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Pheromone synthesis. Part 249: Syntheses of methyl (*R*,*E*)-2,4,5-tetradecatrienoate and methyl (2*E*,4*Z*)-2,4-decadienoate, the pheromone components of the male dried bean beetle, *Acanthoscelides obtectus* (Say)☆

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Dedicated to Professor Masanao Matsui, my Dr. thesis advisor, on the occasion of his 94th birthday

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ABSTRACT

The enantiomers of methyl (*E*)-2,4,5-tetradecatrienoate (**1**), a component of the male pheromone of *Acanthoscelides obtectus*, were synthesized from the enantiomers of 1-undecyn-3-ol (**6**), which were obtained via asymmetric acetylation of (±)-1-trimethylsilyl-1-undecyn-3-ol (**4**) with vinyl acetate as catalyzed by lipase PS (Amano). The ortho ester Claisen rearrangement of **6** with triethyl orthoacetate was the key-step to generate the chiral allenic system. A new synthesis of (±)-**1** was also executed starting from (±)-**6**. Three different syntheses of methyl (2*E*,4*Z*)-2,4-decadienoate (**2**), another component of the male pheromone of *A. obtectus*, were achieved by means of either palladium-catalyzed Heck reaction or a Claisen and an Al_2O_3 catalyzed thermal rearrangements.

1. Introduction

In 1970 Horler isolated (−)-methyl (*E*)-2,4,5-tetradecatrienoate {**1**, Fig. 1, $[\alpha]_D^{23}$ −128 (*c* 0.6, hexane)} as the male-produced pheromone of the dried bean beetle, *Acanthoscelides obtectus* (Say) [COLEOPTERA: Bruchidae].[2] This unique chiral and non-racemic allene soon attracted the attention of synthetic chemists, and Landor et al. were the first to announce the synthesis of (±)-**1** in 1971.[3] Since then a number of syntheses of (±)-, (*R*)-, and (*S*)-**1** were reported.[4–10]

The absolute configuration of the naturally occurring (−)-**1** was determined as *R* by Pirkle and Boeder's first synthesis of the enantiomerically enriched (*R*)- and (*S*)-**1** {$[\alpha]_D$ −98.3 (*c* 3.8, hexane) and +94.7 (*c* 3.3, hexane), respectively} in 1978.[6] The second synthesis of (*R*)- and (*S*)-**1** gave enantiomerically more enriched products {$[\alpha]_D^{23}$ −162 (*c* 0.95, hexane) and $[\alpha]_D^{22}$ +160 (*c* 0.75, hexane), respectively}, and confirmed the *R* configuration of the natural pheromone.[7] Since the magnitude of the specific rotation of the natural (−)-**1** was reported as −128, its enantiomeric purity was speculated to be less than 100%.[7] In 1981 when our previous synthesis was completed, however, there was no good analytical method available to determine the enantiomeric composition of the natural pheromone.

In February 2011, Professor W. Francke (Hamburg University, Germany) informed me that he, in cooperation with the groups of J.A. Pickett (Rothamsted Research, UK) and M. Tóth (Plant Protection Institute, Budapest, Hungary), reinvestigated the male pheromone of *A. obtectus*, and found **1** and methyl (2*E*,4*Z*)-2,4-decadienoate (**2**) to be bioactive as checked by electroantenographic detection (EAD). He also proposed that he would analyze the enantiomeric composition of the natural **1**, employing enantioselective GC analysis on a cyclodextrin-based chiral stationary phase.[11] Of course, availability of the enantiomers of **1** as the reference samples was prerequisite for the analysis. Because the pheromone **1** was reported to be unstable and polymerize readily (half-life of natural **1** was about 20 d at −13 °C),[2] our samples prepared in 1981 were no more useful. I therefore decided to prepare again the enantiomers of **1** by

☆ For Part 248, see Ref. 1.

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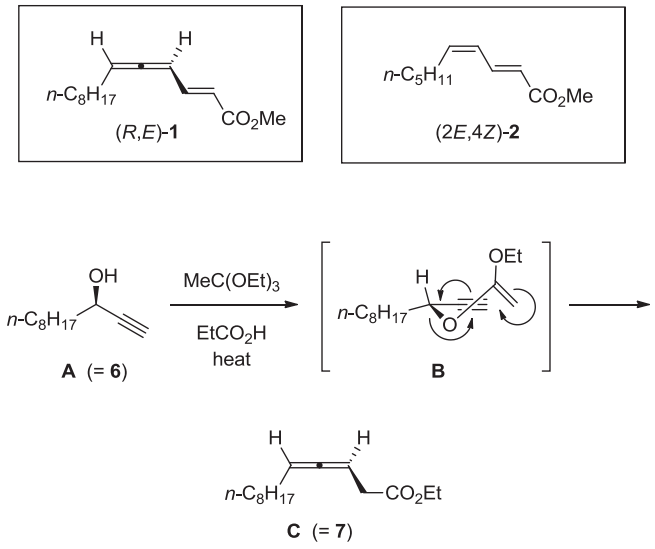
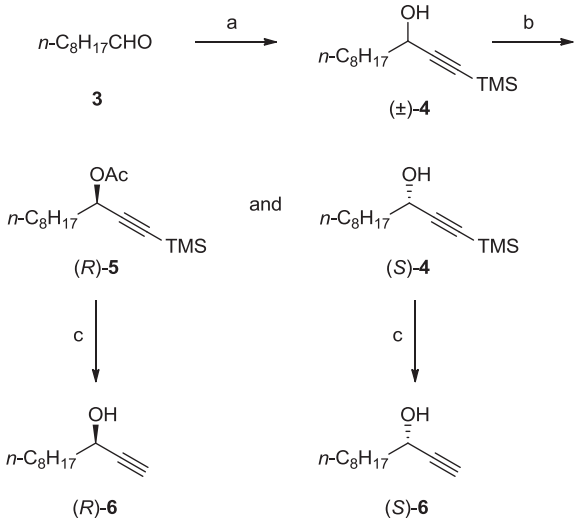


Fig. 1. Structures **1** and **2** of the pheromone components of the male dried bean beetle, *Acanthoscelides obtectus*, and the key-step (ortho ester Claisen rearrangement) to prepare the chiral and non-racemic allene system of **1**.



Scheme 1. Synthesis of the acetylenic alcohols (*R*)- and (*S*)-**6** by lipase-catalyzed asymmetric acetylation of (±)-**4**. Reagents and conditions: (a) HC≡CTMS, *n*-BuLi, THF, −78 °C to room temperature (99%); (b) (i) Lipase PS on Celite 503 (pH 7.0), CH_2=CHOAc, $(i\text{-Pr})_2O$, 30 °C, 3 d; (ii) SiO_2 chromatographic separation [49% for (*R*)-**5** and 36% for (*S*)-**4**]; (c) K_2CO_3, MeOH, 33–40 °C, 2–2.5 h [91% for (*R*)-**6** and 83% for (*S*)-**6**].

improving our 1981 synthesis. This paper describes the results of my efforts along this line together with a new synthesis of (±)-**1** and three different syntheses of **2**.

2. Results and discussion

2.1. Synthesis of the enantiomers of methyl (*E*)-2,4,5-tetradecatrienoate (1)

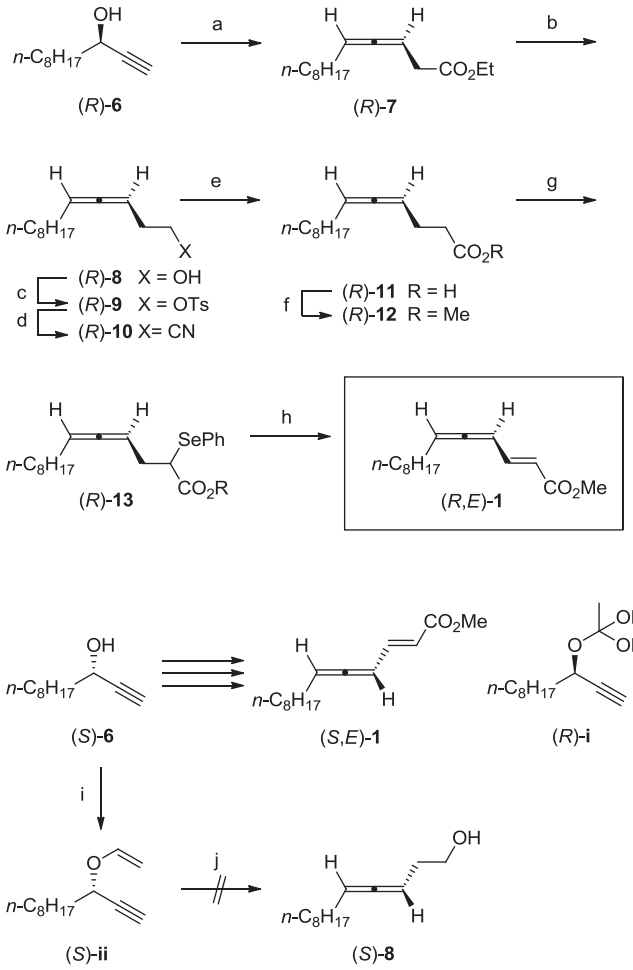
Examination of the five existing syntheses of (*R*)- and (*S*)-**1** indicated that the use of organocopper reagents led to partial racemization of intermediates.[6,8,9] Although Franck-Neumann's method employing allene manganese complexes yielded both (*R*)- and (*S*)-**1** of high enantiomeric purity,[10] it was rather complicated due to the formation and removal of the manganese coordination complexes. Accordingly, ortho ester Claisen rearrangement as shown in Fig. 1 was again adopted as the key-step just like in our previous synthesis to convert acetylenic alcohol **A** into allenic ester **C** via **B**.[7]

Scheme 1 shows the preparation of the enantiomers of 1-undecyn-3-ol (**6**). Since the resolution of (±)-**6** was quite cumbersome by means of chemical derivatization followed by recrystallization or chromatographic separation,[6,7] the enzymatic method was adopted as reported by Anastasia and his coworkers.[12] They achieved lipase-catalyzed enantiomer separation of (±)-1-trimethylsilyl(TMS)-1-alkyn-3-ols.[12] By attaching a TMS group at C-1, the enantioselectivity of asymmetric acetylation with vinyl acetate and lipase could be improved to give optically active and long-chain 1-alkyn-3-ols.[12] Their results were later confirmed by us[13] and others.[14]

Nonanal (**3**) was treated with lithium trimethylsilylacetylide in THF to give (±)-**4** in 99% yield. Immobilized lipase PS (Amano) on Celite 503[15] was added to a stirred and warmed solution of (±)-**4** and vinyl acetate in diisopropyl ether. The mixture was stirred for 3 d at 30 °C, and filtered. After concentration of the filtrate, the mixture was chromatographed over SiO_2 to give acetate (*R*)-**5** and the recovered alcohol (*S*)-**4**.[12] Treatment of (*R*)-**5** with potassium carbonate in methanol furnished (*R*)-**6**, $[\alpha]_D^{14}$ +14.5 (*c* 3.57, Et_2O) {Ref. 12 $[\alpha]_D^{22}$ +14.8 (*c* 1.04, Et_2O)}. Similarly (*S*)-**4** afforded (*S*)-**6**, $[\alpha]_D^{17}$ −14.7 (*c* 3.48, Et_2O) {Ref. 12 $[\alpha]_D^{21}$ −15.0 (*c* 1.02, Et_2O)}. The enantiomeric purities of (*R*)- and (*S*)-**6** were determined by GC analysis on a Chiramix® column[16] as 97.4 and 97.5% ee, respectively. The overall yields of (*R*)- and (*S*)-**6** based on nonanal (**3**) were 40 and 30%, respectively. The present enzymatic preparation of (*R*)- and (*S*)-**6** was far more efficient and easier than the classical resolution of (±)-**6** as its half phthalate as reported in 1981.[7]

Conversion of the acetylenic alcohol (*R*)-**6** to the pheromone (*R*)-**1** is summarized in Scheme 2. The key ortho ester Claisen rearrangement with transfer of the central chirality at C-3 of (*R*)-**6** into the axial chirality of the allenic system of (*R*)-**7** was executed by heating a mixture of (*R*)-**6** and triethyl orthoacetate in the presence of propanoic acid at 145–150 °C for 1–1.5 h with distillative removal of the generated ethanol. Under these conditions, the conversion of (*R*)-**6** to (*R*)-**7** was complete, although slight and partial racemization also took place. The conditions (110 °C for 7 h) previously reported[7] was mild enough to avoid racemization, while the product contained a substantial amount of ortho ester (*R*)-**i**.

