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Biosci. Biotechnol. Biochem., **68** (8), 1768–1778, 2004

Synthesis of the Four Stereoisomers of 7-Acetoxy-15-methylnonacosane, a Component of the Female Sex Pheromone of the Screwworm Fly, *Cochliomyia hominivorax**

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Received April 23, 2004; Accepted May 13, 2004

The four stereoisomers of 7-acetoxy-15-methylnonacosane (1), a component of the female sex pheromone of the New World screwworm fly (*Cochliomyia hominivorax*) were synthesized. The stereogenic center at C-15 of 1 originated from that of the enantiomers of citronellal, and that at C-7 was generated by lipase-catalyzed asymmetric acetylation of (3*RS*,11*R*)- and (3*RS*,11*S*)-17-methyl-1-trimethylsilylpentacos-1-yn-3-ol (13). Three of the stereoisomers of 1 showed equivalent good pheromone activity, while the activity of (7*R*,15*R*)-1 was weak.

Key words: *Cochliomyia hominivorax*; enzymatic kinetic resolution; lipase; methyl-branched secondary acetate; pheromone

Since 2001 we have studied the synthesis of the female sex pheromone of the New World screwworm fly (*Cochliomyia hominivorax*), which is a serious pest to livestock in Central and South America.[1)] Our first attempt was to synthesize five pheromone candidates[1)] such as 7-acetoxy-15-methylnonacosane (**1**) and 6-acetoxy-19-methylnonacosane (Fig. 1) as racemic and diastereomeric mixtures.[2)] Our synthetic products were bioassayed in the United States, and both **1** and 6-acetoxy-19-methylnonacosane were shown to be pheromonally active.[3)] Subsequently, 5-acetoxy-19-methylnonacosane was also synthesized,[4)] and found to be biologically inactive.[3)]

Because each of the pheromonally active acetates possesses two stereogenic centers, it was necessary to synthesize the four stereoisomers of each of them so as to clarify the stereochemistry-pheromone activity relationship. As to 6-acetoxy-19-methylnonacosane, the most potent pheromone component, we recently reported the synthesis of its four stereoisomers together with a precise analysis of their stereochemical purity and the results of their bioassay.[5)] The remaining task is to synthesize all four stereoisomers of **1**, although they may show the same degree of pheromone activity. Herein are described the synthesis (by K.M.), analysis (by T.O. and H.O.), and bioassay (by D.R.B. and D.A.C.) of all the stereoisomers of 7-acetoxy-15-methylnonacosane (**1**).

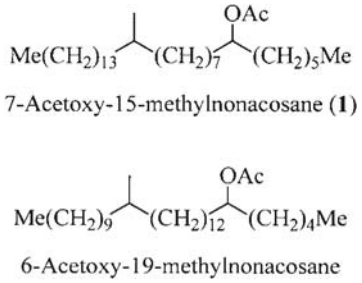

Fig. 1. Structures of the Pheromone Components of the Screwworm Fly, *Cochliomyia hominivorax*.

Results and Discussion

Scheme 1 shows the retrosynthetic analysis of (7*S*,15*R*)-7-acetoxy-15-methylnonacosane (**1**). The carbon skeleton of **1** can be constructed by alkylating (3*R*,11*R*)-**A** with *n*-butyl iodide (**B**). Both (3*R*,11*R*)-**A** and its (3*S*,11*R*)-isomer are available by enzymatic kinetic resolution of (3*RS*,11*R*)-**C**, which is to be prepared by addition of trimethylsilyl (TMS) acetylene (**E**) to (*R*)-9-methyltricosanal (**D**). The aldehyde **D** is obtainable by chain-elongation of (*R*)-4-methyloctadecanal (**F**) with 5-tetrahydropyranyl(THP)oxypentyl bro-

* Pheromone Synthesis, Part 227. For Part 226, see Muto, S., Bando, M., and Mori, K., *Eur. J. Org. Chem.*, 1946–1952 (2004).

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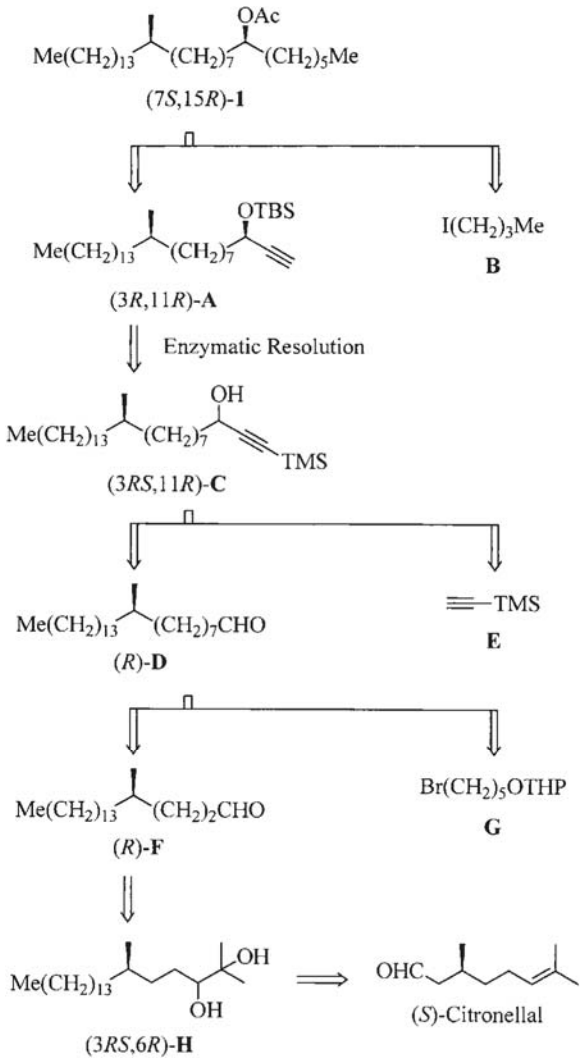


Scheme 1. Retrosynthetic Analysis of (7*S*,15*R*)-7-Acetoxy-15-methylnonacosane (**1**).

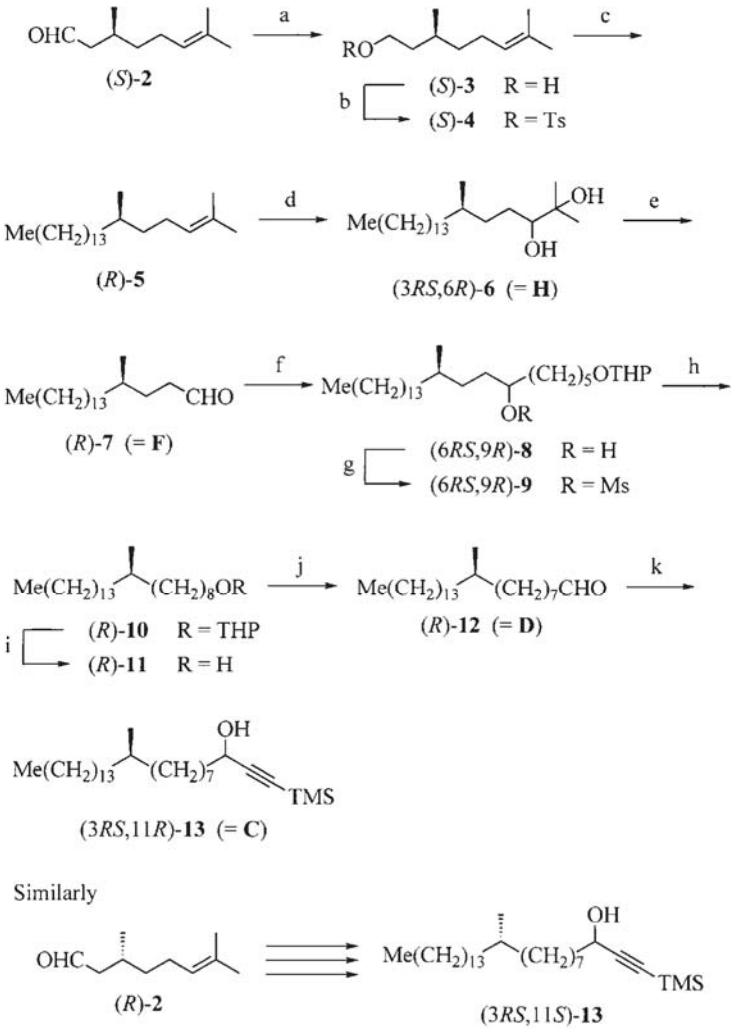
mide (**G**). Preparation of **F** is possible by periodate cleavage of (3*RS*,6*R*)-2,6-dimethylicosane-2,3-diol (**H**), which is to be prepared by starting from (*S*)-citronellal. Similarly, the remaining two stereoisomers of **A** can be prepared from (*R*)-citronellal. As to the key enzymatic resolution step (**C** → **A**), a similar TMS-protected 1-alkyn-3-ol (1-pentadecyn-3-ol)[6] had been resolved successfully by asymmetric acetylation with lipase PS and vinyl acetate according to Anastasia,[7] and therefore we were confident about its feasibility. The plan described above was realized as detailed below.

