly, (*S*)-**10′** was converted to (2*Z*,6*S*)-**2′**.



Scheme 4. Synthesis of (2*Z*,6*R*)-**2** and (2*Z*,6*S*)-**2′**. Reagents and conditions: (a) (*o*-MeC$_6$H$_4$O)$_2$P(O)CHMeCO$_2$Et, NaH, THF, −78 to 5 °C, quant.; (b) Ph$_3$P(Me)Br, *n*-BuLi, THF, quant.; (c) (*i*-Bu)$_2$AlH, toluene, 51% (crude), 22% after purification.

GC–MS analysis of both (2*Z*,6*R*)-**2** and (2*Z*,6*S*)-**2′** indicated that they were obtained as diastereomeric mixtures in ratios of 1.46–1.59:1. The MS of **2** was virtually identical to that of **1** with a molecular ion peak at $m/z = 220$ ($C_{15}H_{24}O$), which was in good accordance with that of the natural pheromone (Table 1). The ^{1}H and ^{13}C NMR spectra of **2** in C_6D_6 were carefully compared with those of the natural pheromone. In the ^{1}H NMR spectrum (400 MHz), synthetic **2** showed signals at $\delta = 0.43$ (1H, dd, *J* 4, 8) and 0.61 (1H, dd, *J* 4, 4) for the cyclopropane protons, 1.75 (3H, 8-Me), 3.97 (2H, 1-C*H*$_2$OH), 4.78 (1H, s), and 4.99 (1H, s) for olefinic methylene protons, and 5.18 (1H, 3-CH=C), while the natural pheromone showed signals in its 600 MHz spectrum at $\delta = 0.40$, 0.57, 1.75, 3.96, 4.78, 4.99, and 5.17. In the ^{13}C NMR spectrum (100 MHz), synthetic **2** exhibited signals at $\delta = 21.3$ (C-8), 61.3 (C-1), 128.1 (C-3), and 134.5 (C-2), while the natural pheromone showed them (125 MHz) at $\delta = 21.3$, 61.5, 128.1, and 135.4. Although the spectra of synthetic **2** were much more complicated than those of the natural pheromone due to the presence of the unnatural diastereomer, all the signals in the spectra of the natural pheromone could be observed in the spectra of **2**.

3. Conclusion

Our synthetic products, (2*E*,6*R*)-**1′**, (2*E*,6*S*)-**1′**, (2*Z*,6*R*)-**2**, and (2*Z*,6*S*)-**2′** were bioassayed against *Erysarcosis lewisi* by Yoshimura and Ishii at Yamagata Prefectural Agricultural Research Center. In three independent field bioassays, 0.408 mg of the natural pheromone attracted 107 stink bugs in sum total, while the same amount of (2*Z*,6*R*)-**2** attracted 40 *Erysarcoris lewisi*. Other isomers attracted only 2–7 bugs. These results suggest that either (2*Z*,6*R*,1′*S*,5′*S*)- or (2*Z*,6*R*,1′*R*,5′*R*)-**2** is the natural pheromone. The synthesis of these two compounds is now being pursued, and the result will be reported in due course.

4. Experimental

4.1. General

Boiling points are uncorrected values. Optical rotations were measured on a Jasco P-1020 polarimeter. IR spectra were measured on a Jasco FT/IR-410 spectrometer. ^{1}H NMR spectra (400 MHz, TMS at $\delta = 0.00$ as internal standard) and ^{13}C NMR spectra (100 MHz, $CDCl_3$ at $\delta = 77.0$ as internal standard) were recorded on a Jeol JNM-AL 400 spectrometer. GC–MS were measured on Agilent Technologies 5975 inert XL. HRMS were recorded on a Jeol JMS-SX102A. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. 3,7-Dimethyl-2-methylene-6-octenal 4 and 4′

4.2.1. (*R*)-(−)-Isomer 4. Propanoic acid (0.54 g, 7.3 mmol) and pyrrolidine (0.52 g, 7.3 mmol) were added to a solution of (*R*)-**3** (Takasago, 97% ee; 11.2 g, 73 mmol) and 37% CH_2O aqueous solution (6.5 mL, ca. 73 mmol) in *i*-PrOH (8 mL). The mixture was stirred at 45 °C for 4 h. It was then diluted with $NaHCO_3$ aqueous solution, and extracted with hexane. The extract was washed with water, $NaHCO_3$ aqueous solution and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was distilled to give 10.9 g (90%) of (*R*)-**4** as an oil, bp 94–97 °C/12 Torr; $n_D^{21} = 1.4660$; $[\alpha]_D^{24} = -13.6$ (*c* 3.45, hexane); ν_{max} (film): 2696 (w, H–C=O), 1697 (s, C=O), 1624 (w, C=C), 945 (m, C=CH_2); $\delta_H(CDCl_3)$: 1.06 (3H, d, *J* 7.2, CHCH_3), 1.32–1.42 (1H, m), 1.48–1.54 (1H, m), 1.57 (3H, s, C=CCH_3), 1.67 (3H, s, C=CCH_3), 1.88–2.00 (1H, m), 2.62–2.78 (1H, m), 5.08 (1H, t, *J* = 7, C=CH), 5.98 (1H, s, C=CH*H*), 6.23 (1H, s, C=C*H*H), 9.53 (1H, s, CHO); $\delta_C(CDCl_3)$: 17.6, 19.5, 25.66, 25.71, 30.9, 35.5, 124.1, 131.6, 133.1, 155.4, 194.7. The spectral data of **4** were identical with those reported by Erkkilä and Pihko.[7] HRMS calcd for $C_{11}H_{18}O$ (M^+) 166.1358; found, 166.1361.

