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Synthesis of all the stereoisomers of 6-methyl-2-octadecanone, 6,14-dimethyl-2-octadecanone, and 14-methyl-2-octadecanone, the components of the female-produced sex pheromone of a moth, *Lyclene dharma dharma*☆

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ABSTRACT

All of the stereoisomers of the components of the female-produced sex pheromone of a moth, *Lyclene dharma dharma*, were synthesized. They are (*R*)- and (*S*)-6-methyl-2-octadecanone, (6*R*,14*R*)-, (6*R*,14*S*)-, (6*S*,14*R*)-, and (6*S*,14*S*)-6,14-dimethyl-2-octadecanone, and (*R*)- and (*S*)-14-methyl-2-octadecanone. Enantiomers of citronellal and methyl (*S*)-3-hydroxy-2-methylpropanoate were the starting materials, and olefin cross metathesis was employed as the key reaction.

1. Introduction

In 2007 Ando and his co-workers investigated the female-produced sex pheromone of a Lithosiinae moth, *Lyclene dharma dharma*, in the Iriomote Islands, Okinawa.[2] They identified three electroantennographically active components of the sex pheromone as 6-methyl-2-octadecanone (**1**, Fig. 1), 6,14-dimethyl-2-octadecanone (**2**), and 14-methyl-2-octadecanone (**3**) in a ratio of about 2:1:1. In continuation of our long-standing project to clarify the absolute configuration of pheromones,[3] I decided to synthesize all the possible stereoisomers of **1**, **2**, and **3**. Their bioassay will hopefully clarify the bioactive stereoisomers.

There are several methyl-branched 2-alkanones among chiral insect pheromones, and they have been prepared by employing traditional carbon–carbon single bond formation reactions such as Grignard reaction and alkylation of alkynes.[4] Advent of olefin cross metathesis reaction[5–7] opened a new possibility to employ it as the key-step in pheromone synthesis.[8,9] Although ring-closing metathesis has frequently been used,[10–14] there are not so many applications of cross metathesis in pheromone synthesis.[15,16] In the present case of the synthesis of all the stereoisomers of **1**–**3**, cross metathesis can be used advantageously to prepare them in a simple manner.

Scheme 1 shows the retrosynthetic analysis of (*R*)-**1**, (6*R*,14*R*)-**2**, and (*R*)-**3**. These ketones can be prepared by hydrogenation of olefinic ketones **A**, **B**, and **C**, respectively, which can be prepared by cross metathesis by employing the Grubbs' first generation catalyst

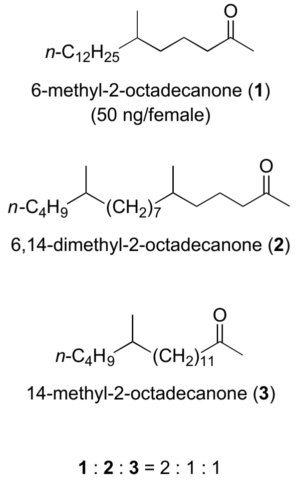

Figure 1. Structures of the components of the female-produced sex pheromone of a moth, *L. dharma dharma*. A female moth produces about 50 ng of **1**.

☆ Pheromone synthesis, Part 239. For Part 238, see Ref. 1.

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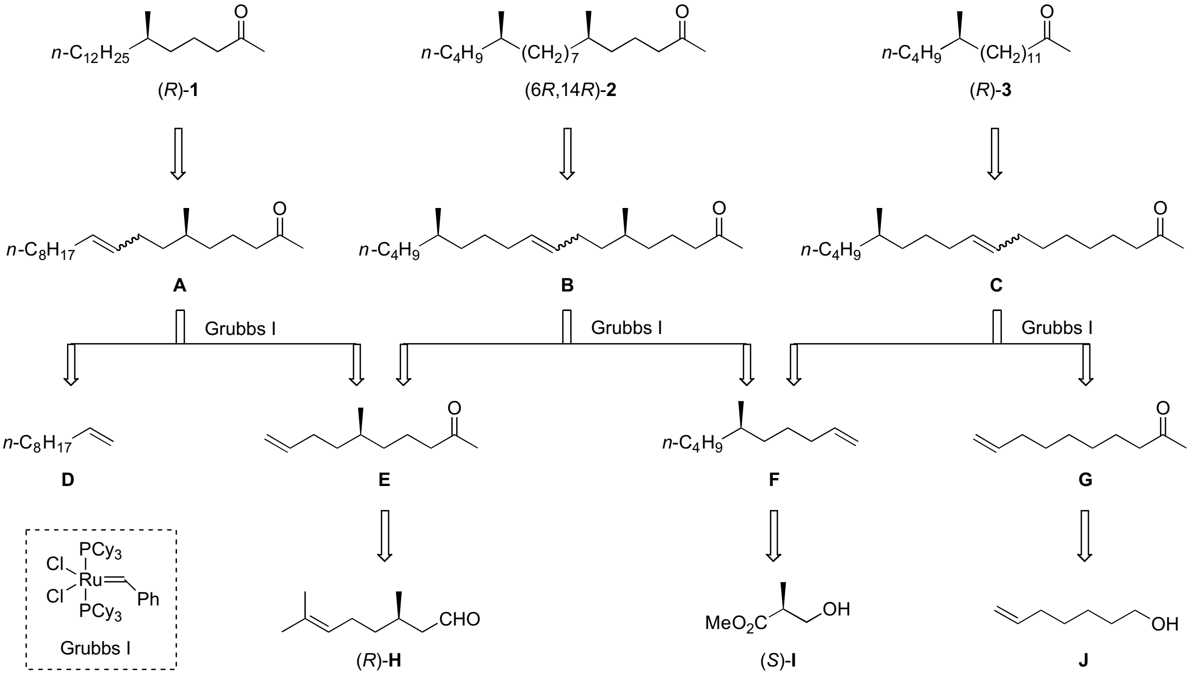


Scheme 1. Retrosynthetic analysis of (*R*)-**1**, (6*R*,14*R*)-**2**, and (*R*)-**3**. The starting materials **D**, **H**, **I**, and **J** are commercially available.

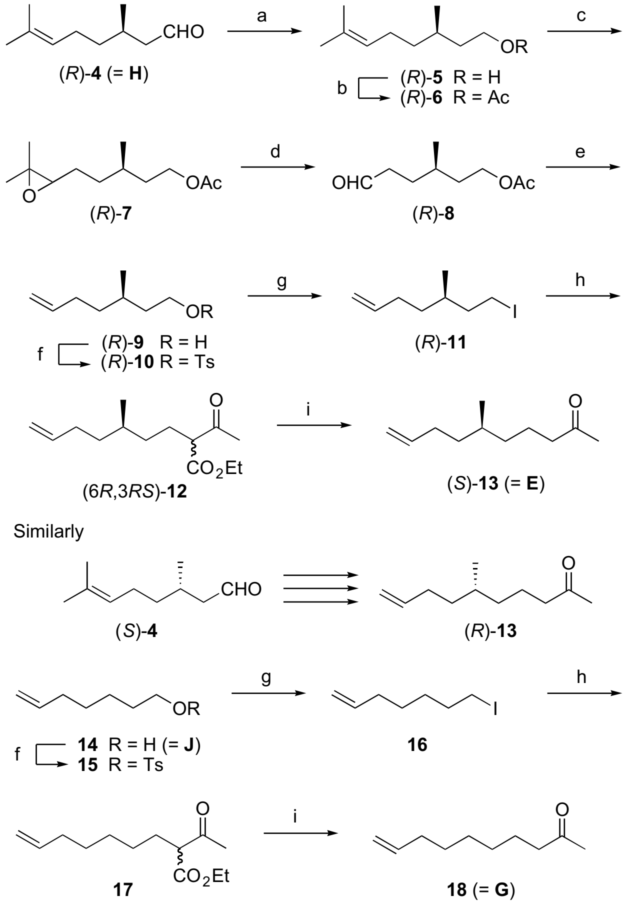
(Grubbs I). Accordingly, cross metathesis of 1-decene (**D**) with (*S*)-6-methyl-9-decen-2-one (**E**) generates **A**, while (*R*)-6-methyl-1-decene (**F**) and **E** gives **B**. The ketone **C** can be prepared from **F** and 9-decen-2-one (**G**). As to the supply of the two metathesis partners, **D** is commercially available, while **G** is readily synthesized from commercially available 6-hepten-1-ol (**J**). The commercially available enantiomers of citronellal (**H**), which are widely used as chiral building blocks,[9,17] are to be converted to the enantiomers of **E**. Another chiral building block **F** can be synthesized from commercially available methyl (*S*)-3-hydroxy-2-methylpropanoate (**I**). This paper reports a successful synthesis of all the stereoisomers of **1**–**3** along the line described above. The present method serves as a general protocol for the synthesis of methyl-branched ketones.