Synthesis of (3*RS*,11*R*)-acetylenic alcohol (**13**) is summarized in Scheme 2. Reduction of (*S*)-citronellal (**2**, 97% e.e.; Takasago) to (*S*)-citronellol (**3**) was followed by its tosylation to give tosylate (*S*)-**4**. Chain-elongation of (*S*)-**4** with dodecylmagnesium bromide in the presence of dilithium tetrachlorocuprate under Schlosser conditions[8] afforded crude alkene (*R*)-**5** contaminated with tetracosane, which was generated in the course of the preparation of the Grignard reagent. Without purification, the crude (*R*)-**5** was oxidized with osmium tetroxide under catalytic conditions[9] to give crystalline diol (3*RS*,6*R*)-**6** after chromatographic purification. Cleavage of the diol (3*RS*,6*R*)-**6** with periodic acid furnished (*R*)-4-methyloctadecanal (**7**).

Five-carbon chain elongation of **7** to give (*R*)-**11** was executed by the method previously described.[4] Accordingly, the aldehyde (*R*)-**7** was treated with 5-THPoxypentylmagnesium bromide to give (6*RS*,9*R*)-**8**. The corresponding mesylate (6*RS*,9*R*)-**9** was reduced with lithium aluminum hydride, and the resulting THP ether (*R*)-**10** was deprotected to provide (*R*)-9-methyltricosan-1-ol (**11**). Oxidation of (*R*)-**11** with pyridinium chlorochromate (PCC) afforded aldehyde (*R*)-**12**. Treatment of (*R*)-**12** with lithium trimethylsilylacetylide gave (3*RS*,11*R*)-**13**, the substrate for lipase-catalyzed asymmetric acetylation. The overall yield of (3*RS*,11*R*)-**13** was 14% based on (*S*)-citronellal (**2**) after 10 steps. Similarly, another substrate (3*RS*,11*S*)-**13** was prepared from (*R*)-citronellal (**2**, 97% e.e.; Takasago).

Scheme 3 shows lipase-catalyzed asymmetric acetylation of **13** and subsequent synthesis of the four stereoisomers of **16**. Asymmetric acetylation of (3*RS*,11*R*)-**13** was executed with lipase PS (Amano) and vinyl acetate in diisopropyl ether for two weeks at room temperature. This acetylation is known to generate (*R*)-acetates leaving (*S*)-alcohols intact.[6,7] Chromatographic separation of the crude product afforded acetate (3*R*,11*R*)-**14** (63% yield) and alcohol (3*S*,11*R*)-**13** (71% yield). Treatment of (3*R*,11*R*)-**14** with potassium carbonate in methanol gave crystalline alcohol (3*R*,11*R*)-**15** with removal of both the acetyl and the TMS groups. Similar treatment of (3*S*,11*R*)-**13** with potassium carbonate in methanol furnished diastereomeric alcohol (3*S*,11*R*)-**15** as crystals. Both (3*R*,11*R*)- and (3*S*,11*R*)-**15** were converted to the corresponding TBS ethers, (3*R*,11*R*)- and (3*S*,11*R*)-**16**. Similarly, (3*RS*,11*S*)-**13** yielded (3*R*,11*S*)- and (3*S*,11*S*)-**16**. Thus we accomplished the synthesis of all four stereoisomers of the intermediate **16**. The stereochemical purities of the four crystalline isomers of acetylenic alcohol **15** were determined by Ohrui's fluorescence-guided HPLC analysis of the derivatives (**17**) of **15**.[10] The stereochemical purities at each of the two stereogenic centers of **15** are shown in Scheme 3. The purity at C-11 of **15** was satisfactory (97.5–99.5% e.e.), reflecting the purity of the starting enantiomers of citronellal (**2**, 97% e.e.). As to the purity at C-3, three isomers of **15** were pure enough (92.5–98% e.e.), but that of (3*R*,11*S*)-**15** was only 79% e.e. Therefore, in the case of (3*R*,11*S*)-**15**, asymmetric acetylation of (3*RS*,11*S*)-**13** was not perfectly successful.

Conversion of the four stereoisomers of **16** to the four stereoisomers of 7-acetoxy-15-methylnonacosane (**1**) is summarized in Scheme 4. The acetylene (3*R*,11*R*)-**16** was treated with a stoichiometric amount of *n*-butyllithium to generate the corresponding anion, which was alkylated with *n*-butyl iodide, yielding (7*R*,15*R*)-**18**.



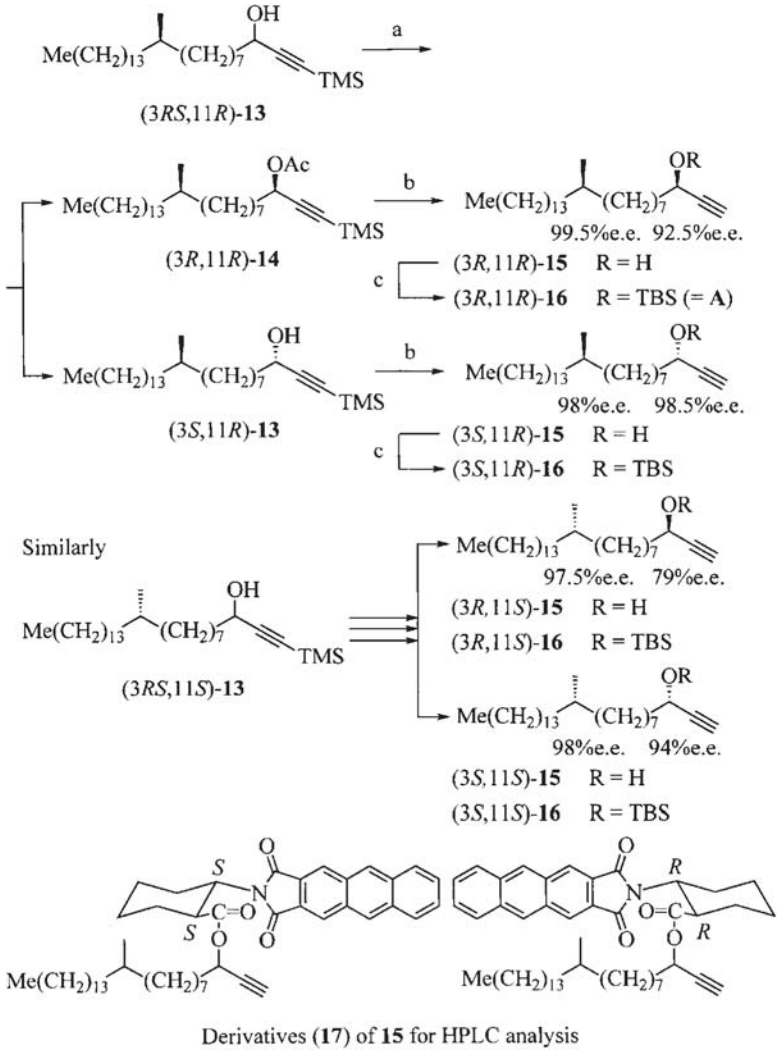
Scheme 2. Synthesis of Substrate **13** for Lipase-catalyzed Asymmetric Acetylation.

Reagents: (a) $LiAlH_4$, Et_2O (96%). (b) TsCl, C_5H_5N. (c) $Me(CH_2)_{11}MgBr$, Li_2CuCl_4, THF. (d) OsO_4, NMO, *tert*-BuOH, Me_2CO, H_2O, 3 d., room temp., then Na_2SO_3 (94% based on **3**). (e) $HIO_4 \cdot 2H_2O$, THF (quant.). (f) $THPO(CH_2)_5MgBr$, THF (64%), (g) MsCl, CH_2Cl_2, C_5H_5N. (h) $LiAlH_4$, THF. (i) $TsOH \cdot 2H_2O$, THF, EtOH (39% based on **8**). (j) PCC, NaOAc, MS 4 Å, CH_2Cl_2 (72%). (k) LiC≡CTMS, THF (86%).

Hydrogenation of (7*R*,15*R*)-**18** in ethyl acetate was performed with Adams' platinum oxide. The reaction was stopped after 15 min at room temperature to avoid racemization at the chiral centers,[5] and the product (7*S*,15*R*)-**19** was treated with tetra(*n*-butyl)ammonium fluoride (TBAF) to furnish alcohol (7*S*,15*R*)-**20** as crystals, mp 68–69 °C, $[\alpha]_D^{25}$ +0.2 (*c* 2.1, hexane). Acetylation of (7*S*,15*R*)-**20** yielded one of the final products (7*S*,15*R*)-7-acetoxy-15-methylnonacosane (**1**) as an oil. The overall yield of (7*S*,15*R*)-**1** was 3% based on (*S*)-citronellal (**2**, 17 steps). Similarly (3*S*,11*R*)-**16** was converted to crystalline (7*R*,15*R*)-**20**, mp 50.5–51.0 °C, $[\alpha]_D^{25}$ −1.5 (*c* 2.1, hexane), whose acetylation yielded oily (7*R*,15*R*)-**1**. Similar conversion of (3*R*,11*S*)- and (3*S*,11*S*)-**16** afforded (7*S*,15*S*)- and (7*R*,15*S*)-**1** respectively.

