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Pheromone synthesis. Part 240: Cross-metathesis with Grubbs I (but not Grubbs II) catalyst for the synthesis of (*R*)-trogodermal (14-methyl-8-hexadecenal) to study the optical rotatory powers of compounds with a terminal *sec*-butyl group☆

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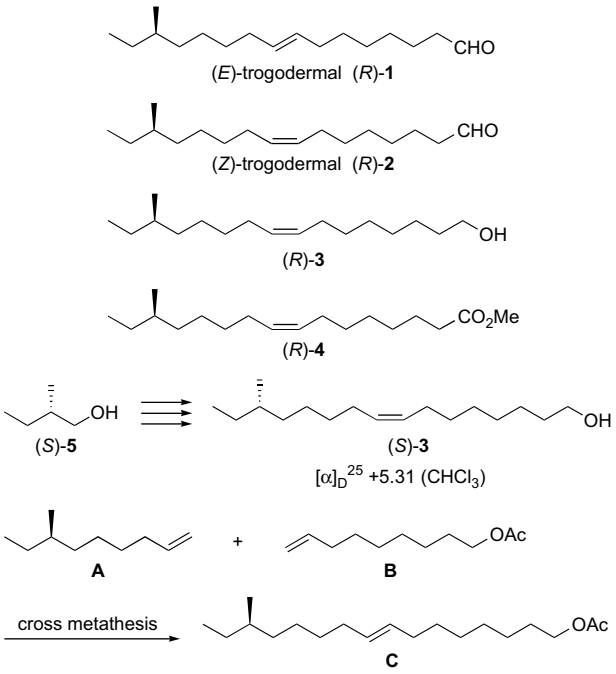
ABSTRACT

(*R*)-Trogodermal (14-methyl-8-hexadecenal), the sex pheromone of *Trogoderma* species of pest insects against stored products, and its (*S*)-isomer were synthesized by using olefin cross-metathesis between (*R*)- or (*S*)-7-methyl-1-nonene and 8-nonenyl acetate as the key step. This step was successful with Grubbs I but not with Grubbs II catalyst. The latter caused randomization of the carbon skeleton to give a mixture of abnormal products with both longer or shorter carbon chains than the desired product. The specific rotations of 18 newly and 6 previously synthesized compounds with a terminal *sec*-butyl group were measured to conclude them to be $[\alpha]_D$ +3.5 to +6.5 or −3.6 to −6.4.

1. Introduction

Trogoderma species of insects are notorious pests of stored products. They use (*E*)-trogodermal and/or its (*Z*)-isomer [(*R*)-**1** and (*R*)-**2**, Scheme 1] as their female-produced sex pheromone.[2] At the early stage of the pheromone isolation in 1969, the alcohol **3** and the methyl ester **4**, both derived from **2**, were erroneously identified as the pheromone candidates.[3] The absolute configuration of the levorotatory **3** and **4** of insect origin was determined as *R* by synthesizing dextrorotatory (*S*)-**3** from the known (*S*)-2-methyl-1-butanol (**5**).[4,5]

Although these two pheromone aldehydes (*R*)-**1** and (*R*)-**2** as well as their enantiomers have been synthesized repeatedly by us[6–8] and also by others,[9–11] it is worthwhile to achieve a simple synthesis of (*R*)-trogodermal (**1**) by olefin cross-metathesis reaction (**A**+**B**→**C**) as shown in Scheme 1. Olefin cross-metathesis[12–14] has been employed advantageously in the synthesis of olefinic pheromones,[15] including aliphatic pheromones with methyl-branchings.[1,16] This paper describes the successful execution of the above-mentioned step (**A**+**B**→**C**) as assisted by Grubbs I (not by Grubbs II) catalyst, leading to a new synthesis of (*R*)-trogodermal.



Scheme 1. Structures of trogodermal and related compounds.

☆ Pheromone synthesis, Part 240. For part 239, see Ref. 1.

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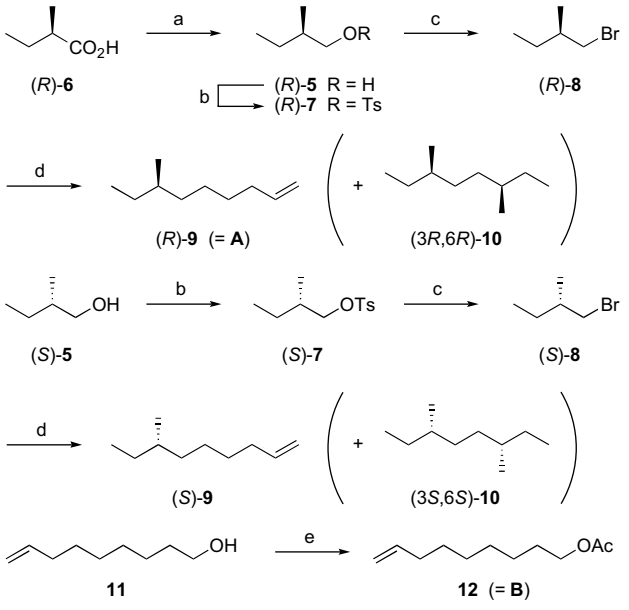
Another important issue discussed in the present paper concerns with the magnitude of specific rotations of compounds with a terminal *sec*-butyl group like trogodermal. As shown in Scheme 1, the specific rotation of (*S*)-**3** was reported as +5.31 in chloroform by myself.[4,5] Others also reported similar values.[6–11] Recently in 2008, however, there was a criticism against this value by an eminent chemist insisting that the value +5.31 was too large and could not happen to be so, because no strongly absorbing chromophore was present in (*S*)-**3**. I therefore decided to synthesize a number of derivatives related to **3** so as to measure their specific rotations.

For many years I have been interested in the relationship between structure and optical rotatory power. The prevailing thought in 1950s was expressed by Shriner, Adams, and Marvel as 'No deductions concerning the molecular rotation of a molecule can be drawn from a knowledge of its structure.'[17] This situation remained unchanged until recent days, despite much efforts to solve the problem.[18,19] The situation has changed, however, due to very recent progress in calculation of optical rotatory power by means of time-dependent density functional theory.[20] It is now possible to calculate the sign of rotation of a certain molecule, although exact prediction is still difficult as to the magnitude of rotation at a given wavelength.[21,22] Accordingly, it is worthwhile to prepare a number of derivatives related to **3** and measure their optical rotations.

2. Results and discussion

2.1. Synthesis of the enantiomers of 7-methyl-1-nonene (9) and 8-nonenyl acetate (12), the metathesis partners

Scheme 2 summarizes the synthesis of (*R*)- and (*S*)-7-methyl-1-nonene (**9**) and 8-nonenyl acetate (**12**), the partners for cross-metathesis reaction. Synthesis of (*R*)-**9** started from (*R*)-2-methylbutanoic acid (**6**, T. Hasegawa Co., >99.0% ee), which was prepared by treating (±)-**6** with *Pseudomonas* sp. TH-252-1.[23] Reduction of (*R*)-**6** with lithium aluminum hydride afforded (*R*)-**5**, whose tosylate (*R*)-**7** was treated with lithium bromide in DMF to give (*R*)-2-methylbutyl bromide (**8**) in 63% overall yield (three steps).

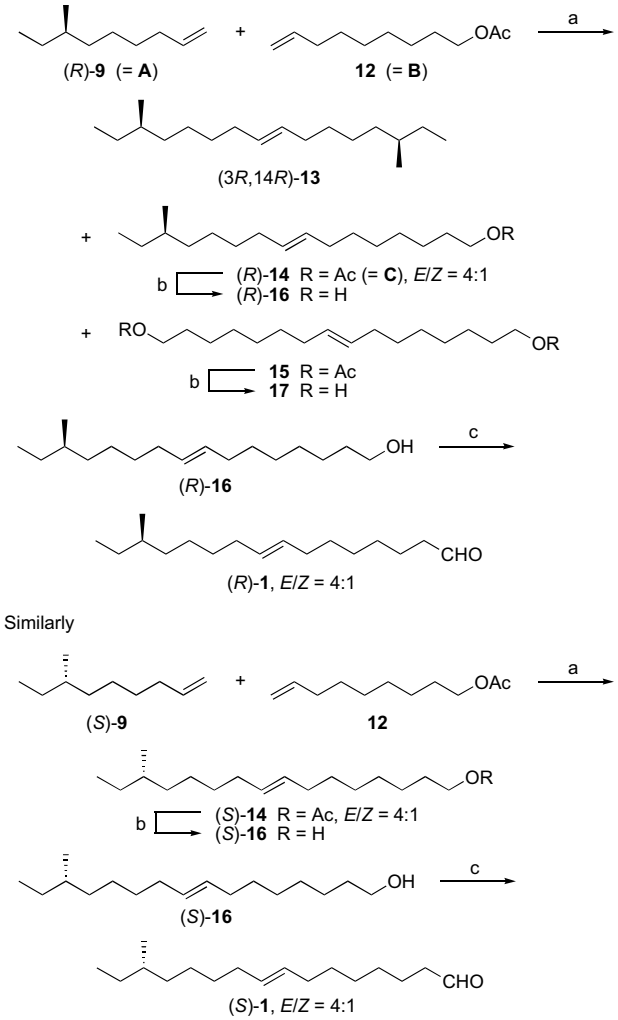


Scheme 2. Synthesis of the enantiomers of 7-methyl-1-nonene (**9**) and 8-nonenyl acetate (**12**), the metathesis partners. Reagents: (a) $LiAlH_4$, Et_2O (quant.); (b) TsCl, C_5H_5N [86% for (*R*)-**7**: quant. for (*S*)-**7**]; (c) LiBr, DMF [63% for (*R*)-**8** based on (*R*)-**6**, three steps; 78% for (*S*)-**8** based on (*S*)-**5**, two steps]; (d) (i) Mg, THF; (ii) $H_2C{=}CH(CH_2)_3OTs$, THF, Li_2CuCl_4 [56% of (*R*)-**9** based on (*R*)-**8**; 58% of (*S*)-**9** based on (*S*)-**8**]; (e) Ac_2O, C_5H_5N (quant.).