2. Results and discussion

2.1. Synthesis of ketones (*R*)- and (*S*)-13 and 18, the metathesis partners

Scheme 2 summarizes the synthesis of the key building blocks (*R*)- and (*S*)-**13** (=**E**) and **18** (=**G**). (*R*)-Citronellal (**4**) was converted to the known aldehyde (*R*)-**8** in 93% overall yield by the steps depicted.[18] Treatment of (*R*)-**8** with methylenetriphenylphosphorane was followed by the hydrolysis of the acetate group with sodium hydroxide to give (*R*)-**9**. Tosylation of (*R*)-**9** afforded (*R*)-**10**, which was treated with sodium iodide in *N*,*N*-dimethylformamide (DMF) to give (*R*)-**11**. Alkylation of ethyl acetoacetate with (*R*)-**11** yielded (6*R*,3*RS*)-**12**, whose hydrolysis and decarboxylation furnished the desired building block (*S*)-**13**, $[\alpha]_D^{26}$ −2.81 (*c* 4.29, hexane), in 27% overall yield based on (*R*)-**4** (eight steps). Similarly, (*R*)-**13**, $[\alpha]_D^{25}$ +2.90 (*c* 3.64, hexane), was prepared from (*S*)-citronellal (**4**). Enantioselective GC analysis of (*R*)- and (*S*)-**13** revealed them to be of 97.2% ee and 97.6% ee, respectively (see Experimental). It should be added that **9** is a useful metathesis partner for the synthesis of 3-methyl-branched 1-alkanols.[19]

Preparation of the achiral ketone **18** was straightforward starting from 6-hepten-1-ol (**14**). The corresponding tosylate **15** was converted to iodide **16**. Alkylation of ethyl acetoacetate with **16**

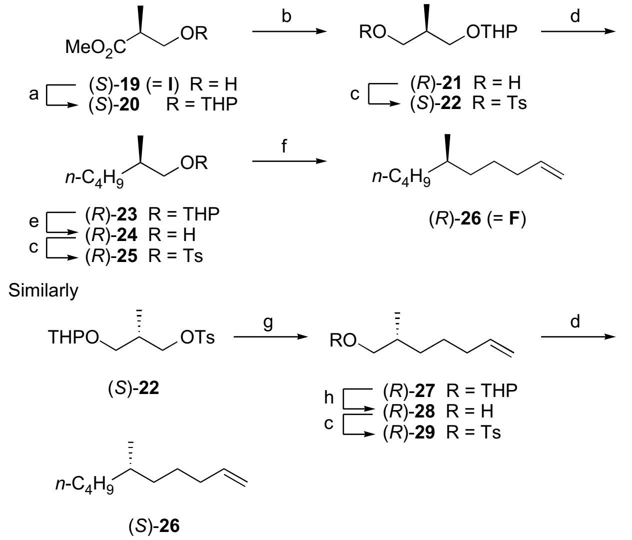


Scheme 2. Synthesis of unsaturated ketones (*R*)- and (*S*)-**13** and **18**. Reagents: (a) $LiAlH_4$, Et_2O; (b) Ac_2O, C_5H_5N (93% for two steps); (c) MCPBA, CH_2Cl_2 (quant.); (d) $HIO_4 \cdot 2H_2O$, THF, Et_2O (quant.); (e) (1) $Ph_3P(Me)Br$, *n*-BuLi, THF; (2) NaOH, MeOH, H_2O (48–50%, two steps); (f) TsCl, C_5H_5N (93–96% for **10**, 69% for **15**); (g) NaI, DMF (82–84%); (h) $MeCOCH_2CO_2Et$, K_2CO_3, DMF, Me_2CO; (i) KOH, MeOH, H_2O (68–72%, two steps).

gave **17**, which was treated with potassium hydroxide in aqueous methanol to give **18** in 42% overall yield based on **14** (four steps).

2.2. Synthesis of alkenes (*R*)- and (*S*)-26, the other metathesis partners

Scheme 3 shows the synthesis of the other key building blocks (*R*)- and (*S*)-**26** (=**F**). Methyl (*S*)-3-hydroxy-2-methylpropanoate (**19**) was chosen as the starting material, and converted to both the enantiomers of **26** by employing Schlosser's copper-catalyzed Grignard coupling reaction as the key chain-elongation methodology.[20] The hydroxy ester (*S*)-**19** was converted to (*R*)-**25** by the known method as depicted.[21] Treatment of (*R*)-**25** with 3-butenylmagnesium bromide in the presence of dilithium tetrachlorocuprate afforded (*R*)-**26**, $[\alpha]_D^{25}$ −1.40 (*c* 3.76, Et_2O), in 43% overall yield based on (*S*)-**19** (seven steps).



Scheme 3. Synthesis of olefins (*R*)- and (*S*)-**26**. Reagents: (a) 3,4-dihydro-2*H*-pyran, TsOH, Et_2O (quant.); (b) $LiAlH_4$, Et_2O (90%); (c) TsCl, C_5H_5N (quant.); (d) *n*-C_3H_7MgBr, Li_2CuCl_4, THF [71% for (*S*)-**26**]; (e) TsOH, MeOH (70%, two steps); (f) $CH_2{=}CH(CH_2)_2MgBr$, Li_2CuCl_4, THF (69%, two steps); (g) $CH_2{=}CH(CH_2)_2MgBr$, Li_2CuCl_4, THF; (h) AcOH, THF, H_2O (55%, two steps).

For the synthesis of (*S*)-**26**, the tosylate (*S*)-**22**, whose (*R*)-isomer was known,[22] was subjected to the Schlosser coupling[20] with 3-butenylmagnesium bromide to give (*R*)-**27**. Tosylate (*R*)-**29** of the corresponding alcohol (*R*)-**28** was then treated with propylmagnesium bromide in the presence of dilithium tetrachlorocuprate to give (*S*)-**26**, $[\alpha]_D^{25}$ +1.71 (*c* 4.20, Et_2O), in 35% overall yield based on (*S*)-**19** (seven steps). The enantiomers of **26** were analyzed by GC on two different chiral stationary phases [octakis-(2,3-di-*O*-methoxymethyl-6-*O*-*t*-butyldimethylsilyl)-γ-cyclodextrin[23] and Chiramix®[24]]. Unfortunately they were inseparable on these two stationary phases. Accordingly, direct evaluation of their enantiomeric purities was impossible. It can be assumed that they are of 99.9% ee, reflecting the high enantiomeric purity (99.9% ee) of the starting (*S*)-**19**.