The stereochemical purities of the final products **1** must be the same as those of the four crystalline stereoisomers of alcohol **20**. Therefore, each of the isomers of **20** was derivatized with Ohrui's reagent to give **21** and analyzed by HPLC.[10] The results are shown in Scheme 4. Like the precursors **15**, the purity at C-15 of **20** was satisfactory (98–98.5% e.e.), while the purity at C-7 was not perfect. In the case of (7*S*,15*S*)-**20**, it was 83% e.e., reflecting the purity (79% e.e.) at C-3 of (3*R*,11*S*)-**15**. A small improvement (79 → 83% e.e.) must have been due to the purification of (7*S*,15*S*)-**20** *via* its recrystallization. Other isomers of **20** were pure enough at C-7 (91–97% e.e.). Nevertheless, our sample of (7*S*,15*S*)-**20** [83% e.e. = 91.5% of (7*S*,15*S*)-**20** + 8.5% of (7*R*,15*S*)-**20**] was thought to be pure enough to give (7*S*,15*S*)-**1** with unambiguous bioactivity, because of the probable activity of all of the stereoisomers of **1** as in the case of 6-acetoxy-19-methylnonacosane.[3]

Bioassays of the four stereoisomers of 7-acetoxy-15-methylnonacosane (**1**) were conducted against male screwworm flies in the U.S.A. Even at a 0.5 μg dosage, (7*S*,15*S*)-**1** was sufficiently active to excite the male insects, and at a 1 μg dosage, all of the stereoisomers of **1** caused a copulatory response in the male *Cochliomyia*



Scheme 3. Lipase-catalyzed Asymmetric Acetylation of **13** and Synthesis of the Four Stereoisomers of **16**.
Reagents: (a) Lipase PS-D, CH_2=CHOAc, $(i\text{-Pr})_2O$, 14 d., room temp., SiO_2 chromatog. [63% of (3*R*,11*R*)-**14** and 71% of (3*S*,11*R*)-**13**]. (b) K_2CO_3, MeOH [79% of (3*R*,11*R*)-**15**; 66% of (3*S*,11*R*)-**15**]. (c) TBSCl, imidazole, DMF [74% of (3*R*,11*R*)-**16**; 80% of (3*S*,11*R*)-**16**].

hominivorax. Accordingly, all the stereoisomers of **1** were pheromonally active, although the activity of (7*R*,15*R*)-**1** was weak (see Fig. 2). All the stereoisomers were bioactive also in the case of 6-acetoxy-19-methylnonacosane.[5)]

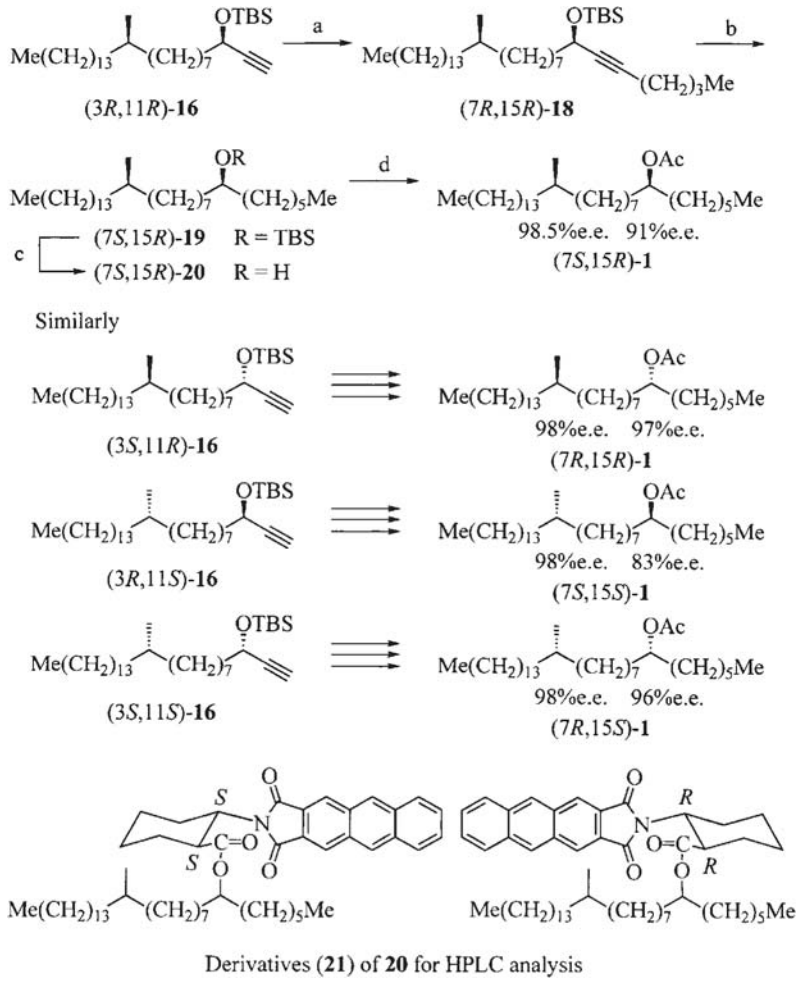
In conclusion, all four stereoisomers of 7-acetoxy-15-methylnonacosane (**1**) were synthesized and shown to be bioactive as a sex pheromone component of the female screwworm fly, *Cochliomyia hominivorax*. Detailed bioassay results will be reported by D.A.C. in due course.

Experimental

Melting point (mp) data are uncorrected. IR spectra were measured with a Horiba FT-720 spectrometer. ^{1}H-NMR spectra were recorded at 300 MHz with a Varian Mercury-300 spectrometer (TMS at $\delta = 0.00$ or $CHCl_3$ at $\delta = 7.26$ as an internal standard). ^{13}C-NMR spectra were recorded at 75 MHz also with the Varian Mercury-300 spectrometer ($CDCl_3$ at $\delta = 77.0$ as an internal standard). Optical rotation values were measured with a Jasco DIP-320 polarimeter and refractive index data with an Atago DMT-1 refractometer.

*2,6-Dimethylicosane-2,3-diol (**6**).*

(i) *(3RS,6R)-Isomer.* (*S*)-Citronellol (**3**, 5.5 g, 35 mmol), prepared by reduction of (*S*)-citronellal (**2**, Takasago, 97% e.e.) with $LiAlH_4$, was treated with TsCl (7.7 g, 40 mmol) in dry pyridine (35 ml) at 0 °C for 3 d to give about 10 g (quant.) of (*S*)-**4**. A stirred solution of (*S*)-**4** (9.9 g) in dry THF (100 ml) was treated with n-$C_{12}H_{25}MgBr$ [prepared from n-$C_{12}H_{25}Br$ (20 g, 80 mmol) and Mg (2.7 g, 110 mmol) in dry THF (90 ml)] and Li_2CuCl_4 in THF (0.5 M, 3.0 ml, 1.5 mmol) at −78 °C under Ar. The mixture was stirred for 30 min at −78 °C and left to stand overnight, allowed to warm to room temperature. The mixture was then poured into ice and sat. NH_4Cl aq. and extracted with hexane. The hexane extract was successively washed with $NaHCO_3$



Scheme 4. Synthesis of the Four Stereoisomers of 7-Acetoxy-19-methylnonacosane (**1**).
Reagents: (a) *n*-BuLi, *n*-BuI, THF, HMPA (75%). (b) H_2, PtO_2, EtOAc, 15 min, room temp. (c) TBAF, THF [92% based on (7*R*,15*R*)-**18**]. (d) Ac_2O, DMAP, CH_2Cl_2, C_5H_5N (83%).

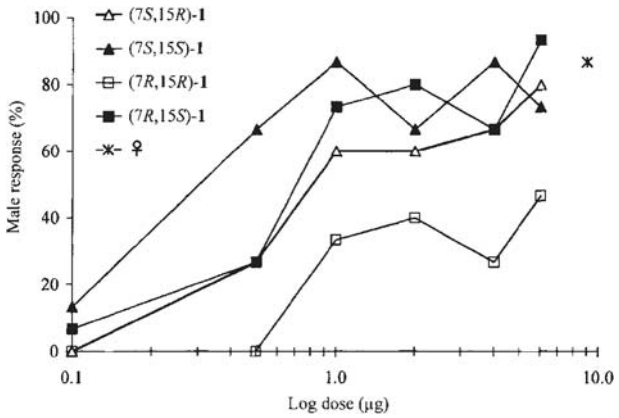


Fig. 2. Response of P-95 Strain of *Cochliomyia hominivorax* Males to the Four Stereoisomers of 7-Acetoxy-15-methylnonacosane (N = 15) Includes the Percentage of Males That Gave Full Copulatory Responses to Treated Decoys and Dead Females.

