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Synthesis and Bioassay of the Eight Analogues of the CH503 Male Pheromone (3-Acetoxy-11,19-octacosadien-1-ol) of the *Drosophila melanogaster* Fruit Fly*

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Eight analogues of (3*R*,11*Z*,19*Z*)-CH503 (3-acetoxy-11,19-octacosadien-1-ol), the anti-aphrodisiac pheromone of male *Drosophila melanogaster*, were synthesized for a bioassay. These were the enantiomers of 3-acetoxy-11,19-octacosadiyn-1-ol (1), 3-acetoxyoctacosan-1-ol (2), (*Z*)-3-acetoxy-11-octacosen-1-ol (3), and (*Z*)-3-acetoxy-19-octacosen-1-ol (4). None of them were pheromonally active, indicating that the two double bonds at C-11 and C-19 were necessary for bioactivity.

Key words: 3-acetoxy-11,19-octacosadiyn-1-ol; 3-acetoxyoctacosan-1-ol; 3-acetoxy-11 or 19-octacosen-1-ol; *Drosophila melanogaster*; pheromone

In 2009, Yew *et al.* isolated a new pheromone named CH503 from the male fruit fly, *Drosophila melanogaster*, and identified it as 3-acetoxy-11,19-octacosadien-1-ol. The CH503 pheromone is transferred from males to females during mating, remains on the surface of females for at least 10 d, and inhibits courtship as an anti-aphrodisiac.[2] Since it has been well established that bioactivity depended on the correct stereochemistry of a pheromone,[3,4] we decided to determine the olefin geometry and absolute configuration at C-3 of CH503.

In 2010, we synthesized the enantiomers of (11*Z*,19*Z*)-CH503 (Fig. 1), and found (3*S*,11*Z*,19*Z*)-CH503 to be bioactive, while (3*R*,11*Z*,19*Z*)-CH503 was only slightly bioactive at the equivalent dose.[5] We therefore thought that (3*S*,11*Z*,19*Z*)-CH503 might be the naturally occurring pheromone.[5] The remaining six stereoisomers of CH503 were subsequently synthesized in 2012.[6] Complete separation of the eight stereoisomers of CH503 by reversed-phase HPLC at −20 °C was achieved after their esterification with (1*R*,2*R*)-2-(2,3-anthracenedicarboximido)cyclohexanecarboxylic acid, and natural CH503 was found to be (3*R*,11*Z*,19*Z*)-CH503.[6] Curiously, regardless of the geometry of the two double bonds, all (*S*)-stereoisomers of CH503 were also bioactive. It was therefore difficult to determine the stereostructure of natural CH503 on the basis of bioassay data alone.

Our next concern was to clarify the structural requirement for anti-aphrodisiac activity against male *Drosophila melanogaster*. Since the terminal hydroxy group and the acetoxy group at C-3 of CH503 seemed necessary for the interaction with its receptor, we planned to modify the two double bonds at C-11 and C-19. Accordingly, the four pairs of enantiomers of the analogues of CH503 were synthesized: (i) 3-acetoxy-11,19-octacosadiyn-1-ol (**1**) to examine whether two triple bonds could substitute for the two double bonds, (ii) 3-acetoxyoctacosan-1-ol (**2**) to see whether fully saturated compound **2** was bioactive or not, (iii) (*Z*)-3-acetoxy-11-octacosen-1-ol (**3**) to examine the role of the double bond at C-19, and (iv) (*Z*)-3-acetoxy-19-octacosen-1-ol (**4**) to clarify whether the double bond at C-11 was indispensable for bioactivity or not.

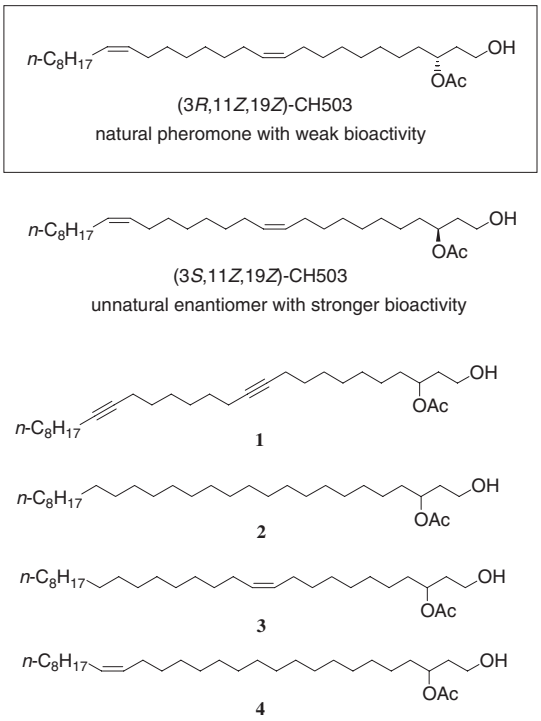

Fig. 1. Structures of (3*R*,11*Z*,19*Z*)-CH503, the Anti-Aphrodisiac Pheromone of the Male Fruit Fly (*Drosophila melanogaster*), and Its Analogues.

This paper reports the synthesis of the enantiomers of **1**–**4**, starting from the known intermediates employed in our previous synthesis of the stereoisomers of CH503.[5,6]

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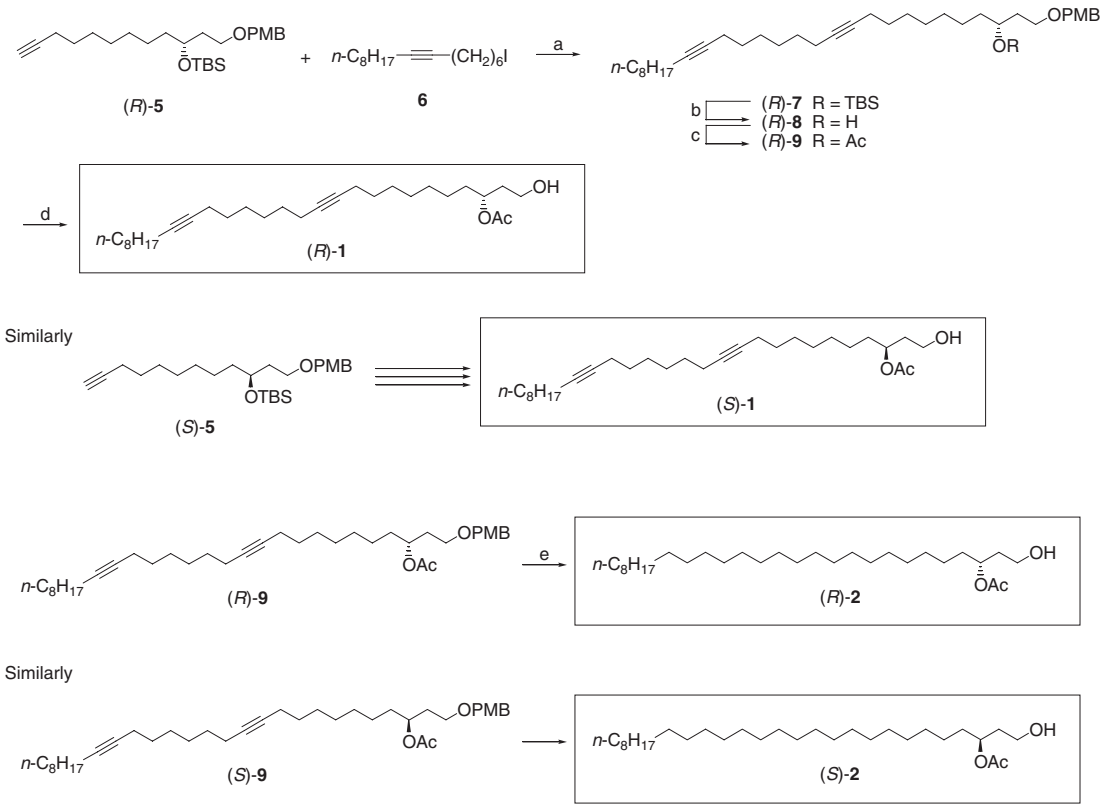


Scheme 1. Synthesis of the Enantiomers of **1** and **2**.
Reagents: (a) *n*-BuLi, THF, HMPA [91% for (*R*)-**7**; 85% for (*S*)-**7**]; (b) TBAF, THF [76% for (*R*)-**8**; 77% for (*S*)-**8**]; (c) Ac_2O, DMAP, C_5H_5N [96% for (*R*)-**9**; 92% for (*S*)-**9**]; (d) DDQ, CH_2Cl_2, H_2O [80% for (*R*)-**1**; 79% for (*S*)-**1**]; (e) H_2, Pd–C, EtOAc [68% for (*R*)-**2**; 83% for (*S*)-**2**].

A bioassay of the eight new analogues [(*R*)- and (*S*)-**1**–**4**] of CH503 revealed none of them to be pheromonally active.