Treatment of (*R*)-**8** with magnesium in THF furnished the corresponding Grignard reagent, which was added to a cooled solution of 4-pentenyl tosylate in THF. Subsequent addition of dilithium tetrachlorocuprate according to Schlosser and Fouquet[24] afforded (*R*)-**9** contaminated with 11% of (3*R*,6*R*)-**10** generated by the self-coupling of (*R*)-**8** in the course of the preparation of the Grignard reagent. Since complete removal of (3*R*,6*R*)-**10** from (*R*)-**9** was difficult, the obtained mixture was used directly for the metathesis reaction. Synthesis of (*S*)-**9** was executed in the same manner, starting from commercially available (*S*)-2-methyl-1-butanol (**5**). 8-Nonenyl acetate (**12**), another partner of the cross-metathesis, was prepared by conventional acetylation of commercially available 8-nonen-1-ol (**11**).

2.2. Synthesis of trogodermal (1) by cross-metathesis

Cross-metathesis between each of the enantiomers of 7-methyl-1-nonene (**9**) and 8-nonenyl acetate (**12**) was achieved by using Grubbs' first generation catalyst [Grubbs I, $(Cy_3P)_2Ru(=CHPh)Cl_2$, Scheme 3].[13,14] A mixture of (*R*)-**9**, **12** and Grubbs I catalyst (molar ratio=121:86:1) in dichloromethane was stirred and heated under reflux for 5 h under argon, and the product was purified by silica gel chromatography to give (3*R*,14*R*)-**13** first, and then the desired (*R*)-**14** in 56% yield based on (*R*)-**9** or 80% yield based on **12**. Finally, a small amount of **15**, the homocoupling product of **12**, was also



Scheme 3. Synthesis of the enantiomers of trogodermal (**1**). Reagents: (a) **9** (17 mmol), **12** (12 mmol), Grubbs I [$(Cy_3P)_2Ru(=CHPh)Cl_2$, 0.14 mmol], CH_2Cl_2, reflux, 6 h [56% of (*R*)-**14** based on (*R*)-**9**; 47% of (*S*)-**14** based on (*S*)-**9**]; (b) NaOH, aq MeOH [62% for (*R*)-**16**; 67% for (*S*)-**16**]; (c) PCC ($CrO_3{\cdot}C_5H_5N{\cdot}HCl$), SiO_2, CH_2Cl_2 [88% for (*R*)-**1**: 91% for (*S*)-**1**].

obtained. Its basic hydrolysis gave crystalline diol (*E*)-**17**, mp 57.5–58.0 °C.

The obtained crude (*R*)-**14** was a mixture of (*R*,*E*)-**14** (71.7%), (*R*,*Z*)-**14** (14.7%) and **15** (13.6%) as estimated by GC–MS. Alkaline hydrolysis of the crude (*R*)-**14** followed by chromatographic purification gave (*R*)-**16** as an *E*/*Z* mixture. Its specific rotation was $[\alpha]_D^{24}$ −5.98 (*c* 4.24, $CHCl_3$). Similarly, (*S*)-**16** was synthesized from (*S*)-**9** and **12** via (*S*)-**14**, and its specific rotation was $[\alpha]_D^{21}$ +5.89 (*c* 4.83, $CHCl_3$). These values were in good accord with the previous value, $[\alpha]_D^{25}$ +5.31 (*c* 4.575, $CHCl_3$), reported in 1973,[4] and confirmed its correctness.

Oxidation of (*R*)-**16** with pyridinium chlorochromate (PCC) in the presence of sodium acetate and silica gel in dichloromethane gave (*R*)-trogodermal (**1**), $[\alpha]_D^{25}$ −6.39 (*c* 4.02, Et_3O), in 88% yield. Addition of silica gel (180 wt % based on PCC) to the reaction mixture facilitated the isolation of (*R*)-**1** by removing the solid material through Celite and concentrating the filtrate. (*R*)-Trogodermal (**1**) was obtained as an *E*/*Z* mixture (*E*/*Z*=81.9:18.1). Similarly, (*S*)-**1**, $[\alpha]_D^{25}$ +6.52 (*c* 3.07, $CHCl_3$), was also synthesized from (*S*)-**16** as an *E*/*Z* mixture (*E*/*Z*=78.1:21.9). The overall yield of (*R*)-**1** was 19% based on (*R*)-**6** (seven steps).

2.3. Grubbs II catalyst causes randomization of the original product of cross-metathesis by double bond migration followed by further cross-metathesis

In one occasion Grubbs' second generation catalyst (Grubbs II) was employed for the cross-metathesis between (*S*)-**9** and **12** under the conditions (7 h in refluxing dichloromethane) successful with Grubbs I catalyst (Fig. 1).

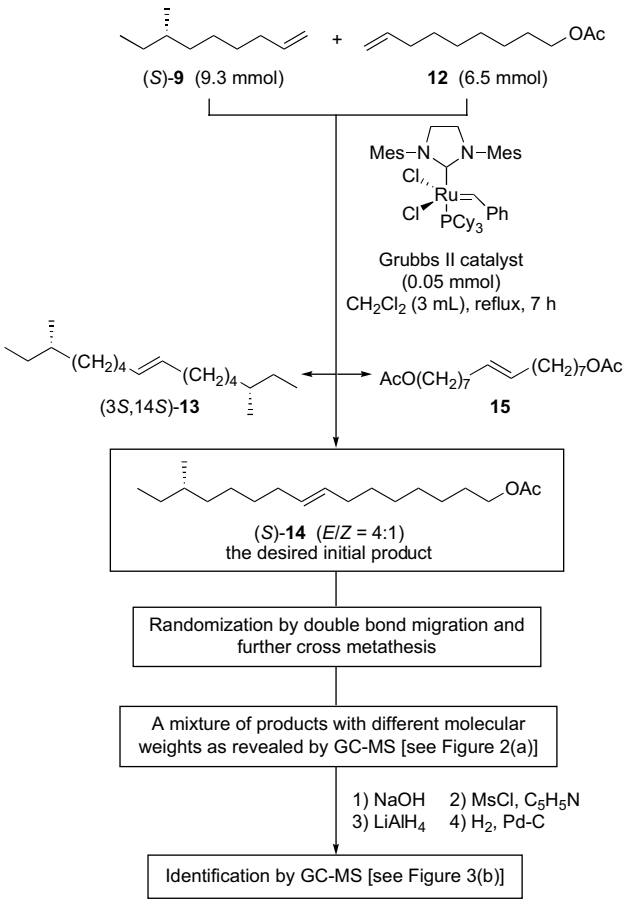


Figure 1. Olefin cross-metathesis between (*S*)-**9** and **12** with Grubbs II catalyst leading to a complex mixture of products.

GC–MS analysis of the acetate part obtained by silica gel chromatography revealed the product to be a complex mixture of acetates, containing only 22% of the desired (*S*)-**14**, with molecular weights different from that of (*S*)-**14** by $\pm 14\times n$ ($=\pm CH_2\times n$) (Fig. 2a). The GC peaks were observed as doublets due to the presence of (*E*)- and (*Z*)-isomers (*E*/*Z*=ca. 4:1). It must be added that the IR, ^1H, and ^{13}C NMR spectra of the mixture was almost indistinguishable from those of (*S*)-**14** except some subtle changes in the olefinic region. Complexity of the product could be noticed only through GC–MS analysis. Then the hydrocarbon part of the metathesis product was also analyzed by GC–MS, and it also turned out to be a complex mixture as shown in Figure 2b. The GC peak at retention time=6.35 min could be identified as 8-methyl-2-decene by comparison of its mass spectrum (MS) with that of the reference MS of (*Z*)-8-methyl-2-decene.[25]

In order to clarify what happened in the course of the metathesis, the acetate mixture was converted to a mixture of alkanes by successive treatments with (1) sodium hydroxide, (2) methanesulfonyl chloride, (3) lithium aluminum hydride, and (4) hydrogen and 10% palladium–charcoal. For the purpose of comparison, (*R*)-**14** as prepared in the presence of Grubbs I catalyst was also subjected to the same sequence of treatments. Figure 3 shows the gas chromatograms of (a) the reference hydrocarbon originating from (*R*)-**14** prepared by Grubbs I-catalyzed metathesis, and (b) the hydrocarbons originating from Grubbs II-catalyzed metathesis. The structure of each of the alkanes was identified by comparison of its MS with the reference MS of the known alkanes.[25] The alkane originated from (*R*)-**14** prepared in the presence of Grubbs I catalyst was (*R*)-3-methylhexadecane (**21**) as expected (Fig. 3a), while the alkane mixture obtained by employing Grubbs II catalyst was a beautiful blend of 3-methylalkanes ranging from 3-methyldodecane to 3-methyldocosane (Fig. 3b).

As shown in Figure 1, the genesis of the mixture must have taken place by double bond migration of the desired product (*S*)-**14** followed by further cross-metathesis leading to randomization of the carbon chain-length. 8-Methyl-2-decene shown in Figure 2b could be generated from 7-methyl-1-nonene (**9**), the starting material, by double bond migration to C-2 followed by the cross-metathesis of the generated 7-methyl-2-nonene with **9**. Double bond migration of 8-nonenyl acetate (**12**), another starting material, to give 7-nonenyl acetate would also give rise to 8-methyl-2-decene after cross-metathesis with **9**.