4.2.2. (*S*)-(+)-Isomer 4′. In the same manner, (*S*)-**3′** (Takasago, 97% ee; 11.2 g, 73 mmol) yielded 10.7 g (86%) of (*S*)-**4′** as an oil, bp 86–88 °C/9 Torr; $n_D^{20} = 1.4661$; $[\alpha]_D^{24} = +13.1$ (*c* 4.72, hexane). Its spectral data were identical with those of **4**. HRMS calcd for $C_{11}H_{18}O$ (M^+) 166.1358; found, 166.1361.

4.3. 3,7-Dimethyl-2-methylene-6-octen-1-ol 5 and 5′

4.3.1. (*R*)-(−)-Isomer 5. A solution of (*R*)-**4** (10.5 g, 63 mmol) in dry Et_2O (50 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (1.3 g, 34 mmol) in dry Et_2O (100 mL) at 0–10 °C. The mixture was stirred for 2 h at 5–10 °C. Subsequently, H_2O (10 mL) was added dropwise to the stirred and ice-cooled reaction mixture to destroy the excess $LiAlH_4$. The voluminous solid was dissolved by the addition of ice-water containing concd HCl (10 mL) and NH_4Cl. Then the organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined Et_2O solution was washed with water, $NaHCO_3$ aqueous solution and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was distilled to give 10.1 g (91%) of (*R*)-**5** as an oil, bp 113–115 °C/11 Torr; $n_D^{21} = 1.4710$; $[\alpha]_D^{25} = -19.4$ (*c* 4.50, hexane); ν_{max} (film): 3305 (s, OH), 1651 (m, C=C), 1045 (s, C–O), 899 (s, C=CH_2); $\delta_H(CDCl_3)$: 1.06 (3H, d, *J* 6.8, CHCH_3), 1.30–1.40 (1H, m), 1.44 (1H, OH), 1.45–1.54 (1H, m), 1.59 (3H, s, C=CCH_3), 1.68 (3H, s, C=CCH_3), 1.92–1.98 (2H, m), 1.92–1.99 (1H, m), 4.09 (2H, d, *J* 3, CH_2OH), 5.05 (1H, s, C=C*H*H), 5.09 (1H, s, C=CH*H*). Anal. Calcd for $C_{11}H_{20}O$ (168.3): C, 78.51; H, 11.98. Found: C, 77.98; H, 12.05.

4.3.2. (*S*)-(+)-Isomer 5′. In the same manner, (*S*)-**4′** (10.5 g, 63 mmol) yielded 9.6 g (90%) of (*S*)-**5′** as an oil, bp 93–96 °C/4 Torr; $n_D^{21} = 1.4705$; $[\alpha]_D^{22} = +19.0$ (*c* 4.19, hexane). Its spectral data were identical with those of **5**. Anal. Calcd for $C_{11}H_{20}O$ (168.3): C, 78.51; H, 11.98. Found: C, 77.81; H, 12.20.

4.4. Ethyl 5,9-dimethyl-4-methylene-8-decenoate 6a and 6a′

4.4.1. (*R*)-(−)-Isomer 6a. Propanoic acid (400 mg, 5 mmol) was added to a solution of (*R*)-**5** (10.0 g, 59 mmol) in $MeC(OEt)_3$ (80 g, 494 mmol), and the mixture was stirred and heated at 150–160 °C for 1 h to remove the ethanol generated. The mixture was then concentrated in vacuo, and the residue was distilled to give 13.5 g (95%) of (*R*)-**6a** as an oil, bp 113–115 °C/3 Torr; $n_D^{22} = 1.4562$; $[\alpha]_D^{21} = -11.6$ (*c* 4.85, hexane); ν_{max} (film): 3078 (m), 1739 (s, C=O), 1643 (m, C=C), 1160 (s, C–O), 891 (m, C=CH_2). $\delta_H(CDCl_3)$: 1.02 (3H, d, *J* 6.8, CHCH_3), 1.26 (3H, t, *J* 7.2, CH_2CH_3), 1.28–1.36 (1H, m), 1.40–1.52 (1H, m), 1.59 (3H, s, C=CCH_3), 1.68 (3H, s, C=CCH_3), 4.13 (2H, q, *J* 7.2, OCH_2CH_3), 4.70 (1H, s, C=CH), 4.78 (1H, s, C=CH), 5.09 (1H, t-like, *J* 7, C=CH); $\delta_C(CDCl_3)$: 14.2, 17.6, 20.0, 25.7, 25.9, 28.2, 32.8, 35.6, 39.9, 60.3, 107.8, 124.5, 131.3, 152.8, 173.4. HRMS calcd for $C_{15}H_{26}O_2$ (M^+) 238.1933; found, 238.1925.