2.3. Synthesis of all the stereoisomers of 1, 2, and 3 by cross metathesis and subsequent hydrogenation

In comparison to ring-closing metathesis, cross metathesis is rather underdeveloped, because it lacks the entropic driving force, and is complicated by self-metathesis of each of the two partners. In the present case, the olefin partners **D** and **F** (see Scheme 4) are more readily available than the unsaturated ketone partners **E** and **G**. It was therefore planned that 6 equiv of **D** or **F** were to be used for 1 equiv of **E** or **G** so as to increase the yield of the desired cross metathesis product based on **E** or **G**. Thus, 5–7 mol % (to **E** or **G**) of Grubbs I catalyst was added to a solution of the two metathesis partners in dichloromethane, and the mixture was stirred and heated under reflux for 4–6 h under argon. The progress of the reaction could be monitored by evolution of ethylene, which enlarged the argon balloon. After the reaction mixture was left to stand overnight or longer to allow the decomposition of the catalyst, which facilitated the removal of the trace of the ruthenium residue, it was concentrated, and the residue was purified by silica gel chromatography. After elution of alkene **i**, the cross metathesis product (*S*)-**31** resulting from **30** and (*S*)-**13** was obtained as an oil in 83% yield based on (*S*)-**13**. The olefinic ketone (*S*)-**31** was immediately hydrogenated over 10% palladium–charcoal in ethyl acetate to give (*R*)-**1**, $[\alpha]_D^{26}$ +0.35 (*c* 4.08, hexane), as an oil in 89% yield. Since the double bond of (*S*)-**31** was immediately hydrogenated and disappeared in the final product (*R*)-**1**, its *E*/*Z* ratio was not determined. The overall yield of (*R*)-**1** was 17% based on citronellal [(*R*)-**4**, ten steps] and 74% based on the utilized alkene **30** (two steps). Similarly, **30** and (*R*)-**13** yielded (*S*)-**1**, $[\alpha]_D^{28}$ −0.38 (*c* 3.63, hexane), as an oil. The mass spectrum of (*R*)- or (*S*)-**1** was identical with that of the naturally occurring pheromone component **1**.[2]

By starting from (*R*)-**26** and (*S*)-**13**, (6*S*,14*R*)-**32** was obtained in 86% yield based on (*S*)-**13**, which was hydrogenated to give (6*R*,14*R*)-**2**, $[\alpha]_D^{27}$ −0.50 (*c* 2.65, hexane), as an oil. Similarly, (*S*)-**26** and (*S*)-**13** afforded (6*R*,14*S*)-**2**, $[\alpha]_D^{24}$ +1.54 (*c* 3.07, hexane), as an oil; (*R*)-**26** and (*R*)-**13** furnished (6*S*,14*R*)-**2**, $[\alpha]_D^{27}$ −1.16 (*c* 3.07, hexane), as an oil; (*S*)-**26** and (*R*)-**13** gave (6*S*,14*S*)-**2**, $[\alpha]_D^{26}$ +0.65 (*c* 3.81, hexane), as an oil. The overall yield of (6*R*,14*R*)-**2** was 21% based on citronellal [(*R*)-**4**, ten steps], or 34% based on methyl (*S*)-3-hydroxy-2-methylpropanoate [**19**, nine steps, based on the utilized (*R*)-**26**], and that of (6*R*,14*S*)-**2** was 24% based on (*S*)-**4** (ten steps) and 32% based on (*S*)-**19** (nine steps). The mass spectrum of each of the synthetic stereoisomers of **2** was identical with that of the naturally occurring pheromone component **2**.

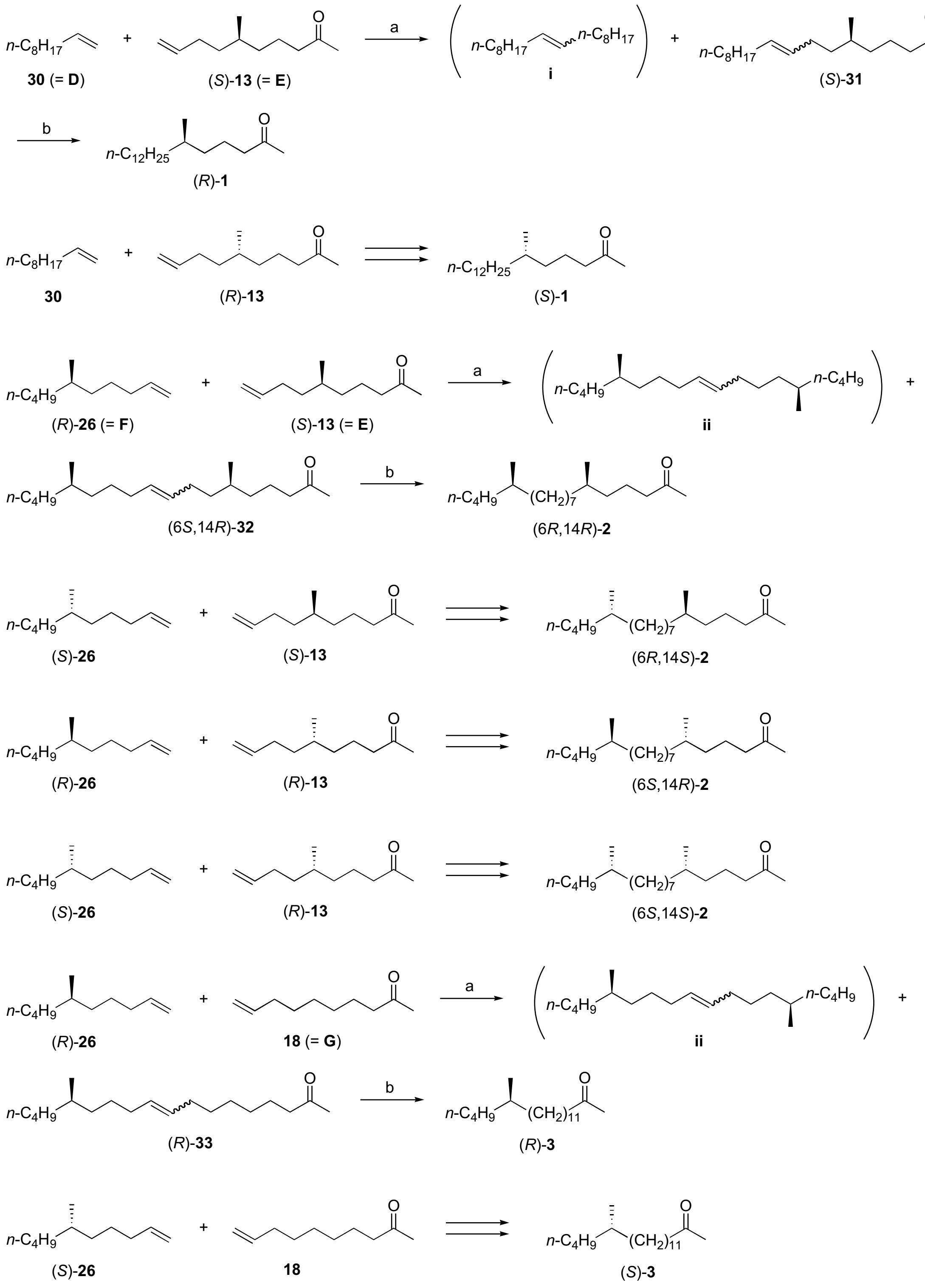
Cross metathesis of (*R*)-**26** with achiral **18** gave (*R*)-**33** in 78% yield based on **18**, which was hydrogenated to give (*R*)-**3**, $[\alpha]_D^{25}$ −0.60 (*c* 3.07, hexane), as an oil. Similarly, (*S*)-**26** and **18** yielded (*S*)-**3**, $[\alpha]_D^{24}$ +1.05 (*c* 3.13, hexane), as an oil. The overall yield of (*R*)-**3** was 27% based on **14** (six steps) or 28% based on (*S*)-**19** [nine steps, based on the utilized (*R*)-**26**], and that of (*S*)-**3** was 23% based on (*S*)-**19** [nine steps, based on the utilized (*S*)-**26**]. The mass spectrum of each of the synthetic stereoisomers of **3** was identical with that of the naturally occurring pheromone component **3**.