It might be possible, however, to employ Grubbs II catalyst successfully for cross-metathesis by lowering the reaction temperature and shortening the reaction time.[15] Indeed, when the metathesis of (*S*)-**9** and **12** with Grubbs II catalyst in dichloromethane was stopped after 30 min at reflux temperature, less randomization took place. Unfortunately, even in this case the generated (*S*)-**14** (M^+=296) was contaminated with about 20% of its lower homologue (M^+=282) and also by some other higher and lower homologues.

It is therefore recommended that the result of cross-metathesis between type I olefins[14] must always be checked by GC–MS or HPLC-MS to secure the desired product only. In the case when the desired product is crystalline and can readily be purified by recrystallization, some extent of randomization may be ignored. If the product is an oil, its purity must be checked carefully. In laboratory scale experiments, Grubbs I catalyst seems to be better than Grubbs II for cross-metathesis between terminal olefins (type I olefin[14]), avoiding extreme randomization.

2.4. Preparation and optical rotatory powers of compounds with a terminal *sec*-butyl group

Although the correctness of the magnitude of the optical rotation of (*S*)-**16** reported in 1973[4] was reconfirmed, it seemed better

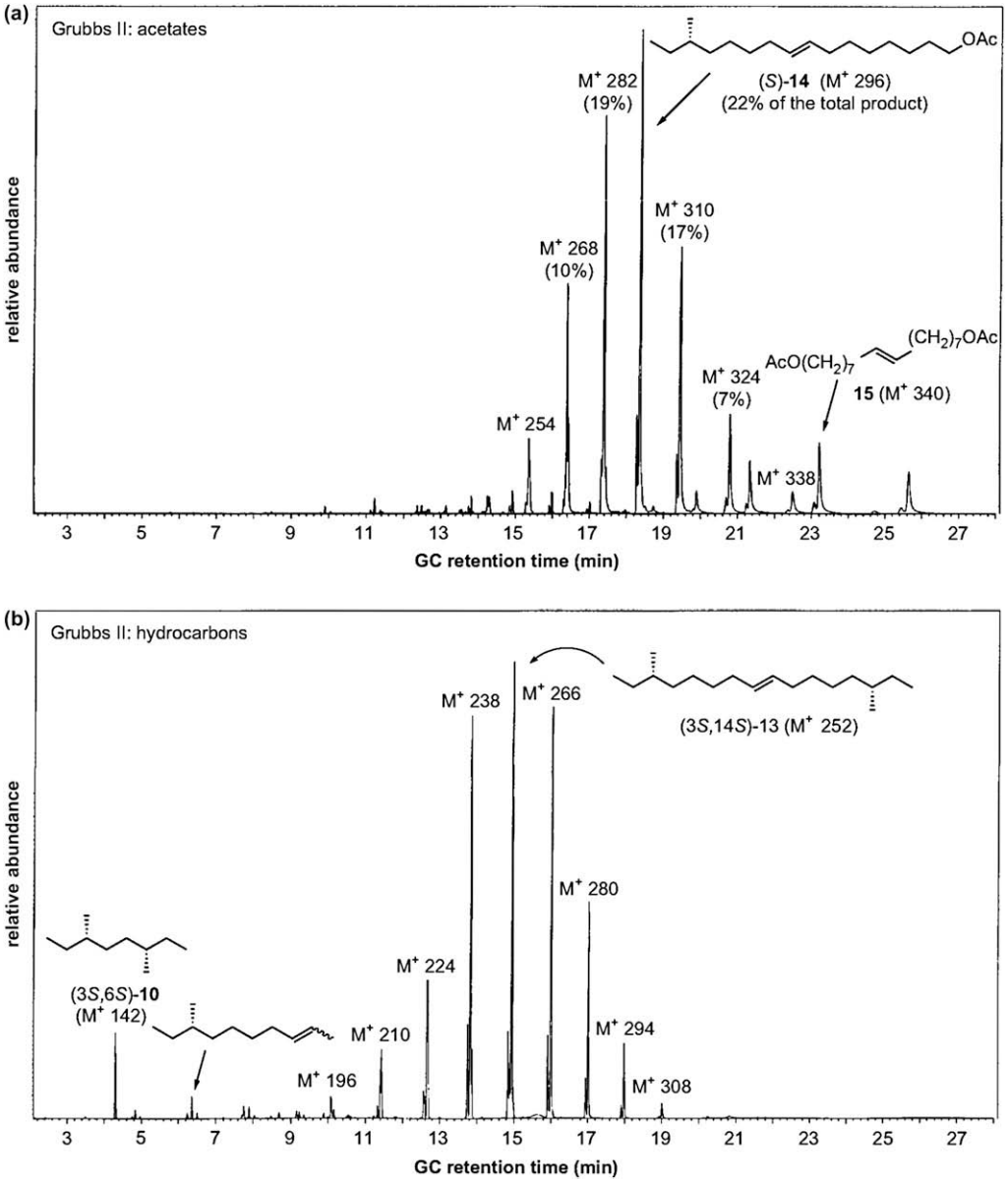


Figure 2. Olefin cross-metathesis between (*S*)-**9** and **12** with Grubbs II catalyst. GC–MS analysis of the resulting mixture after 7 h-reflux in dichloromethane: (a) gas chromatogram of the acetate part, and (b) gas chromatogram of the hydrocarbon part after separation by silica gel chromatography. All the olefinic compounds are *E*/*Z* (ca. 4:1) mixtures.

to further scrutinize the influence of functional groups on the optical rotatory powers of a series of compounds with a terminal *sec*-butyl group. Some people believe that a compound without any chromophore should show only very small specific rotation. My own experience indicates that even 3-methylalkanes with no functional group show measurable specific rotations of $[\alpha]_D$ ±3–4.[26]

Scheme 4 summarizes the route by which (*R*)- and (*S*)-**16** were converted to the enantiomers of unsaturated and saturated acetates **14** and **18**, saturated alcohol **19**, alkane **21**, alkene **23**, alkenyl ether **24**, and alkyl ether **25**. Measurements of specific rotations of these compounds will tell us the influence of a double bond, a hydroxy group, an acetoxy group, and a methoxy group on the magnitude of specific rotation, and will reveal us also the optical rotatory power of the asymmetric carbon framework itself.

Acetylation of **16** (*E*/*Z*=ca. 4:1) gave **14** without contamination of **15**. Catalytic hydrogenation of **14** over palladium–charcoal furnished **18**, while **16** was hydrogenated to give **19**. Preparations of alkane **21** and alkene **23** were achieved via methanesulfonates **20** and **22**, respectively. Accordingly, **19** was methanesulfonylated to **20**, which was reduced with lithium aluminum hydride to give 3-methylhexadecane (**21**). 3-Methyl-8-hexadecene (**23**) was obtained from **16** via methanesulfonate **22**. Hydrogenation of **23** gave **21**, which was identical with the sample prepared from **19**. Methylation of **16** with potassium *tert*-butoxide and methyl iodide in DMF gave **24**, whose hydrogenation afforded **25**.

Table 1 shows the specific rotations $[\alpha]_D$ and molar rotations $[\phi]_D=[\alpha]_D\times MW/100$ of compounds with a terminal (*R*)- or (*S*)-*sec*-butyl group. All the observed specific rotations of 24 compounds prepared by us fell in the range of $[\alpha]_D$ +3.5 to +6.5 and $[\alpha]_D$ −3.6 to −6.4, while the molar rotations were in the range of +12 to +16 −and −12 to −16. Accordingly, presence or absence of functionalities did not alter the magnitude of specific rotation remarkably. In the case of the unsaturated alcohol (*S*)-**16**, its specific rotation was $[\alpha]_D$ +6.1 in hexane, +5.9 in chloroform, and +6.3 in ethanol. This may mean that no strong interaction exists between the hydroxy group and the double bond of **16**.