4.4.2. (*S*)-(+)-Isomer 6a′. In the same manner, (*S*)-**5′** (9.5 g, 56.5 mmol) yielded 12.6 g (94%) of (*S*)-**6a′** as an oil, bp 118–120 °C/4 Torr; $n_D^{22} = 1.4562$; $[\alpha]_D^{24} = +11.5$ (*c* 5.03, hexane). Its spectral data were identical with those of **6a**. HRMS calcd for $C_{15}H_{26}O_2$ (M^+) 238.1933; found, 238.1925.

4.5. 5,9-Dimethyl-4-methylene-8-decenoic acid 6b and 6b′

4.5.1. (*R*)-(−)-Isomer 6b. A solution of KOH (7.0 g, 125 mmol) in H_2O (30 mL) was added to a solution of (*R*)-**6a** (13.5 g, 57 mmol) in 95% EtOH (100 mL). The mixture was stirred and heated at reflux for 2 h. It was then diluted with ice-water, acidified with AcOH (13 mL, ca. 230 mmol), and extracted with hexane. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was distilled to give 9.9 g (83%) of (*R*)-**6b** as an oil, bp 159–160 °C/7 Torr; $n_D^{21} = 1.4715$; $[\alpha]_D^{23} = -14.0$ (*c* 4.41, hexane); ν_{max} (film): 3080–2615 (m, CO_2H), 1712 (s, C=O), 1650 (m, C=C), 890 (m, C=CH_2). $\delta_H(CDCl_3)$: 1.02 (3H, d, *J* 6.8, CHCH_3), 1.25–1.38 (1H, m), 1.40–1.50 (1H, m), 1.58 (3H, s, C=CCH_3), 1.68 (3H, s, C=CCH_3), 2.10–2.20 (1H, m), 2.29–2.36 (2H, m), 2.53 (2H, t-like, *J* 7.6, CH_2CO_2H), 4.72 (1H, s, C=C*H*H), 4.80 (1H, s, C=CH*H*), 5.09 (1H, t-like, *J* 7.2, C=CH); $\delta_C(CDCl_3)$:17.7, 20.0, 25.7, 25.9, 27.8, 32.5, 35.5, 39.9, 108.0, 124.5, 131.4, 152.4, 179.8. Anal. Calcd for $C_{13}H_{22}O_2$ (210.3): C, 74.24; H, 10.54. Found: C, 74.20; H, 10.79.

4.5.2. (*S*)-(+)-Isomer 6b′. In the same manner, (*S*)-**6a′** (12.6 g, 53 mmol) yielded 9.4 g (86%) of (*S*)-**6b′** as an oil, bp 153–156 °C/5 Torr; $n_D^{20} = 1.4712$; $[\alpha]_D^{23} = +13.9$ (*c* 4.28, hexane). Its spectral data were identical with those of **6b**. Anal. Calcd for $C_{13}H_{22}O_2$ (210.3): C, 74.24; H, 10.54. Found: C, 74.32; H, 10.64.

4.6. 1-Diazo-6,10-dimethyl-5-methylene-9-undecen-2-one 8 via sodium 5.9-dimethyl-4-methylene-8-decenoate 6c and 5,9-dimethyl-4-methylene-8-decenoyl chloride 7

4.6.1. (*R*)-Isomer 8. Sodium ethoxide (2.8 g, 41 mmol) was added to a solution of (*R*)-**6b** (8.0 g, 38 mmol) in 99% EtOH (30 mL) and the solution concentrated in vacuo. The residue was dissolved in toluene, and the resulting solution was concentrated in vacuo. This operation was repeated once more to remove EtOH completely. The amorphous solid residue **6c** was suspended in hexane (100 mL), and treated with dry C_5H_5N (0.5 mL) and $(COCl)_2$ (15 g, 118 mmol) with stirring and ice-cooling at 0–5 °C. The mixture was stirred for 1 h at room temp., and then filtered through Celite (vacuum suction). The Celite layer was washed with hexane (100 mL), and the combined filtrate and washings concentrated in vacuo to give 9.0 g (quant.) of crude (*R*)-**7** as an oil, ν_{max} (film): 1801 (s, C=O), 1643 (m, C=C), 1041 (m), 960 (m), 894 (m), 729 (s). A solution of (*R*)-**7** (9.0 g, ca. 38 mmol) in hexane (100 mL) was added dropwise over 15 min to a stirred and ice-cooled solution of CH_2N_2 [prepared from 16 g (155 mmol) of *N*-nitroso-*N*-methylurea, 50 mL of 20% KOH aqueous solution, and Et_2O (400 mL)] in Et_2O (400 mL). The yellow reaction mixture was stirred at 0–5 °C for 1 h, and then concentrated in vacuo to give crude (*R*)-**8** (11.0 g, quant.) as a yellow oil, ν_{max} (film): 3082 (w), 2106 (s, $N^+\equiv N$), 1643 (s, C=O), 891 (m), 733 (m). This was immediately employed for the next step.

4.6.2. (*S*)-Isomer 8′. In the same manner, (*S*)-**6b′** (10.6 g, 50 mmol) yielded 11.0 g (93%) of (*S*)-**8′** as a yellow oil. This was immediately used for the next step.