The enantiomeric purities of the final products **1**, **2**, and **3** were considered to be ca. 97% ee, reflecting the enantiomeric purities of the starting materials. Their direct evaluation by GC was unsuccessful.

3. Conclusion

All of the eight possible stereoisomers of **1**, **2**, and **3**, the components of the female-produced sex pheromone of a moth *L. dharma dharma*, were synthesized by employing cross metathesis as the key-step. The cross metathesis was achieved in the average yield of 82% (79–92%), and shown to be an excellent method to quickly prepare a number of similar compounds.

Bioassay of these isomers of **1**, **2**, and **3** is now in progress by Professor T. Ando and his co-workers, and the results will be published in due course. Preliminary results showed that (*S*)-**1** and (*S*)-**3** were more attractive than (*R*)-**1** and (*R*)-**3** against *L. dharma dharma* males.



Scheme 4. Synthesis of all the stereoisomers of **1**, **2**, and **3**. Reagents: (a) Grubbs I catalyst, CH_2Cl_2 (79–92%, average 82%); (b) H_2, 10% Pd–C, EtOAc (77–93%; average 88%).

4. Experimental

4.1. General

Boiling points are uncorrected values. Refractive indices (n_D) were measured on an Atago DMT-1 refractometer. 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 δ=0.00 as internal standard) and ^{13}C NMR spectra (100 MHz, $CDCl_3$ at δ=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-SX 102A. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. 3-Methyl-6-hepten-1-ol 9

Enantiomers of citronellal (**4**, Takasago, ca. 97% ee) were the starting materials.

4.2.1. *(R)-Isomer*

A solution of *n*-BuLi in hexane (1.6 M, 120 mL, 192 mmol) was added dropwise to a cooled and stirred suspension of $Ph_3P(Me)Br$ (61 g, 171 mmol) in dry THF (250 mL) at −30 °C under Ar. The mixture was stirred for 10 min at 0–5 °C and cooled again at −70 °C. A solution of crude (*R*)-**8** [33.1 g, prepared from 161 mmol of (*R*)-**6**] in dry THF (50 mL) was added to the cooled and stirred Wittig reagent at −60 to −50 °C over 15 min. The stirring was continued overnight, and the temperature was allowed to reach room temperature. The mixture was then shaken with hexane and $MeOH/H_2O$ (2:1, 150 mL). The hexane/THF layer was separated, washed successively with $MeOH/H_2O$ (2:1, 50 mL), water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residual oil (ca. 30 g) was dissolved in MeOH (150 mL), and mixed with NaOH (12 g, 300 mmol) in H_2O (75 mL). The mixture was stirred and heated under reflux for 1 h. It was then diluted with water, and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 10.2 g (50%) of (*R*)-**9** as a colorless oil, bp 110–112 °C/40 Torr, n_D^{21} 1.4430; $[\alpha]_D^{25}$ +4.06 (*c* 3.58, hexane); ν_{max} (film): 3334 (s, OH), 3078 (m, $C=CH_2$), 1641 (m, C=C), 1059 (s, C–O), 908 (s, $CH=CH_2$); δ_H ($CDCl_3$): 0.91 (3H, d, *J* 6.8, $CHCH_3$), 1.25–1.29 (1H, m), 1.37–1.41 (2H, m), 1.57–1.63 (3H, m), 1.64–2.09 (2H, m), 3.60–3.75 (2H, m, CH_2O), 4.92–5.03 (2H, m, $CH=CH_2$), 5.75–5.86 (1H, m, $CH=CH_2$). HRMS calcd for $C_8H_{15}O$ (M^+-H): 127.1123, found: 127.1129.

4.2.2. *(S)-Isomer*

In the same manner, (*S*)-**6** (33.4 g, 156 mmol) yielded 9.5 g (48%) of (*S*)-**9** as a colorless oil, bp 128–134 °C/98 Torr, n_D^{26} 1.4418; $[\alpha]_D^{26}$ −4.04 (*c* 4.54, hexane). Its spectral data were identical with those of (*R*)-**9**. HRMS calcd for $C_8H_{15}O$(M^+-H): 127.1123, found: 127.1129.

4.3. 3-Methyl-6-heptenyl tosylate 10

4.3.1. *(R)-Isomer*

Tosyl chloride (17.2 g, 91 mmol) was added to a stirred and ice-cooled solution of (*R*)-**9** (10.2 g, 80 mmol) in dry pyridine (30 mL) at 5–10 °C. The mixture was left to stand overnight in a refrigerator. It was then diluted with ice-water, and extracted with diethyl ether. The ether solution was washed with water, dil. HCl, water, $NaHCO_3$ aq solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 20.9 g (93%) of (*R*)-**10** as an oil, ν_{max} (film): 3074 (w, $C=CH_2$), 1641 (m, C=C), 1599 (m, arom. C=C), 1360 (s), 1178 (s), 945 (s), 663 (s); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.8, $CHCH_3$), 2.45 (3H, s, $C_6H_4CH_3$), 4.02–4.12 (2H, m, CH_2O), 4.91–4.99 (2H, m, $CH=CH_2$), 5.68–5.80 (1H, m, $CH=CH_2$), 7.35 (2H, *J* 8.0, arom. H), 7.79 (2H, d, *J* 8.0, arom. H). This was employed in the next step without further purification.

4.3.2. *(S)-Isomer*

In the same manner, (*S*)-**9** (9.5 g, 74 mmol) yielded 20.0 g (96%) of (*S*)-**10** as an oil. Its spectral data were identical with those of (*R*)-**10**.

4.4. 3-Methyl-6-heptenyl iodide 11

4.4.1. *(R)-Isomer*

Powdered sodium iodide (31 g, 207 mmol) was added to a solution of (*R*)-**10** (20.9 g, 75 mmol) in dry DMF (150 mL) with vigorous stirring. After exothermic reaction, the homogeneous and colored solution was stirred and heated at 80 °C for 40 min. After cooling, the mixture was diluted with ice-water, and extracted with pentane. The pentane solution was washed with water containing a small amount of $Na_2S_2O_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 15.0 g (84%) of (*R*)-**11** as a colorless and dense oil, bp 116–118 °C/47 Torr, n_D^{27} 1.4968; $[\alpha]_D^{29}$ −12.4 (*c* 4.12, hexane); ν_{max} (film): 3076 (m, $C=CH_2$), 1639 (m, C=C), 910 (s, $CH=CH_2$); δ_H ($CDCl_3$): 0.89 (3H, d, *J* 6.4, $CHCH_3$), 1.18–1.30 (1H, m), 1.37–1.47 (1H, m), 1.54–1.70 (2H, m), 1.84–1.92 (1H, m), 1.95–2.15 (2H, m), 3.12–3.29 (2H, m), 4.92–5.04 (2H, m, $CH=CH_2$), 5.70–5.86 (1H, m, $CH=CH_2$). HRMS calcd for $C_8H_{15}I$: 238.0218, found: 238.0218.

4.4.2. *(S)-Isomer*

In the same manner, (*S*)-**10** (20.0 g, 71 mmol) gave 14.0 g (83%) of (*S*)-**11** as a colorless and dense oil, bp 105–108 °C/28 Torr; n_D^{27} 1.4968; $[\alpha]_D^{25}$ +12.7 (*c* 4.93, hexane). Its spectral data were identical with those of (*R*)-**11**. HRMS calcd for $C_8H_{15}I$: 238.0218, found: 238.0218.