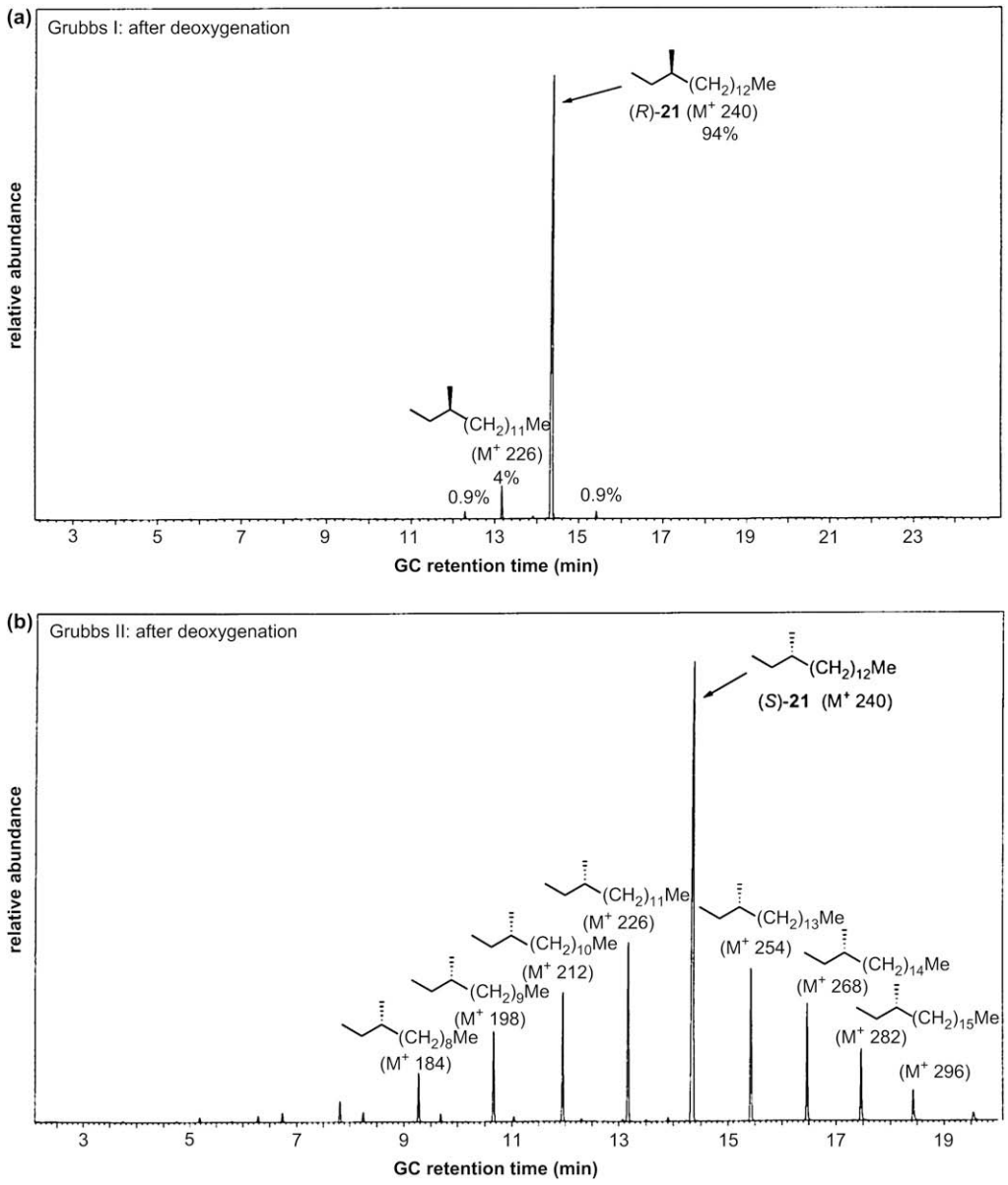


Figure 3. Identification of the hydrocarbon-framework of each of the products generated by olefin cross-metathesis between **9** and **12** by GC–MS of the deoxygenation products, (a) gas chromatogram of the products obtained with Grubbs I catalyst followed by subsequent deoxygenation treatments 1–4 in Figure 1. [(*R*)-**9** was employed]; (b) gas chromatogram of the products obtained with Grubbs II catalyst followed by subsequent deoxygenation treatments. [(*S*)-**9** was employed, and about the same amount of authentic (*S*)-**14** was added to the metathesis product so as to make the deoxygenation experiment successful with a sufficient amount of the starting material].

It is now clear that the compounds with terminal (*R*)- or (*S*)-*sec*-butyl group show specific rotations around −3.6 to −6.4 or +3.5 to +6.5, and the criticism against our experimental data turned out to be without experimental support. It should be added that (*S*)-axinellamine A (Table 1), a marine alkaloid, shows a large specific rotation of $[\alpha]_D^{23}$ +40.1 (*c* 0.38, $CHCl_3$).[27] The conjugated double bond of axinellamine A is located vicinal to the chiral center. This fact must have increased the magnitude of its specific rotation due to the somewhat skewed stereochemistry of the conjugated diene system.

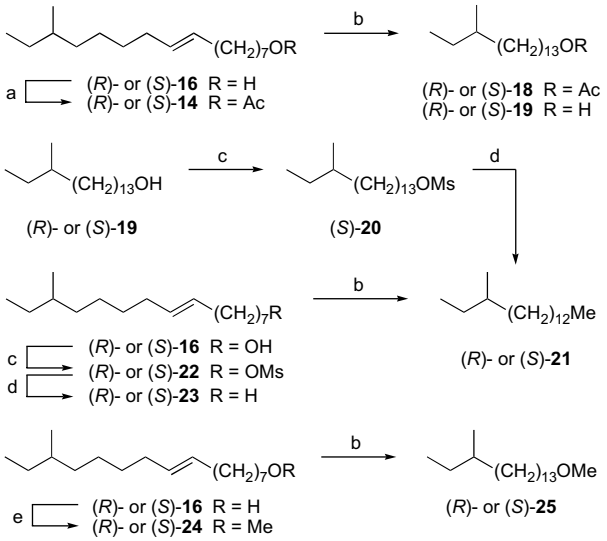
3. Conclusion

Cross-metathesis with Grubbs I catalyst was shown to be a quick way to synthesize an aliphatic pheromone with a stereogenic center such as (*R*)-trogodermal (**1**). Grubbs II catalyst was found to cause extensive side reactions in this particular case.[29] Specific rotations of compounds with (*R*)- or (*S*)-3-methylhexadecane skeleton were shown to be −3.6 to −6.4 or +3.5 to +6.5. The parent alkane 3-methylhexadecane was with $[\alpha]_D$ values of −5.7 [(*R*)-isomer] and +5.7 [(*S*)-isomer].

4. Experimental

4.1. General

Boiling points and a melting point are uncorrected values. Refractive indices (n_D) were measured on 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. ^1H 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



Scheme 4. Synthesis of the enantiomers of 3-methylhexadecane (**21**) and their derivatives from the enantiomers of 14-methyl-8-hexadecen-1-ol (**16**). Reagents: (a) Ac_2O, C_5H_5N [77% for (*R*)-**14**; 70% for (*S*)-**14**]; (b) H_2, Pd–C, EtOAc [99% for (*R*)-**18**; 72% for (*S*)-**18**; 89% for (*R*)-**19**; 90% for (*S*)-**19**; 80% for (*R*)-**21**; 90% for (*S*)-**21**; 93% for (*R*)-**25**; 98% for (*S*)-**25**]; (c) MsCl, C_5H_5N (quant.); (d) $LiAlH_4$, THF, reflux [70% for (*S*)-**21**; 87% for (*R*)-**23**; 78% for (*S*)-**23**]; (e) *t*-BuOK, DMF, MeI [88% for (*R*)-**24**; 80% for (*S*)-**24**].

on Jeol JMS-SX 102A. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. 2-Methylbutyl bromide (8)

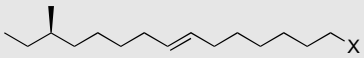
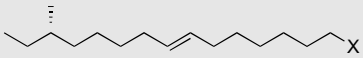
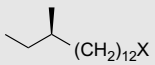
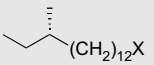
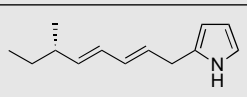
4.2.1. (*R*)-Isomer

(i) A solution of (*R*)-**6** (T. Hasegawa Co., >99.0% ee as analyzed by GC on Chiramix®,[28] 12.0 g, 118 mmol) in dry Et_2O (20 mL) was added dropwise to an ice-cooled and stirred suspension of $LiAlH_4$ (5.0 g, 120 mmol) in dry Et_2O (100 mL). The mixture was stirred for 1 h at 0–5 °C. The excess $LiAlH_4$ was destroyed by slowly adding water. The mixture was then acidified with ice and dil. HCl, and extracted with Et_2O. The extract was washed with satd $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated under atmospheric pressure to give crude (*R*)-**5** (10.6 g, quant.) as an oil. ν_{max} (film): 3348 (s, OH), 1047 (s, C–O), 1016 (m); δ_H ($CDCl_3$): 0.912 (3H, t, *J* 7.2, CH_2CH_3), 0.915 (3H, d, *J* 6.4, $CHCH_3$), 1.19–1.25 (1H, m), 1.40–1.60 (2H, m), 3.40–3.55 (2H, m, CH_2OH).

(ii) Powdered TsCl (27.0 g, 142 mmol) was added portionwise to an ice-cooled and stirred solution of (*R*)-**5** (10.6 g, 118 mmol) in dry pyridine (40 mL) at 0–5 °C. The mixture was stirred for 2 h at 0–5 °C. It was then poured into ice-water and extracted with Et_2O. The extract was washed with dil. HCl, satd $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give (*R*)-**7** (25.2 g, 86%) as an oil. ν_{max} (film): 1599 (w, arom. C=C), 1360 (m), 1176 (s), 964 (m); δ_H ($CDCl_3$): 0.83 (3H, t, *J* 7.6, CH_2CH_3), 0.87 (3H, d, *J* 6.8, $CHCH_3$), 1.10–1.22 (1H, m), 1.32–1.45 (1H, m), 1.65–1.75 (1H, m), 2.45 (3H, s, arom. CH_3), 7.34 (2H, d, *J* 8.8, arom. H), 7.78 (2H, d, *J* 8.8, arom. H).

(iii) Powdered LiBr (15 g, 172 mmol) was added to a solution of (*R*)-**7** (25.2 g, 104 mmol) in dry DMF (70 mL) with shaking. The mixture became homogeneous after exothermic reaction. It was then stirred and heated at 60 °C for 1.5 h. After cooling, the mixture was diluted with ice and water, and the separated heavy oil was collected. The aqueous layer was extracted with a small amount of pentane. The combined organic solution was washed with water and brine, dried ($MgSO_4$), and concentrated under atmospheric pressure. The residue was distilled to give (*R*)-**8** [11.2 g 63% based on (*R*)-**6**; three steps] as an oil. Bp 117–119 °C (atm press); n_D^{22}=1.4434; $[\alpha]_D^{25}$ −3.59 (*c* 3.03, pentane); ν_{max} (film): 2964 (s), 2931 (m), 2875 (m), 1460 (m), 1381 (m), 1230 (m), 650 (m); δ_H ($CDCl_3$): 0.91 (3H, t, *J* 7.2, CH_2CH_3), 1.01 (3H, d, *J* 7.2, $CHCH_3$), 1.20–1.35 (1H, m), 1.40–1.55 (1H, m), 1.65–1.76 (1H, m), 3.30–3.45 (2H, m).