4.7. 2-Methyl-6-(4′-oxobicyclo[3.1.0]hexyl)hept-2-ene 9 and 9′

4.7.1. (*R*)-(−)-Isomer 9. A solution of crude (*R*)-**8** (11.0 g, 38 mmol) in cyclohexane (50 mL) was added dropwise over 30 min to a stirred and refluxing suspension of powdered copper (1.0 g, 16 mmol) and anhyd $CuSO_4$ (0.5 g, 3 mmol) in cyclohexane (200 mL). After the addition, the mixture was stirred and heated at reflux for 1 h, cooled and filtered. The filtrate was concentrated in vacuo to give 8.5 g (quant.) of crude (*R*)-**9**. This was chromatographed over SiO_2 (150 g) in hexane. Elution with hexane/EtOAc (40:1–20:1) gave ca. 1.0 g of by-products. Further elution with hexane/EtOAc (15:1) afforded 6.9 g (85%) of (*R*)-**9**. This was distilled to give 4.7 g (58%) of oily (*R*)-**9** as a mixture of two diastereoisomers, bp 143–144 °C/5 Torr, $n_D^{22} = 1.4869$, $[\alpha]_D^{23} = -2.8$ (*c* 4.51, hexane); ν_{max} (film): 1728 (s, C=O), 1182 (m), 916 (m), 775 (m); $\delta_H(CDCl_3)$: 0.97, 0.99 (total 3H, each d, *J* 7, $CHCH_3$), 1.58 (3H, $C=CCH_3$), 1.70 (3H, $C=CCH_3$), 5.06 (1H, m, CH=C); $\delta_C(CDCl_3)$: 17.0, 17.4, 17.7, 19.3, 21.4, 22.4, 23.3, 25.7, 25.8, 25.9, 27.9, 33.0, 33.1, 33.4, 34.2, 34.5, 37.1, 37.4, 39.9 124.2, 131.7, 215.0; GC–MS (column: TC-Wax, temp: 100–190 °C (+3 °C/min)): t_R 19.9 min (0.5%) 37.1 (51.9%), 37.4 (1.2%), 37.9 (46.5%); MS (70 eV, EI): *m*/*z*: 206 (12) [M^+], 191 (4), 173 (3), 164 (4) 163 (18) 149 (12) 136 (14), 123 (46), 121 (12), 109 (23), 95 (30), 93 (38), 79 (62), 69 (79), 67 (86), 55 (100), 53 (57). Both of the diastereoisomers of (*R*)-**9** showed the identical MS. HRMS calcd for $C_{14}H_{22}O$ (M^+) 206.1671; found, 206.1668.

4.7.2. (*S*)-(+)-Isomer 9′. In the same manner, (*S*)-**6b′** (11.8 g, 56 mmol) yielded 5.0 g (43%) of oily (*S*)-**9′** after SiO_2 chromatography and distillation, bp 142–146 °C/5 Torr, $n_D^{22} = 1.4866$, $[\alpha]_D^{25} = +2.3$ (*c* 5.55, hexane). Its spectral data were identical with those of (*R*)-**6b**. HRMS calcd for $C_{14}H_{22}O$ (M^+) 206.1671; found, 206.1679.

4.8. 4-(4′-Oxobicyclo[3.2.1]hexyl)pentanal 10 and 10′

4.8.1. (*R*)-Isomer 10. A solution of OsO_4 (30 mg) in *t*-BuOH (3 mL) and powdered $NaIO_4$ (3.2 g, 15 mmol) were added to a stirred solution of (*R*)-**9** (1.0 g, 5 mmol) in a mixture of THF (22.5 mL) and H_2O (7.5 mL) at room temp. under N_2. The stirring was continued for 2 d at room temp., while tan-colored mixture turned colorless. It was then diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo to give 0.9 g (quant.) of (*R*)-**10** as an oil, ν_{max} (film): 2723 (w, O=CH), 1722 (s, C=O), 1180 (m), 914 (m); $\delta_H(CDCl_3)$: 0.99, 1.01 (total 3H, each d, *J* 7, $CHCH_3$), 9.78, 9.80 (total 1H each s, CHO); $\delta_C(CDCl_3)$: 201.9, 214.4. This was employed for the next step without further purification.

4.8.2. (*S*)-Isomer 10′. Similarly, (*S*)-**9′** (1.0 g, 5 mmol) yielded 0.8 g (91%) of (*S*)-**10′**, whose IR and ^1H NMR spectra were identical to those of (*R*)-**10**. This was directly employed for the next step.

4.9. Ethyl (*E*)-2-methyl-6-(4′-oxobicyclo[3.1.0]hexyl)hept-2-enoate 11 and 11′

4.9.1. (*R*)-Isomer 11. A solution of (carbethoxyethylidene)triphenylphosphorane (1.8 g, 5.0 mmol) in dry THF (10 mL) was added dropwise to a stirred and ice-cooled solution of (*R*)-**10** (0.90 g, 5.0 mmol) in dry CH_2Cl_2 (10 mL) at 0–5 °C under N_2. The Wittig reaction was exothermic. The mixture was further stirred for 2 d at room temp., and concentrated in vacuo. The residue was chromatographed over SiO_2 (30 g). Elution with hexane/EtOAc (5:1) yielded 0.74 g (57%) of (*R*)-**11** [contaminated with a small amount (7%) of its (*Z*)-isomer] as an oil, ν_{max} (film): 1726 (s, C=O), 1649 (w, C=C), 1261 (m, C–O); $\delta_H(CDCl_3)$: 0.99, 1.02 (total 3H, each d, *J* 7, $CHCH_3$), 1.28 (3H, t, *J* 7, CH_2CH_3), 1.80, 1.82 [total 3H, each s, $C=C(CH_3)CO_2Et$], 4.18 (2H, q, *J* 7, CH_2CH_3), 5.88 [0.07H, m, (*Z*)-$CH=C(CH_3)CO_2Et$] 6.70 [0.93H, m, (*E*)-$CH=C(CH_3)CO_2Et$]. This was employed in the next step without further purification.