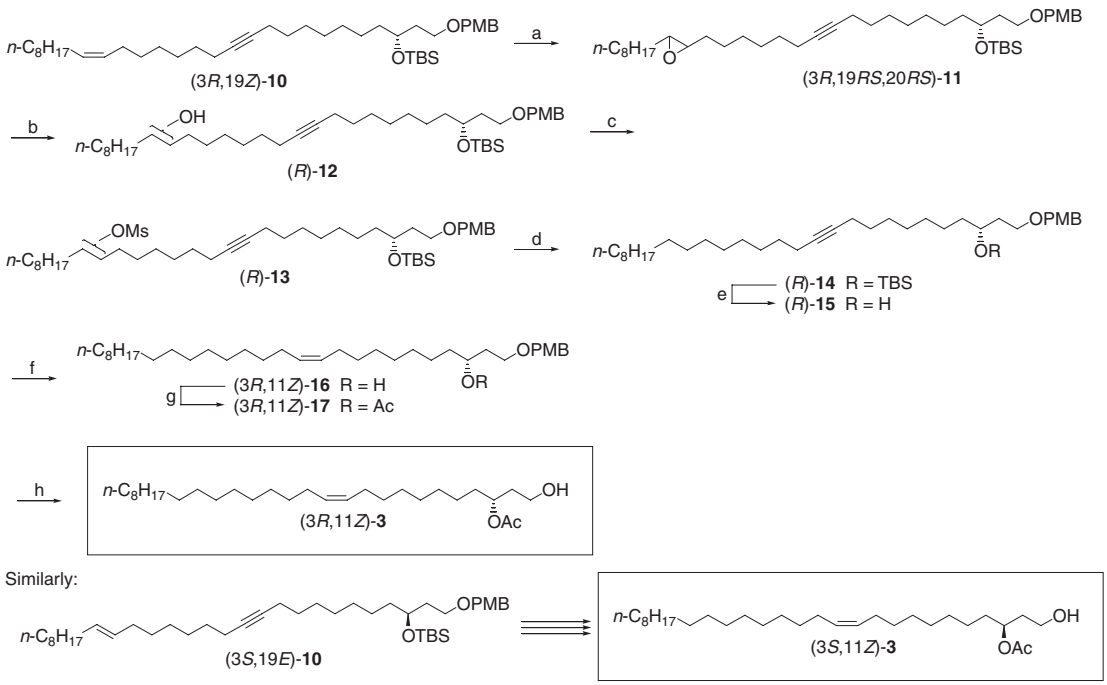
Results and Discussion

The upper part of Scheme 1 summarizes the synthesis of the enantiomers of 3-acetoxy-11,19-octacosadiyn-1-ol (**1**). Known alkyne (*R*)-**5**[6] was alkylated with known iodide **6**,[5] employing *n*-butyllithium as the base in THF/HMPA to give (*R*)-**7**. Removal of the *t*-butyldimethylsilyl (TBS) group of (*R*)-**7** with tetra(*n*-butyl)ammonium fluoride (TBAF) in THF afforded alcohol (*R*)-**8** which was acetylated to give acetate (*R*)-**9** in a 73% yield (two steps). Finally, treatment of (*R*)-**9** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in wet dichloromethane furnished desired diyne analogue (*R*)-**1** as a colorless oil in a 53% overall yield based on (*R*)-**5** (four steps). Similarly, oily (*S*)-**1** was prepared from (*S*)-**5** in a 48% overall yield.

Synthesis of the enantiomers of 3-acetoxyoctacosan-1-ol (**2**) is shown in the lower part of Scheme 1. Hydrogenation of (*R*)-**9** over palladium-charcoal gave (*R*)-**2**, mp 68–69 °C, in a 68% yield with concomitant removal of the *p*-methoxybenzyl (PMB) protective group. Similarly, (*S*)-**9** furnished (*S*)-**2** in an 83% yield.

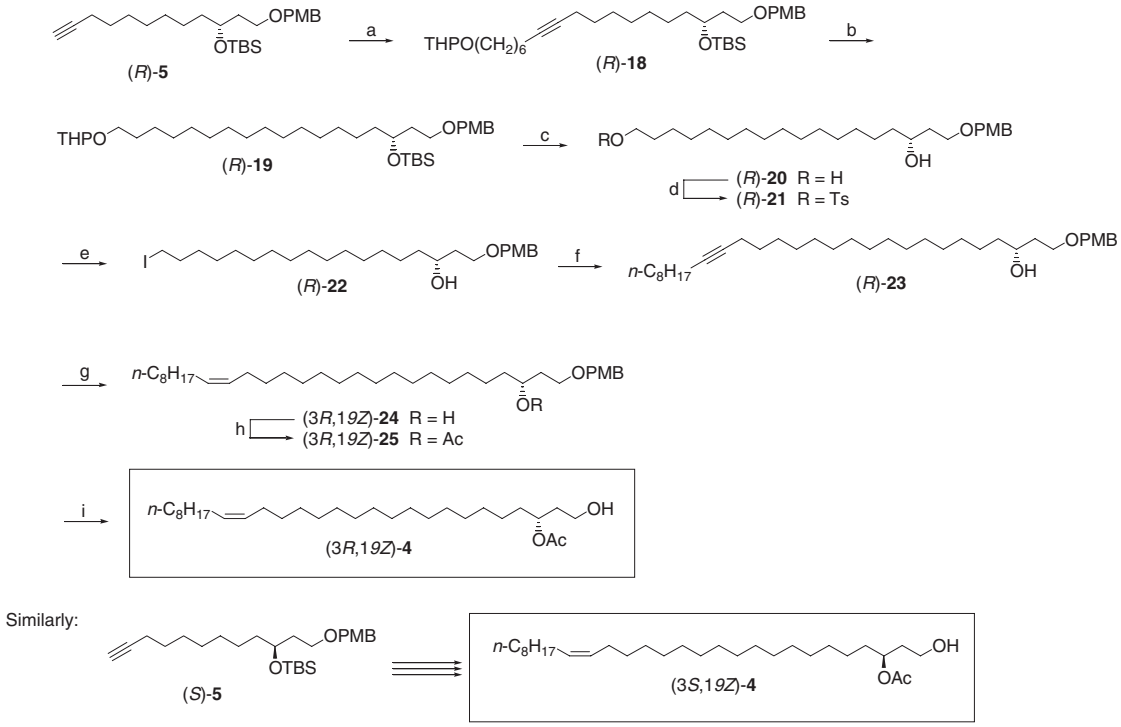
Scheme 2 shows the synthesis of the enantiomers of (*Z*)-3-acetoxy-11-octacosen-1-ol (**3**). Known enyne (3*R*,19*Z*)-**10**[6] was oxidized with *m*-chloroperbenzoic acid (MCPBA) to give epoxide **11** as a diastereomeric mixture. This was reduced with lithium aluminum hydride to furnish a regioisomeric mixture of alcohol (*R*)-**12** which gave a mixture of corresponding mesylate (*R*)-**13** upon mesylation. Reduction of (*R*)-**13** with lithium aluminum hydride in THF removed the mesyloxy group to afford (*R*)-**14** in a 43% yield, together with a 45% yield of desilylated product (*R*)-**15**. The TBS protective group of (*R*)-**14** was then removed with TBAF to yield an additional amount of (*R*)-**15**. The triple bond at C-11 of (*R*)-**15** was subjected to semi-hydrogenation over Lindlar's palladium catalyst in the presence of quinoline to give (3*R*,11*Z*)-**16** which was acetylated to furnish (3*R*,11*Z*)-**17**. Finally, the PMB protective group of **17** was removed by treatingt with DDQ in wet dichloromethane to give desired monoene analogue (3*R*,11*Z*)-**3**, mp 34–36 °C. The overall yield of (3*R*,11*Z*)-**3** was 43% based on (3*R*,19*Z*)-**10** (eight steps). Similarly, (3*S*,11*Z*)-**3** was synthesized from (3*S*,19*E*)-**10** in a 45% overall yield.

Synthesis of the enantiomers of 3-acetoxy-19-octacosen-1-ol (**4**) is summarized in Scheme 3. Known alkyne (*R*)-**5**[6] was alkylated with the 6-iodo-1-hexanol tetrahydropyranyl (THP) ether, employing *n*-butyllithium in THF/HMPA as the base to furnish (*R*)-**18**. This was hydrogenated over palladium-charcoal to give (*R*)-**19**, which was treated with *p*-toluenesulfonic acid (TsOH) in methanol to remove both the THP and TBS protective group, affording diol (*R*)-**20**. Selective tosylation of (*R*)-**20** with 1 eq. of *p*-toluenesulfonyl chloride (TsCl) gave crude (*R*)-**21**. This was subjected to the Finkelstein reaction with sodium iodide in DMF to furnish iodide (*R*)-**22**, mp 58–59 °C, in a 29% yield based on (*R*)-**20** with 59% recovery of (*R*)-**20**. Alkylation of 1-decyne with (*R*)-**22** was achieved by using *n*-butyllithium in THF/HMPA as the base to give (*R*)-**23** in a 75% yield. Lindlar hydrogenation of (*R*)-**23**



Scheme 2. Synthesis of the Enantiomers of **3**.

Reagents: (a) MCPBA CH_2Cl_2 [99% for crude (3*R*,19*RS*,20*RS*)-**11**; 99% for crude (3*S*,19*RS*,20*RS*)-**11**]; (b) $LiAlH_4$, Et_2O, reflux [79% for (*R*)-**12**; 84% for (*S*)-**12**]; (c) MsCl, C_5H_5N [91% for (*R*)-**13**; 92% for (*S*)-**13**]; (d) $LiAlH_4$, THF, reflux [43% for (*R*)-**14** and 45% for (*R*)-**15**; 42% for (*S*)-**14** and 44% for (*S*)-**15**]; (e) TBAF, THF, reflux [94% for (*R*)-**15** and 91% for (*S*)-**15**]; (f) H_2, Lindlar's Pd cat., quinoline, cyclohexane [88% for (3*R*,11*Z*)-**16** and 95% for (3*S*,11*Z*)-**16**]; (g) Ac_2O, C_5H_5N [96% for (3*R*,11*Z*)-**17** and 95% for (3*S*,11*Z*)-**17**]; (h) DDQ, CH_2Cl_2, H_2O [86% for (3*R*,11*Z*)-**3** and 84% for (3*S*,11*Z*)-**3**].