4.5. 3-Ethoxycarbonyl-6-methyl-9-decen-2-one 12

4.5.1. *(3RS,6R)-Isomer*

Powdered K_2CO_3 (32.0 g, 232 mmol) was added to a stirred solution of (*R*)-**11** (14.9 g, 63 mmol), ethyl acetoacetate (11.2 g, 86 mmol), and DMF (10 mL) in acetone (150 mL). The mixture was stirred and heated under reflux for 7 h under Ar, and then concentrated in vacuo to remove acetone. The residue was diluted with water, and extracted with diethyl ether. The ether extract was washed with dil. $NaHCO_3$ aq solution containing a small amount of $Na_2S_2O_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo to give 17.6 g (quant.) of crude (3*RS*, 6*R*)-**12**, ν_{max} (film): 3078 (w, $C=CH_2$), 1718 (s, C=O), 1641 (m, C=C), 1242 (s), 1149 (s), 1041 (m), 910 (m). This was used in the next step without further purification.

4.5.2. *(3RS, 6S)-Isomer*

In the same manner, (*S*)-**11** (14.0 g, 59 mmol) gave 18.0 g (quant.) of crude (3*RS*,6*S*)-**12**. Its IR spectrum was identical with that of (3*RS*,6*R*)-**12**. This was used in the next step without further purification.

4.6. 6-Methyl-9-decen-2-one 13

4.6.1. *(S)-Isomer*

The crude (3*RS*,6*R*)-**12** (17.6 g) was mixed with 10% aq solution of KOH (80 mL, 143 mmol) and MeOH (80 mL), and the mixture was stirred and heated under reflux for 30 min, and left to stand overnight at room temperature. It was then diluted with water, and extracted with diethyl ether. The ether extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 7.6 g (72%, two steps) of (*S*)-**13**. This was redistilled to give 6.8 g of pure (*S*)-**13**, bp 90–92 °C/18 Torr or bp 95–98 °C/10 Torr, n_D^{27} 1.4394; $[\alpha]_D^{26}$ −2.81 (*c* 4.29, hexane); ν_{max} (film): 3076 (m, $C=CH_2$), 1718 (s, C=O), 1641 (m, C=C), 1360 (m), 1165 (m), 995 (m), 910 (m); δ_H ($CDCl_3$): 0.88 (3H, d, *J* 6.4, $CHCH_3$), 1.08–1.15 (1H, m), 1.15–1.34 (2H, m), 1.36–1.48 (2H, m), 1.50–1.65 (2H, m), 1.95–2.10 (2H, m), 2.13 (3H, s, $COCH_3$), 2.40 (2H, t, *J* 7.6, CH_2CO), 4.90–5.03 (2H, m, $CH=CH_2$), 5.74–5.86 (1H, m, $CH=CH_2$). GC [Instrument: Agilent 7890 GC; Column: 50% octakis-(2,3-di-*O*-methoxymethyl-6-*O*-*t*-butyldimethylsilyl)-γ-cyclodextrin (MOMT-BDMSGCD),[23] 30 m×0.25 mm i.d.; carrier gas: He; flow rate: 0.7 mL/min; temp: 40–180 °C (+0.7 °C/min); injection temp: 230 °C; detector (F1D) temp: 250 °C]: t_R=96.4 min (1.2%); 96.9 min (98.8%). Enantiomeric purity of (*S*)-**13** was 97.6% ee. HRMS calcd for $C_{11}H_{20}O$: 168.1515, found: 168.1516.

4.6.2. *(R)-Isomer*

In the same manner, the crude (3*RS*,6*S*)-**12** (18.0 g) gave 7.2 g (76%, two steps) of (*R*)-**13**. This was redistilled to give 6.2 g of pure (*R*)-**13**, bp 89–91 °C/7 Torr or 90–92 °C/7 Torr, n_D^{27} 1.4392; $[\alpha]_D^{25}$ +2.90 (*c* 3.64, hexane). Its spectral data were identical with those of (*S*)-**13**. GC [same conditions as for (*S*)-**13**]: t_R=96.4 min (98.6%);

96.9 min (1.4%). Enantiomeric purity of (*R*)-**13** was 97.2% ee. HRMS calcd for $C_{11}H_{20}O$: 168.1514, found: 168.1513.

4.7. 6-Heptenyl tosylate 15

In the same manner as described for the preparation of **10**, **14** (5.0 g, 44 mmol) gave 8.1 g (69%) of **15** as a slightly yellowish oil, ν_{max} (film): 1641 (w, C=C), 1599 (w, arom. C=C), 1362 (s), 1176 (s); δ_H ($CDCl_3$): 1.25–1.40 (4H, m), 1.60–1.70 (2H, m), 1.94–2.02 (2H, m), 2.45 (3H, s, $C_6H_4CH_3$), 4.02 (2H, t, *J* 6.4, OCH_2), 4.90–5.05 (2H, m, $CH{=}CH_2$), 5.68–5.85 (1H, m, $CH{=}CH_2$), 7.34 (2H, d, *J* 8.0, arom. H), 7.78 (2H, d, *J* 8.0, arom. H). This was employed for the next step without further purification.

4.8. 6-Heptenyl iodide 16

In the same manner as described for the preparation of **11**, **15** (8.1 g, 30 mmol) gave 5.5 g (82%) of **16** as an oil, bp 90–100 °C/40 Torr, n_D^{27} 1.4902; ν_{max} (film): 3076 (w, $C{=}CH_2$), 1641 (m, C=C), 1207 (m), 1173 (m), 993 (m), 912 (s); δ_H ($CDCl_3$): 1.38–1.50 (4H, m), 1.75–1.90 (2H, m), 2.02–2.12 (2H, m), 3.19 (2H, t, *J* 6.8, OCH_2), 4.92–5.05 (2H, m, $CH{=}CH_2$), 5.74–5.87 (1H, m, $CH{=}CH_2$). HRMS calcd for $C_7H_{13}I$: 224.0062, found: 224.0062.

4.9. 9-Decen-2-one 18

In the same manner as described for the preparation of **12** and **13**, **16** (5.5 g, 24 mmol) was converted to 6.3 g of crude **17**, which gave 2.5 g (68%, two steps) of **18**, bp 83–85 °C/7 Torr, n_D^{27} 1.4360; ν_{max} (film): 3076 (w, $C{=}CH_2$), 1718 (s, C=O), 1641 (m, C=C), 1360 (m), 1165 (m), 993 (m), 910 (m); δ_H ($CDCl_3$): 1.24–1.32 (2H, m), 1.32–1.45 (2H, m), 1.54–1.61 (2H, m), 2.00–2.08 (2H, m), 2.13 (3H, s, $COCH_3$), 2.42 (2H, t, *J* 3.2, $COCH_2$), 4.90–5.04 (2H, m, $CH{=}CH_2$), 5.74–5.86 (1H, m, $CH{=}CH_2$). HRMS calcd for $C_{10}H_{18}O$: 154.1358, found: 154.1359.