aq. and brine, dried with $MgSO_4$, and concentrated *in vacuo* to give crude (*R*)-**5** (30.2 g) containing $C_{24}H_{50}$. To a stirred solution of crude (*R*)-**5** (30.2 g) in *tert*-BuOH (100 ml), acetone (240 ml) and water (60 ml) were added a solution of OsO_4 (0.15 g, 0.59 mmol) in *tert*-BuOH (15 ml) and NMO (50% solution, 26.0 g, 111 mmol). The stirring was continued for 3 d at room temperature. The excess oxidant was then destroyed by the addition of $Na_2SO_3 \cdot 7H_2O$ (16 g). After stiring for 30 min at room temperature, the mixture was concentrated *in vacuo*, diluted with water, and extracted with EtOAc. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (180 g in hexane). Elution with hexane gave about 11 g of hydrocarbon. Subsequent elution with hexane/ethyl acetate (10:1-5:1) afforded (3*RS*,6*R*)-**6** [10.7 g, 94% based on (*S*)-**3**] as a solid. Recrystallization from acetone gave an analytical sample of (3*RS*,6*R*)-**6** as needles, mp 51–53 °C, $[\alpha]_D^{22}$ −0.2 (*c* 6.2, hexane). IR ν_{max} (nujol) cm^{-1}: 3360 (s), 1080 (m), NMR δ_H ($CDCl_3$): 0.87 (3H, d, $J = 6.3$ Hz, 6-Me), 0.88 (3H, t, $J = 6.3$ Hz, 20-H), 1.16 (3H, s, 1-H or 2-Me), 1.22 (3H, s, 1-H or 2-Me), 1.00–1.65 [1.26 (br. s), 31H, m], 1.99 (1H, br. s, OH), 2.13 (1H, br. s, OH), 3.34 (1H, m, 3-H). NMR δ_c ($CDCl_3$): 14.1, 19.4, 19.8,

22.7, 23.13, 23.16, 26.5, 27.0, 27.1, 27.8, 29.1, 29.2, 29.3, 29.6, 29.7, 30.0, 31.9, 32.8, 32.9, 34.0, 34.2, 36.8, 37.2, 73.17, 73.19, 78.9, 79.2. *Anal.* Found: C, 77.04; H, 13.62%. Calcd. for $C_{22}H_{46}O_2$: C, 77.13; H, 13.53%.

(ii) *(3RS,6S)-Isomer.* In the same manner as that described for (3*RS*,6*R*)-**6**, (*R*)-**3** (4.7 g) gave (3*RS*,6*S*)-**6** (7.6 g, 74%) as needles from acetone, mp 50–51 °C, $[\alpha]_D^{22}$ +0.1 (*c* 5.8, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (3*RS*,6*R*)-**6**. *Anal.* Found: C, 76.79; H, 13.46%. Calcd. for $C_{22}H_{46}O_2$: C, 77.13; H, 13.53%.

*4-Methyloctadecanal (**7**).*

(i) *(R)-Isomer.* A solution of (3*RS*,6*R*)-**6** (10.1 g, 30 mmol) in THF (50 ml) was added dropwise to a stirred and ice-cooled solution of $HIO_4 \cdot 2H_2O$ (8.0 g, 35 mmol) in THF (150 ml). The stirring was continued for 1 h at 0–5 °C, during which HIO_3 precipitated. The mixture was then diluted with water and extracted with hexane. The hexane extract was successively washed with water, $NaHCO_3$ aq. and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (100 g in hexane). Elution with hexane/EtOAc (50:1) gave (*R*)-**7** (8.4 g, quant.) as an oil, n_D^{26} 1.4465, $[\alpha]_D^{22}$ +1.1 (*c* 2.8, hexane). IR ν_{max} (film) cm^{-1}: 2710 (w), 1725 (s), NMR δ_H ($CDCl_3$): 0.87 (3H, d, $J = 6$ Hz, 4-Me), 0.88 (3H, t, $J = 6.3$ Hz, 18-H), 1.00–1.20 (2H, m), 1.20–1.40 [1.31 (br. s), 26 H, m], 1.39–1.47 (2H, m, 3-H), 1.62–1.70 (1H, m, 4-H), 2.36–2.45 (2H, m, 2-H), 9.77 (1H, t, $J = 2$ Hz, CHO). NMR δ_c ($CDCl_3$): 14.1, 19.3, 22.64, 22.68, 26.9, 28.9, 29.4, 29.5, 29.66, 29.67, 29.68, 29.9, 31.6, 31.9, 32.4, 36.7, 41.7, 203.0. *Anal.* Found: C, 77.87; H, 13.54%. Calcd. for $C_{19}H_{38}O$: C, 80.78; H, 13.56%. This aldehyde is labile and readily oxidized with air to the corresponding acid. Therefore it did not give correct combustion analytical data.

(ii) *(S)-Isomer.* In the same manner as that described for (*R*)-**7**, (3*RS*,6*S*)-**6** (3.24 g) gave (*S*)-**7** (2.43 g, 91%) as an oil, n_D^{22} 1.4472, $[\alpha]_D^{20} = -1.1$ ($c = 4.4$, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (*R*)-**7**. An analytical sample of (*S*)-**7** was air-oxidized after storage and gave correct analytical data as the corresponding carboxylic acid. *Anal.* Found: C, 76.51; H, 12.96%. Calcd. for $C_{19}H_{38}O_2$: C, 76.45; H, 12.83%.

*9-Methyltricosane-1,6-diol 1-Tetrahydropyranyl Ether (**8**).*

(i) *(6RS,9R)-Isomer.* A Grignard reagent was prepared from $Br(CH_2)_5OTHP$ (11.5 g, 45 mmol) and Mg (1.2 g, 50 mmol) in dry THF (60 ml) under Ar. The reaction was initiated by adding a small amount (about 10 mg) of iodine under heating. To the stirred and ice-cooled solution of the Grignard reagent was added a solution of (*R*)-**7** (8.1 g, 28.7 mmol) in dry THF (20 ml). The mixture was left to stand overnight at room temperature, quenched with ice-NH_4Cl aq. soln., and extracted with hexane. The extract was washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (120 g) in hexane. Elution with hexane/EtOAc (20:1-10:1) gave 8.7 g (64%) of (6*RS*,9*R*)-**8** as an oil, n_D^{22} 1.4608. $[\alpha]_D^{21}$ +0.05 (*c* 3.05, hexane). IR ν_{max} (film) cm^{-1}: 3430 (s), 1140 (s), 1035 (s). NMR δ_H ($CDCl_3$): 0.83–0.93 (6H, m, 9-Me, 23-H), 1.02–1.15 (2H, m), 1.15–1.90 [1.26 (br. s), 44H, m], 3.35–3.42 (1H, m), 3.45–3.60 (2H, m), 3.68–3.80 (1H, m), 3.80–3.92 (1H, m), 4.58 (1H, apparently t). NMR δ_C ($CDCl_3$): 14.1, 19.57, 19.63, 19.68, 22.61, 22.65, 25.43, 25.45, 26.25, 26.31, 27.00, 27.03, 29.32, 29.587, 29.594, 29.62, 29.66, 29.68, 29.70, 29.97, 30.716, 30.728, 31.876, 31.884, 32.81, 32.87, 36.9, 37.1, 67.48, 67.52, 98.75, 98.80, 98.83. *Anal.* Found: C, 76.61; H, 12.99%. Calcd. for $C_{29}H_{58}O_3$: C, 76.59; H, 12.86%.

(ii) *(6RS,9S)-Isomer.* In the same manner as that described for (6*RS*,9*R*)-**8**, (*S*)-**7** (2.8 g) gave (6*RS*,9*S*)-**8** (3.3 g, 70%), n_D^{26} 1.4632, $[\alpha]_D^{20}$ −0.05 (*c* 3.93, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (6*RS*,9*R*)-**8**. *Anal.* Found: C,76.69; H, 13.04%. Calcd. for $C_{29}H_{58}O_3$: C, 76.59; H, 12.86%.

*9-Methyl-1-tricosanol (**11**).*

(i) *(R)-Isomer.* MsCl (4.6 g, 40 mmol) was added dropwise to a stirred and ice-cooled solution of (6*RS*,9*R*)-**8** (8.7 g, 18.4 mmol) in CH_2Cl_2 (45 ml) and dry pyridine (30 ml). The mixture was left to stand overnight in a refrigerator, poured into ice-water, and extracted with hexane. The extract was successively washed with $CuSO_4$ aq. soln., water and brine, dried with $MgSO_4$, and concentrated *in vacuo* to give crude mesylate (6*RS*,9*R*)-**9** (8.8 g). IR ν_{max} (film) cm^{-1}: 1355 (m), 1175 (m), 905 (m). NMR δ_H ($CDCl_3$): 0.83–0.92 (6H, m, 9-Me, 23-H), 1.00–1.92 [1.26 (br. s), 45H, m], 3.00 (3H, s, CH_3SO_2), 3.34–3.43 (1H, m), 3.46–3.55 (1H, m), 3.68–3.78 (1H, m), 3.82–3.92 (1H, m), 4.57 (1H, apparntly t), 4.69 (1H, m, CHOMs). A solution of (6*RS*,9*R*)-**9** (8.7 g, 15.8 mmol) in dry THF (30 ml) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (2.0 g, 53 mmol) in dry THF (90 ml). The mixture was stirred and heated under reflux for 1.5 h, then cooled with ice-water. The excess $LiAlH_4$ was destroyed by dropwise addition of water to the stirred and ice-cooled mixture. The inorganic solid was dissolved by addition of dil. HCl and the mixture was extracted with hexane. The extract was successively washed with water, $NaHCO_3$ aq. soln. and brine, dried with $MgSO_4$, and concentrated *in vacuo* to give crude THP ether (*R*)-**10** (6.4 g), ν_{max} (film) cm^{-1}: 1035 (s), as an oil. This was dissolved in EtOH (80 ml) and THF (50 ml), to which was added *p*-$TsOH \cdot 2H_2O$ (0.2 g). The solution was left to stand at room temperature for one week, neutralized with solid $NaHCO_3$, and concentrated *in vacuo*. The residue was diluted with water and extracted with hexane. The hexane extract was washed successively with water and brine, dried with $MgSO_4$,