Table 1
Specific rotation $[\alpha]_D$ and molar rotations $[\phi]_D=[\alpha]_D\times MW/100$ of compounds with a terminal (*R*)- or (*S*)-*sec*-butyl group[a]

	X	$[\alpha]_D$	$[\phi]_D$		X	$[\alpha]_D$	$[\phi]_D$
							
(*R*)-**23**[b]	Me	−6.4	−15	(*S*)-**23**[b]	Me	+6.3	+15
(*R*)-**16**	CH_2OH	−6.0	−15	(*S*)-**16**[c]	CH_2OH	+5.9	+15
(*R*)-**1**	CHO	−6.4	−16	(*S*)-**1**	CHO	+6.5	+16
(*R*)-**14**	CH_2OAc	−5.1	−15	(*S*)-**14**	CH_2OAc	+5.1	+15
(*R*)-**24**	CH_2OMe	−5.8	−15	(*S*)-**24**	CH_2OMe	+5.7	+15
							
(*R*)-**21**	Me	−5.7	−14	(*S*)-**21**	Me	+5.7	+14
(*R*)-**19**	CH_2OH	−5.0	−13	(*S*)-**19**	CH_2OH	+5.3	+14
(*R*)-**18**	CH_2OAc	−4.0	−12	(*S*)-**18**	CH_2OAc	+4.2	+13
(*R*)-**25**	CH_2OMe	−4.8	−13	(*S*)-**25**	CH_2OMe	+4.6	+12
Ref. 26	$(CH_2)_8Me$	−4.1	−15	Ref. 26	$(CH_2)_8Me$	+4.2	+15
	$(CH_2)_{10}Me$	−3.6	−14		$(CH_2)_{10}Me$	+3.7	+15
	$(CH_2)_{12}Me$	−3.6	−15		$(CH_2)_{12}Me$	+3.5	+15
	 (*S*)-axinellamine A (ref. 27)	$[\alpha]_D$ +40	$[\phi]_D$ +76				

[a] All the rotations except for trogodermal (**1**, X=CHO) were measured as $CHCl_3$ solutions.[4–10,26,27] The rotations of (*R*)- and (*S*)-trogodermals (**1**) were measured as Et_2O solutions as reported previously.[7–9]

[b] All of these olefinic compounds are ca. 4:1 mixtures of (*E*)- and (*Z*)-isomers.

[c] This compound (*S*)-**16** showed $[\alpha]_D^{21}$ +6.1 in hexane and $[\alpha]_D^{19}$ +6.3 in EtOH.

4.2.2. (S)-Isomer

In the same manner as described above, (*S*)-**5** [Tokyo Kasei (TCI), 28.4 g, 322 mmol] yielded, via (*S*)-**7**, 38.0 g (78%, two steps) of (*S*)-**8**. Bp 117–119 °C (atm press): n_D^{22}=1.4440; $[\alpha]_D^{25}$ +3.74 (*c* 4.76, pentane). Its spectral data were identical with those of (*R*)-**8**.

4.3. 7-Methyl-1-nonene 9

4.3.1. (R)-Isomer

A Grignard reagent was prepared from (*R*)-**8** (9.1 g, 60 mmol), Mg (1.7 g, 71 mmol) and a catalytic amount of I_2 in dry THF (40 mL) under Ar. This was added through a syringe to a stirred and cooled solution of 4-pentenyl tosylate [ν_{max} (film): 1641 (m, C=C), 1599 (m, arom. C=C), 1362 (s), 1188 (s), 1176 (s), 970 (m), 920 (m); δ_H ($CDCl_3$): 1.71–1.80 (2H, m), 2.05–2.12 (2H, m), 2.45 (3H, s, CH_3), 4.04 (2H, t-like, *J* 10.8), 4.92–5.00 (2H, m), 5.63–5.75 (1H, m), 7.35 (2H, d, *J* 8.0), 7.80 (2H, d, *J* 8.0); 10.0 g, 41 mmol] in dry THF (30 mL) at −70 to −55 °C under Ar. Subsequently, a solution of Li_2CuCl_4 in THF (0.1 M, 1.5 mL, 0.15 mmol) was added through a syringe, and the stirred mixture was left to stand overnight under Ar with gradual warming to room temperature. The mixture was quenched with ice and NH_4Cl solution, and extracted with a small amount of pentane. The pentane solution was washed with water and brine, dried ($MgSO_4$), and concentrated at atmospheric pressure. The residue was distilled to give (*R*)-**9** contaminated with 6% of (3*R*, 6*R*)-**10** [4.7 g, 82% based on the tosylate or 56% based on (*R*)-**8**]. Bp 80–86 °C/57 Torr; n_D^{22}=1.4230; $[\alpha]_D^{26}$ −11.1 (*c* 3.28, pentane); ν_{max} (film): 3078 (w), 1641 (m, C=C), 1462 (m), 1379 (m), 991 (s); δ_H 0.845 (3H, d, *J* 7.6, $CHCH_3$), 0.849 (3H, t, *J* 7.6, CH_2CH_3), 1.05–1.20 (2H, m), 1.20–1.41 (8H, m), 2.00–2.10 (2H, q-like, $C=CCH_2$), 4.90–5.03 (2H, m, $C=CH_2$), 5.75–5.88 (1H, m, CH=C); GC–MS [column: HP-5MS, 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; press: 52.8 kPa; temp: 50–160 °C (+10 °C/min)–220 °C (+4 °C/min)]: t_R 6.08 [6%, (3*R*,6*R*)-**10**], 6.47 min [94%, (*R*)-**9**]. MS of (3*R*,6*R*)-**10** (70 eV, EI): *m*/*z* 142 (3) [M^+, $C_{10}H_{22}$], 113 (24), 112 (10), 85 (8), 71 (77), 57 (100), 56 (25), 43 (38), 41 (26), 29 (17); MS of (*R*)-**9** (70 eV, EI): *m*/*z* 140 (2) [M^+,$C_{10}H_{20}$], 111 (65), 83 (55), 70 (95), 69 (100), 57 (80), 56 (59), 55 (88), 41 (80). HRMS calcd for $C_{10}H_{20}$: 140.1565, found: 140.1555.

4.3.2. (S)-Isomer

In the same manner as described for (*R*)-**9**, (*S*)-**8** (18.9 g, 125 mmol), Mg (3.4 g, 140 mmol), 4-pentenyl tosylate (20.0 g, 83 mmol), and Li_2CuCl_4 in THF (0.1 M, 3 mL, 0.3 mmol) yielded (*S*)-**9** contaminated with 9% of (3*S*,6*S*)-**10** [10.1 g, 87% based on 4-pentenyl tosylate on 58% based on (*S*)-**8**]. Bp 77–80 °C/50 Torr; n_D^{21}=1.4226; $[\alpha]_D^{27}$ +11.3 (*c* 3.44, pentane). Its spectral properties were identical with those of (*R*)-**9**. GC [under the same conditions for (*R*)-**9**]: t_R 6.08 [9%, (3*S*,6*S*)-**10**], 6.48 [91%, (*S*)-**9**]. HRMS calcd for $C_{10}H_{20}$: 140.1565, found: 140.1547.

4.4. 8-Nonenyl acetate (12)

Acetic anhydride (10 mL, 10.8 g, 105 mmol) was added to a solution of **11** (10.0 g, 70 mmol) in dry pyridine (30 mL) with shaking. The mixture was left to stand for 3 days at room temperature. It was then poured into ice-water and extracted with Et_2O. The extract was washed with water, dil. HCl, satd $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give **12** (12.9 g, quant.). Bp 138–140 °C/50 Torr; n_D^{21}=1.4332; ν_{max} (film): 1743 (s), 1641 (w), 1240 (s), 1041 (m), 910 (m); δ_H ($CDCl_3$): 1.27–1.42 (8H,m), 1.58–1.66 (2H, m), 2.05 (3H, s, CH_3CO), 2.00–2.08 (2H, m), 4.05 (2H, t-like, *J* 6.4, CH_2OAc), 4.90–5.03 (2H, m, $C=CH_2$), 5.75–5.87 (1H, m, CH=C). HRMS (doped with LiI) calcd for $C_{11}H_{20}O_2Li$: 191.1623, found: 191.1611.

4.5. 14-Methyl-8-hexadecenyl acetate 14

4.5.1. (R)-Isomer

Grubbs' first generation catalyst (Grubbs I, Aldrich, Lot number 01928CJ, 80 mg, 0.1 mmol) was added to a solution of (*R*)-**9** (2.4 g, 17 mmol) and **12** (2.2 g, 12 mmol) in dry CH_2Cl_2 (5 mL). The wine red solution was stirred and heated under reflux for 3 h under Ar. Then an additional amount of Grubbs I catalyst (30 mg, 0.04 mmol) was added, and the stirring was continued for another 3 h, when the evolution of ethylene ceased. The mixture was left to stand for 3 days at room temperature, and concentrated in vacuo. The residue was chromatographed over SiO_2 (25 g). Elution with hexane gave (3*R*,14*R*)-**13** [1.32 g, ν_{max} (film): 2960 (s), 2925 (s), 2856 (s), 1462 (m), 1377 (m), 966 (m)]. Further elution with hexane/EtOAc (15:1) gave crude (*R*)-**14** [2.84 g, 56% based on (*R*)-**9** or 80% based on **12**] contaminated with 13.6% of **15**. Properties of crude (*R*)-**14**: ν_{max} (film): 1743 (s, C=O), 1238 (s, C–O), 1038 (m), 968 (m); δ_H ($CDCl_3$): 0.80–0.90 (6H, m, CH_3×2), 1.02–1.18 (2H, m), 1.20–1.40 (17H, m), 1.56–1.65 (2H, m), 1.92–2.06 (2H, m), 2.04 (3H, s, CH_3CO), 4.05 (2H, t-like, *J* 6.8, CH_2O), 5.32–5.41 (2H, m, CH=CH); GC–MS [column: HP-5MS, 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; press: 60.7 kPa; 70–230 °C (+10 °C/min)]: t_R 18.3 [14.7%; (*R*,*Z*)-**14**], 18.4 [71.7%; (*R*,*E*)-**14**], 23.2 min (13.6%, **15**); MS of (*R*,*Z*)-**14** (70 eV, EI): *m*/*z* 296 (1) [M^+, $C_{19}H_{36}O_2$], 236 (36, M^+−AcOH), 137 (19), 123 (38), 110 (40), 109 (63), 97 (48), 96 (100), 95 (85), 82 (90), 81 (90), 67 (75), 55 (69), 43 (73); MS of (*R*,*E*)-**14** is identical with that of (*R*,*Z*)-**14**; MS of **15** (70 eV, EI): *m*/*z* 340 (1) [M^+, $C_{20}H_{36}O_4$], 280 (2), 251 (1), 237 (2), 220 (2, M^+−2AcOH), 149 (10), 135 (28), 121 (34), 95 (58), 81 (70), 67 (72), 55 (48), 43 (100). Pure (*R*)-**14** could be prepared by acetylation of (*R*)-**16** (see 4.8.1). The crude (*R*)-**14** was used directly in the next step. Further elution with hexane/EtOAc (15:1) gave **15** (0.3 g); ν_{max} (film): 1741 (s, CO), 1240 (s, C–O), 1039 (m), 968 (w); δ_H ($CDCl_3$): 1.25–1.40 (16H, br s), 1.58–1.68 (4H, m), 1.94–2.02 (4H, m), 2.04 (6H, s, CH_3CO×2), 4.05 (4H, t-like, *J* 6.8, CH_2O), 5.33–5.40 (2H, m, CH=CH).