4.9.2. (*S*)-Isomer 11′. In the same manner, (*S*)-**10′** (0.80 g, 4.4 mmol) afforded 0.62 g (53%) of (*S*)-**11′** as an oil. Its spectral data were identical to those of (*R*)-**11**. This was used directly for the next step.

4.10. Ethyl (*E*)-2-methyl-6-(4′-methylenebicyclo-[3.1.0]hexyl)hept-2-enoate 12 and 12′

4.10.1. (*R*)-Isomer 12. Methylenetriphenylphosphorane was prepared by the addition of a solution of *n*-BuLi in hexane (1.6 M, 2.1 mL, 3.4 mmol) to a suspension of $(C_6H_5)_3P(CH_3)Br$ (1.10 g, 3.0 mmol) in dry THF (10 mL) at −78 °C under N_2. The mixture was stirred for 15 min at −78 °C to generate an orange solution of the Wittig reagent. This was added through a syringe to a stirred and cooled solution of (*R*)-**11** (0.70 g, 2.65 mmol) in dry THF (7 mL) at −78 °C under N_2. The solution was stirred for 30 min at −78 °C to room temp. It was then poured into ice-water, and extracted with Et_2O. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (10:3) gave 0.67 g (96%) of (*R*)-**12**, ν_{max} (film): 3074 (w), 1712 (s, C=O), 1651 (m, C=C), 1243 (s, C–O), 863 (m); $\delta_H(CDCl_3)$: 0.55–0.78 (2H, m, cyclopropane CH_2), 0.84–0.98 (3H, m, $CHCH_3$), 1.23–1.35 (3H, m, OCH_2CH_3), 4.16–4.28 (2H, m, OCH_2CH_3), 4.62 (1H, s, C=CHH), 4.80 (1H, s, C=CHH), 6.74 [1H, m, $CH=C(CH_3)CO_2Et$]. This was employed for the next step without further purification.

4.10.2. (*S*)-Isomer 12′. In the same manner, (*S*)-**11**′ (0.62 g, 2.35 mmol) gave 0.56 g (91%) of (*S*)-**12**′. Its spectral data were identical to those of (*R*)-**12**. This was employed for the next step without further purification.

4.11. (*E*)-2-Methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol 1 and 1′

4.11.1. (*R*)-Isomer 1. A solution of $(i\text{-Bu})_2AlH$ in toluene (1 M, 6 mL, 6 mmol) was added to a stirred and cooled solution of (*R*)-**11** (0.5 g, 1.9 mmol) in toluene (10 mL) at −78 °C under N_2. After 5 min at −78 to 0 °C, an additional amount (4 mL, 4 mmol) of $(i\text{-Bu})_2AlH$ in toluene was added, and the stirring was continued for 30 min at 0–5 °C. MeOH (10 mL) was then added to destroy excess $(i\text{-Bu})_2AlH$, and the mixture was stirred for 30 min at room temp. It was filtered through Celite, and the Celite layer was washed with hexane. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed over SiO_2 (10 g). Elution with hexane/EtOAc (4:1) yielded 0.23 g (55%) of (*R*)-**1**. This was further purified by SiO_2 chromatography to give pure (*R*)-**1** as a mixture of two diastereoisomers, $n_D^{21} = 1.5052$; $[\alpha]_D^{24} = -10.7$ (*c* 1.11, hexane); ν_{max} (film): 3344 (s, OH), 1651 (m, C=C) 1116 (m, C–O), 864 (m); $\delta_H(CDCl_3)$: 0.56 (0.5H, m, cyclopropane CH), 0.67 (1H, m, cyclopropane CH), 0.74 (0.5H, m cyclopropane CH), 0.94, 0.97 (total 3H, each d, *J* 7, $CHCH_3$), 1.68 [3H, $CH=C(CH_3)$], 3.98 (2H, s, CH_2OH), 4.65 (1H, s, C=CHH), 4.81 (1H, s, C=CHH), 5.40 [1H, m, $CH=C(CH_3)$]; $\delta_C(CDCl_3)$: 13.7, 16.2, 17.5, 18.1, 18.3, 25.7, 26.3, 26.6, 28.8, 29.7, 31.2, 34.3, 34.9, 36.6, 38.1, 69.0, 101.7, 126.6, 134.5, 154.1; $\delta_H(C_6D_6)$: 0.42, 0.57, 0.60, 0.67 (total 2H, each m, cyclopropane CH_2), 0.88, 0.90 (total 3H, each d, *J* 7, $CHCH_3$), 1.59 [3H, s, $CH=C(CH_3)$], 3.80, 3.82 (total 2H, each s, CH_2OH), 4.78 (1H, s, C=CHH), 4.98 (1H, s, C=CHH) 5.34 [1H, m, $CH=C(CH_3)$]; $\delta_C(C_6D_6)$: 13.7, 14.3, 16.2, 17.6, 18.3, 23.1, 26.0, 26.5, 29.1, 29.8, 30.1, 31.7, 32.3, 34.6, 35.2, 36.6, 38.2, 68.6, 102.3, 125.6, 135.0, 153.7, GC–MS [Column: HP-5MS, 35% phenylmethylsiloxane, 30 m × 0.25 mm i.d.; press: 60.7 kPa; 70–230 °C (+10 °C/min)]; t_R 14.74 min (2.2%), 14.96 (2.2%) 15.03 (44.5%), 15.18 (40.8%), 15.37 (4.2%), 15.68 (2.6%). The peaks at $t_R = 15.03$ and 15.18 min were due to the two diastereoisomers (1.09:1) of (*R*)-**1** showing the same MS. MS (70 eV, EI): *m*/*z*: 220 (7) [M^+], 202 (9), 187 (12), 161 (13), 159 (10), 145 (19), 133 (24), 132 (32), 121 (52), 120 (32), 119 (78), 105 (37), 93 (100), 91 (59), 79 (41), 77 (41), 69 (23), 67 (20), 55 (23), 43 (35), 41 (26). HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827; found, 220.1827.