4.10. 6-Methyl-1-decene 26

4.10.1. (R)-Isomer

Hydroxy ester (*S*)-**19** (Mitsubishi Rayon Co., 99.9% ee as estimated and guaranteed by Dr. K. Sakashita of Mitsubishi Rayon Co. The enantiomeric purity of **19** can be determined by HPLC analysis of the corresponding MTPA ester.[22]) was converted to (*R*)-**25** by the known method.[21] A solution of the Grignard reagent was prepared from 3-butenyl bromide (22 g, 163 mmol) and Mg (4.3 g, 179 mmol) in dry THF (90 mL) in a usual manner under Ar. This was added dropwise to a stirred and cooled solution of (*R*)-**25** (23.4 g, 86.5 mmol) in dry THF (80 mL) at −60 to −50 °C under Ar. Subsequently, a solution of Li_2CuCl_4 in THF (0.1 M, 3 mL, 0.3 mmol) was added dropwise to the stirred mixture, which was left to stand overnight with gradual rise of the temperature to room temperature. The mixture was poured into ice–dil. NH_4Cl aq solution, and extracted with diethyl ether. The ether extract was washed with ether and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 9.3 g (69%, two steps) of (*R*)-**26** as a colorless oil, bp 90–95 °C/43 Torr, n_D^{27} 1.4260, $[\alpha]_D^{25}$ −1.40 (*c* 3.76, Et_2O); ν_{max} (film): 3078 (m, $C{=}CH_2$), 1641 (m, C=C), 993 (m), 910 (s); δ_H ($CDCl_3$): 0.85 (3H, d, *J* 6.4, $CHCH_3$), 0.89 (3H, t, *J* 6.8, CH_2CH_3), 1.05–1.15 (2H, m), 1.20–1.50 (9H, m), 2.00–2.09 (2H, m), 4.90–5.03 (2H, m, $CH{=}CH_2$), 5.75–5.90 (1H, m $CH{=}CH_2$). HRMS calcd for $C_{11}H_{22}$: 154.1721, found: 154.1723.

4.10.2. (S)-Isomer

A solution of *n*-propylmagnesium bromide was prepared from *n*-propyl bromide (14.8 g, 120 mmol) and Mg (3.0 g, 125 mmol) in dry THF (50 mL) under Ar. This was added dropwise to a stirred and cooled solution of (*R*)-**29** (15.7 g, 56 mmol) in dry THF (60 mL) at −60 to −50 °C under Ar. Subsequently, a solution of Li_2CuCl_4 in THF (0.1 M, 3 mL, 0.3 mmol) was added dropwise to the stirred mixture, which was left to stand overnight with gradual rise of the temperature to room temperature. The mixture was worked up as described for the preparation of (*R*)-**26**. The residual oil was distilled to give 6.1 g (71%, two steps) of (*S*)-**26** as a colorless oil, bp 93–98 °C/48 Torr, n_D^{27} 1.4240; $[\alpha]_D^{25}$ +1.71 (*c* 4.20, Et_2O). Its spectral data were identical with those of (*R*)-**26**. HRMS calcd for $C_{11}H_{22}$: 154.1721, found: 154.1713.

4.11. (*R*)-2-Methyl-6-hepten-1-ol THP ether 27

A solution of the Grignard reagent was prepared from 3-butenyl bromide (28.0 g, 207 mmol) and Mg (5.4 g, 235 mmol) in dry THF (100 mL) under Ar. This was added dropwise to a stirred and cooled solution of (*S*)-**22** (33.0 g, 100 mmol) in dry THF (120 mL) at −60 to −50 °C under Ar. Subsequently, a solution of Li_2CuCl_4 in THF (0.1 M, 4 mL, 0.4 mmol) was added dropwise to the stirred mixture, which was left to stand overnight with gradual rise of the temperature to room temperature. The mixture was worked up as described for the preparation of (*R*)-**26** to give crude (*R*)-**27** (23.5 g) as a colorless oil, ν_{max} (film): 3076 (w, $C{=}CH_2$), 1641 (w, C=C), 1120 (m), 1034 (s), 908 (m). This was employed for the next step without further purification.

4.12. (*R*)-2-Methyl-6-hepten-1-ol 28

The above described crude (*R*)-**27** (23.5 g) was dissolved in a mixture of THF (100 mL), AcOH (50 mL) and H_2O (50 mL). The mixture was stirred and heated under reflux for 6 h. After cooling, it was diluted with water, and extracted with diethyl ether. The ether extract was washed with water, 10% NaOH aq solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give a crude oil (17.6 g). This was chromatographed over SiO_2 (80 g). Elution with hexane gave 4.7 g of non-polar impurities, and further elution with pentane/Et_2O (2:1) gave 12.8 g of crude (*R*)-**28**. This was distilled to give 7.1 g (55%, three steps) of pure (*R*)-**28**, bp 106–109 °C/43 Torr, n_D^{27} 1.4412; $[\alpha]_D^{25}$ +12.8 (*c* 3.22, hexane); ν_{max} (film): 3348 (s, OH), 3078 (m, $C{=}CH_2$), 1641 (m, C=C), 1034 (s, C–O), 995 (m), 910 (s); δ_H ($CDCl_3$): 0.92 (3H, d, *J* 6.8, $CHCH_3$), 1.07–1.18 (1H, m), 1.20–1.50 (3H, m), 1.58–1.68 (2H, m), 2.00–2.10 (2H, m), 3.41 (1H, dd *J* 7.2, 6.0, CHOH), 3.50 (1H, dd, *J* 7.2, 6.0, CHOH), 4.92–5.04 (2H, m, $CH{=}CH_2$), 5.75–5.88 (1H, m, $CH{=}CH_2$). HRMS calcd for $C_8H_{16}O$: 128.1201, found: 128.1198.

4.13. (*R*)-2-Methyl-6-heptenyl tosylate 29

Tosyl chloride (13.3 g, 70 mmol) was added to a stirred and ice-cooled solution of (*R*)-**28** (7.1 g, 55 mmol) in pyridine (30 mL) at 5–10 °C. The mixture was left to stand overnight in a refrigerator. Usual work-up as described for the preparation of (*R*)-**10** afforded (*R*)-**29** (15.7 g, quant.) as a colorless oil, ν_{max} (film): 2932 (w, $C{=}CH_2$), 1641 (w, C=C), 1598 (m, arom. C=C), 1362 (s), 1178 (s), 1097 (m), 964 (s), 814 (s), 667 (s); δ_H ($CDCl_3$): 0.88 (3H, d, *J* 6.8, $CHCH_3$), 1.06–1.16 (1H, m), 1.20–1.40 (3H, m), 1.72–1.81 (1H, m), 1.92–2.02 (2H, m), 3.80 (1H, dd *J* 6.4, 5.2, CHO), 3.88 (1H, dd, *J* 6.4, 5.2, CHO), 4.90–5.00 (2H, m, $CH{=}CH_2$), 5.70–5.80 (1H, m, $CH{=}CH_2$), 7.34 (2H,d, *J* 8.4, arom. H), 7.78 (2H,d, *J* 8.4, arom. H). This was employed for the next step without further purification.

4.14. 6-Methyl-9-octadecen-2-one 31

4.14.1. (S)-Isomer

A wine-red solution of $(Cy_3P)_2Ru({=}CHPh)Cl_2$ (Grubbs I catalyst, Aldrich, 82 mg, 0.1 mmol), **30** (2.82 g, 20 mmol), and (*S*)-**13**

(535 mg, 3.2 mmol) in dry CH_2Cl_2 (5 mL) was stirred and heated under reflux for 4 h under Ar. The mixture was left to stand overnight at room temperature. Then the solvent was removed in vacuo, and the dark residue in hexane was chromatographed over SiO_2 (23 g). Elution with hexane gave *n*-$C_8H_{17}CH{=}CH$*n*-C_8H_{17} (**i**, 2.5 g). Further elution with hexane/EtOAc (15:1) afforded (*S*)-**31** [737 mg, 83% based on (*S*)-**13**] as a slightly yellowish oil, ν_{max} (film): 1720 (s, C=O), 1163 (m), 968 (m); δ_H ($CDCl_3$): 0.86 (3H, d, *J* 6.4, CHCH_3), 0.87 (3H, t, *J* 6.4, CH_2CH_3), 1.05–1.20 (2H, m), 1.20–1.50 (14H, m), 1.50–1.65 (3H, m), 1.90–2.05 (4H, m), 2.13 (3H, s, $COCH_3$), 2.40 (2H, t, *J* 7.2, $COCH_2$), 5.30–5.42 (2H, CH=CH). This was employed in the next step without further purification.