4.5.2. (S)-Isomer

In the same manner as described for (*R*)-**14**, (*S*)-**9** (5.02 g, 35.7 mmol), **12** (4.23 g, 22.8 mmol) and Grubbs I catalyst (200 mg, 0.24 mmol) in dry CH_2Cl_2 (10 mL) gave 2.9 g of (3*S*,14*S*)-**13** and 5.0 g [47% based on (*S*)-**9** and 74% based on **12**] of crude (*S*)-**14**. Pure (*S*)-**14** could be prepared by acetylation of (*S*)-**16** (see 4.8.2). The crude (*S*)-**14** was used directly in the next step.

4.5.3. Metathesis with Grubbs II catalyst

In the same manner as described for (*R*)-**14**, a solution of (*S*)-**9** (1.30 g, 9.3 mmol), **12** (1.20 g, 6.5 mmol) and Grubbs II catalyst (Aldrich, Lot number 08410TC, 43 mg, 0.05 mmol) in dry CH_2Cl_2 (3 mL) was stirred and heated under reflux for 7 h. The mixture was concentrated, and the residue was chromatographed over SiO_2 (20 g). Elution with hexane gave hydrocarbon fraction (719 mg, for its GC–MS see Fig. 2b). Elution with hexane/EtOAc (15:1) gave acetate fraction (1.440 g, for its GC–MS see Fig. 2a). Further elution with hexane/EtOAc (15:1) gave the second acetate fraction (194 mg).

4.6. 14-Methyl-8-hexadecen-1-ol 16

4.6.1. (R)-Isomer

A solution of crude (*R*)-**14** (2.8 g, 9.5 mmol) in THF (30 mL) was added to a solution of NaOH (3.0 g, 75 mmol) in H_2O (15 mL) and MeOH (30 mL). The mixture was stirred and heated under reflux for 40 min, and then 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 (20 g). Elution with hexane/EtOAc (5:1) gave 1.5 g (62%) of (*R*)-**16** as an oil. n_D^{21}=1.4598;

$[\alpha]_D^{21}$ −5.98 (*c* 4.34, $CHCl_3$); ν_{max} (film): 3334 (s, OH), 1057 (m, C–O), 966 (m); δ_H ($CDCl_3$): 0.844 (3H, d, *J* 7.6, $CHCH_3$), 0.846 (3H, t, *J* 6.4, CH_2CH_3), 1.04–1.19 (2H, m), 1.20–1.92 (18H, m), 1.52–1.62 (2H, m), 1.92–2.06 (4H, m), 3.64 (2H, m, CH_2O), 5.34–5.42 (2H, m, CH=CH); δ_C ($CDCl_3$): 11.5, 12.3, 25.8, 26.6, 27.0, 27.02, 27.2, 27.3, 30.0, 31.6, 32.8, 63.1, 130.1, 130.3. HRMS calcd for $C_{17}H_{34}O$: 254.2610, found: 254.2606. Further elution with EtOAc gave (*E*)-**17** as rhombs from EtOAc/hexane. Mp 57.5–58.0 °C; ν_{max} (Nujol): 3351 (s, OH), 1065 (m, C–O), 966 (s); δ_H ($CDCl_3$): 1.23–1.50 (18H, m), 1.50–1.60 (4H, m), 1.92–2.05 (4H, m), 3.64 (4H, t-like, *J* 6.4, $CH_2O\times2$), 5.32–5.42 (2H, m); δ_C ($CDCl_3$): 25.8, 29.1, 29.3, 29.6, 32.6, 32.8, 63.1, 130.3. HRMS calcd for $C_{16}H_{32}O_2$: 256.2402, found: 256.2404.

4.6.2. (S)-Isomer

In the same manner as described for (*R*)-**16**, crude (*S*)-**14** (5.6 g, 18.9 mmol) and NaOH (4.0 g, 100 mmol) gave 3.2 g (67%) of (*S*)-**16** as a colorless oil after chromatography over SiO_2 (40 g). Crystalline (*E*)-**17** (1.1 g) was also obtained. Properties of (*S*)-**16**: n_D^{21}=1.4590; $[\alpha]_D^{21}$ +5.89 (*c* 4.83, $CHCl_3$). Its spectral properties were identical with those of (*R*)-**16**. HRMS calcd for $C_{17}H_{34}O$: 254.2610, found: 254.2610.

4.7. 14-Methyl-8-hexadecenal 1

4.7.1. (R)-Isomer

A solution of (*R*)-**16** (604 mg, 2.3 mmol) in dry CH_2Cl_2 (10 mL) was added to a stirred and ice-cooled suspension of pyridinium chlorochromate (PCC, 3.6 g, 16.7 mmol), SiO_2 (6.5 g), and sodium acetate (0.5 g) at 0–5 °C under Ar. Addition of SiO_2 facilitates the isolation of the product. After stirring for 2 h at 0–5 °C, the brown-colored mixture was filtered through Celite. The Celite layer was washed with Et_2O, and the combined filtrates were concentrated in vacuo. The residue was chromatographed over SiO_2 (12 g). Elution with hexane/EtOAc (15:1) gave (*R*)-**1** as a colorless oil (531 mg, 88%). n_D^{21}=1.4573; $[\alpha]_D^{25}$ −6.39 (*c* 4.02, Et_2O); ν_{max} (film): 1728 (s, C=O), 966 (m); δ_H ($CDCl_3$): 0.841 (3H, d, *J* 7.6, $CHCH_3$), 0.845 (3H, t, *J* 7.6, CH_2CH_3), 1.05–1.18 (2H, m), 1.20–1.41 (15H, m), 1.58–1.70 (2H, m), 1.92–2.08 (4H, m), 2.40–2.48 (2H, m), 5.32–5.42 (2H, m, CH=CH), 9.76 (1H, s-like, CHO); δ_C ($CDCl_3$): 11.4, 19.2, 22.0, 26.7, 28.9, 29.0, 30.1, 32.4, 32.6, 34.4, 36.5, 43.8, 64.3, 129.4 and 130.0 [(*Z*)-isomer], 129.9 and 130.4 [(*E*)-isomer] (*E*/*Z*=4:1), 202.6; 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 16.46 min [18.1%, (*Z*)-isomer], 16.53 min [81.9%, (*E*)-isomer]; MS of (*R*,*E*)-**1** (70 eV, EI): *m*/*z* 252 (10) [M^+, $C_{17}H_{32}O$], 234 (11), 223 (6), 205 (4), 149 (10), 135 (18), 123 (20), 121 (27), 109 (35), 98 (42), 97 (45), 96 (35), 95 (47), 83 (67), 81 (52), 70 (100), 55 (81), 41 (55). (*R*,*Z*)-**1** showed the same MS. HRMS calcd for $C_{17}H_{32}O$: 252.2453, found: 252.2447.

4.7.2. (S)-Isomer

In the same manner as described for (*R*)-**1**, (*S*)-**15** (602 mg, 2.4 mmol) was oxidized with PCC (3.6 g, 16.7 mmol) in the presence of NaOAc (0.5 g) and SiO_2 (6.5 g) in CH_2Cl_2 (40 mL) to give 550 mg (91%) of (*S*)-**1**. n_D^{24}=1.4578; $[\alpha]_D^{24}$ +6.52 (*c* 3.07, Et_2O). The spectral properties of (*S*)-**1** were identical with those of (*R*)-**1**. GC [same conditions as for (*R*)-**1**]: t_R 16.46 min [21.9%, (*Z*)-isomer], 16.54 min [78.1%, (*E*)-isomer]. HRMS calcd for $C_{17}H_{32}O$: 252.2453, found: 252.2448.