4.11.2. (*S*)-Isomer 1′. In the same manner, (*S*)-**11**′ (530 mg, 2 mmol) afforded 380 mg (85%) of (*S*)-**1**′, $n_D^{21} = 1.5053$; $[\alpha]_D^{21} = +4.5$ (*c* 1.08, hexane). Its spectral properties were identical with those of (*R*)-**1**. GC–MS [same conditions as for (*R*)-**1**]: t_R 14.75 min (3.1%), 14.96 (3.1%), 15.05 (44.8%), 15.20 (42.1%), 15.37 (2.3%), 15.68 (1.3%). The peaks at $t_R = 15.05$ and 15.20 min were those of the two diastereoisomers (1.06:1) of (*S*)-**1**′. Their MS were identical to those of the two diastereoisomers of (*R*)-**1**. HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827; found, 220.1833.

4.12. 1-Ethoxycarbonylethylphosphonic dichloride 20

According to Ref. 15, **17** and **18** were converted to **19**, bp 97–99 °C/2 Torr; ν_{max} (film): 1737 (s, C=O); $\delta_H(CDCl_3)$: 1.27–1.37 (9H, m, OCH_2CH_3), 1.47 (3H, ddd, *J* 18, 7, 2, $CHCH_3$), 3.03 (1H, dqd, *J* 18, 7, 2, $CHCH_3$), 4.13–4.23 (6H, m, OCH_2CH_3). Solid PCl_5 (39 g, 187 mmol) was added portionwise to stirred and ice-cooled **19** (17.5 g, 73.5 mmol). After stirring for 30 min at 0–5 °C, the stirred mixture was heated at 75–80 °C for 14 h in a draft chamber. It was then concentrated in vacuo. The residue was distilled to give **20** (10.8 g 67%) as an oil, bp 87–89 °C/2 Torr; $n_D^{23} = 1.4748$; ν_{max} (film): 1743 (s, C=O), 1279 (s, C–O); $\delta_H(CDCl_3)$: 1.33 (3H, t, *J* 7, OCH_2CH_3), 1.69 (3H, dd, *J* 27, 7, $PCHCH_3$), 2.03–2.32 (sextet, P), 3.67 (1H, dq, *J* 20, 7, $PCHCH_3$), 4.23–4.51 (2H, m, $OCHCH_3$). HRMS calcd for $C_5H_8PO_3Cl$ [$(M-H)^+$] 216.9588; found, 216.9590.

4.13. Ethyl 2-(di-*o*-tolylphosphono)propanoate 15

Triethylamine (10.4 g, 10 mmol) was added dropwise to a stirred and ice-cooled solution of **20** (9.3 g, 42.5 mmol) and *o*-cresol (9.3 g, 86 mmol) in CH_2Cl_2 (40 mL) at 0–5 °C. The mixture soon solidified, and then became paste-like. The stirring was continued for 30 min at 0–5 °C, and then for 1 h at room temp. The mixture turned to a slurry of solid $Et_3N{\cdot}HCl$, which was stirred vigorously. Subsequently, the slurry was poured into ice-water, and extracted with hexane. The extract was washed with ice-cooled dilute NaOH aqueous solution, ice-cooled dilute HCl, saturated $NaHCO_3$ aqueous solution and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was distilled to give **15** as a viscous oil (9.3 g, 60%), bp 210–215 °C/2 Torr; $n_D^{22} = 1.5162$; ν_{max} (film): 1738 (s, C=O), 1585 (m, aromatic C=C) 1228 (s), 1168 (s), 1109 (s), 949 (vs), 808 (m), 760 (m); $\delta_H(CDCl_3)$: 1.24 (3H, t, *J* 7, OCH_2CH_3).

1.69 (3H, dd, *J* 19, 7, PCHCH_3), 2.22 (3H, s, $C_6H_4CH_3$), 2.25 (3H, s, $C_6H_4CH_3$), 3.43 (1H, dq, *J* 19, 7, PC*H*CH_3), 4.21 (2H, q, *J* 7, OCH_2CH_3), 7.00–7.32 (8H, m, aromatic H); GC–MS [same conditions as for (*R*)-**1**]: t_R 23.76 min (92.7%, **15**), 25.25 (4.1%, unknown, $M^+ = 396$); MS (70 eV, EI): *m*/*z* 362 (72) [M^+], 317 (31), 273 (36), 227 (100), 108 (23), 91 (35). HRMS calcd for $C_{19}H_{23}PO_5$ (M^+) 362.1283; found, 362.1271.