Reduction of (*R*)-**7** with lithium aluminum hydride gave (*R*)-**8** without any event, although reduction of (±)-**7** with the same reagent had been reported to give a poor yield of (±)-**8**, recommending the use of diisobutylaluminum hydride.[17] The corresponding tosylate (*R*)-**9** was converted to methyl ester (*R*)-**12** via (*R*)-**10** and (*R*)-**11**.[7] Phenylselenenylation of (*R*)-**12** at C-2 was first attempted with excess lithium diisopropylamide [$LiN(i\text{-Pr})_2$] and phenylselenenyl chloride. The product (*R*)-**13**, however, was contaminated with the starting (*R*)-**12**. Chromatographic separation over silica gel of (*R*)-**12** from (*R*)-**13** was rather difficult.[7] Fortunately, use of potassium hexamethyldisilazide [$KN(SiMe_3)_2$] solved the problem, and the desired (*R*)-**13** could be secured without contamination of (*R*)-**12**. Finally, selenide (*R*)-**13** was oxidized with sodium periodate to give the pheromone component (*R*)-**1**, $[\alpha]_D^{24}$ −130.3 (*c* 2.23, hexane) {Ref. 7 $[\alpha]_D^{23}$ −162 (*c* 0.95, hexane)}. Its enantiomeric purity was determined as 74.7% ee by GC analysis employing Chiramix® as the chiral stationary phase (see Experimental 4.12.1). Another batch of (*R*)-**13** prepared by employing $LiN(i\text{-Pr})_2$ as the base yielded (*R*)-**1** contaminated with (*R*)-**12** (**1**/**12**=65.6:33.3), $[\alpha]_D^{23}$ −117.1 (*c* 1.09, hexane). Due to the contamination with (*R*)-**12**, $[\alpha]_D^{23}$ −62.0, a smaller $[\alpha]_D$ value was observed for the product. However, GC analysis of this batch of (*R*)-**1** revealed its enantiomeric purity as 87.9% ee. Similarly, (*S*)-**6** afforded (*S*)-**1**, $[\alpha]_D^{25}$ +122.8 (*c* 1.75, hexane). Since (*S*)-**13** was prepared by using $LiN(i\text{-Pr})_2$ as the base, both (*S*)-**13** and (*S*)-**1** were contaminated with (*S*)-**12**. The enantiomeric purity of (*S*)-**1** was



Scheme 2. Synthesis of (*R*)- and (*S*)-**1**. Reagents and conditions: (a) $MeC(OEt)_3$, Et-CO_2H, 145–150 °C, 1.5 h (83%); (b) $LiAlH_4$, THF, 0–5 °C, 1.5 h (98%); (c) TsCl, C_5H_5N, DMAP, 0–5 °C, 2.5 h (98%); (d) KCN, DMSO, room temperature, 4 d (93%); (e) NaOH, EtOH, H_2O, reflux, 7 h (89%); (f) CH_2N_2, Et_2O (78%); (g) $KN(SiMe_3)_2$, PhSeCl, THF, −78 to −70 °C, 1 h (59%) or $LiN(i\text{-}Pr)_2$, THF, −65 °C, 1 h (49%); (h) $NaIO_4$, THF, H_2O, room temperature, 2.5 h (74%); (i) $EtOCH{=}CH_2$, room temperature, 5 h (5%); (j) $[(Ph_3PAu)_3O]BF_4$, CH_2Cl_2, room temperature, 6.5 h; then $NaBH_4$, MeOH (0%).

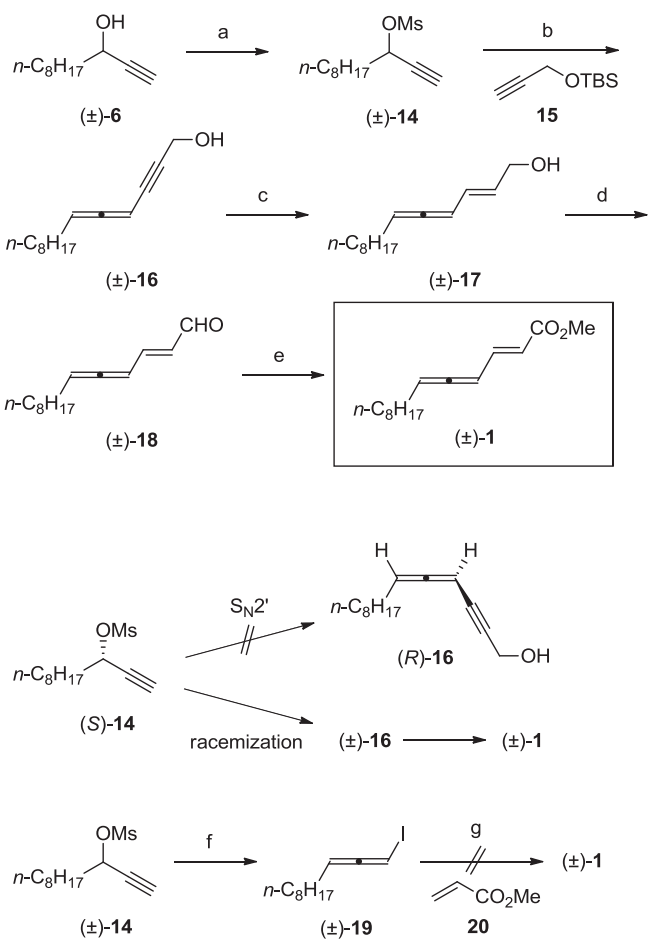
94.4% ee. In this case, the Claisen rearrangement was executed by heating at 110 °C for 7 h. Apparently under the low temperature conditions, the chirality transfer from (*S*)-**6** to (*S*)-**7** could be achieved more perfectly. Because the objective of the present work was to supply reference samples to the GC analysis of the naturally occurring pheromone (*R*)-**1**, the synthetic samples of 70–90% ee could be utilized successfully. The overall yields of (*R*)- and (*S*)-**1** based on (*R*)- and (*S*)-**6** were 22 and 12% (eight steps).

These synthetic enantiomers of **1** enabled Professor Francke to determine the enantiomeric purity of the naturally occurring (*R*)-**1** as 87% ee (W. Francke, private communication, May 19, 2011). The result added another example to known cases of enantiomerically impure pheromones.[18–20]

In 2004, Sherry and Toste reported a new variant of propargyl Claisen rearrangement under gold(I) catalysis at room temperature.[21] Their procedure yielded, with remarkably efficient chirality transfer (>90%), homoallenic alcohols after reduction with sodium borohydride. The acetylenic alcohol (*S*)-**6** was therefore converted to vinyl ether (*S*)-**ii** by treatment with ethyl vinyl ether in the presence of mercury(II) acetate.[22,23] The transetherification proceeded in very poor yield (5%), presumably due to the presence of the terminal alkyne group, which reacted with Hg^{2+} ion. Attempted conversion of (*S*)-**ii** to (*S*)-**8** under the reported condition with gold catalyst $[(Ph_3PAu)_3O]BF_4$[21] was unsuccessful, giving only the recovered (*S*)-**ii** (33%) and other products with no allenic absorption (1960–1967 cm^{-1}) in their IR spectrum. In this particular case, gold(I)-catalyzed propargyl Claisen rearrangement failed to give the desired (*S*)-**8**.

2.2. Synthesis of (±)-methyl (*E*)-2,4,5-tetradecatrienoate (1)

Because the absolute configuration of the major enantiomer of the natural pheromone (−)-**1** was *R*, it would be advantageous to prepare (*R*)-**1** from (*S*)-**6**. Of course Mitsunobu inversion of (*S*)-**6** affords (*R*)-**6**, the starting material for (*R*)-**1**. It was expected, however, that S_N2'-type conversion of (*S*)-**14** (Scheme 3) to (*R*)-**16** might eventually lead to (*R*)-**1**, in view of the success of S_N2'-type allene synthesis in the past.[24,25] In order to explore this possibility, a synthesis of (±)-**1** was first executed starting from (±)-**6** as shown in Scheme 3. The key-step was the allene formation from mesylate (±)-**14** and acetylene **15** by the attack of a carbanion generated from **15**. The present allene formation reaction was reported previously by Boudouy and Gore under the Cadiot conditions (CuCl, *t*-$BuNH_2$, DMF) employing (±)-**14** and propargyl alcohol.[26]



Scheme 3. Synthesis of (±)-**1**. Reagents and conditions: (a) MsCl, C_5H_5N, DMAP, 0-5 °C, 2 h (85%); (b) (i) **15**, *n*-BuLi, $CuBr{\cdot}Me_2S$, THF, −78 °C, 2 h; (ii) 46% HF aq, MeCN, room temperature, 45 min (89%, two steps); (c) $LiAlH_4$, THF, room temperature, 2.5 h (50%); (d) DMP, CH_2Cl_2, 0 °C to room temperature, 50 min (60%); (e) KCN, AcOH, MnO_2, MeOH, room temperature, 4 h (79%); (f) NaI, DMF, 50 °C, 1.5 h (86%); (g) **20**, $Pd(OAc)_2$, K_2CO_3, $(n\text{-}Bu)_4NCl$, DMF, room temperature, 4.5 h (0%).

Treatment of (±)-**6** with mesyl chloride and pyridine in the presence of 4-dimethylaminopyridine (DMAP) gave crystalline (±)-**14**, which was treated with the lithio salt of **15** in THF in the presence of copper(I) bromide at −78 °C to give (±)-**16** after

deprotection of the TBS group with hydrofluoric acid. Reduction of (±)-**16** with lithium aluminum hydride furnished alcohol (±)-**17**. Dess–Martin periodinane (DMP) oxidized (±)-**17** to aldehyde (±)-**18**. Finally, aldehyde (±)-**18** was treated with potassium cyanide, manganese dioxide, and acetic acid in methanol[27] to furnish (±)-**1**. The overall yield of (±)-**1** based on (±)-**6** was 18% (six steps).

Conversion of **14** to **16** was then carried out employing oily (*S*)-**14**, $[\alpha]_D^{27}$ −49.4 (*c* 3.26, hexane). The generated **16** showed $[\alpha]_D^{26}$ −0.33 (*c* 3.19, hexane), indicating that extensive racemization took place in the course of the reaction.[28] The present (−)-**16** eventually afforded almost racemic **1**, $[\alpha]_D^{27}$ −0.12 (*c* 1.35, hexane). Attempted synthesis of (*R*)-**1** from (*S*)-**14** via S_N2' mechanism was thus proved to be unsuccessful. Since Sarandeses and co-workers found that organoindium reagents react with optically active propargylic esters to give optically active allenes via S_N2' mechanism under palladium catalysis, their conditions were also examined in the present case of the reaction of (*S*)-**14** with **15** to give no useful results.[14,25]

Another attempt was made to prepare (±)-**1** by means of palladium-catalyzed Heck reaction[29] between allenic iodide (±)-**19** and methyl acrylate **20**. Although the iodoallene (±)-**19** could be synthesized readily by treatment of (±)-**14** with sodium iodide in DMF, the attempted Heck reaction was unsuccessful, giving a messy mixture of unsaturated esters including methyl 2,4,6-tetradecatrienoate.