4.14.2. (R)-Isomer

In the same manner, **30** (2.8 g) and (*R*)-**13** (533 mg) with Grubbs I catalyst (82 mg) in CH_2Cl_2 (5 mL) furnished 710 mg [80% based on (*R*)-**13**] of (*R*)-**31**. Its spectral data were identical with those of (*S*)-**31**. This was employed in the next step without further purification.

4.15. 6-Methyl-2-octadecanone 1

4.15.1. (R)-Isomer

10% Palladium on charcoal (300 mg) was added to a solution of (*S*)-**31** (730 mg, 2.6 mmol) in EtOAc (15 mL). The suspension was stirred under H_2 (balloon) for 3 h at room temperature. The mixture was then filtered through Celite and the catalyst and Celite were washed with EtOAc. The filtrate was concentrated in vacuo, and the residue was chromatographed over SiO_2 (15 g). The column was washed with hexane. Elution with hexane/EtOAc (50:1) gave (*R*)-**1** (652 mg, 89%) as a colorless oil, which solidified in a deep freezer, n_D^{27} 1.4434; $[\alpha]_D^{26}$ +0.35 (*c* 4.08, hexane); ν_{max} (film): 1720 (s, C=O), 1464 (m), 1360 (m), 1165 (m), 721 (w); δ_H ($CDCl_3$): 0.85 (3H, d, *J* 6.4, CHCH_3), 0.88 (3H, t, *J* 6.4, CH_2CH_3), 1.05–1.15 (2H, m), 1.20–1.35 [22H, m, (1.26, s)], 1.85–1.95 (1H, m), 1.50–1.65 (2H, m), 2.13 (3H, s, $COCH_3$), 2.07 (2H, t, *J* 7.6, $COCH_2$); δ_C ($CDCl_3$): 14.2, 19.6, 21.5, 22.7, 23.0, 27.1, 29.4, 29.7, 29.9, 30.0, 32.0, 32.7, 36.6, 36.9, 44.2, 209.1 (C=O); GC–MS [Column: HP-5MS 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; press: 60.7 kPa; temp: 70–230 °C (+10 °C/min)]: t_R 8.97 min (1.7%), 17.24 (4.1%), 18.25 (92.0%, **1**). MS of (*R*)-**1** (70 eV, EI): *m*/*z*: 282 (4) [M^+, $C_{19}H_{38}O$], 264 (68), 239 (18), 123 (16), 110 (30), 109 (35), 95 (30), 85 (43), 71 (57), 58 (100), 43 (87). The MS was identical with that of the naturally occurring **1**. HRMS calcd for $C_{19}H_{38}O$: 282.2923, found: 282.2921.

4.15.2. (S)-Isomer

In the same manner, (*R*)-**31** (700 mg) afforded 657 mg (93%) of (*S*)-**1** as a colorless oil. This solidifies in a deep freezer, n_D^{27} 1.4438; $[\alpha]_D^{28}$ −0.38 (*c* 3.63, hexane). GC [same conditions as reported for (*R*)-**1**]: t_R 8.97 min (3.4%), 17.2 (3.0%), 18.2 (91.5%, **1**). Its spectral data (IR, ^1H, and ^{13}C NMR, MS) were identical with those of (*R*)-**1**. HRMS calcd for $C_{19}H_{38}O$: 282.2923, found: 282.2928.

4.16. 6,14-Dimethyl-9-octadecen-2-one-32

4.16.1. (6S,14R)-Isomer

A wine-red solution of Grubbs I catalyst (85 mg, 0.1 mmol), (*R*)-**26** (2.018 g, 13.1 mmol) and (*S*)-**13** (358 mg, 2.1 mmol) in dry CH_2Cl_2 (5 mL) was stirred and heated under reflux for 4 h under Ar, when evolution of ethylene almost ceased. An additional amount of Grubbs I (36 mg, 0.04 mmol) was added to the mixture, and the stirring and refluxing were continued for additional 1.75 h. The mixture was left to stand overnight at room temperature. Then the mixture was concentrated in vacuo, and the residue was chromatographed over SiO_2 (20 g). Elution with hexane gave alkene **ii** (1.52 g). Further elution with hexane/EtOAc (15:1) gave 543 mg [86% based on (*S*)-**13**] of (6*S*,14*R*)-**32** as a yellowish oil, ν_{max} (film): 1720 (s, C=O), 1163 (m), 968 (m); δ_H ($CDCl_3$): 0.80–0.92 (9H, m, CH_3), 1.05–1.18 (2H, m), 1.18–1.47 (14H, m), 1.48–1.68 (2H, m), 1.90–2.08 (4H, m), 2.13 (3H, s, $COCH_3$), 2.40 (2H, t, *J* 7.2, $COCH_2$), 5.30–5.43 (2H, m, CH=CH); MS (70 eV, EI): *m*/*z*: 294 (11) [M^+, $C_{20}H_{38}O$], 276 (6), 236 (17), 139 (20), 123 (16), 111 (35), 109 (36), 95 (39), 81 (35), 69 (41), 55 (45), 43 (100). This was employed in the next step without further purification. Further elution with hexane/EtOAc (3:1) gave 82 mg of polar and colored by-product, presumably enedione generated from (*S*)-**13**.

4.16.2. (6S,14S)-Isomer

In the same manner, a solution of (*S*)-**26** (2.025 g, 13.2 mmol), (*S*)-**13** (336 mg, 2.0 mmol), and Grubbs I catalyst (85 mg initially and 30 mg after 2 h) in CH_2Cl_2(5 mL) was stirred and heated under reflux for 5 h under Ar. Subsequent work-up gave 470 mg (92%) of (6*S*,14*S*)-**32** as an oil. Its IR and ^1H NMR spectra were identical with those of (6*S*,14*R*)-**32**.

4.16.3. (6R,14R)-Isomer

In the same manner, a solution of (*R*)-**26** (2.0195 g, 13.1 mmol), (*R*)-**13** (362 mg, 2.2 mmol), and Grubbs I catalyst (85 mg+35 mg) in CH_2Cl_2 (5 mL) was stirred and heated under reflux for 6.5 h under Ar. Subsequent work-up gave 480 mg (76%) of (6*R*,14*R*)-**32** as an oil. Its IR and ^1H NMR spectra were identical with those of (6*S*,14*R*)-**32**.

4.16.4. (6R,14S)-Isomer

In the same manner, a solution of (*S*)-**26** (2.023 g, 13.1 mmol), (*R*)-**13** (364 mg, 2.2 mmol), and Grubbs I catalyst (82 mg+ 50 mg) was stirred and heated under reflux for 5 h under Ar. Subsequent work-up gave 465 mg (73%) of (6*R*,14*S*)-**32** as an oil. Its IR and ^1H NMR spectra were identical with those of (6*S*,14*R*)-**32**.