4.8. Pure 14-methyl-8-hexadecenyl acetate 14

4.8.1. (R)-Isomer

Acetic anhydride (3 mL) was added to a solution of (*R*)-**16** (500 mg, 2 mmol) in dry pyridine (5 mL), and the mixture was left to stand at room temperature for 3 days. The mixture was poured into ice-water and extracted with Et_2O. The ether solution was washed with dil. HCl, satd $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 450 mg (77%) of (*R*)-**14**. n_D^{23}=1.4506; $[\alpha]_D^{25}$ −5.12 (*c* 2.36, $CHCl_3$); ν_{max} (film): 1743 (s, C=O), 1238 (s, C–O), 1039 (m), 966 (m), 758 (m); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 8, $CHCH_3$), 0.85 (3H, t, *J* 7.6, CH_2CH_3), 1.05–1.20 (2H, m), 1.20–1.40 (15H, m), 1.62 (2H, m), 1.98 (4H, m), 2.04 (3H, s, $COCH_3$), 4.05 (2H, t, *J* 6.8, CH_2OAc), 5.32–5.46 (2H, m); δ_C ($CDCl_3$): 25.8, 25.9, 26.6, 26.7, 27.1, 27.2, 28.6, 29.0, 29.1, 29.46, 29.52, 29.6, 29.9, 30.1, 32.5, 32.6, 34.4, 36.4, 64.6, 129.6 and 130.0 [(*Z*)-isomer], 129.9 and 130.4 [(*E*)-isomer] (*E*/*Z*=4:1), 171.0 (C=O); GC–MS [same conditions as for (*R*)-**1**]: t_R 18.30 [19.4%, (*Z*)-isomer], 18.40 min [80.6% (*E*)-isomer]; MS of (*R*,*E*)-**14** (70 eV, EI): *m*/*z* 296 (2) [M^+, $C_{19}H_{36}O_2$], 236 (29), 207 (7), 166 (6), 151 (10), 137 (21), 123 (39), 109 (63), 96 (100), 82 (85), 67 (70), 55 (62), 43 (64). (*R*,*Z*)-**14** showed the same MS. HRMS (doped with LiI) calcd for $C_{19}H_{36}O_2Li$: 303.2875, found: 303.2874.

4.8.2. (S)-Isomer

In the same manner as described for (*R*)-**14**, (*S*)-**16** (500 mg) yielded 410 mg (70%) of (*S*)-**14**. n_D^{24}=1.4492; $[\alpha]_D^{24}$ +5.07 (*c* 3.30, $CHCl_3$). Its spectral data were identical with those of (*R*)-**14**. GC [same conditions as for (*R*)-**14**]: t_R 18.30 [21.0%, (*Z*)-isomer], 18.40 min [79.0%, (*E*)-isomer]. HRMS (doped with LiI) calcd for $C_{19}H_{36}OLi$: 303.2875, found: 303.2884.

4.9. 14-Methylhexadecyl acetate 18

4.9.1. (R)-Isomer

Palladium–charcoal (10%, 0.1 g) was added to a solution of (*R*)-**14** (330 mg, 1.1 mmol) in EtOAc (10 mL). The suspension was stirred under H_2 (balloon) for 2 h at room temperature. The suspension was filtered through SiO_2 (5.0 g). The SiO_2 column was washed with EtOAc, and the combined EtOAc solution was concentrated in vacuo to give (*R*)-**18** (330 mg, 99%). n_D^{23}=1.4422; $[\alpha]_D^{25}$ −4.02 (*c* 2.59, $CHCl_3$); ν_{max} (film): 1743 (s, C=O), 1238 (s, C–O), 1041 (m); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.0, $CHCH_3$), 0.85 (3H, t *J* 6.8, CH_2CH_3), 1.04–1.18 (2H, m), 1.20–1.40 (23H, m), 1.61 (2H, m), 2.04 (3H, s, $COCH_3$), 4.05 (2H, t, *J* 6.8, CH_2OAc); δ_C ($CDCl_3$): 27.1, 28.6, 29.2, 29.47, 29.48, 29.5, 29.6, 29.62, 29.65, 29.67, 29.7, 29.9, 30.0, 34.4, 36.6, 64.6, 171.0 (C=O); GC–MS [same conditions as for (*R*)-**1**]: t_R 18.58 min (92.8%); MS (70 eV, EI): *m*/*z* 299 (0.5) [M^++1, $C_{19}H_{38}O_2$+1], 238 (3) [M^+−AcOH], 209 (18), 139 (15),125 (31), 111 (54), 97 (92), 83 (88), 70 (100), 57 (64), 43 (78). HRMS (doped with LiI) calcd for $C_{19}H_{38}O_2Li$: 305.3032, found: 305.3024.

4.9.2. (S)-Isomer

In the same manner as described for (*R*)-**18**, (*S*)-**14** (500 mg, 1.7 mmol) yielded 424 mg (72%) of (*S*)-**18**. n_D^{24}=1.4426; $[\alpha]_D^{22}$ +4.23 (*c* 4.24, $CHCl_3$). Its spectral data were identical with those of (*R*)-**18**. GC [same conditions as for (*R*)-**1**]: t_R 18.58 min (94.9%). HRMS (doped with LiI) calcd for $C_{19}H_{38}O_2Li$: 305.3032, found: 305.3032.

4.10. 14-Methyl-1-hexadecanol 19

4.10.1. (R)-Isomer

Palladium–charcoal (10%, 0.1 g) was added to a solution of (*R*)-**16** (200 mg, 0.8 mmol) in EtOAc (5 mL). The suspension was stirred under H_2 (balloon) for 1.5 h at room temperature. The suspension was filtered through SiO_2 (2 g). The SiO_2 column was washed with EtOAc, and the combined EtOAc solution was concentrated in vacuo to give (*R*)-**19** (180 mg, 89%), which was a solid in a refrigerator but remained as an oil at room temperature. n_D^{24}=1.4516; $[\alpha]_D^{23}$ −4.98 (*c* 2.55, $CHCl_3$); ν_{max} (film): 3330 (m, OH), 1057 (m, C–O); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.0, $CHCH_3$), 0.85 (3H, t, *J* 6.8, CH_2CH_3), 1.05–1.17 (2H, m), 1.26 (24H, m), 1.55 (2H, m), 3.64 (2H, t, *J* 6.4, CH_2OH); δ_C ($CDCl_3$): 29.4, 29.5, 29.59, 29.61, 29.65, 29.67, 29.68, 29.72, 30.0, 32.8, 34.4, 36.6, 63.0. HRMS (doped with LiI) calcd for $C_{17}H_{36}OLi$: 263.2926, found: 263.2928.

4.10.2. (S)-Isomer

In the same manner as described for (*R*)-**19**, (*S*)-**16** (1.87 g, 7.4 mmol) yielded 1.70 g (90%) of (*S*)-**19**. n_D^{24}=1.4516; $[\alpha]_D^{22}$ +5.27 (*c* 2.51, $CHCl_3$). Its spectral data were identical with those of (*R*)-**19**. HRMS (doped with LiI) calcd for $C_{17}H_{36}OLi$: 263.2926, found: 263.2922.

4.11. (*S*)-14-Methylhexadecyl methanesulfonate 20

Methanesulfonyl chloride (1.0 mL, 1.48 g, 12.9 mmol) was added dropwise to a stirred and ice-cooled solution of (*S*)-**19** (1.22 g, 4.8 mmol) in dichloromethane (3 mL) and dry pyridine (3 mL) at 0–5 °C. The stirring was continued for 1 h at 0–5 °C. The mixture was then poured into ice-water and extracted with Et_2O. The ether solution was washed with dil. HCl, satd $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 1.60 g (quant.) of crude (*S*)-**20**, ν_{max} (film): 1344 (s), 1169 (s), 983 (s), 947 (s). This was employed in the next step without further purification.

4.12. 3-Methylhexadecane 21

4.12.1. (R)-Isomer

Palladium–charcoal (10%, 0.1 g) was added to a solution of (*R*)-**23** (350 mg, 1.5 mmol) in EtOAc (10 mL). The suspension was stirred under H_2 (balloon) for 1.5 h at room temperature. The suspension was filtered through SiO_2 (6.0 g). The SiO_2 column was washed with hexane, and the combined organic solution was concentrated in vacuo to give (*R*)-**21** (282 mg, 80%). n_D^{22}=1.4372; $[\alpha]_D^{23}$ −5.73 (*c* 1.97, $CHCl_3$); ν_{max} (film): 2958 (m), 2924 (s), 2854 (s), 1464 (m), 1377 (w); δ_H ($CDCl_3$): 0.84 (3H, d, *J* 6.0, $CHCH_3$), 0.85 (3H, t, *J* 6.8, CH_2CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 1.05–1.20 (2H, m), 1.20–1.35 (25H, m); δ_C ($CDCl_3$): 11.4, 14.1, 15.5, 19.2, 22.7, 27.1, 29.3, 29.4, 29.5, 29.65, 29.70, 29.73, 30.0, 31.9, 34.4; GC–MS [same condition as for (*R*)-**1**]: t_R 14.37 min (94.0%). MS (70 eV, EI): *m*/*z* 240 (1) [M^+, $C_{17}H_{36}$], 211 (54), 182 (9), 169 (5), 155 (9), 141 (13), 127 (15), 113 (19), 99 (26), 85 (61), 71 (72), 57 (100), 43 (40). HRMS calcd for $C_{17}H_{36}$: 240.2817, found: 240.2823.

*4.12.2. (S)-Isomer from (S)-**20***

A solution of (*S*)-**20** (1.60 g, 0.5 mmol) in THF (10 mL) was added to a stirred suspension of $LiAlH_4$ (0.8 g, 21 mmol) in THF (20 mL) under Ar. The mixture was stirred and heated under reflux for 1 h, then poured into ice–dil. HCl, and extracted with Et_2O. The ether solution was washed with water, satd $NaHCO_3$ solution, brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (10 g). Elution with pentane gave (*S*)-**21** (840 mg, 70%). n_D^{24}=1.4372; $[\alpha]_D^{23}$ +5.66 (*c* 6.38, $CHCl_3$). Its spectral data were identical with those of (*R*)-**21**. GC [same conditions as for (*R*)-**1**]: t_R 14.37 min (90.0%). HRMS calcd for $C_{17}H_{36}$: 240.2817, found: 240.2815.