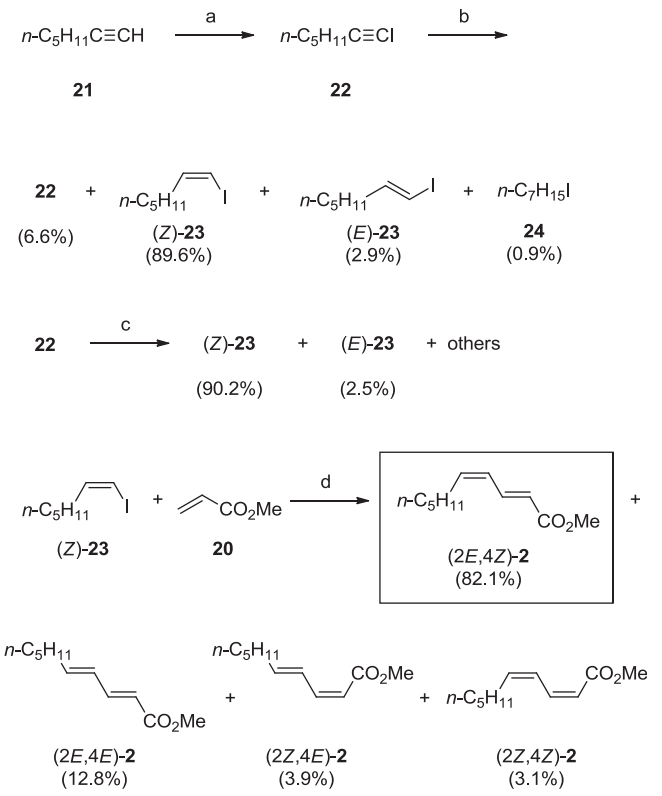
2.3. Synthesis of methyl (2*E*,4*Z*)-2,4-decadienoate (2) via three different routes

Palladium-catalyzed Heck reaction was employed to prepare methyl (2*E*,4*Z*)-2,4-decadienoate (**2**), the second component of the male dried bean beetle pheromone.[29,30] Scheme 4 summarizes the first attempt, which consists in the coupling of (*Z*)-1-iodo-1-heptene (**23**) with methyl acrylate (**20**).

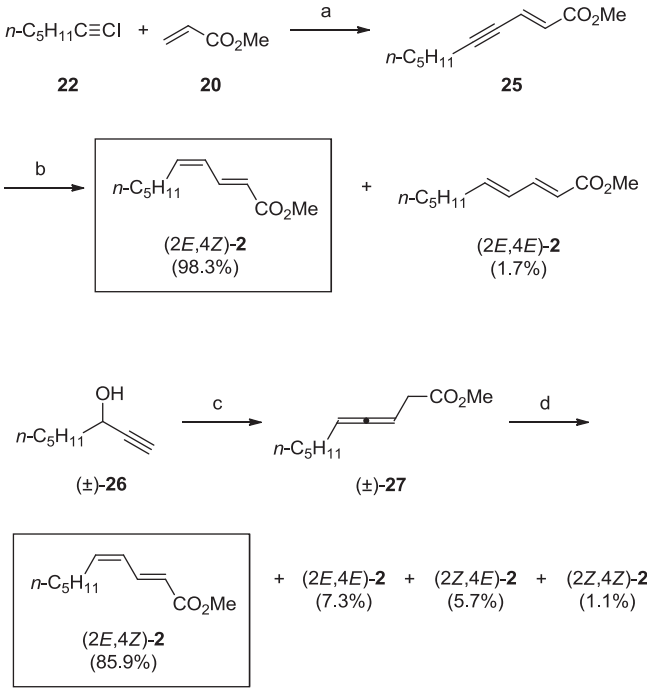
(*Z*)-1-Iodo-1-heptene (**23**) was synthesized in two different ways. At first, 1-heptyne (**21**) was warmed with iodine and morpholine in benzene at reflux to give 1-iodo-1-heptyne (**22**).[31] Diimide reduction of **22** gave in 67% yield a mixture of the desired (*Z*)-**23** (89.6%), its (*E*)-isomer (2.9%) and the over-reduction product 1-iodoheptane (**24**, 0.9%) together with the recovered **22** (6.6%).[31] In the second route, hydroboration-protonolysis of **22** with dicyclohexylborane followed by acetic acid furnished in 57% yield a mixture of (*Z*)-**23** (90.2%) and (*E*)-**23** (2.5%) together with other unidentified products.

The iodoalkene mixture containing 90.2% of (*Z*)-**23** and 2.5% of (*E*)-**23** was allowed to react with methyl acrylate (**20**) in the presence of palladium(II) acetate, potassium carbonate, and tetrabutylammonium chloride in DMF[29] to give in 75% yield a mixture of the desired (2*E*,4*Z*)-**2** (82.1%) and its isomers [(2*E*,4*E*)-**2** (12.8%), (2*Z*,4*E*)-**2** (3.9%), and (2*Z*,4*Z*)-**2** (3.1%)]. Isomerization of the desired (2*E*,4*Z*)-**2** to other *E*/*Z*-isomers was an inevitable side-reaction of the present Heck reaction owing to the gradual generation of palladium(0) in the reaction mixture. Further attempts were therefore made to obtain purer (2*E*,4*Z*)-**2** (Scheme 5).

In the second attempt, as shown in the upper part of Scheme 5, 1-iodo-1-heptyne (**22**) was subjected to the Heck reaction with methyl acrylate (**20**) under Jeffrey's conditions,[30] similar to those employed for the coupling of (*Z*)-**23** with **20**. The reaction afforded **25** in 47% yield. The enyne ester **25** was thermally unstable, and its purification by distillation caused severe decrease in its yield (47 into 27%). Hydroboration-protonolysis of **25** furnished (2*E*,4*Z*)-**2** (98.3% purity) contaminated with 1.7% of (2*E*,4*E*)-**2** in 23% yield after chromatographic purification and distillation. The present method provided (2*E*,4*Z*)-**2** of a better purity (98.3%) than that (82.1%) obtained by the first method.



Scheme 4. Synthesis of (2*E*,4*Z*)-**2** via (*Z*)-**23**. Reagents and conditions: (a) I_2, morpholine, C_6H_6, 45 °C, 21 h (79%); (b) (i) $KO_2CN{=}NCO_2K$, C_5H_5N, MeOH, AcOH, room temperature, overnight; (ii) Me_2NH, H_2O, Et_2O, room temperature, 5 h (67%); (c) (i) $(C_6H_{11})_2BH$, THF, 0–5 °C, 30 min, then room temperature, 1.5 h; (ii) AcOH, 50 °C, 30 min (57%); (d) $Pd(OAc)_2$, K_2CO_3, $(n\text{-}Bu)_4NCl$, DMF, room temperature, 1 h (75%).



Scheme 5. Syntheses of (2*E*,4*Z*)-**2** via hydroboration-protonolysis of **25** and rearrangement of (±)-**27**. Reagents and conditions: (a) $Pd(OAc)_2$, K_2CO_3, $(n\text{-}Bu)_4NCl$, DMF, room temperature, 4.5 h (47%, 29% after distillation); (b) (i) $(C_6H_{11})_2BH$, THF, 0–5 °C for 30 min, then room temperature for 2 h; (ii) AcOH, 50 °C, 140 min (23%); (c) (i) $MeC(OMe)_3$, $EtCO_2H$, 145 °C, 1.5 h; (ii) $EtCO_2H$, *o*-xylene, 160–170 °C, 2 h (72–87%); (d) basic Al_2O_3, *o*-xylene, 160 °C, 2 h (55%).

Aiming a more efficient synthesis, the third attempt was made to prepare (2*E*,4*Z*)-**2** as shown in the lower part of Scheme 5. In 1982 Tsuboi et al. discovered a thermal rearrangement of 3,4-allenic esters with alumina catalyst in aprotic solvents to give (2*E*,4*Z*)-dienoic esters.[32] Indeed, rearrangement of (±)-ethyl 3,4-decadienoate to ethyl (2*E*,4*Z*)-2,4-decadienoate was established as an *Organic Syntheses* procedure.[33]

Accordingly, (±)-ethyl 3,4-decadienoate (**27**) was prepared from (±)-1-octyn-3-ol (**26**) by treatment with trimethyl orthoacetate in the presence of propanoic acid followed by Claisen rearrangement in *o*-xylene at 160–170 °C. The key thermal rearrangement of (±)-**27** to (2*E*,4*Z*)-**2** was executed in the presence of basic alumina in *o*-xylene at 160 °C for 2 h to give the pheromone component (2*E*,4*Z*)-**2** in 40–48% overall yield based on the commercially available (±)-**26** (two steps). The purity of (2*E*,4*Z*)-**2** obtained by this method was 85.9% with contaminating three isomers [(2*E*,4*E*)-**2** (7.3%), (2*Z*,4*E*)-**2** (5.7%), and (2*Z*,4*Z*)-**2** (1.2%)]. Consequently, the present short and efficient route according to Tsuboi et al. was the best one to prepare a substantial amount of (2*E*,4*Z*)-**2**, although the second method (hydroboration-protonolysis) afforded (2*E*,4*Z*)-**2** with a better purity.

3. Conclusion

The two pheromone components **1** and **2** of the male dried bean beetle were synthesized.

Firstly, enzymatic resolution of (±)-1-trimethylsilyl-1-undecyn-3-ol (**4**) very much facilitated the synthesis of methyl (*R*,*E*)-2,4,5-tetradecatrienoate (**1**) and its (*S*)-isomer. Samples with 74.7–94.4% ee of the enantiomers of **1** were prepared, and employed as reference samples for the determination of the enantiomeric purity of the naturally occurring (*R*)-**1** to be 87% ee. Secondly, a modified synthesis of (±)-**1** was developed to give it in 18% overall yield (six steps) based on (±)-1-undecyn-3-ol (**6**). Thirdly, three different routes were developed for the synthesis of methyl (2*E*,4*Z*)-2,4-decadienoate (**2**). Alumina-catalyzed rearrangement of (±)-methyl 3,4-decadienoate (**27**) to **2** was simpler and more efficient than other two methods based on palladium-catalysis.

4. Experimental

4.1. General

Boiling points and a melting point 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 Jeol JMS-SX 102A. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. (±)-1-Trimethylsilyl-1-undecyn-3-ol (4)

A solution of *n*-BuLi in hexane (1.6 M, 81 mL, 130 mmol) was added dropwise to a stirred and cooled solution of TMSC≡CH (12.3 g, 125 mmol) in dry THF (200 mL) at −75 °C under Ar. The mixture was stirred for 30 min with gradual raise of temperature up to −10 °C. It was then cooled again, and a solution of nonanal (**3**, 14.2 g, 100 mmol) in dry THF (30 mL) was added dropwise to the stirred and cooled mixture at −65 to −78 °C. The stirring was continued for 1 h at −78 °C to room temperature. The reaction mixture was quenched with ice and aqueous NH_4Cl solution, and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give a residual oil (28.8 g). This was chromatographed over SiO_2 (160 g). Elution with hexane/EtOAc (20:1–15:1) gave 23.8 g (99%) of (±)-**4** as a colorless oil, n_D^{23}=1.4502; ν_{max} (film): 3332 (m), 2956 (s), 2925 (s), 2856 (s), 2171 (m), 1250 (s), 1011 (m), 843 (s), 760 (m); δ_H ($CDCl_3$): 0.17 (9H, s), 0.88 (3H, t, *J* 6.8), 1.23–1.35 (10H, br), 1.40–1.47 (2H, m), 1.68–1.73 (2H, m), 1.79 (1H, br), 4.35 (1H, dt, *J* 6.0, 6.4); GC–MS [column: HP-5MS, 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; carrier gas, He; press: 60.7 kPa, temp: 70–230 °C (+10 °C/min)]: t_R 13.18 min (99.3%); MS of (±)-**4** (70 eV, EI): *m*/*z* 239 (1) [(M−1)$^+$], 225 (3), 207 (8), 167 (10), 127 (100), 99 (65), 75 (98), 73 (38). HRMS calcd for $C_{13}H_{25}OSi$ [(M−CH_3)$^+$]: 225.1675, found: 225.1680.