4.14. Ethyl (*Z*)-2-methyl-6-(4′-oxobicyclo[3.1.0]hexyl)hept-2-enoate 21 and 21′

4.14.1. (*R*)-Isomer 21. A solution of the Horner-type Wittig reagent in THF was prepared by the addition of a solution of **15** (1.6 g, 4.4 mmol) in dry THF (10 mL) to a stirred and ice-cooled suspension of NaH (60% in mineral oil, 175 mg, 4.4 mmol) in dry THF (10 mL) at 0–5 °C under N_2. A clear solution of the Wittig reagent was obtained after stirring for 15 min at 0–5 °C. This solution was added to a stirred and cooled solution of (*R*)-**10** (800 mg, 4.4 mmol) in dry THF (10 mL) at −78 °C under N_2. The mixture was stirred for 30 min at −78 °C and for 1 h at 0–5 °C. It was then poured into ice and NH_4Cl aqueous solution, and extracted with Et_2O. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed over SiO_2 (30 g). Elution with hexane/EtOAc (4:1–3:1) yielded 1.2 g (quant.) of crude (*R*)-**21** as an oil, ν_{max} (film): 1728 (s, C=O), 1645 (w, C=C); $\delta_H(CDCl_3)$: 0.99, 1.01 (total 3H, each d, *J* 7, CHCH_3), 1.28 (3H, t, *J* 7, OCH_2CH_3), 1.89, 1.90 [total 3H, each s, C=C(CH_3)CO_2Et], 4.20 (2H, m, OCH_2CH_3), 5.88 [1H, m, C*H*=C(CH_3)CO_2Et]. This was employed for the next step without further purification.

4.14.2. (*S*)-Isomer 21′. In the same manner, (*S*)-**10**′ (800 mg, 4.4 mmol) gave 1.16 g (quant.) of crude (*S*)-**21**′. Its spectral properties were identical with those of (*R*)-**21**. This was employed for the next step without further purification.

4.15. Ethyl (*Z*)-2-methyl-6-(4′-methylenebicyclo-[3.1.0]hexyl)hept-2-enoate 22 and 22′

4.15.1. (*R*)-Isomer 22. Methylenetriphenylphosphorane was prepared by the addition of a solution of *n*-BuLi in hexane (1.6 M, 3.6 mL, 5.8 mmol) to a suspension of $(C_6H_5)_3P(CH_3)Br$ (1.7 g, 5.8 mmol) in dry THF (15 mL) at −78 °C under N_2. The mixture was stirred for 15 min at −78 °C to generate an orange solution of the Wittig reagent. This was added through a syringe over 5 min to a stirred and cooled solution of (*R*)-**21** (1.2 g, 4.5 mmol) in dry THF (7 mL) at −78 °C under N_2. The solution was stirred for 30 min at room temperature. It was then poured into ice-water, and extracted with Et_2O. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (10:3) gave 1.19 g (quant.) of (*R*)-**22**, ν_{max} (film): 1714 (s, C=O), 1651 (m, C=C), 1225 (s, C–O), 862 (m); $\delta_H(CDCl_3)$: 0.55–0.78 (2H, m, cyclopropane CH_2), 0.84–0.98 (3H, m, CHCH_3), 1.23–1.35 (3H, m, OCH_2CH_3), 4.15–4.25 (2H, m, OCH_2CH_3), 4.62 (1H, s, C=C*H*H), 4.80 (1H, s, C=CH*H*), 5.90 [1H, m, C*H*=C(CH_3)CO_2Et]. This was employed for the next step without further purification.

4.15.2. (*S*)-Isomer 22′. In the same manner (*S*)-**21**′ (1.16 g, 4.4 mmol) afforded (*S*)-**22**′ (0.97 g, 84%). Its spectral data were identical with those of (*R*)-**22**. This was employed for the next step without further purification.