Scheme 3. Synthesis of the Enantiomers of **4**.

Reagents: (a) $THPO(CH_2)_6I$, *n*-BuLi, THF, HMPA [83% for (*R*)-**18** and 83% for (*S*)-**18**]; (b) H_2, Pd–C, EtOAc [91% for (*R*)-**19** and 92% for (*S*)-**19**]; (c) TsOH, MeOH [76% for (*R*)-**20** and 76% for (*S*)-**20**]; (d) TsCl, C_5H_5N; (e) NaI, DMF [29%, 2 steps for (*R*)-**22**; 34%, 2 steps for (*S*)-**22**]; (f) 1-decyne [4.5 eq. for (*R*)-**23** and 3.0 eq. for (*S*)-**23**], *n*-BuLi [4.2 eq. for (*R*)-**23** and 2.8 eq. for (*S*)-**23**], THF, HMPA [75% for (*R*)-**23** and 54% for (*S*)-**23**]; (g) H_2, Lindlar's Pd cat., quinoline, cyclohexane [83% for (3*R*,19*Z*)-**24** and 82% for (3*S*,19*Z*)-**24**]; (h) Ac_2O, C_5H_5N [89% for (3*R*,19*Z*)-**25** and 97% for (3*S*,11*Z*)-**25**]; (i) DDQ, CH_2Cl_2, H_2O [89% for (3*R*,19*Z*)-**4** and 88% for (3*S*,19*Z*)-**4**].

Table 1. The Analogues of (3*R*,11*Z*,19*Z*)-CH503 and (3*S*,11*Z*,19*Z*)-CH503 Were Tested in a Courtship Assay at Respective Doses of 2667 ng/fly and 83 ng/fly, Respectively

Compound	Concentration (ng/fly)	Courtship percentage[a,b]
Chloroform (control)	0	100% (n = 18)
Hexane (control)	0	95% (n = 38)
(*R*)-**1**	2667	100% (n = 18)
(*S*)-**1**	83	100% (n = 15)
(*R*)-**2**	2667	100% (n = 16)
(*S*)-**2**	83	94% (n = 18)
(3*R*,11*Z*)-**3**	2667	83% (n = 18)
(3*S*,11*Z*)-**3**	83	82% (n = 17)
(3*R*,19*Z*)-**4**	2667	89% (n = 18)
(3*S*,19*Z*)-**4**	83	94% (n = 16)

[a]The sample size for each experimental trial is indicated; no significant difference in courtship percentage was found between the control and experimental conditions.
[b]At the time of these bioassays, (3*S*,11*Z*,19*Z*)-CH503 was also assayed on a nearly weekly basis, which showing 40–50% courtship suppression at a dose of 83 ng/fly.

afforded (3*R*,19*Z*)-**24**, whose acetylation gave (3*R*,19*Z*)-**25**. Finally, its PMB protective group was removed to furnish another monoene analogue, (3*R*,19*Z*)-**4**, mp 27–28 °C. The overall yield of (3*R*,19*Z*)-**4** was 8% based on (*R*)-**5** (nine steps). Similarly, (3*S*,19*Z*)-**4** was prepared from (*S*)-**5** in a 7% overall yield.

To determine whether any of the synthesized analogues was biologically active as a male anti-aphrodisiac, a standardized courtship assay was used to determine whether male *Drosophila* courtship behavior was suppressed in the presence of a female fly perfumed with each of the analogues. Each analogue was tested at the same dose that was found to be sufficient for the bioactivity of (3*R*,11*Z*,19*Z*)-CH503 (2667 ng/fly) or (3*S*,11*Z*,19*Z*)-CH503 (83 ng/fly). In all cases, no significant suppression of male courtship behavior was apparent (Table 1).

Conclusion

The enantiomers of 3-acetoxy-11,19-octacosadiyn-1-ol (**1**), 3-acetoxyoctacosan-1-ol (**2**), (*Z*)-3-acetoxy-11-octacosen-1-ol (**3**), and (*Z*)-3-acetoxy-19-octacosen-1-ol (**4**) were synthesized, and their function as a male anti-aphrodisiac tested by using a courtship assay. Unlike CH503 [(3*R*,11*Z*,19*Z*)-3-acetoxy-11,19-octacosadien-1-ol], none of the analogues was pheromonally active as an anti-aphrodisiac against male *Drosophila melanogaster*. Accordingly, the two double bonds at C-11 and C-19 of CH503 were found indispensable for its bioactivity.

Experimental

All boiling point (bp) data are uncorrected values. Refractive indices (n_D) were measured with a DR-M2 refractometer (Atago, Tokyo, Japan). Melting points were measured with an EXSTAR DSC 6220 instrument (SII, Chiba, Japan), and optical rotation values were measured with a P-1020 polarimeter (Jasco, Tokyo, Japan). IR spectra were measured with an FT/IR-410 spectrometer (Jasco, Tokyo, Japan), and ^{1}H-NMR spectra (400 MHz, TMS at $\delta = 0.00$ as an internal standard) and ^{13}C-NMR spectra (100 MHz, $CDCl_3$ at $\delta = 77.0$ as an internal standard) were recorded with a JNM-AL 400 spectrometer (Jeol, Tokyo, Japan). GC-MS data were measured with a 5975 Inert XL instrument (Agilent Technologies, CA, USA), and HRMS data were recorded on a 6530 Accurate Mass Q-TOF LC/MS instrument (Agilent Technologies, CA, USA). Column chromatography was carried out on Kieselgel 60 Art. 1.07734 (Merck, Darmstadt, Germany).

*3-*t*-Butyldimethylsilyloxy-11,19-octacosadiyn-1-ol PMB ether (**7**).*

*(i) (*R*)-Isomer.* In the same manner as that previously described,[5] known (*R*)-**5** (1.01 g, 2.33 mmol)[6] and 7-hexadecynyl iodide (**6**, 896 mg, 2.57 mmol)[5] gave 1.39 g (91%) of (*R*)-**7** as a colorless oil, n_D^{23} 1.4872; $[\alpha]_D^{22}$ −5.71 (*c* 4.09, hexane); IR ν_{max} (film) cm^{-1}: 2930 (s), 2856 (s), 1613 (m, arom. C=C), 1586 (w), 1514 (s), 1464 (m), 1249 (s), 1098 (m), 1040 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.03 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.84–0.94 (12H, m), 1.18–1.54 (33H, m), 1.63–1.80 (2H, m), 2.07–2.24 (8H, br, 4 × C≡CCH_2), 3.50 (2H, t, $J = 6.8$ Hz), 3.80 (3H, s, OCH_3), 4.36–4.46 (2H, m, OCH_2Ar), 6.87 (2H, d, $J = 8.6$ Hz, arom. H), 7.25 (2H, d, $J = 8.6$ Hz, arom. H). HRMS of (*R*)-**7** [ESI ionization, positive polarity, 150 V fragmentor, N_2 (50 psi) nebulizer, N_2 (10 L/min, 350 °C) drying gas, 3500 V capillary current, 0.01 M HCO_2H aq./MeCN (10/90) eluent]: calcd. for $C_{42}H_{73}O_3Si$ [$(M + H)^+$], 653.5323; found, 653.5322.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**5** (1.01 g, 2.33 mmol) gave 1.29 g (85%) of (*S*)-**7** as a colorless oil, n_D^{23} 1.4869; $[\alpha]_D^{22}$ +5.66 (*c* 4.16, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**7**. HRMS of (*S*)-**7**: calcd. for $C_{42}H_{73}O_3Si$ [$(M + H)^+$], 653.5323; found, 653.5322.

*11,19-Octacosadiyne-1,3-diol 1-PMB ether (**8**).*

*(i) (*R*)-Isomer.* In the same manner as that previously described,[6] (*R*)-**7** (1.37 g, 2.10 mmol) gave 863 mg (76%) of (*R*)-**8** as a colorless solid. Mp 36 °C; $[\alpha]_D^{25}$ +6.04 (*c* 4.11, hexane); IR ν_{max} (film) cm^{-1}: 3505 (s, O–H), 2930 (s), 2849 (s), 1613 (m, arom. C=C), 1586 (w), 1518 (m), 1462 (s), 1252 (s), 1092 (m), 1032 (m), 813 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, $J = 6.8$ Hz), 1.21–1.55 (32H, m), 1.68–1.75 (2H, m), 2.08–2.18 (8H, br, 4 × C≡CCH_2), 2.89 (1H, d, $J = 3.2$ Hz), 3.58–3.64 (1H, m), 3.66–3.73 (1H, m), 3.74–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, OCH_2Ar), 6.88 (2H, d, $J = 8.6$ Hz, arom. H), 7.25 (2H, d, $J = 8.6$ Hz, arom. H). HRMS of (*R*)-**8** [same conditions as those for **7**]: calcd. for $C_{36}H_{59}O_3$ [$(M + H)^+$], 539.4459; found, 539.4459.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**7** (1.26 g, 1.93 mmol) gave 804 mg (77%) of (*S*)-**8** as a colorless solid. Mp 35–36 °C; $[\alpha]_D^{24}$ −5.97 (*c* 4.14, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**8**. HRMS of (*S*)-**8**: calcd. for $C_{36}H_{59}O_3$ [$(M + H)^+$], 539.4459; found, 539.4458.