4.3. Asymmetric acetylation of (±)-4 with vinyl acetate and lipase PS (Amano)

4.3.1. Preparation of immobilized lipase PS on Celite 503.[15] Lipase PS (Amano, 9.0 g) and Celite 503 (30.0 g) were mixed thoroughly by shaking in a 300 mL Erlenmeyer flask with a glass stopper. Phosphate buffer (pH 7.0, 1/15 M, 30 mL) was added portionwise to the mixture, which was vigorously shaken to make it homogeneous. It was then dried in vacuo for 1 d to give 53.0 g of immobilized lipase PS, and kept in a refrigerator at 0–5 °C.

*4.3.2. Asymmetric acetylation of (±)-**4**.*[12] Immobilized lipase PS (15.0 g) was added to a solution of (±)-**4** (15.0 g, 62.5 mmol) and vinyl acetate (150 mL) in diisopropyl ether (350 mL). The suspension was stirred at 30 °C for 3 d, and then filtered. The filtrate was concentrated in vacuo to give an oil (17.7 g). This was chromatographed over SiO_2 (200 g). Elution with hexane/EtOAc (150:1 to 200:1) first gave (*R*)-**5** (7.22 g) and then (*S*)-**4** (5.39 g). The intermediate fractions were rechromatographed over SiO_2 (50 g) to give additional amounts of (*R*)-**5** and (*S*)-**4**. The total yield of (*R*)-**5** was 8.63 g (98% of the theoretical) and that of (*S*)-**4** was 5.39 g (72%). *Properties of (R)-**5***: a colorless oil, n_D^{23}=1.4456; $[\alpha]_D^{22}$ +74.4 (*c* 3.12, $CHCl_3$) {Ref. 12 $[\alpha]_D^{22}$ +67.7 (*c* 1, $CHCl_3$)}; $[\alpha]_D^{13}$ +63.6 (*c* 3.32, hexane); ν_{max} (film): 2957 (s), 2927 (s), 2857 (m), 2179 (w), 1748 (s), 1467 (w), 1371 (m), 1250 (s), 1231 (s), 1019 (m), 845 (s), 761 (m); δ_H ($CDCl_3$): 0.17 (9H, s), 0.88 (3H, t, *J* 6.8), 1.22–1.35 (10H, br), 1.41 (2H, m),1.73 (2H, m), 2.08 (3H, s), 5.38 (1H, t, *J* 6.8); GC–MS [same conditions as those for (±)-**4**]: t_R 14.08 min (99.6%); MS (70 eV, EI): *m*/*z* 282 (1) [M$^+$], 239 (37), 207 (40), 184 (16), 169 (15), 142 (13), 127 (40), 117 (100), 109 (29), 99 (13), 83 (13), 75 (60), 73 (93), 59 (13), 43 (38). HRMS calcd for $C_{16}H_{30}O_2Si$: 282.2015, found: 282.2012. *Properties of (S)-**4***: a colorless oil, n_D^{23}=1.4536; $[\alpha]_D^{23}$ +1.34 (*c* 3.16, $CHCl_3$) {Ref. 12 $[\alpha]_D^{25}$ +1.2 (*c* 1, $CHCl_3$)}; $[\alpha]_D^{14}$ −5.22 (*c* 3.68, hexane). Its IR, ^{1}H NMR, and mass spectra were identical to those of (±)-**4**. HRMS calcd for $C_{13}H_{25}OSi$ [(M−CH_3)$^+$]: 225.1675, found: 225.1675.

4.4. 1-Undecyn-3-ol (6)

4.4.1. (R)-Isomer. Potassium carbonate (11.6 g, 84 mmol) was added to a solution of (*R*)-**5** (9.65 g, 34.2 mmol) in MeOH (150 mL) and water (5 mL). The mixture was stirred for 2.5 h at 33–35 °C, and concentrated in vacuo. The residue was diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 5.21 g (91%) of (*R*)-**6** as a colorless oil, bp 94.0–94.5 °C/4 Torr; n_D^{23}=1.4478; $[\alpha]_D^{14}$ +14.5 (*c* 3.57, Et_2O) {Ref. 7 $[\alpha]_D^{22}$ +14.8 (*c* 1.04, Et_2O)}; ν_{max} (film): 3350 (m), 3311 (s), 2925 (s), 2856 (s), 2116 (w), 1466 (m), 1029 (m), 655 (m), 627 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7.2), 1.20–1.38 (10H, br), 1.40–1.50 (2H, m), 1.64–1.79 (2H, m), 2.00

(1H, br), 2.46 (1H, d, *J* 2); 4.37 (1H, dt *J* 2, 6); GC–MS [same conditions as those for (±)-**4**]: t_R 9.55 min (94.2%); MS (70 eV, EI): *m*/*z* 167 (<1) [$(M-1)^+$], 153 (<1), 121 (11), 107 (21), 97 (24), 93 (44), 83 (44), 79 (64), 71 (55), 70 (72), 57 (70), 55 (100), 43 (69), 41 (65), 39 (22). HRMS calcd for $C_{10}H_{17}O$ [$(M-CH_3)^+$]: 153.1279, found: 153.1274.

4.4.2. (S)-Isomer. Potassium carbonate (7.0 g, 51 mmol) was added to a solution of (*S*)-**4** (8.30 g, 34.6 mmol) in MeOH (150 mL) and water (5 mL). The mixture was stirred at 40 °C for 2 h, and concentrated in vacuo. The residue was worked up in the same manner as described above for (*R*)-**6** to give 4.84 g (83%) of (*S*)-**6** as a colorless oil, bp 97–98 °C/5 Torr; n_D^{23}=1.4478; $[\alpha]_D^{17}$ −14.7 (*c* 3.48, Et_2O) {Ref. 7 $[\alpha]_D^{21}$ −15.0 (*c* 1.02, Et_2O)}. Its IR, ^1H NMR, and mass spectra were identical to those of (*R*)-**6**. GC–MS [same conditions as those for (±)-**4**]: t_R 9.57 min (95.0%). HRMS calcd for $C_{10}H_{17}O$ [$(M-CH_3)^+$]: 153.1279, found: 153.1278.

4.4.3. Enantioselective GC analysis of ***6****.* Instrument: Agilent 7890; column: Chiramix® 30 m×0.25 mm i.d.; carrier gas: He; flow rate: 0.7 mL/min; temp: 40–180 °C (0.7 °C/min); detector: FID; injection port temp: 230 °C; detector temp: 250 °C; t_R 129.56 min [(*S*)-**6**], 131.24 min [(*R*)-**6**]. Synthetic (*R*)-**6**: (*S*)-isomer/(*R*)-isomer=1.29:98.71. Enantiomeric purity=97.4% ee. Synthetic (*S*)-**6**: (*S*)-isomer/(*R*)-isomer=98.73:1.27. Enantiomeric purity=97.5% ee.

4.5. Ethyl 3,4-tridecadienoate (7)

4.5.1. (R)-Isomer. Propanoic acid (0.15 g) was added to a solution of (*R*)-**6** (5.30 g, 31.5 mmol) in triethyl orthoacetate (38 mL), and the solution was stirred and heated at 135 °C for 1 h with distillative removal of EtOH. The mixture was cooled and concentrated in vacuo. The residue was diluted with Et_2O. The Et_2O solution was washed with $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 6.26 g (83%) of (*R*)-**7** as a colorless oil, bp 120–122 °C/4 Torr; n_D^{23}=1.4542; $[\alpha]_D^{16}$ −30.1 (*c* 3.64, Et_2O); ν_{max} (film): 2956 (m), 2926 (s), 2855 (m), 1967 (w), 1741 (s), 1242 (m), 1159 (s), 1040 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.18–1.22 (1H, m), 1.23–1.34 (9H, br), 1.27 (3H, t, *J* 7.2), 1.35–1.45 (2H, m), 1.95–2.02 (2H, m), 3.01 (2H, q, *J* 7.2), 4.15 (2H, q, *J* 7.2), 5.16–5.25 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 13.97 [8.1%, ortho ester (*R*)-**i**], 14.70 min [91.9%, (*R*)-**7**]; MS of (*R*)-**i** (70 eV, EI): *m*/*z* 281 (<1), 239 (2), 139 (2), 117 ($C_6H_{13}O_2^+$, 100), 89 (46), 79 (18), 61 (35), 43 (46); MS of (*R*)-**7** (70 eV, EI): *m*/*z* 238 (10) [M^+], 209 (9), 193 (6), 181 (10), 167 (9), 150 (16), 140 (38), 139 (26), 125 (25), 112 (32), 111 (46), 98 (29), 83 (70), 81 (42), 79 (35), 67 (100), 55 (39), 41 (38). HRMS calcd for $C_{15}H_{26}O_2$: 238.1933, found: 238.1940. This batch of (*R*)-**7** finally yielded (*R*)-**1** with 87.9% ee. When the Claisen rearrangement was executed at 145–150 °C at 1.5 h, the ortho ester (*R*)-**i** almost disappeared, and (*R*)-**7** was obtained in a better purity [(*R*)-**7**/(*R*)-**i**=96.7:1.8]. That batch of (*R*)-**7** finally afforded (*R*)-**1** with 74.7% ee. This indicated that the attempt to force complete conversion of (*R*)-**i** to (*R*)-**7** by raising the reaction temperature caused partial racemization of (*R*)-**7**. Enantiomer separation of **7** by GC was unsuccessful.

4.5.2. (S)-Isomer. In the same manner as described above (*S*)-**6** (3.00 g, 18 mmol) was stirred and heated with triethyl orthoacetate (35 mL) in the presence of propanoic acid (0.12 g) at 110 °C for 7 h to give 3.10 g (72%) of (*S*)-**7** as a colorless oil, bp 124–135 °C/5 Torr; n_D^{23}=1.4540; $[\alpha]_D^{21}$ +29.8 (*c* 3.12, Et_2O). Its IR, ^1H NMR, and mass spectra were identical to those of (*R*)-**7**. GC–MS [same conditions as those for (±)-**4**]: t_R 13.97 [8.3%, (*S*)-**i**], 14.70 min [89.8%, (*S*)-**7**]. HRMS calcd for $C_{15}H_{26}O_2$: 238.1933, found: 238.1940. This batch of (*S*)-**7** finally afforded (*S*)-**1** with 94.4% ee. Racemization of (*S*)-**7** could be avoided at a lower reaction temperature.