and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (100 g in hexane). Elution with hexane/EtOAc (15:1) gave (*R*)-**11** [2.6 g, 39% based on (6*RS*,9*R*)-**8**] as a solid. In another run, the yield of (*R*)-**11** was 65% based on (6*RS*,9*R*)-**8**. Recrystallization from acetone gave an analytical sample of (*R*)-**11** as leaflets, mp 39–40 °C, $[\alpha]_D^{20}$ +0.20 (*c* 4.0, hexane). IR ν_{max} (nujol) cm^{-1}: 3390 (m), 1055 (m), 720 (m). NMR δ_H ($CDCl_3$): 0.83 (3H, d, $J = 6.6$ Hz, 9-Me), 0.88 (3H, t, $J = 6.3$ Hz, 23-H), 1.00–1.18 (2H, m), 1.18–1.40 [1.26 (br. s), 38H, m], 1.50–1.62 (2H, m), 3.64 (2H, t, $J = 6.6$ Hz, 1-H). NMR δ_c ($CDCl_3$): 14.1, 19.7, 22.7, 25.7, 27.06, 27.09, 29.36, 29.45, 29.66, 29.70, 29.73, 29.9, 30.0, 31.9, 32.7, 32.8, 37.08, 37.09, 63.1. *Anal.* Found: C, 81.31; H, 14.04%. Calcd. for $C_{24}H_{50}O$: C, 81.28; H, 14.21%.

(ii) *(S)-Isomer.* In the same manner as that described for (*R*)-**11**, (6*RS*,9*S*)-**8** (3.3 g) gave (*S*)-**11** (1.6 g, 63%) as leaflets, mp 38–39 °C, $[\alpha]_D^{20}$ −0.20 (*c* 4.2, hexane). In another run, the yield was 60%. Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (*R*)-**11**. *Anal.* Found: C, 80.97: H, 13.88%. Calcd. for $C_{24}H_{50}O$: C, 81.28; H, 14.21%.

*9-Methyltricosanal (**12**).*

(i) *(R)-Isomer.* Powdered MS 4 Å (0.6 g) and NaOAc (1.4 g, 17 mmol) were added to a solution of (*R*)-**11** (6.3 g, 17.8 mmol) in dry CH_2Cl_2 (150 ml). To this stirred and ice-cooled suspension was added PCC (17.0 g, 79 mmol). Stirring was continued for 20 min at 0–5 °C and then for 2 h at room temperature. The mixture was diluted with Et_2O (200 ml), filtered through SiO_2 (70 g in Et_2O), and concentrated *in vacuo* to give a brown oil (7.2 g). This was chromatographed on SiO_2 (70 g in hexane). Elution with hexane/EtOAc (50:1) gave (*R*)-**12** (4.5 g, 72%) as an oil, n_D^{26} 1.4530, $[\alpha]_D^{21}$ +0.1 (*c* 4.3, hexane). IR ν_{max} (film) cm^{-1}: 2715 (w), 1725 (s), 725 (w). NMR δ_H ($CDCl_3$): 0.83, m (3H, d, $J = 6.2$ Hz, 9-Me), 0.86 (3H, t, $J = 6.6$ Hz, 23-H), 1.00–1.18 (2H, m), 1.18–1.50 [1.26 (br. s), 35H, m], 1.50–1.70 (2H, m, 3-H), 2.42 (2H, dt, $J = 1.5$, 7.2 Hz, 2-H), 9.76 (1H, t, $J = 1.5$ Hz, 1-H). NMR δ_c ($CDCl_3$): 14.1, 19.7, 22.1, 22.7, 27.0, 27.1, 29.2, 29.36, 29.39, 29.65, 29.73, 29.77, 30.0, 31.9, 32.7, 37.0, 37.1, 43.9, 202.9. *Anal.* Found: C, 80.90; H, 13.70%. Calcd. for $C_{24}H_{48}O$: C, 81.74; H, 13.72%.

(ii) *(S)-Isomer.* In the same manner as that described for (*R*)-**12**, (*S*)-**11** (5.2 g) gave (*S*)-**12** (4.7 g, 91%) as an oil, n_D^{26} 1.4532. $[\alpha]_D^{22}$ −0.1 (*c* 4.24, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (*R*)-**12**. *Anal.* Found: C, 81.26; H, 13.92%. Calcd for $C_{24}H_{48}O$: C, 81.74; H, 13.72%.

*11-Methyl-1-trimethylsilylpentacos-1-yn-3-ol (**13**).*

(i) *(3RS,11R)-Isomer.* A solution of *n*-BuLi in hexane (1.6 M, 16 ml, 26 mmol) was added to a stirred and cooled solution of TMSC≡CH (2.6 g, 26 mmol) in dry THF (30 ml) at −78 °C under Ar. The mixture was warmed to −20 °C and then cooled again to −78 °C. A solution of (*R*)-**12** (4.5 g, 13 mmol) in dry THF (30 ml) was added dropwise to the stirred and cooled solution of TMSC≡CLi at −78 °C. The mixture was stirred and warmed gradually to room temperature and left to stand for 3 d. It was then poured into ice and sat. NH_4Cl aq. soln. and extracted with hexane. The extract was washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (70 g in hexane). Elution with hexane/EtOAc (50:1) gave (3*RS*,11*R*)-**13** (4.8 g, 86%) as an oil, n_D^{25} 1.4599, $[\alpha]_D^{21}$ +0.14 (*c* 4.0, hexane). IR ν_{max} (film) cm^{-1}: 3300 (m), 1250 (m), 1020 (m), 850 (s). NMR δ_H ($CDCl_3$): 0.17 (9H, s, TMS), 0.83 (3H, d, $J = 6.3$ Hz, 11-Me), 0.88 (3H, t, $J = 6.6$ Hz, 25-H), 1.00–1.18 (2H, m), 1.18–1.50 [1.25 (br. s), 37H, m], 1.60–1.75 (2H, m, 4-H), 1.90 (1H, br.), 4.35 (1H, m, 3-H). NMR δ_c ($CDCl_3$): −0.12, 14.1, 19.7, 22.65, 22.69, 22.7, 25.1, 27.05, 27.09, 29.2, 29.4, 29.5, 29.65, 29.66, 29.67, 29.70, 29.74, 29.90, 30.0, 31.6, 31.9, 32.8, 37.1, 37.7, 62.9, 89.3, 106.9. *Anal.* Found; C, 77.07; H, 12.97%. Calcd. for $C_{29}H_{58}OSi$; C, 77.26; H, 12.97%.

(ii) *(3RS,11S)-Isomer.* In the same manner as that described for (3*RS*,11*R*)-**13**, (*S*)-**12** (4.7 g) gave (3*RS*,11*S*)-**13** (4.6 g, 78%) as an oil, n_D^{26} 1.4602, $[\alpha]_D^{23}$ −0.13 (*c* 4.77, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (3*RS*,11*R*)-**13**. *Anal.* Found: C, 76.91; H, 12.91%. Calcd. for $C_{29}H_{58}OSi$: C, 77.26; H, 12.97%.