4.17. 6,14-Dimethyl-2-octadecanone 2

4.17.1. (6R,14R)-Isomer

10% Palladium–charcoal (200 mg) was added to a solution of (6*R*,14*R*)-**32** (530 mg, 1.8 mmol) in EtOAc (15 mL). The suspension was stirred under H_2 (balloon) for 3 h at room temperature. Subsequent work-up and chromatographic purification over SiO_2 (6.5 g) gave 484 mg (91%) of (6*R*,14*R*)-**2** as a colorless oil, n_D^{27} 1.4460; $[\alpha]_D^{27}$ −0.50 (*c* 2.65, hexane); ν_{max} (film): 1720 (s, C=O), 1462 (s), 1377 (m), 725 (m); δ_H ($CDCl_3$): 0.80–0.92 (9H, m, CH_3), 1.05–1.15 (4H, m), 1.15–1.40 (20H, m), 1.50–1.65 (2H, m), 2.13 (3H, s, $COCH_3$), 2.40 (2H, t, *J* 7.2, $COCH_2$); δ_C ($CDCl_3$): 14.1, 19.5, 19.7, 21.4, 22.6, 23.0, 27.0, 27.1, 29.2, 29.3, 29.7, 29.8, 32.59, 32.63, 36.5, 36.8, 36.9, 37.1, 44.1, 209.1 (C=O); GC–MS [same conditions as for (*R*)-**1**]: t_R 8.98 min (6%), 18.77 (92%, **2**), 19.30 (2%). MS of (6*R*,14*R*)-**2** (70 eV, EI): *m*/*z*: 296 (6%) [M^+, $C_{20}H_{40}O$], 278 (63), 253 (15), 236 (13), 123 (20), 110 (42), 109 (41), 95 (32), 85 (45), 71 (55), 58 (92), 43 (100). The MS was identical with that of the naturally occurring **2**. HRMS calcd for $C_{20}H_{40}O$: 296.3079, found: 296.3082.

4.17.2. (6R,14S)-Isomer

In the same manner, (6*S*,14*S*)-**32** (470 mg, 1.9 mmol) gave 459 mg (96%) of (6*R*,14*S*)-**2**, n_D^{27} 1.4462; $[\alpha]_D^{24}$ +1.54 (*c* 3.07, hexane). GC [same conditions as for (*R*)-**1**]: t_R 17.73 min (2%), 18.77 (95%), 19.30 (3%). Its spectral data (IR, ^1H, and ^{13}C NMR and MS) were identical with those described for (6*R*,14*R*)-**2**. HRMS calcd for $C_{20}H_{40}O$: 296.3079, found: 296.3079.

4.17.3. (6S,14R)-Isomer

In the same manner, (6*R*,14*R*)-**32** (475 mg, 1.6 mmol) gave 440 mg (92%) of (6*S*,14*R*)-**2**, n_D^{27} 1.4470; $[\alpha]_D^{27}$ −1.16 (*c* 3.07, hexane). GC [same conditions as for (*R*)-**1**]: t_R 16.68 min (3%), 17.73 (2%), 18.77 [95%, (6*R*,14*R*)-**2**]. Its spectral data (IR, ^1H, and ^{13}C NMR and

MS) were identical with those described for (6*R*,14*R*)-**2**. HRMS calcd for $C_{20}H_{40}O$: 296.3079, found: 296.3077.

4.17.4. (6S,14S)-Isomer

In the same manner, (6*R*,14*S*)-**32** (400 mg, 1.6 mmol) gave 352 mg (77%) of (6*S*,14*S*)-**2**, n_D^{27} 1.4466; $[\alpha]_D^{26}$ +0.65 (*c* 3.81, hexane). GC [same conditions as for (*R*)-**1**]: t_R 16.68 min (1%), 17.73 (2%), 18.77 [97%, (6*S*,14*S*)-**2**]. Its spectral data (IR, ^1H, and ^{13}C NMR and MS) were identical with those described for (6*R*,14*R*)-**2**. HRMS calcd for $C_{20}H_{40}O$: 296.3079, found: 296.3082.

4.18. 14-Methyl-9-octadecen-2-one 33

4.18.1. (R)-Isomer

A solution of Grubbs I catalyst (82 mg and then 30 mg, total 112 mg, 0.14 mmol), (*R*)-**26** (2.00 g, 13 mmol), and **18** (325 mg, 2.1 mmol) in CH_2Cl_2 (5 mL) was stirred and heated under reflux for 5 h under Ar. The mixture was left to stand overnight at room temperature. Subsequent work-up gave 460 mg (78% based on **18**) of (*R*)-**33**, ν_{max} (film): 1720 (s, C═O), 1163 (m), 968 (m); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.8, $CHCH_3$), 0.90 (3H, t, *J* 6.8, CH_2CH_3), 1.00–1.11 (2H, m), 1.15–1.40 (14H, m), 1.45–1.60 (3H, m), 1.85–2.00 (4H, m), 2.13 (3H, s, $COCH_3$), 2.41 (2H, t, *J* 7.6, $COCH_2$), 5.30–5.40 (2H, m, HC═CH). This was employed in the next step without further purification.

4.18.2. (S)-Isomer

In the same manner, Grubbs I catalyst (85 mg and then 25 mg, total 110 mg, 0.14 mmol), (*S*)-**26** (1.50 g, 9.7 mmol), and **18** (334 mg, 2.2 mmol) in CH_2Cl_2 (5 mL) were stirred and heated under reflux for 7 h under Ar. The mixture was left to stand overnight at room temperature. Subsequent work-up gave 501 mg (81%) of (*S*)-**33**. Its IR and ^1H NMR spectra were identical with those of (*R*)-**33**. This was employed in the next step without further purification.

4.19. 14-Methyl-2-octadecanone 3

4.19.1. (R)-Isomer

10% Palladium–charcoal (200 mg) was added to a solution of (*R*)-**33** (438 mg, 1.6 mmol) in EtOAc (15 mL). The suspension was stirred under H_2 (balloon) for 2 h at room temperature. Subsequent work-up and chromatographic purification over SiO_2 (5 g) gave 361 mg (82%) of (*R*)-**3**. This solidifies in a deep freezer, n_D^{27} 1.4428; $[\alpha]_D^{25}$ −0.60 (*c* 3.07, hexane); ν_{max} (film): 1720 (s, C═O), 1466 (s), 1360 (m), 1163 (m), 721 (m); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.8, $CHCH_3$), 0.89 (3H, t, *J* 6.4, CH_2CH_3), 1.03–1.12 (2H, m), 1.18–1.90 (23H, m), 1.55–1.60 (2H, m), 2.13 (3H, s, $O{=}CCH_3$), 2.41 (2H, t, *J* 7.6, $O{=}CCH_2$), δ_C ($CDCl_3$): 14.1, 19.7, 22.6, 23.0, 23.9, 27.1, 28.9, 29.2, 29.3, 29.4, 29.5, 29.6, 30.0, 36.8, 37.1, 43.8, 209.1, (C═O); GC–MS [same conditions as for (*R*)-**1**]: t_R 18.34 min [90%, (*R*)-**3**], 18.82 (10%). MS of (*R*)-**3** (70 eV, EI): *m*/*z*: 282 (21) [M^+, $C_{19}H_{38}O$], 264 (16), 222 (11), 127 (8), 109 (13), 96 (21), 85 (28), 71 (62), 59 (71), 58 (100), 43 (94). The MS is identical with that of the naturally occurring **3**. HRMS calcd for $C_{19}H_{38}O$: 282.2923, found: 282.2923.

4.19.2. (S)-Isomer

In the same manner, (*S*)-**33** (495 mg, 1.8 mmol) gave 405 mg (82%) of (*S*)-**3**, n_D^{27} 1.4468; $[\alpha]_D^{24}$ +1.05 (*c* 3.13, hexane). GC [same conditions as for (*R*)-**1**] t_R 17.27 min (2%), 17.66 (2%), 18.34 [96%, (*S*)-**3**]. Its spectral data (IR, ^1H, and ^{13}C NMR and MS) were identical with those of (*R*)-**3**. HRMS calcd for $C_{19}H_{38}O$: 282.2923, found: 282.2926.

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