4.6. 3,4-Tridecadien-1-ol (8)

4.6.1. (R)-Isomer. A solution of (*R*)-**7** (5.83 g, 24.5 mmol) in dry THF (10 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (1.00 g, 26 mmol) in dry THF (40 mL) at 5–10 °C. The mixture was stirred for 1.5 h at 0–5 °C. The excess $LiAlH_4$ was then destroyed by dropwise addition of water to the stirred and ice-cooled mixture. Subsequently, the mixture was diluted with ice-cooled dil. HCl and NH_4Cl solution, and extracted with Et_2O. The Et_2O solution was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (60 g). Elution with hexane/EtOAc (20:1–10:1) gave 4.71 g (98%) of (*R*)-**8** as a colorless oil, n_D^{23}=1.4716; $[\alpha]_D^{21}$ −62.5 (*c* 3.15, Et_2O) {Ref. 7 $[\alpha]_D^{20}$ −66.3 (*c* 1.17, Et_2O)}; ν_{max} (film): 3332 (m), 2955 (s), 2925 (s), 2854 (s), 1963 (w), 1466 (m), 1050 (m), 874 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.36 (10H, br), 1.36–1.45 (2H, m), 1.68 (1H, br), 1.95–2.02 (2H, m), 2.21–2.30 (2H, m), 3.70 (2H, q-like, *J* 5.6), 5.05–5.20 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 9.51(2.5%), 13.28 min [97.5%, (*R*)-**8**]; MS (70 eV, EI): *m*/*z* 196 (2) [M^+], 178 (2), 166 (4), 153 (3), 135 (3), 124 (5), 121 (6), 109 (7), 107 (8), 98 (81), 97 (50), 83 (37), 81 (45), 80 (44), 79 (61), 69 (56), 68 (100), 67 (92), 55 (60), 41 (63). HRMS calcd for $C_{13}H_{24}O$: 196.1827, found: 196.1823.

4.6.2. (S)-Isomer. In the same manner as described above, 3.10 g (13 mmol) of (*S*)-**7** was treated with 0.60 g (16 mmol) of $LiAlH_4$ in THF (33 mL) to give 2.10 g (82%) of (*S*)-**8** as a colorless oil, n_D^{23}=1.4720; $[\alpha]_D^{21}$ +64.8 (*c* 3.20, Et_2O) {Ref. 7 $[\alpha]_D^{24}$ +66.9 (*c* 1.20, Et_2O)}. Its IR, ^1H NMR, and mass spectra were identical to those of (*R*)-**8**. GC–MS [same conditions as those for (±)-**4**]: t_R 9.52 (0.3%), 13.27 min [99.7%, (*R*)-**8**]. HRMS calcd for $C_{13}H_{24}O$: 196.1827, found: 196.1827.

4.7. 3,4-Tridecadienyl tosylate (9)

4.7.1. (R)-Isomer. Tosyl chloride (5.25 g, 25 mmol) was added portionwise to a stirred and ice-cooled solution of (*R*)-**8** (4.62 g, 23.6 mmol) in dry pyridine (30 mL) containing 4-dimethylaminopyridine (DMAP, 50 mg) at 0–5 °C. The mixture was stirred for 2.5 h at 0–5 °C, poured into ice-water, and extracted with Et_2O. The Et_2O solution was washed with $CuSO_4$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 7.80 g (98%) of (*R*)-**9** as a colorless oil; ν_{max} (film): 2954 (m), 2925 (s), 2854 (m), 1964 (w), 1598 (m), 1364 (s), 1189 (s), 1177 (s), 972 (m), 915 (m), 814 (m), 664 (m), 573 (m), 555 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.40 (12H, br), 1.90–1.98 (2H, m), 2.28–2.35 (2H, m), 2.45 (3H, s), 4.07 (2H, t, *J* 6.8), 4.92–5.06 (1H, m), 5.06–5.62 (1H, m), 7.34 (2H, d, *J* 8.0), 7.79 (2H, d, *J* 8.0). This was employed in the next step without further purification.

4.7.2. (S)-Isomer. In the same manner as described above, 2.00 g (10 mmol) of (*S*)-**8** gave 2.60 g (quant.) of (*S*)-**9** as a colorless oil. Its IR and ^1H NMR spectra were identical to those of (*R*)-**9**. This was employed in the next step without further purification.

4.8. 4,5-Tetradecadienenitrile (10)

4.8.1. (R)-Isomer. Potassium cyanide (2.50 g, 38 mmol) was added to a stirred solution of (*R*)-**9** [7.80 g (crude), 23 mmol] in dry DMSO (35 mL). The mixture was stirred for 4 d under Ar at room temperature, then diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 4.36 g (93%) of (*R*)-**10** as an oil; ν_{max}

(film): 2955 (s), 2925 (s), 2854 (s), 2247 (w), 1964 (w), 1341 (m), 722 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.35 (10H, br), 1.35–1.50 (2H, m), 1.98–2.05 (2H, m), 2.29–2.36 (2H, m), 2.41 (2H, t, *J* 6.8), 5.12–5.20 (1H, m), 5.22–5.30 (1H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 9.52 (4.0%), 11.22 (3.9%), 14.65 [85.4%, (*R*)-**10**], 16.91 (1.4%), 17.00 min (3.1%); MS (70 eV, EI) of (*R*)-**10**: *m*/*z* 205 (<1) [M^+], 204 (3) [$(M-1)^+$], 190 (3), 176 (4), 162 (5), 148 (9), 134 (13), 120 (13), 107 (44), 106 (25), 79 (32), 67 (100), 55 (13), 41 (22). This was employed in the next step without further purification.

4.8.2. (S)-Isomer. In the same manner as described above, 3.62 g (10 mmol) of crude (*S*)-**9** was treated with 1.3 g (20 mmol) of KCN to give 2.08 g (99%) of crude (*S*)-**10** as an oil. Its IR, ^{1}H NMR, and mass spectra were identical to those of (*R*)-**10**. GC–MS [same conditions as those (±)-**4**]: t_R 9.52 (2.0%), 13.26 (1.4%), 14.65 [89.6%, (*S*)-**10**], 16.91 (1.5%), 17.00 min (3.4%).This was employed in the next step without further purification.

4.9. 4,5-Tetradecadienoic acid (11)

4.9.1. (R)-Isomer. An aqueous solution of NaOH [10.0 g (250 mmol) in 15 mL water] was added to a solution of (*R*)-**10** (4.30 g, 21 mmol) in 99% EtOH (50 mL). The mixture was stirred and heated at reflux for 7 h, and concentrated in vacuo. The residue was diluted with water, and extracted with Et_2O to remove neutral impurities. The aqueous layer was acidified with ice and dil. HCl (containing 30 mL of concd HCl), and extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with hexane/EtOAc (25:1) gave 3.54 g (75%) of (*R*)-**11** as a colorless oil; ν_{max} (film): 3200 (m, br), 2956 (s), 2925 (s), 2855 (s), 2669 (m, br), 1964 (w), 1712 (s), 1436 (m), 1278 (m), 1250 (m), 936 (m, br), 875 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.35 (10H, br), 1.35–1.45 (2H, m), 1.92–2.05 (2H, m), 2.26–2.34 (2H, m), 2.47 (2H, t, *J* 6.4), 5.10–5.20 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 15.50 min (99.8%); MS (70 eV, EI): *m*/*z* 224 (<1) [M^+], 126 (100), 111 (6), 93 (16), 84 (41), 81 (68), 67 (31), 55 (19), 41 (24). This was employed in the next step without further purification.

4.9.2. (S)-Isomer. In the same manner as described above, 2.06 g (10 mmol) of (*S*)-**10** afforded 2.00 g (89%) of (*S*)-**11**. Its IR, ^{1}H NMR, and mass spectra were identical to those of (*R*)-**11**. GC–MS [same conditions as those (±)-**4**]: t_R 15.44 min (100%). This was employed in the next step without further purification.

4.10. Methyl 4,5-tetradecadienoate (12)

4.10.1. (R)-Isomer. A solution of (*R*)-**11** (4.20 g, 19 mmol) in Et_2O (20 mL) was treated with CH_2N_2 in Et_2O (prepared from 7.0 g of *N*-nitroso-*N*-methylurea), and the product was purified by distillation to give 3.54 g (78%) of (*R*)-**12** as a colorless oil, bp 105–106 °C/2 Torr; n_D^{23}=1.4620; $[\alpha]_D^{23}$ −62.0 (*c* 3.51, hexane) {Ref. 7 $[\alpha]_D^{22}$ −63.3 (*c* 2.07, hexane)}; ν_{max} (film): 2953 (s), 2925 (vs), 2854 (s), 1963 (w), 1743 (vs), 1437 (m), 1252 (m), 1227 (m), 1200 (m), 1161 (s), 1058 (w), 1032 (w), 996 (w), 875 (m), 721 (w); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.35 (10H, br), 1.35–1.42 (2H, m), 1.92–2.00 (2H, m), 2.25–2.32 (2H, m), 2.43 (2H, t, *J* 6.8), 3.67 (3H, s), 5.13 (2H, quintlike, *J* 4.8); GC–MS [same conditions as those for (±)-**4**]: t_R 14.99 min (99.5%); MS (70 eV, EI): *m*/*z* 238 (4) [M^+], 207 (3), 164 (4), 149 (4), 140 (80), 121 (10), 111 (14), 98 (40), 81 (56), 80 (100), 79 (52), 67 (28), 55 (16), 41 (24). HRMS calcd for $C_{15}H_{26}O_2$: 238.1933, found: 238.1940.

4.10.2. (S)-Isomer. In the same manner as described above, (*S*)-**11** (2.00 g, 8.9 mmol) was treated with CH_2N_2 in Et_2O (prepared from 3.5 g of *N*-nitroso-*N*-methylurea) to give 1.50 g (71%) of (*S*)-**12** as a colorless oil, bp 102–103 °C/1.5 Torr; n_D^{23}=1.4621; $[\alpha]_D^{23}$ +61.7 (*c* 3.66, hexane) {Ref. 7 $[\alpha]_D^{22}$ +63.3 (*c* 2.17, hexane)}. Its IR, ^{1}H NMR, and mass spectra were identical to those of (*R*)-**12**. GC–MS [same conditions as those for (±)-**4**]: t_R 14.98 min (96.9%). HRMS calcd for $C_{15}H_{26}O_2$: 238.1933, found: 238.1944.

4.11. Methyl 2-phenylseleno-4,5-tetradecadienoate (13)

4.11.1. (R)-Isomer employing KN(SiMe$_3$)$_2$. A solution of $KN(SiMe_3)_2$ in toluene (Tokyo Kasei, 0.5 M, 24 mL, 12 mmol) was added dropwise to a stirred and cooled solution of (*R*)-**12** (714 mg, 3 mmol) in dry THF (10 mL) at −78 to −65 °C under Ar. After stirring for 30 min at −78 °C, a dark red solution of PhSeCl (997 mg, 5.2 mmol) in dry THF (10 mL) was added dropwise to the stirred and cooled yellowish solution of the K-enolate of (*R*)-**12** at −78 to −65 °C. The stirring was continued for 1 h at −78 to −70 °C. The reaction was quenched with aqueous NH_4Cl solution, and the mixture was extracted with Et_2O. The Et_2O solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The orange-yellow residual oil was chromatographed over SiO_2 (30 g). Elution with hexane gave Ph_2Se_2 (0.12 g). Further elution with hexane/EtOAc (200:1) furnished 695 mg (59%) of (*R*)-**13** as a yellow oil; ν_{max} (film): 3058 (w), 2952 (s), 2925 (s), 2854 (s), 1962 (w), 1733 (s), 1436 (m), 1251 (m), 1224 (m), 1160 (m), 741 (m), 691 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7.2), 1.20–1.30 (10H, br), 1.30–1.40 (2H, br), 1.90–2.00 (2H, m), 2.40–2.50 (1H, m), 2.52–2.62 (1H, m), 3.62 (3H, s), 3.66–3.72 (1H, m), 5.05–5.15 (2H, m), 7.25–7.35 (3H, m), 7.57–7.62 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 28.06 min (98.6%); MS (70 eV, EI): *m*/*z* 394 (21) [$(M+1)^+$], 295 (100), 293 (48), 237 (12), 177 (17), 157 (36), 137 (16), 121 (21), 107 (19), 95 (29), 93 (25), 91 (28), 79 (52), 77 (36). 67 (24), 53 (35), 44 (28). This was employed in the next step without further purification to give (*R*)-**1** with 74.7% ee.