*Lipase-catalyzed Asymmetric Acetylation of **13**.*

(i) *(3RS,11R)-Isomer.* Vinyl acetate (62 ml, 670 mmol) and lipase PS-D (Amano, 2.6 g) were added to a stirred solution of (3*RS*,11*R*)-**13** (4.8 g, 10.9 mmol) in $(i\text{-Pr})_2O$ (125 ml). The mixture was stirred for 2 weeks at room temperature, then filtered through a pad of Celite. The Celite pad was washed with Et_2O, and the filtrate and washings were concentrated *in vacuo*. The residue was chromatographed over SiO_2 (120 g in hexane). Elution with hexane/EtOAc (100:1) gave impure acetate (3*R*,11*R*)-**14** (2.9 g). Further elution with hexane/EtOAc (50:1) first furnished impure alcohol (3*S*,11*R*)-**13** (1.3 g) followed by pure alcohol (3*S*,11*R*)-**13** (0.9 g). The combined impure (3*S*,11*R*)-**13** and (3*R*,11*R*)-**14** (4.2 g) were rechromatographed over SiO_2 (80 g in hexane) to give pure (3*R*,11*R*)-**14** (1.7 g, 63%) and pure (3*S*,11*R*)-**13** (0.8 g). The combined yield of (3*S*,11*R*)-**13** was 71% (1.7 g). The alcohol (3*S*,11*R*)-**13** was an oil, n_D^{26} 1.4592. $[\alpha]_D^{22}$ −1.7 (*c* 2.3, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those reported for (3*RS*,11*R*)-**13**. *Anal.* Found: C, 77.26; H, 13.05%. Calcd. for $C_{29}H_{58}OSi$:C, 77.26, H, 12.97%. The acetate (3*R*,11*R*)-**14** was also an oil, n_D^{26} 1.4565, $[\alpha]_D^{22}$ +29.8 (*c* 3.14, hexane). IR ν_{max} (film) cm^{-1}: 1750 (s), 1235 (s), 850 (s). NMR δ_H ($CDCl_3$): 0.16 (9H, s, TMS), 0.82 (3H, d, $J = 6.3$ Hz, 11-Me), 0.88 (3H, t, $J = 6.3$ Hz, 25-H), 1.00–1.20 (2H, m), 1.20–1.50 [1.25 (br. s), 37H, m], 1.65–1.80 (2H, m, 4-H), 2.07 (3H, s, Ac),

5.37 (1H, t, $J = 6.6$ Hz, 3-H). NMR δ_C ($CDCl_3$): 0.2, 14.1, 19.7, 21.1, 22.65, 22,68, 24.9, 27.0, 27.1, 29.1, 29.4, 29.5, 29.65, 29.67, 29.70, 29.73, 29.9, 30.0, 31.6, 31.9, 32.8, 34.8, 37.08, 37.1, 64.4, 90.2, 102.8, 169.9. *Anal.* Found: C, 75.92; H, 12.59%. Calcd. for $C_{31}H_{60}O_2Si$: C, 75.54; H, 12.27%.

(ii) *(3RS,11S)-Isomer.* In the same manner as that described for enzymatic acetylation of (3*RS*,11*R*)-**13**, (3*RS*,11*S*)-**13** (4.4 g) gave (3*S*,11*S*)-**13** (1.2 g, 55%) and (3*R*,11*S*)-**14** (2.2 g, 88%). The alcohol (3*S*,11*S*)-**13** was an oil, n_D^{26} 1.4620. $[\alpha]_D^{23}$ −1.7 (*c* 3.0, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those reported for (3*RS*,11*S*)-**13**. *Anal.* Found: C, 77.22; H, 12.95%. Calcd. for $C_{29}H_{58}OSi$: C, 77.26; H, 12.97%. The acetate (3*R*,11*S*)-**14** was also an oil, n_D^{26} 1.4562, $[\alpha]_D^{22}$ +26.2 (*c* 3.3, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those reported for (3*R*,11*R*)-**14**. *Anal.* Found: C, 75.14; H, 12.27%. Calcd. for $C_{31}H_{60}O_2Si$: C, 75.54; H, 12.27%.

*11-Methylpentacos-1-yn-3-ol (**15**).*

(i) *(3R,11R)-Isomer.* To a stirred solution of (3*R*,11*R*)-**14** (1.65 g, 3.3 mmol) in MeOH (30 ml) and H_2O (2 ml) was added K_2CO_3 (2.0 g, 14 mmol). The suspension was stirred for 2 d at room temperature. The mixture was then diluted with water and extracted with hexane. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (15 g in hexane). Elution with hexane/EtOAc (50:1) gave (3*R*,11*R*)-**15** (1.0 g, 79%) as a solid. Recrystallization from acetone yielded an analytical sample of (3*R*,11*R*)-**15** as needles, mp 38.0–38.5 °C, $[\alpha]_D^{25}$ +4.3 (*c* 0.84, hexane). IR ν_{max} (nujol) cm^{-1}: 3285 (m), 1065 (m), 630 (m). NMR δ_H ($CDCl_3$): 0.83 (3H, d, $J = 6.3$ Hz, 3-Me), 0.86 (3H, t, $J = 6.6$ Hz, 25-H), 1.00–1.18 (2H, m), 1.18–1.52 [1.26 (br. s), 38H, m], 1.65–1.78 (2H, m, 4-H), 2.46 (1H, d, $J = 2.4$ Hz, 1-H), 4.37 (1H, dt, $J = 2.4$, 6.6 Hz, 3-H). NMR δ_c ($CDCl_3$): 14.1, 19.7, 22.7, 25.0, 27.1, 29.2, 29.4, 29.6, 29.66, 29.74, 29.9, 30.0, 31.9, 32.8, 37.08, 37.10, 37.7, 62.4, 72.8, 85.0. *Anal.* Found: C, 81.84; H, 13.41%. Calcd. for $C_{26}H_{50}O$: C, 82.46; H, 13.31%.

(ii) *(3S,11S)-Isomer.* In the same manner as described for (3*R*,11*R*)-**15**, (3*S*,11*S*)-**13** (1.05 g) gave (3*S*,11*S*)-**15** (0.83 g, 92%). Recrystallization from acetone yielded an analytical sample as needles, mp 37.5–38.0 °C, $[\alpha]_D^{25}$ −4.0 (*c* 2.24, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (3*R*,11*R*)-**15**. *Anal.* Found: C, 82.30; H, 13.45%. Calcd. for $C_{26}H_{50}O$: C, 82.46; H, 13.31%.

(iii) *(3S,11R)-Isomer.* In the same manner as described for (3*R*,11*R*)-**15**, (3*S*,11*R*)-**13** (0.90 g) gave (3*S*,11*R*)-**15** (0.51 g, 66%) as an oil, n_D^{26} 1.4621, $[\alpha]_D^{22}$ −4.0 (*c* 2.38, hexane). IR ν_{max} (film) cm^{-1}: 3310 (m), 1025 (m), 655 (m). NMR δ_H ($CDCl_3$): 0.83 (3H, d, $J = 6.3$ Hz, 11-Me), 0.88 (3H, t, $J = 6.6$ Hz, 25-H), 1.10–1.18 (2H, m), 1.18–1.40 [1.26 (br. s), 35H, m], 1.40–1.52 (2H, m, 5-H), 1.60–1.80 (2H, m, 4-H), 2.05 (1H, br. s, OH), 2.45 (1H, dt, $J = 0.2$, 1.2 Hz, 1-H), 4.37 (1H, $J = 0.2$, 2.7 Hz, 3-H). NMR δ_c ($CDCl_3$): 14.1, 19.7, 22.6, 22.7, 25.0, 27.04, 27.09, 29.2, 29.4, 29.56, 29.66, 29.74, 29.9, 30.0, 31.9, 32.7, 37.07, 37.09, 37.6, 62.3, 72.8, 85.0. *Anal.* Found: C, 83.02; H, 13.48%. Calcd. for $C_{26}H_{50}O$: C, 82.46; H, 13.31%.

(iv) *(3R,11S)-Isomer.* In the same manner as described for (3*R*,11*R*)-**15**, (3*R*,11*S*)-**14** (1.3 g) gave (3*R*,11*S*)-**15** (0.87 g, 87%) as an oil, n_D^{26} 1.4619, $[\alpha]_D^{22}$ +3.0 (*c* 2.3, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (3*S*,11*R*)-**15**. *Anal.* Found: C, 82.27; H, 13.32%. Calcd. for $C_{26}H_{50}O$: C, 82.46; H, 13.31%.

*11-Methylpentacos-1-yn-3-ol TBS Ether (**16**).*

(i) *(3R,11R)-Isomer.* To a stirred and ice-cooled solution of (3*R*,11*R*)-**15** (1.35 g, 3.6 mmol) in dry DMF (10 ml) were added imidazole (0.98 g, 14 mmol) and TBSCl (0.65 g, 4.3 mmol). The mixture was stirred overnight at room temperature, then poured into ice-water and extracted with hexane. The extract was washed successively with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (25 g). Elution with hexane gave (3*R*,11*R*)-**16** (1.3 g, 74%) as an oil, n_D^{26} 1.4540, $[\alpha]_D^{25}$ +18.4 (*c* 2.22, hexane). IR ν_{max} (film) cm^{-1}: 3310 (m), 1260 (m), 1080 (s), 840 (s), 760 (m). NMR δ_H ($CDCl_3$): 0.10, 0.12 (6H, SiMe), 0.83 (3H, d, $J = 6.3$ Hz, 11-Me), 0.88 (3H, t, $J = 6.9$ Hz, 25-H), 0.91 (9H, s, *t*-Bu), 1.00–1.18 (2H, m), 1.18–1.50 [1.26 (br. s), 37H, m], 1.60–1.74 (2H, m, 4-H), 2.36 (1H, d, $J = 2.1$ Hz, 1-H), 4.33 (1H, dt, $J = 2.1$, 6.3 Hz, 3-H). NMR δ_c ($CDCl_3$): −5.1, −4.6, 14.1, 18.2, 19.7, 22.66, 22.70, 25.1, 25.8, 27.06, 27.11, 29.26, 29.38, 29.60, 29.67, 29.72, 29.76, 29.9, 30.1, 31.6, 31.9, 32.8, 37.09, 37.11, 38.6, 62.8, 74.8, 85.8. *Anal.* Found: C, 76.53; H, 12.71%. Calcd. for $C_{32}H_{64}OSi$: C, 77.97; H, 13.09%. This TBS ether was slightly volatile and did not give correct analytical data.