4.16. (*Z*)-2-Methyl-6-(4′-methylenebicyclo[3.1.0]hexyl)hept-2-en-1-ol 2 and 2′

4.16.1. (*R*)-Isomer 2. A solution of (*i*-Bu)$_2$AlH in toluene (1 M, 12 mL, 12 mmol) was added to a stirred and cooled solution of (*R*)-**22** (1.19 g, 4.5 mmol) in dry toluene (10 mL) at −78 °C under N_2. After 5 min at −78 to 0 °C, an additional amount of (*i*-Bu)$_2$AlH (8 mL, 8 mmol) in toluene was added, after which stirring was continued for 30 min at 0–5 °C. MeOH (20 mL) was then added to destroy excess (*i*-Bu)$_2$AlH, and the mixture was stirred for 1 h at room temp., after which it was filtered through Celite, and the Celite layer washed with hexane. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (3:1) gave 0.51 g (51%) of crude (*R*)-**2** contaminated with some phosphorus compounds. In order to remove the phosphorus compounds, crude (*R*)-**2** (510 mg) was heated at reflux for 1.5 h in the presence of KOH (0.5 g) in 95% EtOH (4 mL) and H_2O (1 mL). The solution was concentrated in vacuo, diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed over SiO_2 (5 g). Elution with hexane/EtOAc (10:3) gave 220 mg (22%) of (*R*)-**2**. This was further purified by SiO_2 chromatography, $n_D^{21} = 1.5056$; $[\alpha]_D^{23} = +12.6$ (*c* 1.20, hexane); ν_{max} (film): 3394 (m, OH), 1651 (w, C=C), 1246 (m, C–O); $\delta_H(CDCl_3)$: 0.60 (1H, dd, *J* 4, 8, cyclopropane CH), 0.71 (1H, dd, *J* 4, 4, cyclopropane CH), 0.91, 0.93 (total 3H, each d, *J* 7, CHCH_3), 1.78 [3H, s, CH=C(CH_3)CH_2OH], 4.15 (2H, s, CH_2OH), 4.63 (1H, s, C=C*H*H), 4.81 (1H, s, C=CH*H*), 5.29 [1H, m, C*H*=C(CH_3)CH_2OH]; $\delta_C(CDCl_3)$: 14.2, 16.2, 17.5, 18.3, 21.3, 22.7, 25.7, 26.3, 26.6, 28.8, 29.7, 31.2, 31.6, 34.9, 35.5, 36.6, 37.9, 38.0, 61.6, 101.7, 128.7, 134.0, 154.1; $\delta_H(C_6D_6)$: 0.43 (1H, dd, *J* 4, 8, cyclopropane CH), 0.61 (1H, dd, *J* 4, 4, cyclopropane CH), 0.86, 0.87 (total 3H, each d, *J* 7, CHCH_3), 1.75 (3H, s, C=CCH_3), 3.97 (2H, s, CH_2OH), 4.78 (1H, s, C=C*H*H), 4.99 (1H, s, C=CH*H*), 5.18 [1H, m, C*H*=C(CH_3)CH_2OH]; $\delta_C(C_6D_6)$: 14.3, 15.9, 16.2, 17.6, 18.2, 18.4, 21.3, 23.0, 25.8, 26.0, 26.4, 26.6 29.0, 29.2, 30.1, 31.7, 32.3, 35.1, 35.7, 36.5, 38.1, 61.3, 102.3, 128.1, 134.5, 153.6, 154.7; GC–MS [Column: HP-5MS, 35% phenylmethylsiloxane, 30 m × 0.25 mm i.d.; press: 60.7 kPa; 70–130 °C (+10 °C/min)]. t_R 14.74 min (50.1%), 14.95 (34.4%), 15.12 (5.7%), 15.45 (7.3%). The peaks at $t_R = 14.74$ and 14.95 min were due to the two diastereomers (1.46:1) of (*R*)-**2**, showing virtually the same MS as those of (*R*)-**1** and (*S*)-**1**′. MS of the peaks at $t_R = 15.12$ and 15.45 min were different from those of the major peaks. MS (70 eV, EI): *m*/*z* 220 (7) [M^+], 202 (13), 187 (15), 161 (13), 159 (14), 145 (23), 133 (27), 132 (42), 121 (57), 120 (36) 119 (89) 105 (43), 93 (100), 91 (72), 79 (45), 77 (43), 69 (25), 67 (23), 55 (25),

43 (37), 41 (29). The MS of (*R*)-**2** was virtually identical with those of the other isomers, (*R*)-**1**, (*S*)-**1′**, and (*S*)-**2′**; HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827; found, 220.1831.

4.16.2. (*S*)-Isomer 2′. In the same manner, (*S*)-**22′** (970 mg) yielded (*S*)-**2′** (550 mg, 67%). This was further purified by SiO_2 chromatography. All of its spectral data were identical with those of (*R*)-**2**, $n_D^{21} = 1.5058$; $[\alpha]_D^{21} = -2.2$ (*c* 1.14, hexane); GC–MS [same conditions as for (*R*)-**2**]: $t_R = 14.76$ min (54.1%), 14.96 (34.0%), 15.13 (5.0%), 15.46 (5.1%). The peaks at $t_R = 14.76$ and 14.96 min were those of the two diastereomers (1.59:1) of (*S*)-**2′**. Their MS were virtually identical to those of (*R*)-**1** and (*S*)-**1′**. HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827; found, 229,1821. The reason for the small rotation value was unclear.

Acknowledgments

Thanks are due to Mr. Masateru Kimura (President, Toyo Gosei Co.) for his support. I am grateful to Ms. Masami Takita (Yamagata Prefecture Mogami Office) and Dr. Hajime Sugie (National Institute for Agro-Environmental Sciences) for their supply of the ^1H NMR, ^{13}C NMR and MS spectral charts of the natural pheromone. Ms. Tomoko Yoshimura and Dr. Shoichi Ishii (Yamagata Prefectural Agricultural Research Center) kindly carried out the bioassays of (2*E*,6*R*)-**1**, (2*S*,6*S*)-**1′**, (2*Z*,6*R*)-**2**, and (2*Z*,6*S*)-**2′**. Dr. Takuya Tashiro (RIKEN) helped the final purification of the four pheromone candidates as well as the preparation of the Figure and Schemes. I also thank Mr. Yasumasa Shikichi (Toyo Gosei Co.) for NMR and GC–MS analysis. Professor H. Watanabe (Univ. Tokyo) kindly helped my literature survey.

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