*3-Acetoxy-11,19-octacosadiyn-1-ol PMB ether (**9**).*

*(i) (*R*)-Isomer.* In the same manner as that previously described,[5] (*R*)-**8** (812 mg, 1.51 mmol) gave 836 mg (96%) of (*R*)-**9** as a colorless oil, n_D^{23} 1.4926; $[\alpha]_D^{25}$ −13.3 (*c* 4.03, hexane); IR ν_{max} (film) cm^{-1}: 2930 (s), 2856 (s), 1737 (s, C=O), 1613 (m), 1586 (w), 1514 (s), 1465 (m), 1371 (m), 1246 (s), 1097 (m), 1038 (m), 822 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, $J = 6.8$ Hz), 1.14–1.66 (32H, m), 1.77–1.92 (2H, m), 2.00 (3H, s, $COCH_3$), 2.07–2.26 (8H, br, 4 × C≡CCH_2), 3.39–3.55 (2H, m), 3.80 (3H, s, OCH_3), 4.40 (2H, s, OCH_2Ar), 4.97–5.11 (1H, m), 6.87 (2H, d, $J = 8.4$ Hz, arom. H), 7.25 (2H, d, $J = 8.4$ Hz, arom. H). HRMS of (*R*)-**9** [same conditions as those for **7**]: calcd. for $C_{38}H_{61}O_4$ [$(M + H)^+$], 581.4564; found, 581.4568.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**8** (654 mg, 1.21 mmol) gave 647 mg (92%) of (*S*)-**9** as a colorless oil, n_D^{23} 1.4925; $[\alpha]_D^{22}$ +13.7 (*c* 4.03, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**9**. HRMS of (*S*)-**9**: calcd. for $C_{38}H_{61}O_4$ [$(M + H)^+$], 581.4564; found, 581.4563.

*3-Acetoxy-11,19-octacosadiyn-1-ol (**1**).*

*(i) (*R*)-Isomer.* In the same manner as that previously described,[5] (*R*)-**9** (328 mg, 0.565 mmol) gave 208 mg (80%) of (*R*)-**1** as a colorless oil which solidified in a refrigerator, n_D^{23} 1.4732; $[\alpha]_D^{20}$ −7.71 (*c* 1.14, hexane); IR ν_{max} (film) cm^{-1}: 3453 (br, O–H), 2930 (s), 2856 (s), 1738 (s, C=O), 1464 (m), 1373 (m), 1245 (s, C–O), 1056 (m), 1023 (m), 724 (w); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, $J = 6.8$ Hz), 1.18–1.53 (31H, m), 1.53–1.71 (2H, m), 1.79–1.89 (1H, m), 2.09 (3H, s, $COCH_3$), 2.09–2.20 (8H, br, 4 × C≡CCH_2), 2.33–2.39 (1H, br), 3.48–3.58 (1H, m,

CH*H*OH), 3.59–3.68 (1H, m, C*H*HOH), 4.98–5.06 (1H, m, CHOAc); ^{13}C-NMR δ_C ($CDCl_3$): 14.1, 18.7, 18.8, 21.1, 22.7, 25.5, 28.39, 28.40, 28.8, 28.9, 29.04, 29.07, 29.13, 29.14, 29.18, 29.24, 29.3, 31.9, 34.6, 37.5, 58.6, 71.6, 80.10, 80.18, 80.19, 80.3, 172.1; GC-MS [HP-5MS 5% phenylmethylsiloxane column, 30 m × 0.25 mm i.d., 52.7 kPa pressure; 50–325 °C temperature (+15 °C/min)], t_R 24.43 min (96.9%). MS of (*R*)-**1** (70 eV, EI) *m/z*: 460 (0.4) [M^+, $C_{30}H_{52}O_3$], 417 (1), 361 (2), 343 (2), 329 (2), 315 (4), 301 (6), 287 (6), 273 (9), 259 (18), 245 (26), 231 (9), 215 (6), 201 (8), 187 (14), 175 (25), 161 (44), 147 (53), 133 (49), 119 (47), 105 (57),95 (69), 93 (70), 91 (72), 81 (94), 67 (100), 55 (72), 43 (86). HRMS of (*R*)-**1** [same conditions as those for **7**]: calcd. for $C_{30}H_{53}O_3$ [$(M+H)^+$], 461.3989; found, 461.3986.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**9** (301 mg, 0.518 mmol) gave 190 mg (79%) of (*S*)-**1** as a colorless oil which solidified in a refrigerator, n_D^{23} 1.4741; $[\alpha]_D^{23}$ +7.51 (*c* 1.06, hexane). GC-MS [same conditions as those for (*R*)-**1**]: t_R 24.43 min (95.0%). Its spectral data (IR, ^{1}H- and ^{13}C-NMR, and MS) were identical to those of (*R*)-**1**. HRMS of (*S*)-**1**: calcd. for $C_{30}H_{53}O_3$ [$(M+H)^+$], 461.3989; found, 461.3989.

*3-Acetoxyoctacosan-1-ol (**2**).*

*(i) (*R*)-Isomer.* Palladium on charcoal (10%, 80 mg) was added to a solution of (*R*)-**9** (211 mg, 0.363 mmol) in EtOAc (8 mL). The suspension was stirred under H_2 (balloon) for 3 h at room temperature. The mixture was then filtered through Celite, and the catalyst and Celite were washed with Et_2O. The filtrate and washings were concentrated *in vacuo*. The residue (219 mg) was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc = 10:1–5:1 gave 115 mg (68%) of (*R*)-**2** as a colorless solid. Mp 68–69 °C; $[\alpha]_D^{22}$ −8.05 (*c* 1.13, Et_2O); IR ν_{max} (thin film) cm^{-1}: 3414 (br, O–H), 2916 (s), 2848 (s), 1736 (s, C=O), 1463 (m), 1375 (m), 1243 (s, C–O), 1051 (m), 1025 (m), 729 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.20–1.37 (46H, br), 1.48–1.70 (3H, m), 1.79–1.88 (1H, m), 2.09 (3H, s, $COCH_3$), 2.30–2.36 (1H, m), 3.48–3.57 (1H, m, CH*H*OH), 3.59–3.68 (1H, m, C*H*HOH), 4.98–5.06 (1H, m, CHOAc); ^{13}C-NMR δ_C ($CDCl_3$): 14.1, 21.1, 22.7, 25.5, 29.37, 29.40, 29.52, 29.57, 29.65, 29.67, 29.69, 29.71, 31.9, 34.7, 37.5, 58.6, 71.62,172.1; GC-MS [same conditions as those for (*R*)-**1**]: t_R 24.23 min (95.0%). MS of (*R*)-**2** (70 eV, EI) *m/z*: 468 (0.1) [M^+, $C_{30}H_{60}O_3$], 450 (0.2) [M–18], 425 (4), 390 (10), 379 (11), 362 (8), 348 (2), 334 (3), 320 (1), 306 (1), 292 (2), 278 (2), 264 (2), 250 (2), 236 (2), 222 (2), 207 (2), 194 (1), 180 (1), 166 (2), 152 (3), 137 (6), 117 (71), 97 (40), 88 (66), 82 (44), 71 (51), 57 (100), 43 (88). HRMS of (*R*)-**2** [APCI ionization, positive polarity, 6 µA corona current, N_2 (35 psi) nebulizer, N_2 (5 L/min, 350 °C) drying gas, 350 °C vaporizer, 3500 V capillary current, 0.01 M HCO_2H aq./MeOH (10/90) eluent]: calcd. for $C_{30}H_{61}O_3$ [$(M+H)^+$], 469.4615; found, 469.4619.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**9** (218 mg, 0.375 mmol) gave 146 mg (83%) of (*S*)-**2** as a colorless solid. Mp 68–69 °C; $[\alpha]_D^{24}$ +8.70 (*c* 1.07, Et_2O). GC-MS [same conditions as those for (*R*)-**1**]: t_R 24.20 min (94.2%). Its spectral data (IR, ^{1}H- and ^{13}C-NMR, and MS) were identical to those of (*R*)-**2**. HRMS of (*S*)-**2**: calcd. for $C_{30}H_{61}O_3$ [$(M+H)^+$], 469.4615; found, 469.4618.

*3-t-Butyldimethylsilyloxy-19,20-epoxy-11-octacosyn-1-ol PMB ether (**11**).*

*(i) (3*R*,19*RS*,20*RS*)-Isomer.* In the usual manner, known (3*R*,19*Z*)-**10** (509 mg, 0.777 mmol)[6] in CH_2Cl_2 (5 mL) was treated with MCPBA (69% purity, 215 mg, 0.858 mmol) to give 516 mg (99%) of crude (3*R*,19*RS*,20*RS*)-**11** as an oil. IR ν_{max} (film) cm^{-1}: 2927 (s), 2855 (s), 1613 (m), 1586 (w), 1514 (m), 1464 (m), 1249 (m), 1098 (m, C–O), 1040 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.84–0.94 (12H, m), 1.20–1.56 (36H, m), 1.64–1.80 (2H, m), 2.09–2.18 (4H, m, 2 × C≡CCH_2), 2.86–2.94 (2H, br), 3.50 (2H, t, J = 6.8 Hz, CH_2OAr), 3.76–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.37–4.45 (2H, m, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). This oil was employed for the next step without further purification.