(ii) *(3S,11R)-Isomer.* In the same manner as described for (3*R*,11*R*)-**16**, (3*S*,11*R*)-**15** (0.79 g) gave (3*S*,11*R*)-**16** (0.82 g, 80%) as an oil, n_D^{26} 1.4518, $[\alpha]_D^{22}$ −18.9 (*c* 2.34, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those reported for (3*R*,11*R*)-**16**. *Anal.* Found: C, 74.31; H, 12.53%. Calcd. for $C_{32}H_{64}OSi$: C, 77.97; H, 13.09%.

(iii) *(3R,11S)-Isomer.* In the same manner as described for (3*R*,11*R*)-**16**, (3*R*,11*S*)-**15** (0.57 g) gave (3*R*,11*S*)-**16** (0.59 g, 73%) as an oil, n_D^{26} 1.4500, $[\alpha]_D^{22}$ +14.1 (*c* 2.40, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those reported for (3*S*,11*R*)-**16**. *Anal.* Found: C, 75.70; H, 12.52%. Calcd. for $C_{32}H_{64}OSi$: C, 77.97; H, 13.09%.

(iv) *(3S,11S)-Isomer.* In the same manner as described for (3*R*,11*R*)-**16**, (3*S*,11*S*)-**15** (0.78 g) gave (3*S*,11*S*)-**16** (0.83 g, 82%) as an oil, n_D^{26} 1.4550, $[\alpha]_D^{25}$ −20.0 (*c* 2.21, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (3*R*,11*R*)-**16**. *Anal.* Found: C,

76.47; H, 12.54%. Calcd. for $C_{32}H_{62}OSi$: C, 77.97; H, 13.09%.

*15-Methylnonacos-5-yn-7-ol TBS Ether (**18**).*

(i) *(7R,15R)-Isomer.* A solution of *n*-BuLi in hexane (1.6 M, 1.9 ml, 3 mmol) was added to a stirred and cooled solution of (3*R*,11*R*)-**16** (1.2 g, 2.4 mmol) in dry THF (5 ml) and dry HMPA (1.6 ml) at −40 °C under Ar. The mixture was warmed to 0 °C and then cooled again to −40 °C. *n*-BuI (1.12 g, 6.1 mmol) in dry THF (3 ml) was then added to the mixture at −40 °C. The mixture was gradually warmed to room temperature and left to stand overnight. It was then poured into ice and sat. NH_4Cl aq. soln., and extracted with hexane. The extract was successively washed with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (20 g in hexane). Elution with hexane gave (7*R*,15*R*)-**18** (1.0 g, 75%) as an oil. IR ν_{max} (film) cm^{-1}: 1250 (m), 1090 (s), 840 (s). NMR δ_H ($CDCl_3$): 0.10, 0.12 (6H, SiMe), 0.80–0.95 (9H, m, 1-H, 15-Me, 29-H), 0.90 (9H, s, *t*-Bu), 1.00–1.15 (2H, m), 1.18–1.50 [1.26 (br. s), 43H, m], 1.60–1.70 (2H, m), 4.32 (1H, t, $J = 6.3$ Hz, 7-H). NMR δ_c ($CDCl_3$): −5.1, −4.6, 13.6, 14.1, 18.3, 19.7, 21.9, 22.7, 25.1, 25.3, 25.7, 25.8, 27.1, 29.2, 29.4, 29.6, 29.7, 29.9, 30.1, 30.8, 31.6, 31.9, 32.8, 37.1, 38.6, 39.0, 62.8, 63.3, 71.8, 82.0, 84.3. This was used for the next step without further purification.

(ii) *(7S,15R)-Isomer.* In the same manner as described for (7*R*,15*R*)-**18**, (3*S*,11*R*)-**16** (703 mg, 1.4 mmol) gave (7*S*,15*R*)-**18** (526 mg, 67%). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those of (7*R*,15*R*)-**18**. This was used for the next step without further purification.

(iii) *(7R,15S)-Isomer.* In the same manner as described for (7*R*,15*R*)-**18**, (3*R*,11*S*)-**16** (780 mg, 1.6 mmol) gave (7*R*,15*S*)-**18** (743 mg, 85%). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*S*,15*R*)-**18**. This was used for the next step without further purification.

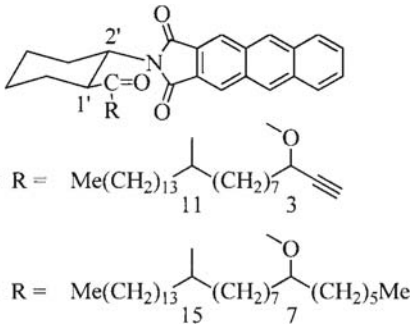
(iv) *(7S,15S)-Isomer.* In the same manner as described for (7*R*,15*R*)-**18**, (3*S*,11*S*)-**16** (789 mg, 1.6 mmol) gave (7*S*,15*S*)-**18** (530 mg, 59%). Its IR ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*R*,15*R*)-**18**. This too was used for the next step without further purification.

*15-Methylnonacosan-7-ol (**20**).*

(i) *(7S,15R)-Isomer.* Adams' PtO_2 (66 mg) was added to a solution of (7*R*,15*R*)-**18** (928 mg, 1.7 mmol) in EtOAc (10 ml). The suspension was vigorously stirred under H_2 at 1 atm for 15 min at room temperature, then filtered. The Pt black was washed with EtOAc. The filtrate and washings were combined and concentrated *in vacuo* to give (7*S*,15*R*)-**19** (846 mg, 91%), whose ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) lacked the broad 2H signal at δ 1.60–1.70 ($CH_2C{\equiv}C$), and showed a signal at δ 4.16 (1H, m, CHOTBS) instead of a signal at d 4.32 (1H, t, C≡CCHOTBS) in the case of (7*R*,15*R*)-**18**. The crude product (7*S*,15*R*)-**19** (846 mg, 1.5 mmol) was dissolved in THF (11 ml). TBAF (1.0 M in THF, 7.2 ml, 7.2 mmol) was added to the stirred solution and the mixture was left to stand at room temperature for 4 d. It was then poured into water and extracted with hexane. The extract was successively washed with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (20 g in hexane). Elution with hexane/EtOAc (50:1) gave crude (7*S*,15*R*)-**20** (620 mg, 92%) as a solid. Recrystallization from acetone gave an analytical sample as fine needles, mp 68–69 °C, $[\alpha]_D^{25}$ +0.2 (*c* 2.1, hexane). IR ν_{max} (nujol) cm^{-1}: 3325 (s), 3230 (s), 1125 (m), 980 (m), 725 (s). NMR δ_H ($CDCl_3$): 0.83 (3H, d, $J = 6.3$ Hz, 15-Me), 0.880 (3H, t, $J = 6.6$ Hz, 1- or 29-H), 0.885 (3H, t, $J = 6.6$ Hz, 1- or 29-H), 1.00–1.10 (2H, m), 1.10–1.32 [1.26 (br. s), 46H, m], 1.32–1.50 (3H, m), 1.56 (1H, s, OH), 3.59 (1H, br., 7-H). NMR δ_c ($CDCl_3$): 14.08, 14.11, 19.7, 22.6, 22.7, 25.6, 25.7, 27.06, 27.10, 29.36, 29.38, 29.67, 29.68, 29.73, 29.75, 29.97, 30.0, 31.85, 31.93, 32.7, 37.08, 37.10, 37.5, 72.0. *Anal.* Found: C, 81.94; H, 14.46%. Calcd. for $C_{30}H_{62}O$: C, 82.11; H, 14.24%.

(ii) *(7R,15R)-Isomer.* In the same manner as described for (7*S*,15*R*)-**20**, (7*S*,15*R*)-**18** (526 mg, 0.96 mmol) gave crystalline (7*R*,15*R*)-**20** (412 mg, 98%). Recrystallization from acetone gave fine needles, mp 50.5–51.0 °C, $[\alpha]_D^{25}$ −1.5 ($c = 2.1$, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those of (7*S*,15*R*)-**20**. *Anal.* Found: C, 81.64; H, 14.37%. Calcd. for

Table 1. HPLC Retention Times of the Stereoisomers of **17** and **21**



Stereoisomers	Retention times[a] (min)
(3*S*,11*S*,1′*R*,2′*R*)- and (3*R*,11*R*,1′*S*,2′*S*)-**17**	348.6[b]
(3*R*,11*S*,1′*R*,2′*R*)- and (3*S*,11*R*,1′*S*,2′*S*)-**17**	372.4[b]
(3*R*,11*R*,1′*R*,2′*R*)- and (3*S*,11*S*,1′*S*,2′*S*)-**17**	386.8[b]
(3*S*,11*R*,1′*R*,2′*R*)- and (3*R*,11*S*,1′*S*,2′*S*)-**17**	483.6[b]
(7*S*,15*S*,1′*R*,2′*R*)- and (7*R*,15*R*,1′*S*,2′*S*)-**21**	62.2[c]
(7*S*,15*R*,1′*R*,2′*R*)- and (7*R*,15*S*,1′*S*,2′*S*)-**21**	79.5[c]
(7*R*,15*S*,1′*R*,2′*R*)- and (7*S*,15*R*,1′*S*,2′*S*)-**21**	91.4[c]
(7*R*,15*R*,1′*R*,2′*R*)- and (7*S*,15*S*,1′*S*,2′*S*)-**21**	294.8[c]

[a] Column: Develosil C30-UG-3 (4.6 mm i.d. × 150 mm) × 2.
[b] Column temp.: −20 °C; Eluent: MeCN/THF/hexane/MeOH = 140:20:25:100; Flow rate: 0.2 ml/min.
[c] Column temp.: −30 °C; Eluent: MeCN/THF/hexane/MeOH = 50:80:70:50; Flow rate: 0.2 ml/min.