*4.12.3. (S)-Isomer from (S)-**23***

In the same manner as described for (*R*)-**21**, (*S*)-**23** (996 mg, 4.2 mmol) was hydrogenated over 10% palladium–charcoal to give (*S*)-**21** (900 mg, 90%). n_D^{24}=1.4372; $[\alpha]_D^{23}$ +4.92 (*c* 4.63, $CHCl_3$). Its spectral data were identical with those of (*R*)-**21**. GC [same conditions as for (*R*)-**1**]: t_R 14.37 min (93.4%). HRMS calcd for $C_{17}H_{30}$: 240.2817, found: 240.2818.

4.13. 14-Methyl-8-hexadecenyl methanesulfonate 22

4.13.1. (R)-Isomer

Methanesulfonyl chloride (0.5 mL, 0.74 g, 6.5 mmol) was added dropwise to a stirred and ice-cooled solution of (*R*)-**16** (602 mg, 2.4 mmol) in dichloromethane (2 mL) and dry pyridine (2 mL) at 0–5 °C. The stirring was continued for 2 h at 0–5 °C. The mixture was then poured into ice-water, and worked up as described for (*S*)-**20** to give crude (*R*)-**22** (830 mg, quant.), ν_{max} (film): 1356 (s), 1176 (s), 970 (s). This was used for the next step without further purification.

4.13.2. (S)-Isomer

In the same manner as described above, (*S*)-**16** (2.0 g, 7.9 mmol) yielded crude (*S*)-**22** (3.3 g, quant.). This was used for the next step without further purification.

4.14. 3-Methyl-8-hexadecene 23

4.14.1. (R)-Isomer

A solution of crude (*R*)-**22** (830 mg, 2.4 mmol) in dry THF (5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (200 mg, 5.3 mmol) in dry THF (7 mL). The mixture was stirred and heated under reflux for 1.5 h. It was then poured into ice–dil. HCl and extracted with Et_2O. The ether solution was washed with water, satd $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (3.5 g). Elution with pentane gave (*R*)-**23** [500 mg, 87% based on (*R*)-**16**]. n_D^{24}=1.4444; $[\alpha]_D^{24}$ −6.35 (*c* 2.15, $CHCl_3$); ν_{max} (film): 2958 (s), 2925 (s), 2854 (s), 1462 (m), 1377 (w), 966 (m); δ_H ($CDCl_3$): 0.84 (3H, t, *J* 6.0, CH_2CH_3), 0.84 (3H, d, *J* 7.2, $CHCH_3$), 0.88 (3H, t, *J* 6.4, CH_2CH_3), 1.04–1.20 (2H, m), 1.20–1.40 (17H, m), 1.92–2.08 (4H, m), 5.33–5.36 [0.4H, m, (*Z*)-isomer], 5.37–5.43 [1.6H, m, (*E*)-isomer]; δ_C ($CDCl_3$): 11.4, 14.1, 19.2, 22.6, 26.6, 26.8, 27.22, 27.24, 29.1, 29.20, 29.23, 29.48, 29.49, 29.67, 29.78, 29.97, 30.1, 31.9, 32.60, 32.87, 34.3, 34.4, 36.5, 129.73 and 129.76 [(*Z*)-isomer], 130.20 and 130.23 [(*E*)-isomer], (*E*/*Z*=ca. 4:1); GC–MS [same conditions as for (*R*)-**1**]: t_R 14.09 [20.0%, (*R*,*Z*)-**23**], 14.18 min [74.9%, (*R*,*E*)-**23**]; MS of (*R*,*E*)-**23** [same as that of (*R*,*Z*)-**23**; 70 eV, EI]: *m*/*z* 238 (19) [M^+, $C_{17}H_{34}$], 209 (8), 181 (1), 168 (3), 153 (5), 139 (8), 125 (18), 111 (30), 97 (54), 83 (69), 70 (100), 55 (52), 41 (43). HRMS calcd for $C_{17}H_{34}$: 238.2661, found: 238.2652.

4.14.2. (S)-Isomer

In the same manner as described for (*R*)-**23**, crude (*S*)-**22**, (3.3 g, 7.9 mmol) yielded (*S*)-**23** [1.48 g, 78% based on (*S*)-**16**], n_D^{24}=1.4440; $[\alpha]_D^{23}$ +6.28 (*c* 3.88, $CHCl_3$). Its spectral data were identical with those reported for (*R*)-**23**. GC [same conditions as for (*R*)-**1**]: t_R 14.09 [23.2%, (*S*,*Z*)-**23**], 14.20 min [70.0% (*S*,*E*)-**23**]. HRMS calcd for $C_{17}H_{34}$: 238.2661, found: 238.2667.

4.15. 1-Methoxy-14-methyl-8-hexadecene 24

4.15.1. (R)-Isomer

Potassium *tert*-butoxide (500 mg, 4.5 mmol) was added to a stirred solution of (*R*)-**16** (505 mg, 2 mmol) in dry DMF (5 mL) at 50 °C under Ar. After stirring for 30 min, methyl iodide (2 mL, 3.1 g, 21 mmol) was added in one portion to the stirred and homogeneous solution. After the exotheromic reaction, KI separated. The mixture was stirred and heated at 80 °C for 1 h, then poured into ice-water, and extracted with hexane. The hexane solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (5 g). Elution with hexane/EtOAc (15:1) gave (*R*)-**24** (470 mg, 88%). n_D^{24}=1.4492; $[\alpha]_D^{24}$ −5.77 (*c* 2.63, $CHCl_3$); ν_{max} (film): 1377 (m, C–O), 966 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, $CHCH_3$), 0.85 (3H, t, *J* 7.2, CH_2CH_3), 1.02–1.18 (2H, m), 1.20–1.40 (15H, m), 1.52–1.61 (2H, m), 1.92–2.07 (4H, m), 3.33 (3H, s, OCH_3), 3.36 (2H, t, *J* 6.8, CH_2O), 5.32–5.34 [0.4H, m, (*R*,*Z*)-**24**], 5.34–5.42 [1.6H, m, (*R*,*E*)-**24**]; δ_C ($CDCl_3$): 11.4, 19.2, 26.1, 26.6, 29.1, 29.3, 29.5, 29.56, 29.63, 30.0, 32.55, 32.60, 34.4, 36.44, 36.48, 58.5, 129.6 and 129.8 [(*Z*)-isomer], 130.13 and 130.25 [(*E*)-isomer]. HRMS [same conditions as for (*R*)-**1**]: t_R 16.52 [17.3%, (*R*,*Z*)-**24**], 16.61 min [71.8% (*R*,*E*)-**24**]. MS of (*R*,*E*)-**24** [same as that of (*R*,*Z*)-**24**; 70 eV, EI]: *m*/*z* 268 (3) [M^+, $C_{18}H_{36}O$], 236 (21), 208 (5), 194 (2), 179 (2), 166 (3), 151 (6), 137 (15), 123 (28), 109 (51), 96 (82),

82 (100), 67 (72), 55 (62), 45 (46). HRMS calcd for $C_{18}H_{36}O$: 268.2766, found: 268.2757.

4.15.2. (S)-Isomer

In the same manner as described for (*R*)-**24**, (*S*)-**16** (2.03 g, 8 mmol) yielded (*S*)-**24** (1.71 g, 80%). n_D^{24}=1.4490; $[\alpha]_D^{22}$ +5.68 (*c* 4.94, $CHCl_3$). Its spectral data were identical with those of (*R*)-**24**. GC [same conditions as for (*R*)-**1**]: t_R 16.53 [22.2%, (*R*,*Z*)-**24**], 16.63 min [67.6%, (*R*,*E*)-**24**]. HRMS calcd for $C_{18}H_{36}O$: 268.2766, found: 268.2762.

4.16. 1-Methoxy-14-methylhexadecane 25

4.16.1. (R)-Isomer

Palladium–charcoal (0.1 g) was added to a solution of (*R*)-**24** (335 mg, 1.25 mmol) in EtOAc (10 mL). The suspension was stirred under H_2 (balloon) for 1.5 h at room temperature. The suspension was filtered through SiO_2 (6.0 g). The SiO_2 column was washed with EtOAc, and the combined organic solution was concentrated in vacuo to give (*R*)-**25** (311 mg, 93%). n_D^{22}=1.4425; $[\alpha]_D^{24}$ −4.83 (*c* 2.18, $CHCl_3$); ν_{max} (film): 1464 (m), 1377 (w), 1120 (m); δ_H ($CDCl_3$): 0.838 (3H, d, *J* 6.4, CHC*H*$_3$), 0.853 (3H, t, *J* 7.2, CH_2CH_3), 1.02–1.19 (2H, m), 1.20–1.40 (23H, m), 1.51–1.60 (2H, m), 3.33 (3H, s, OCH_3), 3.36 (2H, t, *J* 6.4, CH_2O); δ_C ($CDCl_3$): 11.4, 19.2, 26.1, 27.1, 29.48, 29.50, 29.6, 29.65, 29.68, 30.0, 32.8, 34.4, 36.6, 58.5, 63.0, 72.9; GC–MS [same conditions as for (*R*)-**1**]: t_R 16.81 min (90%). MS (70 eV, EI): *m*/*z* 269 (0.5) [M^+, ($C_{18}H_{36}O$)−1], 238 (8), 209 (26), 181 (11), 168 (5), 153 (10), 139 (18), 125 (38), 111 (59), 97 (96), 83 (96), 70 (100), 57 (62), 45 (65). HRMS calcd for $C_{18}H_{38}O$: 270.2923, found: 270.2912.

4.16.2. (S)-Isomer

In the same manner as described for (*R*)-**25**, (*S*)-**24** (958 mg, 3.6 mmol) yielded (*S*)-**25** (950 mg, 98%), n_D^{24}=1.4410; $[\alpha]_D^{23}$ +4.55 (*c* 4.44, $CHCl_3$). Its spectral data were identical with those of (*R*)-**25**. GC [same conditions as for (*R*)-**1**]: t_R 16.79 min (91%). HRMS calcd for $C_{18}H_{38}O$: 270.2923, found: 270.2935.

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