*(ii) (3*S*,19*RS*,20*RS*)-Isomer.* Similarly, known (3*S*,19*E*)-**10** (507 mg, 0.774 mmol)[6] gave 512 mg (99%) of crude (3*S*,19*RS*,20*RS*)-**11** as an oil. ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.84–0.94 (12H, m), 1.20–1.56 (36H, m), 1.64–1.80 (2H, m), 2.09–2.18 (4H, m, 2 × C≡CCH_2), 2.62–2.67 (2H, m), 3.50 (2H, t, J = 6.8 Hz, CH_2OAr), 3.76–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.37–4.45 (2H, m, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). Its IR spectrum was indistinguishable from that of (3*R*,19*RS*,20*RS*)-**11**.

*3-t-Butyldimethylsilyloxy-11-octacosyne-1,19-diol 1-PMB ether and 3-t-butyldimethylsilyloxy-11-octacosyne-1,20-diol 1-PMB ether (**12**).*

*(i) (3*R*,19*RS*)- and (3*R*,20*RS*)-Isomer.* (3*R*,19*RS*,20*RS*)-**11** (496 mg, 0.739 mmol) in dry Et_2O (9 mL) was treated with $LiAlH_4$ (121 mg, 3.19 mmol) under reflux for 1.5 h to give 496 mg of a crude mixture. This mixture was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc = 10:1 gave 395 mg (79%) of a mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**12** as an oil. IR ν_{max} (film) cm^{-1}: 3375 (s, OH), 2927 (s), 2854 (s), 1613 (m), 1586 (w), 1514 (m), 1464 (m), 1249 (m), 1099 (m, C–O), 1040 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.84–0.93 (12H, m), 1.20–1.54 (39H, m), 1.65–1.80 (2H, m), 2.09–2.17 (4H, m, 2 × C≡CCH_2), 3.50 (2H, t, J = 6.8 Hz, CH_2OAr), 3.53–3.61 (1H, br), 3.74–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.37–4.45 (2H, m, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H).

*(ii) (3*S*,19*RS*)- and (3*S*,20*RS*)-Isomer.* Similarly, (3*S*,19*RS*,20*RS*)-**11** (484 mg, 0.721 mmol) gave 409 mg (84%) of a mixture of (3*S*,19*RS*)- and (3*S*,20*RS*)-**12** as an oil. Its IR and ^{1}H-NMR spectra were identical to those of the mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**12**.

*3-t-Butyldimethylsilyloxy-19-methanesulfonyloxy-11-octacosyn-1-ol PMB ether and 3-t-butyldimethylsilyloxy-20-methanesulfonyloxy-11-octacosyn-1-ol PMB ether (**13**).*

*(i) (3*R*,19*RS*)- and (3*R*,20*RS*)-Isomer.* The mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**12** (380 mg, 0.565 mmol) in dry C_5H_5N (5 mL) was treated with methanesulfonyl chloride (0.31 mL, 4.0 mmol) at 0–5 °C to give 414 mg of a crude mixture. This mixture was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc = 10:1 gave 384 mg (91%) of a mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**13** as an oil. IR ν_{max} (film) cm^{-1}: 2927 (s), 2855 (s), 1613 (m), 1586 (w), 1514 (m), 1464 (m), 1358 (m), 1249 (m), 1175 (m), 1098 (m, C–O), 1039 (m), 905 (m), 836 (m), 775 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.84–0.92 (12H, m), 1.20–1.52 (34H, m), 1.62–1.80 (6H, m), 2.10–2.17 (4H, m, 2 × C≡CCH_2), 2.99 (3H, s, CH_3SO_2), 3.50 (2H, t, J = 6.8 Hz, CH_2OAr), 3.76–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.37–4.45 (2H, m, ArCH_2), 4.65–4.73 (1H, m, CHOMs), 6.87 (2H, d, J = 8.8 Hz, arom. H), 7.25 (2H, d, J = 8.8 Hz, arom. H).

*(ii) (3*S*,19*RS*)- and (3*S*,20*RS*)-Isomer.* Similarly, the mixture of (3*S*,19*RS*)- and (3*S*,20*RS*)-**12** (393 mg, 0.584 mmol) gave 402 mg (92%) of a mixture of (3*S*,19*RS*)- and (3*S*,20*RS*)-**13** as an oil. Its IR and ^{1}H-NMR spectra were identical to those of the mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**13**.

*3-t-Butyldimethylsilyloxy-11-octacosyn-1-ol PMB ether (**14**).*

*(i) (*R*)-Isomer.* The mixture of (3*R*,19*RS*)- and (3*R*,20*RS*)-**13** (381 mg, 0.507 mmol) in dry THF (5 mL) was treated with $LiAlH_4$ (77 mg, 2.0 mmol) under reflux for 1.5 h to give 285 mg of a crude mixture. This mixture was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc = 10:1–5:1 gave 143 mg (43%) of (*R*)-**14** as a colorless oil and 123 mg (45%) of (*R*)-**15** as a colorless solid. Properties of (*R*)-**14**: n_D^{17} 1.4837; $[\alpha]_D^{25}$ −5.90 (*c* 1.04, hexane); IR ν_{max} (film) cm^{-1}: 2925 (s), 2854 (s), 1613 (m), 1586 (w), 1514 (m), 1464 (m), 1249 (m), 1098 (m, C–O), 1041 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.84–0.93 (12H, m), 1.19–1.51 (40H, m), 1.65–1.80 (2H, m), 2.13 (4H, t, J = 7.2 Hz, 2 × C≡CCH_2), 3.50 (2H, t, J = 6.8 Hz, CH_2OAr), 3.76–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.37–4.45 (2H, m, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (*R*)-**14** [same conditions as those for **7**]: calcd. for $C_{42}H_{77}O_3Si$ [$(M+H)^+$], 657.5636; found, 657.5640.

*(ii) (*S*)-Isomer.* Similarly, a mixture of (3*S*,19*RS*)- and (3*S*,20*RS*)-**14** (386 mg, 0.514 mmol) gave 142 mg (42%) of (*S*)-**14** as a colorless oil and 124 mg (44%) of (*S*)-**15** as a colorless solid. Properties of (*S*)-**14**: n_D^{17} 1.4835; $[\alpha]_D^{26}$ +6.03 (*c* 0.935, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**14**. HRMS of (*S*)-**14**: calcd. for $C_{42}H_{77}O_3Si$ [$(M+H)^+$], 657.5636; found, 657.5632.

*11-Octacosyne-1,3-diol 1-PMB ether (**15**).*

*(i) (*R*)-Isomer.* (*R*)-**14** (132 mg, 0.201 mmol) in dry THF (1 mL) was treated with a solution of TBAF in THF (1.0 M, 0.6 mL, 0.6 mmol) under reflux for 1.5 h to give 126 mg of a crude mixture. This mixture was chromatographed over SiO_2 (8 g). Elution with hexane/EtOAc = 5:1 gave 102 mg (94%) of (*R*)-**15** as a colorless solid. Mp 50–51 °C; $[\alpha]_D^{24}$ +7.15 (*c* 1.98, hexane); IR ν_{max} (thin film) cm^{-1}: 3508 (m, OH), 2919 (s), 2848 (s), 1613 (m), 1586 (w), 1517 (m), 1466 (m), 1250 (m), 1126 (w), 1091 (m, C–O), 1033 (m), 812 (w), 721 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.19–1.54 (40H, m), 1.68–1.76 (2H, m), 2.13 (4H, t, J = 7.0 Hz, 2 × C≡CCH_2), 2.89 (1H, d, J = 2.9 Hz), 3.58–3.73 (2H, m, CH_2OAr), 3.74–3.84 (1H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, ArCH_2), 6.88 (2H, d, J = 8.6 Hz, arom. H), 7.25 (2H, d, J = 8.6 Hz, arom. H). HRMS of (*R*)-**15** [same conditions as those for **7**]: calcd. for $C_{36}H_{63}O_3$ [$(M + H)^+$], 543.4772; found, 543.4773.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**14** (132 mg, 0.201 mmol) gave 99 mg (91%) of (*S*)-**15** as a colorless solid. Mp 50–51 °C; $[\alpha]_D^{25}$ −7.11 (*c* 1.48, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**15**. HRMS of (*S*)-**15**: calcd. for $C_{36}H_{63}O_3$ [$(M + H)^+$], 543.4772; found, 543.4777.