4.11.2. (R)-Isomer employing LiN(i-Pr)$_2$. A solution of LiN(*i*-Pr)$_2$ in THF was prepared by adding a solution of *n*-BuLi in hexane (1.6 M, 14 mL, 22 mmol) to a stirred and cooled solution of (*i*-Pr)$_2$NH (2.35 g, 3.2 mL, 23 mmol) in dry THF (15 mL) at −78 °C under Ar. The mixture was stirred for 30 min at −78 °C. Subsequently, a solution of (*R*)-**12** (1.428 g, 6 mmol) in dry THF (10 mL) was added dropwise to the stirred and cooled solution of LiN(*i*-Pr)$_2$ at −65 °C. The stirring was continued for 30 min at −65 °C. A solution of PhSeCl (1.15 g, 6 mmol) in dry THF (10 mL) was then added dropwise to the stirred and cooled solution of the Li-enolate at −65 °C. The stirring was continued for 1 h at −65 to −78 °C. The reaction was quenched with aqueous NH_4Cl solution, and the mixture was extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with hexane gave Ph_2Se_2 (0.41 g). Further elution with hexane/EtOAc (200:1 to 25:1) gave a mixture (1.91 g) of (*R*)-**12** and (*R*)-**13**. This was rechromatographed over SiO_2 (35 g). Elution with hexane/EtOAc (200:1) gave 1.15 g (49%) of crude (*R*)-**13** as a yellow oil. GC–MS analysis of this oil revealed it to be a 65.6:33.3 mixture of (*R*)-**13** and (*R*)-**12**. This was employed for the next step, and yielded (*R*)-**1** (87.9% ee) contaminated with (*R*)-**12**.

4.11.3. (S)-Isomer employing LiN(i-Pr)$_2$. In the same manner as described above, 1.50 g (6.3 mmol) of (*S*)-**12** gave 1.65 g (67%) of crude (*S*)-**13**, whose GC–MS analysis revealed it to be a 64.5:33.3 mixture of (*S*)-**13** and (*S*)-**12**. This was employed for the next step, and yielded (*S*)-**1** (94.4% ee) contaminated with (*S*)-**12**.

4.12. Methyl 2,4,5-tetradecatrienoate (1)

*4.12.1. (R)-Isomer from (R)-**13** prepared by employing KN(SiMe$_3$)$_2$.* A solution of (*R*)-**13** (670 mg, 1.7 mmol) in THF(16 mL) was added to

a suspension of $NaIO_4$ (2.14 g, 10 mmol) in water (8 mL), and the mixture was stirred for 2.5 h at room temperature. The mixture became paste-like due to the precipitation of fine crystals of $NaIO_3$. It was then diluted with aqueous Na_2CO_3 solution, and extracted with Et_2O. The Et_2O solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (30 g). Elution with hexane/EtOAc (50:1) gave 297 mg (74%) of (*R*)-**1** as a slightly yellow oil, n_D^{26}=1.5024; $[\alpha]_D^{24}$ −130.3 (*c* 2.23, hexane); ν_{max} (film): 2952 (s), 2925 (s), 2855 (s), 1942 (m), 1721 (s), 1628 (s), 1458 (m), 1436 (m), 1306 (m), 1265 (s), 1240 (s), 1176 (m), 1138 (m), 984 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7), 1.22–1.36 (10H, br), 1.37–1.48 (2H, m), 2.02–2.10 (2H, m), 3.74 (3H, s), 5.44 (1H, q, *J* 6), 5.85 (1H, dd, *J* 0.7, 15), 5.86–5.92 (1H, m), 7.14–7.27 (1H, m); δ_C ($CDCl_3$): 14.1, 22.7, 28.1, 28.9, 29.1, 29.26, 29.35, 31.9, 51.5, 92.9, 93.0, 118.9, 143.0, 167.2, 211.6; GC–MS [same conditions as those for (±)-**4**]: t_R 16.05 min (98.3%); MS (70 eV, EI): *m*/*z* 236 (2) [M^+], 138 (52), 137 (29), 119 (13), 107 (22), 106 (21), 105 (21), 91 (26), 79 (100), 78 (34), 77 (22), 67 (15), 55 (11), 41 (17). HRMS calcd for $C_{15}H_{24}O_2$: 236.1776, found: 236.1775. Enantioselective GC [instrument: Agilent 7890; column: Chiramix® (30 m×0.25 mm i.d.); column temp: 40–180 °C (+0.7 °C/min); carrier gas: He (flow rate, 0.7 mL/min); injection temp: 230 °C; detector temp: 250 °C]: t_R 171.2 [87.37%, (*R*)-**1**], 172.5 min [12.63%, (*S*)-**1**]. Enantiomeric purity of the sample: 74.74 (ca.75)% ee. The specific rotation of pure (*R*)-**1** was therefore calculated as −174. Another experiment gave 884 mg of (*R*)-**1′** with n_D^{21}=1.5074, $[\alpha]_D^{24}$ −122.7 (*c* 3.06, hexane).

*4.12.2. (R)-Isomer from (R)-**13** prepared by employing LiN(i-Pr)$_2$.* Oxidation of crude (*R*)-**13** [(*R*)-**13**/(*R*)-**12**=65.6:33.3] (678 mg) gave impure (*R*)-**1** [(*R*)-**1**/(*R*)-**12**=65.6:33.3] (312.5 mg), $[\alpha]_D^{23}$ −117.1 (*c* 1.09, hexane). Enantioselective GC analysis of this impure (*R*)-**1** showed its enantiomeric purity as 87.9% ee: t_R 187.7 [93.95%, (*R*)-**1**], 189.1 min [6.05%, (*S*)-**1**]. Enantiomers of **12** could not be separated.

*4.12.3. (S)-Isomer from (S)-**13** prepared by employing LiN(i-Pr)$_2$.* Oxidation of crude (*S*)-**13** [(*S*)-**13**/(*S*)-**12**=64.5:33.3] (754 mg) gave impure (*S*)-**1** [(*S*)-**1**/(*S*)-**12**=64.5:33.3] (358.0 mg), $[\alpha]_D^{25}$ −122.8 (*c* 1.75, hexane). Enantioselective GC analysis of this impure (*S*)-**1** revealed its enantiomeric purity as 94.4% ee [(*S*)-**1**/(*R*)-**1**=97.21:2.79]. The allenic ester **1** was unstable and polymerized readily unless it was kept as a hexane solution.

4.13. (*S*)-1-Ethynylnonyl vinyl ether (ii) and its attempted conversion to (*S*)-8

Mercury(II) acetate (1.40 g, 4.4 mmol) was added to a solution of (*S*)-**6** (3.71 g, 22 mmol) in EtOCH=CH_2 (65 mL), and the mixture was stirred for 5 h at room temperature under Ar. It was then mixed with 5% KOH aqueous solution (60 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O. The combined organic solution was washed with water and brine, dried (K_2CO_3), and concentrated in vacuo. The residue was chromatographed over SiO_2 (30 g). Elution with hexane gave 221 mg (5%) of (*S*)-**ii**, and further elution with hexane/EtOAc (10:1) afforded 2.00 g (54%) of the recovered (*S*)-**8**. *Properties of (S)-**ii***: ν_{max} (film): 3311 (m), 2925 (s), 2856 (s), 1638 (m), 1189 (s), 1057 (m), 821 (w); GC–MS [same conditions as those for (±)-**4**]: t_R 10.01 min (73%); MS (70 eV, EI): *m*/*z* 194 (<1) [M^+], 151 (2), 137 (4), 123 (10), 109 (18), 95 (100), 81 (86), 67 (63), 55 (52), 41 (49), 29 (16).

The gold catalyst $[(Ph_3PAu)_3O]BF_4$ (Aldrich, 151 mg, 0.1 mmol, 5 mol % to **ii**) was added to a solution of (*S*)-**ii** (403 mg, 2.08 mmol) in dry CH_2Cl_2 (2 mL). The yellowish solution was stirred for 6.5 h at room temperature under Ar. Then $NaBH_4$ (100 mg, 2.6 mmol) and MeOH (2 mL) were added and the dark colored mixture was stirred for 30 min at room temperature. It was diluted with water, and extracted with Et_2O. The Et_2O solution was washed with water and brine, dried (K_2CO_3), and concentrated in vacuo. The residue was chromatographed over SiO_2 (10 g). Elution with hexane recovered 134 mg (33%) of (*S*)-**ii**. Further elution with hexane/EtOAc (10:1) gave an oil without any IR absorption at 1960–1967 cm^{-1} due to C=C=C, indicating the failure of the reaction.

4.14. 1-Ethynylnonyl methanesulfonate 14

4.14.1. Racemate. Methanesulfonyl chloride (2.30 g, 20 mmol) and DMAP (50 mg, 0.4 mmol) were added to a stirred and ice-cooled solution of (±)-**6** (1.68 g, 10 mmol) in dry C_5H_5N (5 mL). The mixture was stirred for 2 h at 0–5 °C. It was then poured into ice-water, and extracted with hexane. The extract was washed with water, dil. HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The solid residue of crude (±)-**14** (2.09 g, 85%) was recrystallized from EtOAc/hexane to give pure (±)-**14** as colorless rods, mp 44–45 °C (Ref. 26 mp 40–41 °C); ν_{max} (Nujol): 3264 (m), 3020 (w), 2127 (w), 1469 (m), 1348 (s), 1332 (s), 1175 (s), 986 (m), 957 (m), 920 (s), 865 (s); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.21–1.40 (10H, m), 1.45–1.55 (2H, m), 1.82–1.98 (2H, m), 2.70 (1H, d *J* 1.5), 3.13 (3H, s), 5.16 (1H, dt, *J* 1.5, 6.4); GC–MS [same conditions as those for (±)-**4**]: t_R 14.84 min (99.2%); MS (70 eV, EI): *m*/*z* 246 (<1) [M^+], 148 (4), 133 (13), 121 (19), 107 (25), 93 (52), 79 (100), 67 (25), 55 (34), 41 (36). HRMS (FAB, NaI matrix) calcd for $C_{12}H_{22}O_3^{23}NaS$: 269.1187, found: 269.1189.

4.14.2. (S)-Isomer. In the same manner as described above (*S*)-**6** (2.1 g) gave 2.51 g (82%) of (*S*)-**14** as an oil, n_D^{26}=1.4516; $[\alpha]_D^{27}$ −49.4 (*c* 3.26, hexane). Its spectral data were identical to those of (±)-**14**. HRMS (FAB, LiI matrix) calcd for $C_{12}H_{22}O_3LiS$: 253.1450, found: 253.1458.

4.15. *tert*-Butyldimethylsilyl ether (15) of propargyl alcohol

A solution of propargyl alcohol (5.61 g, 100 mmol) in DMF (100 mL) was treated with TBSCl (16.6 g, 110 mmol) and imidazole (16.4 g, 280 mmol) for 4 h at room temperature. Usual work-up and distillation gave 15.8 g (93%) of **15** as a colorless oil, bp 73–74 °C/43 Torr; ν_{max} (film): 3312 (m), 2956 (s), 2931 (s), 2887 (m), 2859 (s), 2121 (w), 1256 (m), 1098 (s), 838 (s), 779 (s).