$C_{30}H_{62}O$: C, 82.11; H, 14.24%.

(iii) *(7S,15S)-Isomer.* In the same manner as described for (7*S*,15*R*)-**20**, (7*R*,15*S*)-**18** (743 mg, 1.35 mmol) gave crystalline (7*S*,15*S*)-**20** (514 mg, 87%). Recrystallization from acetone gave fine needles, mp 51–52 °C,. $[\alpha]_D^{25}$ +2.2 (*c* 0.51, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*R*,15*R*)-**20**. *Anal.* Found: C, 81.43; H, 14.42%. Calcd. for $C_{32}H_{62}O$: C, 82.11; H, 14.24%.

(iv) *(7R,15S)-Isomer.* In the same manner as described for (7*S*,15*R*)-**20**, (7*S*,15*S*)-**18** (742 mg, 1.35 mmol) gave crystalline (7*R*,15*S*)-**20** (410 mg, 69%). Recrystallization from acetone gave fine needles, mp 71–72 °C, $[\alpha]_D^{25}$ −0.2 (*c* 2.19, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*S*,15*R*)-**20**. *Anal.* Found: C, 81.97; H, 14.59%. Calcd. for $C_{30}H_{62}O$: C, 82.11; H, 14.24%.

*7-Acetoxy-15-methylnonacosane (**1**).*

(i) *(7S,15R)-Isomer.* To a stirred and ice-cooled solution of (7*S*,15*R*)-**20** (600 mg, 1.37 mmol) in pyridine (4 ml) and dichloromethane (5 ml) were added Ac_2O (1 ml, 9 mmol) and DMAP (50 mg, 0.4 mmol). The mixture was left to stand at room temperature for 3 d. It was then diluted with ice-water. The mixture was acidified with dil. HCl and extracted with hexane. The hexane extract was successively washed with water, $NaHCO_3$ aq. soln. and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (15 g in hexane). Elution with hexane/EtOAc (70:1) gave (7*S*,15*R*)-**1** (545 mg, 83%) as an oil, n_D^{27} 1.4492, $[\alpha]_D^{25}$ −0.3 (*c* 2.67, hexane). IR ν_{max} (film) cm^{-1}: 1745 (s), 1240 (s), 1020 (m), 725 (w). NMR δ_H ($CDCl_3$): 0.83 (3H, d, $J = 6.3$ Hz, 15-Me), 0.875 (3H, t, $J = 7.2$ Hz, 1- or 29-H), 0.877 (3H, t, $J = 7.2$ Hz, 1- or 29-H), 1.00–1.10 (2H, m), 1.10–1.40 [1.26 (br. s), 45H, m]. 1.40–1.60 (4H, m), 2.04 (3H, s, Ac), 4.86 (1H, m, CHOAc). NMR δ_c ($CDCl_3$): 9.6, 14.1, 19.7, 21.3, 22.58, 22.65, 22.7, 25.28, 25.32, 26.9, 27.05, 27.1, 29.2, 29.4, 29.57, 29.59, 29.66, 29.67, 29.71, 29.74, 29.93, 30.0, 31.6, 31.7, 31.9, 32.8, 33.6, 34.1, 37.08, 37.1, 74.5, 170.9. *Anal.* Found: C, 80.03; H, 13.70%. Calcd. for $C_{32}H_{64}O_2$: C, 79.93; H, 13.42%.

(ii) *(7R,15R)-Isomer.* In the same manner as described for (7*S*,15*R*)-**1**, (7*R*,15*R*)-**20** (252 mg, 0.57 mmol) gave (7*R*,15*R*)-**1** (255 mg, 92%) as an oil, n_D^{27} 1.4508, $[\alpha]_D^{24}$ +0.1 (*c* 1.85, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were virtually identical with those of (7*S*,15*R*)-**1**. *Anal.* Found: C, 79.74; H, 13.67%. Calcd. for $C_{32}H_{64}O_2$: C, 79.93: H, 13.42%.

(iii) *(7S,15S)-Isomer.* In the same manner as described for (7*S*,15*R*)-**1**, (7*S*,15*S*)-**20** (90 mg, 0.2 mmol) gave (7*S*,15*S*)-**1** (85 mg, 87%) as an oil, n_D^{26} 1.4514, $[\alpha]_D^{21}$ −0.2 (*c* 0.9, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*R*,15*R*)-**1**. *Anal.* Found: C, 79.98; H, 13.68%. Calcd. for $C_{32}H_{64}O_2$: C, 79.93; H, 13.42%.

(iv) *(7R,15S)-Isomer.* In the same manner as described for (7*S*,15*R*)-**1**, (7*R*,15*S*)-**20** (390 mg, 0.89 mmol) gave (7*R*,15*S*)-**1** (397 mg, 93%) as an oil, n_D^{27} 1.4484, $[\alpha]_D^{25}$ +0.2 (*c* 2.45, hexane). Its IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (7*S*,15*R*)-**1**. *Anal.* Found: C, 79.62; H, 13.72%. Calcd. for $C_{32}H_{64}O_2$: C, 79.93; H, 13.42%.

Sample Preparation Procedure for Analytical HPLC: (1*S*,2*S*)- or (1*R*,2*R*)-2-(2,3-Anthracenedicarboximido)-cyclohexanecarboxylic acid (1.5 mg, 10 *eq* to **15** or 1.3 mg, 10 *eq* to **20**) and DMAP (a catalytic amount) were added to each stereoisomer of **15** or **20** (0.15 mg) in a mixture of toluene and MeCN (1:1, 0.3 ml). After the addition of 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide hydrochloride [EDC, Tokyo Kasei (TCI), 2.3 mg, 30 *eq* to **15** or 2.0 mg, 30 *eq* to **20**], the mixture was kept at room temperature for more than 10 h. An aliquot was then loaded onto a silica gel TLC plate (10 cm in length, Silica gel 60 F_{254}, Art-5744, Merck), and developed with hexane/EtOAc (4:1, v/v). The target spot **17** or **21** detected by fluorescence was collected, packed in a Pasteur pipette, and eluted with EtOAc/EtOH (4:1, v/v). After evaporation of the solvent with an N_2 gas stream, the residue was dissolved in MeOH and analyzed by HPLC. For preparation of the chiral derivatizing acid, which is not yet commercially available, see ref. 10)

HPLC Separation: The derivatives **17** or **21** were separated on a reversed-phase column (Develosil C30-UG-3, 3 μm, (4.6 mm i.d. × 150 mm) × 2, Nomura Chemical Co., Aichi, Japan). Detection was performed by monitoring the fluorescence intensity at 462 nm (excitation at 298 nm). Separation was performed with (a) a mixture of MeCN/THF/hexane/MeOH (140:20:25:100) at a flow rate of 0.2 ml/min, or (b) a mixture of MeCN/THF/hexane/MeOH (50:80:70:50) at a flow rate of 0.25 ml/min. The column temperature was kept at −20° or −30 °C. The temperature of the sample solution was gradually raised to room temperature by using a loop, and detection was carried out at room temperature. The results of HPLC separation are listed in Table 1.

Behavioral Dose-Response Studies: Insects were resting at the start of each behavioral assay. Males did not respond to solvent-washed decoys. The percentage of males responding increased with the dose of the test stimulus. (7*S*,15*S*)-**1** appeared to be the most active, eliciting a 50% response level at the lowest calculated dose of ~0.3 μg based only on doses up to 1 μg. The 50% response level was ~0.7 μg for (7*R*,15*S*)-**1** and ~0.8 μg for (7*S*,15*R*)-**1**. Responses reached a plateau above 1 μg for these three stereoisomers (Fig. 2). Mean responses to all doses of these three stereoisomers were not significantly different. Response to the (7*R*,15*R*)-**1** stereoisomer was poor. It never achieved 50%, and was significantly different from the other three stereoisomers. The 83% copulatory response level to dead females was well within the range of responses to the three most active stereoisomers at doses from 1 to 6 μg.

Acknowledgments

Thanks are due to Dr. Y. Hirose (Amano Enzyme Inc.) for generously donating lipase PS. K.M. is grateful to Mr. M. Hagihara, the president of Fuji Flavor Co., Ltd., Dr. T. Chuman, Dr. M. Chiba, and other members of Insect Pheromone and Traps Division of Fuji Flavor Co., Ltd., for their support.

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