*(11Z)-11-Octacosene-1,3-diol 1-PMB ether (**16**).*

*(i) (3*R*,11Z)-Isomer.* Lindlar's Pd catalyst on $CaCO_3$ with Pb^{2+} (Aldrich, 12 mg) and quinoline (24 μL) were added to a solution of (*R*)-**15** (220 mg, 0.405 mmol) in cyclohexane (2 mL). The mixture was stirred for 5.5 h under an H_2 atmosphere (gas cylinder, 1 atm) at room temperature. The mixture was then filtered through Celite, and the catalyst and Celite were washed with Et_2O. The filtrate and washings were diluted with Et_2O, and successively washed with dil. HCl, water, an $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue (222 mg) was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc = 5:1 gave 194 mg (88%) of (3*R*,11*Z*)-**16** as a colorless solid. Mp 40–41 °C; $[\alpha]_D^{27}$ +7.41 (*c* 1.48, hexane); IR ν_{max} (thin film) cm^{-1}: 3421 (s, OH), 3002 (m), 2924 (s), 2852 (s), 1613 (m), 1586 (w), 1514 (m), 1466 (m), 1248 (m), 1092 (m), 1038 (m), 821 (m), 720 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.20–1.62 (40H, m), 1.68–1.76 (2H, m), 1.96–2.06 (4H, m, 2× = CHCH_2), 2.84–2.88 (1H, br), 3.57–3.72 (2H, m, CH_2OAr), 3.74–3.83 (1H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, ArCH_2), 5.28–5.38 (2H, m, CH=CH), 6.87 (2H, d, J = 8.6 Hz, arom. H), 7.25 (2H, d, J = 8.6 Hz, arom. H). HRMS of (3*R*,11*Z*)-**16** [same conditions as those for **7**]: calcd. for $C_{36}H_{65}O_3$ [$(M + H)^+$], 545.4928; found, 545.4926.

*(ii) (3*S*,11Z)-Isomer.* Similarly, (*S*)-**15** (110 mg, 0.203 mmol) gave 105 mg (95%) of (3*S*,11*Z*)-**16** as a colorless solid. Mp 40–41 °C; $[\alpha]_D^{26}$ −7.07 (*c* 1.23, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (3*R*,11*Z*)-**16**. HRMS of (3*S*,11*Z*)-**16**: calcd. for $C_{36}H_{65}O_3$ [$(M + H)^+$], 545.4928; found, 545.4932.

*3-Acetoxy-11-octacosyn-1-ol PMB ether (**17**).*

*(i) (3*R*,11Z)-Isomer.* In the same manner as that previously described,[5] (3*R*,11*Z*)-**16** (180 mg, 0.330 mmol) gave 187 mg (96%) of (3*R*,11*Z*)-**17** as a colorless oil, n_D^{18} 1.4839; $[\alpha]_D^{27}$ −13.2 (*c* 1.54, hexane); IR ν_{max} (film) cm^{-1}: 3003 (m), 2925 (s), 2852 (s), 1738 (s, C=O), 1613 (m), 1586 (w), 1514 (m), 1465 (m), 1370 (m), 1245 (m), 1097 (m), 1038 (m), 957 (w), 821 (m), 722 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.19–1.38 (38H, m), 1.49–1.58 (2H, br), 1.79–1.87 (2H, m), 1.95–2.06 (4H, m, 2× = CHCH_2), 1.99 (3H, s, $COCH_3$), 3.40–3.51 (2H, m, CH_2OAr), 3.80 (3H, s, OCH_3), 4.40 (2H, s, ArCH_2), 4.97–5.05 (1H, m), 5.28–5.41 (2H, m, CH=CH), 6.87 (2H, d, J = 8.6 Hz, arom. H), 7.25 (2H, d, J = 8.6 Hz, arom. H). HRMS of (3*R*,11*Z*)-**17** [same conditions as those for **2**]: calcd. for $C_{38}H_{67}O_4$ [$(M + H)^+$], 587.5034; found, 587.5027.

*(ii) (3*S*,11Z)-Isomer.* Similarly, (3*S*,11*Z*)-**16** (174 mg, 0.319 mmol) gave 178 mg (95%) of (3*S*,11*Z*)-**17** as a colorless oil, n_D^{19} 1.4841; $[\alpha]_D^{27}$ +13.4 (*c* 1.33, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (3*R*,11*Z*)-**17**. HRMS of (3*S*,11*Z*)-**17**: calcd. for $C_{38}H_{67}O_4$ [$(M + H)^+$], 587.5034; found, 587.5032.

*3-Acetoxy-11-octacosen-1-ol (**3**).*

*(i) (3*R*,11Z)-Isomer.* In the same manner as that previously described,[5] (3*R*,11*Z*)-**17** (162 mg, 0.276 mmol) gave 111 mg (86%) of (3*R*,11*Z*)-**3** as a colorless solid. Mp 34–36 °C; $[\alpha]_D^{23}$ −8.87 (*c* 1.03, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3460 (s, OH), 3004 (w), 2924 (s), 2853 (s), 1739 (s, C=O), 1465 (m), 1374 (m), 1244 (s, C–O), 1053 (m), 1025 (m), 955 (w), 721 (w); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.18–1.38 (38H, br), 1.47–1.70 (3H, m), 1.79–1.89 (1H, m), 1.95–2.06 (4H, m, 2× = CHCH_2), 2.08 (3H, s, $COCH_3$), 2.32–2.40 (1H, br), 3.48–3.58 (1H, m, CH*H*OH), 3.59–3.68 (1H, m, C*H*HOH), 4.98–5.06 (1H, m, CHOAc), 5.28–5.40 (2H, m, CH=CH); ^{13}C-NMR δ_C ($CDCl_3$): 14.1, 21.1, 22.7, 25.5, 27.19, 27.24, 29.2, 29.35, 29.37, 29.42, 29.59, 29.67, 29.71, 29.73, 29.79, 31.9, 34.7, 37.5, 58.6, 71.6, 129.8, 130.0, 172.1; GC-MS [same conditions as those for **1**]: t_R 23.36 min (13.0%, broad, decomposition peak), 23.72 min (82.0%), 24.28 min (4.8%, broad, decomposition peak). The observed GC purity of (3*R*,11*Z*)-**3** was less than the reality due to thermal decomposition. Its ^{1}H-NMR spectrum guaranteed the high purity of the sample. Similar decomposition was apparent with other mono-olefin samples (3*S*,11*Z*)-**3**, (3*R*,19*Z*)-**4**, and (3*S*,19*Z*)-**4**. MS of (3*R*,11*Z*)-**3** (70 eV, EI) *m/z*: 448 (3) [M-18], 406 (3), 388 (6), 360 (2), 334 (2), 320 (2), 281 (7), 264 (2), 253 (2), 222 (2), 207 (23), 191 (4), 177 (4), 163 (9), 149 (22), 135 (33), 121 (27), 109 (32), 95 (60), 81 (67), 67 (58), 55 (67), 43 (100). HRMS of (3*R*,11*Z*)-**3** [same conditions as those for **2**]: calcd. for $C_{30}H_{59}O_3$ [$(M + H)^+$], 467.4459; found, 467.4454.

*(ii) (3*S*,11Z)-Isomer.* Similarly, (3*S*,11*Z*)-**17** (160 mg, 0.273 mmol) gave 107 mg (84%) of (3*S*,11*Z*)-**3** as a colorless solid. Mp 34–36 °C; $[\alpha]_D^{20}$ +8.59 (*c* 1.02, $CHCl_3$). GC-MS [same conditions as those for (*R*)-**1**]: t_R 23.34 min (9.2%, broad, decomposition peak), 23.72 min (83.1%), 24.29 min (6.7%, broad, decomposition peak). Its spectral data (IR, ^{1}H- and ^{13}C-NMR, and MS) were identical to those of (3*R*,11*Z*)-**3**. HRMS of (3*S*,11*Z*)-**3**: calcd. for $C_{30}H_{59}O_3$ [$(M + H)^+$], 467.4459; found, 467.4453.

*3-*t*-Butyldimethylsilyloxy-18-tetrahydropyranyloxy-11-octadecyn-1-ol PMB ether (**18**).*

*(i) (*R*)-Isomer.* In the same manner as that previously described,[5] (*R*)-**5** (859 mg, 1.99 mmol)[6] and 6-iodo-1-hexanol THP ether (748 mg, 2.40 mmol) gave 1.01 g (83%) of (*R*)-**18** as a colorless oil, n_D^{21} 1.4919; $[\alpha]_D^{26}$ −5.96 (*c* 4.17, hexane); IR ν_{max} (film) cm^{-1}: 2928 (s), 2855 (s), 1613 (m), 1586 (w), 1514 (m), 1464 (m), 1249 (m), 1119 (m), 1078 (m), 1036 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.029 (3H, s, CH_3Si), 0.034 (3H, s, CH_3Si), 0.87 (9H, s), 1.22–1.90 (28H, m), 2.09–2.17 (4H, m, 2 × C≡CCH_2), 3.34–3.42 (1H, m), 3.46–3.54 (3H, m), 3.70–3.76 (1H, m), 3.76–3.83 (1H, br), 3.80 (3H, s, OCH_3), 3.83–3.90 (1H, m), 4.36–4.46 (2H, m, ArCH_2), 4.55–4.59 (1H, m), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (*R*)-**18** [same conditions as those for **7**]: calcd. for $C_{37}H_{65}O_5Si$ [$(M + H)^+$], 617.4596; found, 617.4596.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**5** (971 mg, 2.24 mmol) gave 1.14 g (83%) of (*S*)-**18** as a colorless oil, n_D^{19} 1.4919; $[\alpha]_D^{23}$ +6.12 (*c* 4.05, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**18**. HRMS of (*S*)-**18**: calcd. for $C_{37}H_{65}O_5Si$ [$(M + H)^+$], 617.4596; found, 617.4608.