4.16. (±)-4,5-Tetradecadien-2-yn-1-ol (16)

A solution of *n*-BuLi in hexane (1.6 M, 8.25 mL, 13.2 mmol) was added dropwise to a stirred and cooled mixture of **15** (2.04 g, 12 mmol) and $CuBr\cdot Me_2S$ (246 mg, 1.2 mmol) in dry THF (30 mL) at −78 °C under Ar. The mixture was stirred for 30 min at −78 °C to give a clear and light-yellow solution. Subsequently, a solution of (±)-**14** (1.476 g, 66 mmol) in dry THF (10 mL) was added dropwise to the mixture, and the resulting clear and yellow-colored solution was stirred for 2 h at −78 °C. It was then quenched by the addition of NH_4Cl solution, and extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 2.82 g of a mixture of (±)-**16** and excess **15**. This was dissolved in MeCN (50 mL). Hydrofluoric acid (46% HF in H_2O, 3 mL) was added to the stirred solution and the stirring was continued for 45 min at room temperature. The mixture was diluted with ice-water, and extracted with hexane. The extract was washed with $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give an oil (1.34 g).This was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (100:1 to 10:1) gave 1.10 g (89%) of (±)-**16** as a colorless oil, n_D^{26}=1.5058; ν_{max} (film): 3331 (m), 2955 (s), 2925 (s), 2855 (s), 2220 (w), 1950 (m), 1265 (m), 1015 (s), 865 (m), 724 (m), δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.21–1.40 (10H, br), 1.40–1.50 (2H, m), 1.66 (1H, br), 2.02–2.10 (2H, m), 4.37 (2H, s), 5.36

(1H, m), 5.42 (1H, dt, *J* 6.8, 6.4); GC–MS [same conditions as those for (±)-**4**]: t_R 15.47 min (99.1%); MS (70 eV, EI): *m*/*z* 206 (<1) [M^+], 131 (4), 124 (5), 117 (5), 108 (35), 107 (34), 103 (6), 91 (26), 79 (100), 77 (33), 67 (12), 55 (9), 41 (17). HRMS calcd for $C_{14}H_{22}O$: 206.1671, found: 206.1674.

When (*S*)-**14** was employed, an oily **16**, $[\alpha]_D^{20}$ −0.33 (*c* 3.29, hexane), was obtained.

4.17. (±)-2,4,5-Tetradecatrien-1-ol (17)

A solution of (±)-**16** (1.00 g, 4.9 mmol) in dry THF (5 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (250 mg, 6.6 mmol) in dry THF (10 mL). The mixture was stirred for 2.5 h at room temperature. The excess $LiAlH_4$ was then destroyed by adding water with ice-cooling. The mixture was acidified with dil. HCl/NH_4Cl solution, and extracted with Et_2O. The extract was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (10:1) gave (±)-**17** (0.51 g, 50%) as a colorless oil, n_D^{26}=1.5060; ν_{max} (film): 3338 (m), 2955 (s), 2925 (s), 2854 (s), 1946 (w), 1643 (w), 1465 (m), 1097 (w), 1004 (w), 967 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.35 (10H, br), 1.35–1.45 (2H, m), 1.90–2.05 (3H, m), 4.16 (2H, d, *J* 6), 5.30–5.35 (1H, m), 5.73–5.83 (2H, m), 6.04–6.11 (1H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 15.09 min (95.2%); MS (70 eV, EI): *m*/*z* 208 (1) [M^+], 190 (12), 133 (12), 124 (8), 119 (15), 110 (57), 105 (36), 96 (20), 95 (55), 91 (98), 82 (92), 81 (75), 79 (100), 67 (88), 55 (62), 41 (55). HRMS calcd for $C_{14}H_{24}O$: 208.1827, found: 208.1823.

When (*S*)-**14** was employed as the starting material, an oily **17**, $[\alpha]_D^{27}$ −0.10 (*c* 1.60, hexane), was obtained.

4.18. (±)-2,4,5-Tetradecatrienal (18)

Dess–Martin periodinane (933 mg, 2.2 mmol) was added portionwise to a stirred and ice-cooled solution of (±)-**17** (312 mg, 1.5 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. The homogeneous solution was stirred for 45 min at room temperature to give a suspension of colorless crystals of *o*-iodobenzoic acid. The reaction was quenched by adding a solution of $NaHCO_3$ and $Na_2S_2O_3$, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (10 g). Elution with hexane/EtOAc (50:1) gave 185 mg (60%) of (±)-**18** as a slightly yellowish oil; ν_{max} (film): 2955 (s), 2925 (s), 2855 (s), 2719 (w), 2208 (w), 1940 (m), 1685 (s), 1607 (m), 1465 (m), 1150 (m), 1132 (m), 972 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7.2), 1.20–1.40 (10H, br), 1.40–1.50 (2H, m), 2.08–2.15 (2H, m), 5.42–5.53 (1H, dt, *J* 6, 6), 6.00–6.06 (1H, m), 6.15 (1H, dd, *J* 8, 15), 7.02 (1H, dd, *J* 8, 15), 9.52 (1H, d, *J* 8); GC–MS [same conditions as those for (±)-**4**]: t_R 14.97 min (91.9%); MS (70 eV, EI): *m*/*z* 206 (9) [M^+], 177 (2), 163 (3), 149 (5), 135 (6), 121 (15), 108 (66), 107 (64), 91 (23), 79 (100), 67 (18), 55 (14), 41 (25). This was employed in the next step without further purification.

4.19. (±)-Methyl 2,4,5-tetradecatrienoate (1)

A mixture of (±)-**18** (180 mg, 0.9 mmol), MnO_2 [Aldrich (217646, activated), 1.5 g], KCN (300 mg, 4.6 mmol), and AcOH (150 mg, 2.5 mmol) in MeOH (8 mL) was stirred for 4 h at room temperature. It was then filtered through Celite, and the Celite layer was washed with Et_2O. The combined filtrate and washings were concentrated in vacuo. The residue was diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (10 g). Elution with hexane/EtOAc (50:1) gave 142 mg (79%) of (±)-**1** as a slightly yellowish oil, n_D^{28}=1.4994. Its IR, ^1H NMR, and mass spectra were identical with those of (*R*)-**1**;GC–MS [same conditions as those for (±)-**4**]: t_R 11.95 (7.6%, unidentified impurity), 16.03 min [89.5%, (±)-**1**]. HRMS calcd for $C_{15}H_{24}O_2$: 236.1776, found: 236.1775.

When (*S*)-**14** was employed as the starting material, an oily **1**, $[\alpha]_D^{27}$ −0.12 (*c* 1.35, hexane), was obtained, indicating racemization in the course of the synthesis, particularly at the stage of conversion of (*S*)-**14** to (*R*)-**16**.

4.20. (±)-1-Iodo-1,2-undecadiene (19)

Sodium iodide (5.01 g, 33 mmol) was added to a stirred solution of (±)-**14** (4.30 g, 17.5 mmol) in DMF (30 mL). The mixture was stirred and heated at 50 °C for 1.5 h. The initial homogeneous solution turned to a suspension of solid NaOMs. It was cooled, 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 4.09 g (86%) of (±)-**19** as a slightly yellowish oil, bp 107–109 °C/4 Torr; n_D^{23}=1.5044; ν_{max} (film): 3038 (w), 2954 (s), 2925 (s), 2854 (s), 1944 (w), 1464 (m), 1377 (w), 1165 (m), 1103 (w), 835 (w), 601 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.38 (10H, br), 1.40–1.51 (2H, m), 2.05–2.15 (2H, m), 5.09 (1H, dd, *J* 6.8, 12), 5.65–5.68 (1H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 13.12 min (88.0%); MS (70 eV, EI): *m*/*z* 278 (<1) [M^+], 180 (100), 124 (5), 109 (4), 95 (17), 81 (21), 67 (19), 55 (15), 41 (18). HRMS calcd for $C_{11}H_{19}I$: 278.0531, found: 278.0531.

4.21. 1-Iodo-1-heptyne (22)

Iodine (35.7 g, 140.6 mmol) was dissolved in stirred and warmed benzene (350 mL) at 40 °C. A solution of morpholine (35 mL, 402 mmol) in benzene (45 mL) was added dropwise to the above iodine solution with stirring to generate dark orange-colored iodine–morpholine complex. After 10 min, a solution of **21** (9.01 g, 93.9 mmol) in benzene (10 mL) was added to the mixture, and stirring was continued for 21 h at 45 °C. After cooling, the precipitated morpholine hydroiodide was removed by filtration through a glass filter under suction. The filter-cake was washed with Et_2O (50 mL×3). The combined filtrate and washings were washed successively with $Na_2S_2O_3$ solution, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 16.04 g (79%) of **22** as a colorless oil, bp 53–54 °C/2 Torr; n_D^{28}=1.5088; ν_{max} (film): 2956 (s), 2931 (s), 2859 (s), 2186 (w), 1465 (m), 1427 (m), 1378 (m), 728 (m); δ_H ($CDCl_3$): 0.90 (3H, t, *J* 6.8), 1.28–1.40 (4H, m), 1.52 (2H, quint-like, *J* 7.2), 2.35 (2H, t, *J* 7.2); GC–MS [same conditions as those for (±)-**4**]: t_R 7.10 min (99.6%); MS (70 eV, EI): *m*/*z* 222 (48) [M^+], 165 (54), 95 (100), 67 (79), 55 (62), 41 (41). HRMS calcd for $C_7H_{11}I$: 221.9905, found: 221.9905.

4.22. (*Z*)-1-Iodo-1-heptene (23)

4.22.1. Reduction with diimide. To a stirred and ice-cooled mixture of **22** (8.0 g, 36 mmol), yellow-colored $KO_2CN{=}NCO_2K$ (14.9 g, 72 mmol), C_5H_5N (17 mL), and MeOH (50 mL), AcOH (9.0 mL, 158 mmol) was added dropwise over 2 h at 5–10 °C. The mixture was stirred for 4 h at room temperature. An additional amount (12.0 g, 62 mmol) of $KO_2CN{=}NCO_2K$ (*CAUTION*. This reagent once exploded when stored in a refrigerator.) was added to the mixture. AcOH (7.2 mL, 126 mmol) was then added dropwise to the mixture, and the stirring was continued overnight. The reaction was quenched by acidification with 5% HCl (70 mL) and the mixture was extracted with pentane. The extract was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated by fractional distillation using a Vigreux column under atmospheric pressure. The residue was dissolved in Et_2O (50 mL). A 50% aqueous solution (15 mL) of Me_2NH was added to the Et_2O solution, and the mixture was stirred for 5 h at room temperature. It was then

washed with water, 5% HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated by fractional distillation (Vigreux column) under atmospheric pressure. The residue was distilled to give 5.43 g (67%) of (*Z*)-**23** as an oil, bp 47–48 °C/3 Torr; n_D^{27}=1.5005; ν_{max} (film): 3067 (w), 2956 (s), 2856 (s), 1608 (m), 1296 (m), 1277 (s), 1233 (m), 688 (s), 627 (m), ; δ_H ($CDCl_3$): 0.90 (3H, t, *J* 7.2), 1.25–1.38 (4H, m), 1.43 (2H, quint-like, *J* 7.8), 2.10–2.17 (2H, m), 6.13–6.20 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 6.65 [89.6%, (*Z*)-**23**], 6.86 [2.9%, (*E*)-**23**], 7.07 (6.6%, **22**), 7.23 min (0.9%, **24**); MS of (*Z*)-**23** (70 eV, EI): *m*/*z* 224 (88) [M^+], 167 (21), 154 (49), 127 (5), 97 (26), 55 (100), 41 (40). HRMS calcd for $C_7H_{13}I$: 224.0062, found: 224.0059. Without treatment with Me_2NH, the product contained ca. 10% of **24**.