*3-*t*-Butyldimethylsilyloxy-18-tetrahydropyranyloxy-11-octadecan-1-ol PMB ether (**19**).*

*(i) (*R*)-Isomer.* In the same manner as that described for (*R*)-**2**, (*R*)-**18** (991 mg, 1.61 mmol) gave 910 mg (91%) of (*R*)-**19** as a colorless oil. The THP group remained intact in this step. n_D^{18} 1.4841; $[\alpha]_D^{22}$ −6.20 (*c* 4.17, hexane); IR ν_{max} (film) cm^{-1}: 2926 (s), 2853 (s), 1614 (m), 1586 (w), 1514 (m), 1464 (m), 1249 (m), 1119 (m), 1079 (m), 1037 (m), 836 (m), 774 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.03 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.87 (9H, s), 1.18–1.92 (36H, m), 3.34–3.42 (1H, m), 3.46–3.54 (3H, m), 3.69–3.76 (1H, m), 3.76–3.83 (1H, br), 3.80 (3H, s, OCH_3), 3.83–3.91 (1H, m), 4.36–4.46 (2H, m, ArCH_2), 4.55–4.60 (1H, m), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (*R*)-**19** [same conditions as those for **2**]: calcd. for $C_{37}H_{69}O_5Si$ [$(M + H)^+$], 621.4909; found, 621.4911.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**18** (612 mg, 0.992 mmol) gave 565 mg (92%) of (*S*)-**19** as a colorless oil, n_D^{18} 1.4838; $[\alpha]_D^{27}$ +6.27 (*c* 4.02, hexane). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**19**. HRMS of (*S*)-**19**: calcd. for $C_{37}H_{69}O_5Si$ [$(M + H)^+$], 621.4909; found, 621.4903.

*1,3,18-Octadecanetriol 1-PMB ether (**20**).*

*(i) (*R*)-Isomer.* *p*-Toluenesulfonic acid monohydrate (32 mg, 0.17 mmol) was added to a solution of (*R*)-**19** (877 mg, 1.41 mmol) in methanol (12 mL). The solution was stirred and heated under reflux for 1.5 h, before being diluted with water and extracted with EtOAc. The EtOAc solution was successively washed with an $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was recrystallized from hexane to give 455 mg (76%) of (*R*)-**20** as a colorless solid. Mp 57–61 °C; $[\alpha]_D^{22}$ +5.47 (*c* 0.448, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3312 (s, OH), 2916 (s), 2848 (s), 1609 (w), 1508 (m), 1465 (m), 1246 (m), 1075 (m), 1038 (w); ^{1}H-NMR δ_H ($CDCl_3$): 1.18–1.68 (28H, m), 1.68–1.80 (2H, m), 2.23–2.45 (1H, br), 2.82–2.90 (1H, br), 3.58–3.74 (3H, m), 3.74–3.95 (2H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (*R*)-**20** [same conditions as those for **2**]: calcd. for $C_{26}H_{47}O_4$ [(M + H)$^+$], 423.3469; found, 423.3473.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**19** (946 mg, 1.52 mmol) gave 487 mg (76%) of (*S*)-**20** as a colorless solid. Mp 57–61 °C; $[\alpha]_D^{25}$ −5.80 (*c* 1.05, $CHCl_3$). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**20**. HRMS of (*S*)-**20**: calcd. for $C_{26}H_{47}O_4$ [(M + H)$^+$], 423.3469; found, 423.3467.

*18-*p*-Toluenesulfonyloxy-1,3-octadecanediol 1-PMB ether (**21**).*

*(i) (*R*)-Isomer.* Tosyl chloride (207 mg, 1.09 mmol) was added portionwise to a solution of (*R*)-**20** (449 mg, 1.06 mmol) in dry pyridine (4.5 mL) at 0–5 °C. The solution was stirred at 0–5 °C for 5 h, before being diluted with ice-cooled dil. HCl, and extracted with EtOAc. The EtOAc solution was successively washed with water, a dil. $CuSO_4$ solution, water, an $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 675 mg (quant.) of crude (*R*)-**21** as a colorless solid. IR ν_{max} (thin film) cm^{-1}: 3463 (s, OH), 2916 (s), 2848 (s), 1613 (m), 1514 (m), 1469 (m), 1358 (m), 1249 (m), 1176 (m), 1098 (m), 1071 (m), 1033 (m); ^{1}H-NMR δ_H ($CDCl_3$): 1.10–1.92 (30H, m), 2.45 (3H, s), 2.87–2.97 (1H, br), 3.58–3.74 (2H, m), 3.74–3.93 (1H, br), 3.80 (3H, s, OCH_3), 4.02 (2H, t, J = 6.4 Hz, CH_2OTs), 4.45 (2H, s, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H), 7.34 (2H, d, J = 8.4 Hz, arom. H), 7.79 (2H, d, J = 8.4 Hz, arom. H). This crude (*R*)-**21** was employed for the next step without further purification.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**20** (652 mg, 1.54 mmol) gave 1.05 g (quant.) of crude (*S*)-**21** as a colorless solid. Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**21**.

*18-Iodo-1,3-octadecanediol 1-PMB ether (**22**).*

*(i) (*R*)-Isomer.* Sodium iodide (407 mg, 2.72 mmol) was added to a solution of crude (*R*)-**21** (0.67 g, <1.06 mmol) in DMF (6 mL) at room temperature. After the addition, the mixture was stirred and heated at 50 °C for 5 h, before being diluted with water and extracted with EtOAc. The EtOAc solution was successively washed with a dil. $Na_2S_2O_3$ solution, an $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue (550 mg) was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc = 5:1 gave 165 mg (29%, 2 steps) of (*R*)-**22** as a colorless solid. Further elution with EtOAc recovered 266 mg (59%) of (*R*)-**20**. Properties of (*R*)-**22**: mp 58–59 °C; $[\alpha]_D^{24}$ +5.50 (*c* 1.03, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3456 (s, OH), 2915 (s), 2848 (s), 1612 (m), 1514 (m), 1469 (m), 1249 (m), 1167 (m), 1077 (m), 1025 (m); ^{1}H-NMR δ_H ($CDCl_3$): 1.18–1.55 (26H, m), 1.69–1.77 (2H, m), 1.77–1.87 (2H, m), 2.91 (1H, d, J = 3.2 Hz), 3.19 (2H, t, J = 7.2 Hz), 3.57–3.73 (2H, m), 3.73–3.88 (1H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, ArCH_2), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (*R*)-**22** [same conditions as those for **7**]: calcd. for $C_{26}H_{46}IO_3$ [(M + H)$^+$], 533.2486; found, 533.2484.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**21** (1.0 g, <1.54 mmol) gave 283 mg (34%, 2 steps) of (*S*)-**22** as a colorless solid and recovered 288 mg (44%) of (*S*)-**20**. Properties of (*S*)-**22**: mp 57–59 °C; $[\alpha]_D^{24}$ −4.89 (*c* 2.64, $CHCl_3$). Its IR and ^{1}H-NMR spectra were identical to those of (*R*)-**22**. HRMS of (*S*)-**22**: calcd. for $C_{26}H_{46}IO_3$ [(M + H)$^+$], 533.2486; found, 533.2487.

*19-Octacosyne-1,3-diol 1-PMB ether (**23**).*

*(i) (*R*)-Isomer.* A solution of *n*-BuLi in hexane (1.6 M, 1.28 mL, 2.05 mmol, 4.2 eq.) was added dropwise to a solution of 1-decyne (304 mg, 2.20 mmol, 4.5 eq.) in dry THF (2 mL) and HMPA (0.9 mL) at −65–−40 °C under Ar. The mixture was warmed to −10 °C for 10 min, and then cooled again to −65 °C. A solution of (*R*)-**22** (260 mg, 0.488 mmol) in dry THF (2 mL) was added dropwise to the mixture at −65 °C, and the temperature was gradually raised to room temperature. After stirring for 24 h at room temperature, the mixture was diluted with water and extracted with EtOAc. The EtOAc solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue (841 mg) was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc = 5:1 gave 198 mg (75%) of (*R*)-**23** as a colorless solid. Mp 52–53 °C; $[\alpha]_D^{22}$ +5.47 (*c* 0.790, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3507 (m, OH), 2918 (s), 2847 (s), 1613 (m), 1518 (m), 1466 (m), 1251 (m), 1129 (w), 1091 (m), 1033 (m), 812 (w), 721 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.17–1.54 (40H, m), 1.67–1.76 (2H, m), 2.10–2.20 (4H, m, 2 × C ≡ CCH_2), 2.91–2.96 (1H, br), 3.58–3.74 (2H, m, CH_2OAr), 3.74–3.87 (1H, br), 3.81 (3H, s, OCH_3), 4.46 (2H, s, ArCH_2), 6.88 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). GC-MS [same conditions as those for **1**]: t_R 48.13 min (95.2%). HRMS of (*R*)-**23** [same conditions as those for **7**]: calcd. for $C_{36}H_{63}O_3$ [(M + H)$^+$], 543.4772; found, 543.4767.

*(ii) (*S*)-Isomer.* Similarly, (*S*)-**22** (274 mg, 0.515 mmol), 1-decyne (213 mg, 1.54 mmol, 3.0 eq.) and *n*-BuLi in hexane (1.6 M, 0.90 mL, 1.44 mmol, 2.8 eq.) gave 151 mg (54%) of (*S*)-**23** as a colorless solid. Mp 38–41 °C; $[\alpha]_D^{22}$ −6.08 (*c* 0.653, $CHCl_3$). Its IR and ^{1}H-NMR spectra were indistinguishable with those of (*R*)-**23**. The low mp of this stereoisomer was due to its slightly lower purity than that of the (*R*)-isomer as determined by GC-MS. GC-MS [same conditions as those for **1**]: t_R 48.04 min (82.6%). HRMS of (*S*)-**23**: calcd. for $C_{36}H_{63}O_3$ [(M + H)$^+$], 543.4772; found, 543.4771.

*(19*Z*)-19-Octacosene-1,3-diol 1-PMB ether (**24**).*

*(i) (3*R*,19*Z*)-Isomer.* In the same manner as that described for (3*R*,11*Z*)-**16**, (*R*)-**23** (150 mg, 0.276 mmol) gave 126 mg (83%) of (3*R*,19*Z*)-**24** as a colorless solid. Mp 45–46 °C; $[\alpha]_D^{23}$ +5.42 (*c* 1.13, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3507 (s, OH), 3002 (m), 2918 (s), 2848 (s), 1613 (m), 1585 (w), 1519 (m), 1470 (m), 1251 (m), 1092 (m), 1033 (m), 817 (m), 718 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.14–1.54 (40H, m), 1.68–1.77 (2H, m), 1.96–2.06 (4H, m, 2× = CHCH_2), 2.86–2.92 (1H, br), 3.58–3.72 (2H, m, CH_2OAr), 3.74–3.85 (1H, br), 3.80 (3H, s, OCH_3), 4.45 (2H, s, ArCH_2), 5.29–5.39 (2H, m, CH=CH), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (3*R*,19*Z*)-**24** [same conditions as those for **7**]: calcd. for $C_{36}H_{65}O_3$ [(M + H)$^+$], 545.4928; found, 545.4917.

*(ii) (3*S*,19*Z*)-Isomer.* Similarly, (*S*)-**23** (100 mg, 0.184 mmol) gave 82 mg (82%) of (3*S*,19*Z*)-**24** as a colorless solid. Mp 46–47 °C; $[\alpha]_D^{21}$ −6.03 (*c* 0.762, $CHCl_3$). Its IR and ^{1}H-NMR spectra were identical to those of (3*R*,19*Z*)-**24**. HRMS of (3*S*,19*Z*)-**24**: calcd for $C_{36}H_{65}O_3$ [(M + H)$^+$], 545.4928; found, 545.4939.

*(19*Z*)-3-Acetoxy-11-octacosen-1-ol PMB ether (**25**).*

*(i) (3*R*,19*Z*)-Isomer.* In the same manner as that previously described,[5] (3*R*,19*Z*)-**24** (121 mg, 0.222 mmol) gave 116 mg (89%) of (3*R*,19*Z*)-**25** as a colorless oil, n_D^{17} 1.4845; $[\alpha]_D^{20}$ −9.47 (*c* 0.913, $CHCl_3$); IR ν_{max} (film) cm^{-1}: 3003 (m), 2925 (s), 2852 (s), 1739 (s, C=O), 1613 (m), 1586 (w), 1514 (m), 1465 (m), 1371 (m), 1245 (s), 1097 (m), 1038 (m), 957 (w), 821 (m), 721 (m); ^{1}H-NMR δ_H ($CDCl_3$): 0.88 (3H, t, J = 6.8 Hz), 1.19–1.44 (38H, m), 1.48–1.58 (2H, br), 1.79–1.88 (2H, m), 1.94–2.08 (4H, m, 2× = CHCH_2), 2.00 (3H, s, $COCH_3$), 3.40–3.51 (2H, m, CH_2OAr), 3.80 (3H, s, OCH_3), 4.40 (2H, s, ArCH_2), 4.97–5.06 (1H, m), 5.29–5.42 (2H, m, CH=CH), 6.87 (2H, d, J = 8.4 Hz, arom. H), 7.25 (2H, d, J = 8.4 Hz, arom. H). HRMS of (3*R*,19*Z*)-**25** [same conditions as those for **2**]: calcd. for $C_{38}H_{67}O_4$ [(M + H)$^+$], 587.5034; found, 587.5026.

*(ii) (3*S*,19*Z*)-Isomer.* Similarly, (3*S*,19*Z*)-**24** (80 mg, 0.15 mmol) gave 83 mg (97%) of (3*S*,19*Z*)-**25** as a colorless oil, n_D^{17} 1.4846; $[\alpha]_D^{20}$ +9.56 (*c* 0.831, $CHCl_3$). Its IR and ^{1}H-NMR spectra were identical to those of (3*R*,19*Z*)-**25**. HRMS of (3*S*,19*Z*)-**25**: calcd. for $C_{38}H_{67}O_4$ [(M + H)$^+$], 587.5034; found, 587.5039.

*3-Acetoxy-19-octacosen-1-ol (**4**).*

*(i) (3*R*,19*Z*)-Isomer.* In the same manner as that previously described,[5] (3*R*,19*Z*)-**25** (104 mg, 0.177 mmol) gave 74 mg (89%) of

(3*R*,19*Z*)-**4** as a colorless solid. Mp 27–28 °C; $[\alpha]_D^{21}$ −8.63 (*c* 0.742, $CHCl_3$); IR ν_{max} (thin film) cm^{-1}: 3455 (s, OH), 3004 (w), 2924 (s), 2853 (s), 1739 (s, C=O), 1466 (m), 1374 (m), 1244 (s, C–O), 1054 (m), 1022 (m), 957 (w), 721 (w); ^{1}H-NMR δ_H ($CDCl_3$): 0.89 (3H, t, J = 6.8 Hz), 1.18–1.42 (38H, br), 1.50–1.70 (3H, m), 1.80–1.89 (1H, m), 1.96–2.06 (4H, m, 2× = C*H*$_2$), 2.09 (3H, s, $COCH_3$), 2.32–2.40 (1H, br), 3.48–3.58 (1H, m, CH*H*OH), 3.59–3.68 (1H, m, C*H*HOH), 4.98–5.06 (1H, m, CHOAc), 5.32–5.42 (2H, m, CH=CH); ^{13}C-NMR δ_C ($CDCl_3$): 14.07, 14.09, 21.09, 21.11, 21.20, 22.64, 22.66, 22.67, 25.43, 25.45, 25.46, 27.2, 29.29, 29.36, 29.50, 29.54, 29.65, 29.66, 29.74, 58.5, 71.6, 129.9, 172.2; GC-MS [same conditions as those for **1**]: t_R 23.50 min (8.8%, broad, decomposition peak), 23.91 min (78.6%), 24.49 min (10.8%, broad, decomposition peak). MS of (3*R*,19*Z*)-**4** (70 eV, EI): *m*/*z*: 448 (3) [M-18], 406 (3), 388 (4), 360 (3), 331 (2), 289 (4), 275 (6), 261 (4), 247 (2), 222 (2), 207 (20), 193 (4), 179 (2), 166 (3), 151 (6), 135 (12), 117 (36), 95 (57), 83 (66), 69 (68), 55 (93), 43 (100). HRMS of (3*R*,19*Z*)-**4** [same conditions as those for **2**]: calcd. for $C_{30}H_{59}O_3$ $[(M+H)^+]$, 467.4459; found, 467.4458.

(ii) (3S,19Z)-Isomer. Similarly, (3*S*,19*Z*)-**25** (75 mg, 0.13 mmol) gave 53 mg (88%) of (3*S*,19*Z*)-**4** as a colorless solid, mp 27–28 °C; $[\alpha]_D^{22}$ +8.36 (*c* 0.505, $CHCl_3$). GC-MS [same conditions as those for (*R*)-**1**]: t_R 23.50 min (15.0%, broad, decomposition peak), 23.89 min (81.3%), 24.50 min (2.3%, broad, decomposition peak). Its spectral data (IR, ^{1}H- and ^{13}C-NMR, and MS) were identical to those of (3*R*,19*Z*)-**4**. HRMS of (3*S*,19*Z*)-**4**: calcd. for $C_{30}H_{59}O_3$ $[(M+H)^+]$, 467.4459; found, 467.4466.

Fly stocks and husbandry. The CantonS flies used for the assay were raised at 25 °C on cornmeal agar food. Socially naïve flies aged between 4–6 d were used for the assay.

Courtship behavior assays with perfumed targets. Courtship assays were performed in chambers of 10 mm diameter and 3 mm depth. One male fly and one perfumed female target were placed in each chamber and videotaped for 30 min. Wet filter paper was put into each chamber to maintain humidity. The perfuming method has been described elsewhere.[2,7] Briefly, for (*R*)-3-acetoxy-11,19-octacosadiyn-1-ol (**1**), (*R*)-3-acetoxyoctacosan-1-ol (**2**), (*R*)-3-acetoxy-11-octacosen-1-ol (**3**), and (*R*)-3-acetoxy-19-octacosen-1-ol (**4**), glass vials (Wheaton, USA) were coated with 64 μg of the analogue diluted in 200 μL of hexane or $CHCl_3$, and the solvent was evaporated under a stream of N_2. For (*S*)-3-acetoxy-11,19-octacosadiyn-1-ol (**1**), (*S*)-3-acetoxyoctacosan-1-ol (**2**), (*S*)-3-acetoxy-11-octacosen-1-ol (**3**), and (*S*)-3-acetoxy-19-octacosen-1-ol (**4**), 2 μg of the analogue was used to coat each glass vial. Six live females were placed in each vial and gently vortexed for three 20-s bouts with a 20-s pause between each bout. It has been estimated that approximately 25% of the vial contents would be transferred to the flies.[7] Control flies were vortexed in a vial in which hexane or chloroform had been placed and then evaporated. The heads of perfumed flies were crushed immediately before the assay.

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