4.22.2. Reduction via hydroboration-protonolysis. Borane-dimethyl sulfide complex (4.25 mL, 5.47 g, 72 mmol) was added dropwise to a stirred and ice-cooled solution of cyclohexene (11.8 g, 144 mmol) in dry THF (70 mL) at 0–5 °C to give colorless crystals of dicyclohexylborane. A solution of **22** (8.0 g, 36 mmol) in THF (10 mL) was added dropwise to the stirred and ice-cooled suspension of dicyclohexylborane, and the mixture was stirred at 0–5 °C for 30 min, and for 1.5 h at room temperature to give a homogeneous solution. AcOH (10 mL) was then added dropwise, and the mixture was stirred at 50 °C for 30 min. It was cooled, poured into ice and NaOH aqueous solution (2 M, 200 mL), and extracted with pentane. The pentane solution was washed with water and brine, dried ($MgSO_4$), and concentrated by fractional distillation (Vigreux column) under atmospheric pressure. The residue was distilled to give 4.57 g (57%) of (*Z*)-**23** as a colorless oil, bp 52–56 °C/5 Torr; n_D^{27}=1.5001. A substantial amount of high bp oil resulting from dicyclohexylborane remained in the distillation flask. The spectral data (IR, ^1H NMR, and MS) of (*Z*)-**23** was identical to those of (*Z*)-**23** obtained by diimide reduction except that the present sample contained neither **21** nor **24**. GC–MS [same conditions as those for (±)-**4**]: t_R 6.64 [90.2%, (*Z*)-**23**], 6.91 min [2.5%, (*E*)-**23**]. The product contained several unidentified impurities at t_R=3.6 (0.7%), 6.3 (4.3%), 9.0 (0.3%), 9.8 (0.5%), 10.2 (1.1%), and 10.4 min (0.4%).

4.23. Methyl (2*E*,4*Z*)-2,4-decadienoate (2) via Heck reaction

Palladium(II) acetate (136 mg, 0.6 mmol) was added to a mixture of **20** (8.66 g, 100 mmol), (*Z*)-**23** (2.24 g, 10 mmol), K_2CO_3 (2.77 g, 20 mmol), and $(n\text{-Bu})_4NCl$ (2.21 g, 8 mmol) in DMF (40 mL). The mixture was vigorously stirred under argon for 1 h at room temperature. The reaction was slightly exothermic, and the initially yellow-colored mixture turned brown after 1 h. It was diluted with Et_2O (50 mL), and filtered through Celite. The filter-cake was washed with Et_2O. The combined Et_2O solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (30 g). Elution with hexane gave the recovered **23** (0.31 g). Further elution with hexane/EtOAc (50:1) furnished 1.27 g (75% or 82% based on the consumed **23**) of **2** as a colorless oil, n_D^{27}=1.4825; ν_{max} (film): 3011 (w), 2954 (s), 2929 (s), 2858 (m), 1721 (vs), 1639 (s), 1605 (w), 1435 (m), 1308 (m), 1269 (vs), 1172 (s), 1140 (s), 998 (m), 869 (m); δ_H ($CDCl_3$): 0.89 (3H, t, *J* 7.2), 1.25–1.35 (4H, m), 1.38–1.47 (2H, quint-like, *J* 7.2), 2.30 (2H, q-like, *J* 7.2), 3.75 (3H, s), 5.85–5.92 (2H, m), 6.08–6.18 (1H, q-like *J* 9), 7.58–7.66 (1H, m); δ_C ($CDCl_3$): 14.0, 22.5, 28.3, 29.1, 31.4, 51.1, 120.7, 126.4, 139.8, 141.9, 167.8; GC–MS [same conditions as those for (±)-**4**]: t_R 10.75 [3.1%, (2*Z*,4*Z*)-**2**], 10.98 [82.1%, (2*E*,4*Z*)-**2**], 11.02 [3.9% (2*Z*,4*E*)-**2**], 11.38 min [12.8%, (2*E*,4*E*)-**2**]; MS of (2*E*,4*Z*)-**2** (70 eV, EI): *m*/*z* 182 (20) [M^+], 151 (9), 139 (7), 122 (6), 111 (100), 97 (9), 93 (9), 81 (29), 79 (24), 67 (18), 55 (10), 41 (13). HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1306.

The isomeric ratio of the four isomers of **2** fluctuates. Even when the reaction was stopped after 30 min, the product was a mixture of (2*Z*,4*Z*)-**2** (2.1%), (2*E*,4*Z*)-**2** (68.9%),(2*Z*,4*E*)-**2** (3.1%), and (2*E*,4*E*)-**2** (25.6%).When the reaction was continued for 3 h, the product was a mixture of (2*Z*,4*Z*)-**2** (2.7%), (2*E*,4*Z*)-**2** (65.0%), (2*Z*,4*E*)-**2** (2.6%), and (2*E*,4*E*)-**2** (24.9%). Pd(0) equilibrates (2*E*,4*Z*)-**2** to give 2.6–2.7:1 ratio of (2*E*,4*Z*)-**2** nd (2*E*,4*E*)-**2**.

4.24. Methyl (*E*)-2-decen-4-ynoate (25)

A mixture of K_2CO_3 (10.35 g, 75 mmol), $(n\text{-Bu})_4NCl$ (8.34 g, 30 mmol), and **20** (27 mL, 25.9 g, 301 mmol) in DMF (5 mL) was stirred for 10 min at room temperature to dissolve $(n\text{-Bu})_4NCl$. Then $Pd(OAc)_2$ (330 mg, 1.47 mmol) was added to the mixture, which was stirred for 5 min under Ar to give a yellow suspension. A solution of **22** (8.30 g, 37 mmol) in DMF (20 mL) was added dropwise over 10 min to the stirred mixture under Ar at room temperature. The reaction was exothermic, and the mixture turned dark brown in color. Stirring was continued for 4.5 h at room temperature. It was then worked up in the same manner as described for **2**, and the residue (8.30 g) was chromatographed over SiO_2 (70 g). Elution with hexane and hexane/EtOAc (50:1) gave 3.16 g (47%) of **25**, which was distilled to give pure **25** (1.93 g, 29%), bp 98–99 °C/3 Torr; n_D^{27}=1.4864; ν_{max} (film): 2956 (s), 2933 (s), 2860 (m), 2215 (m), 1727 (s), 1621 (m), 1459 (m), 1434 (m), 1304 (s), 1267 (m), 1158 (s), 962 (m), 860 (w); δ_H ($CDCl_3$): 0.91 (3H, t, *J* 7.2), 1.28–1.42 (4H, m), 1.50–1.60 (2H, quint-like, *J* 6.8), 2.37 (2H, dt, *J* 1.6, 7.2), 3.75 (3H, s), 6.15 (1H, d, *J* 16), 6.76 (1H, dt, *J* 16, 2.4); GC–MS [same conditions as for (±)-**4**]: t_R 11.24 min (97.3%) (After distillation, an unidentified compound was detected at t_R 13.03 min, and the purity dropped to 87.9% with 10.9% of the unknown compound.); MS (70 eV, EI): *m*/*z* 180 (3) [M^+], 179 (3), 165 (74), 149 (60), 137 (46), 134 (43), 121 (60), 120 (45), 119 (59), 109 (63), 105 (83), 93 (63), 92 (59), 91 (89), 79 (100), 63 (47), 55 (38), 41 (36). HRMS calcd for $C_{11}H_{16}O_2$: 180.1150, found: 180.1153.

4.25. Methyl (2*E*,4*Z*)-2,4-decadienoate (2) via hydroboration-protonolysis

Borane-dimethyl sulfide complex (1.2 mL, 1.52 g, 20 mmol) was added dropwise to a stirred and ice-cooled solution of cyclohexene (3.28 g, 40 mmol) in dry THF (20 mL) at 0–5 °C under Ar. Stirring was continued for 30 min at 0–5 °C to give colorless crystals of dicyclohexylborane. A solution of **25** (1.84 g, 10.2 mmol) in dry THF (5 mL) was added dropwise to the stirred and ice-cooled suspension of dicyclohexylborane, and the mixture was stirred for 30 min at 0–5 °C and for 2 h at room temperature to give a homogeneous solution. AcOH (3 mL) was then added dropwise, and the mixture was stirred and heated at 50 °C for 140 min. It was cooled, poured into ice and K_2CO_3 (13 g) in water (100 mL), and extracted with hexane. The hexane solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (4.82 g) was chromatographed over SiO_2 (60 g). Elution with hexane/EtOAc (50:1) gave 1.68 g (90%) of crude **2**. This was distilled to furnish 427 mg (23%) of pure **2** as a colorless oil, bp 99–100 °C/5 Torr; n_D^{27}=1.4834. Its IR, ^1H and ^{13}C NMR, and mass spectra were identical to those of **2** prepared from **23** and **20**. GC–MS [same conditions as those for (±)-**4**]: t_R 10.38 (7.41%, dicyclohexyl ether), 10.98 [82.81%, (2*E*,4*Z*)-**2**], 11.38 [1.38%, (2*E*,4*E*)-**2**], 12.04 min [2.20%, unidentified]. (2*E*,4*Z*)-**2**/(2*E*,4*E*)-**2**=98.3:1.7.

4.26. (±)-Methyl 3,4-decadienoate (27)

Propanoic acid (0.30 g) was added to a solution of (±)-**26** (12.6 g, 100 mmol) in methyl orthoacetate (100 g, 833 mmol), and the mixture was stirred and heated at 145 °C (bath temperature) for 1.5 h with distillative removal of the low bp materials (<100 °C) through a Vigreux column to give a mixture of a mixed

ortho ester containing (±)-**26** and the allenic ester (±)-**27**. After cooling, the mixture was concentrated in vacuo. The residue (ca. 30 g) was dissolved in *o*-xylene (150 mL) containing 0.30 g of propanoic acid. The mixture was stirred and heated at 160–170 °C (bath temperature) for 2 h with removal of low bp materials through a Vigreux column. After cooling, the mixture was concentrated in vacuo. The residue was distilled to give 13.1 g-15.8 g (72–87%) of (±)-**27** as a colorless oil, bp 136–138 °C/41 Torr or 87–90 °C/3 Torr; n_D^{21}=1.4596; ν_{max} (film): 2929 (s), 2857 (m), 1966 (w), 1744 (vs), 1437 (m), 1334 (m), 1248 (m), 1164 (s), 1027 (w), 872 (m), 728 (w); δ_H ($CDCl_3$): 0.89 (3H, t, *J* 7.2), 1.26–1.36 (4H, br m), 1.36–1.50 (2H, m), 1.96–2.08 (2H, m), 3.01–3.05 (2H, m), 3.70 (3H, s), 5.14–5.26 (2H, m); GC–MS [same conditions as those for (±)-**4**]: t_R 10.31 min (96.8%); MS (70 eV, EI): *m*/*z* 182 (4) [M^+], 167 (4), 151 (3), 139 (6), 126 (54), 125 (29), 111 (31), 97 (100), 84 (93), 79 (47), 67 (83), 59 (30), 41 (29). HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1305.

4.27. Methyl (2*E*,4*Z*)-2,4-decadienoate (2) via isomerization of (±)-27

Aluminum oxide (Aldrich 199443, basic Brockmann 1, 30 g) was placed in a 300 mL round-bottomed flask, and heated at 200 °C (bath temperature) for 2 h under reduced pressure (5 Torr). After cooling, a solution of (±)-**27** (9.20 g, 51 mmol) in *o*-xylene (60 mL) was added to Al_2O_3, and the mixture was vigorously stirred and heated at 160 °C (bath temperature) for 2 h under argon. Vigorous stirring was essential to convert (±)-**27** to **2** within 2 h at 160 °C. After cooling, the mixture was filtered through a glass filter, and Al_2O_3 was washed with EtOAc (50 mL). The combined filtrate and washings were concentrated in vacuo. The residue was distilled to give 5.06 g (55%) of **2** as a colorless oil, bp 80–82 °C/2–3 Torr or 93–96 °C/5 Torr; n_D^{21}=1.4902. Its IR, ^{1}H NMR, and mass spectra were identical to those of **2** prepared by other routes. GC–MS [same conditions as those for (±)-**4**]: t_R 10.75 [1.1%, (2*Z*,4*Z*)-**2**], 10.99 [85.9%, (2*E*,4*Z*)-**2**], 11.03 [5.7%, (2*Z*,4*E*)-**2**], 11.38 min [7.3%, (2*E*,4*E*)-**2**]. In other experiments, the isomeric ratios were 0.4:86.4:5.3:7.9 and 1.3:83.3:8.7:6.7%.

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