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Regio- and Stereochemical Study of Sex Pheromone of Pine Sawfly; *Diprion nipponica*

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Regio- and stereoisomers of 1,2,ω-trimethyldecyl propionate (ω = 5–9) were prepared from stereochemically pure chiral building blocks as sex pheromone candidates of a pine sawfly; *Diprion nipponica*. Among the synthesized candidates, (1*S*,2*R*,8*S*)-1,2,8-trimethyldecyl propionate was found to be the sex pheromone of *D. nipponica*, based on compatibility of its GC-MS data with that of the extract of females, and its significantly high pheromone activity in a field bioassay. The field bioassay of the synthesized compounds also revealed that (1*S*,2*R*,8*R*)-1,2,8-trimethyldecyl propionate, (1*S*,2*R*,7*S*)-1,2,7-trimethyldecyl propionate, and (1*S*,2*R*,6*S*)-1,2,6-trimethyldecyl propionate could attract male sawflies to some extent as pheromone mimics.

Pine sawflies (Hymenopetra: *Diprionidae*) consisting of more than 120 spices are common insects in conifer forests. Several of their species are considered to be severe pests of pine trees. In 1976, Jewtt and co-workers[1] found that 1,2,6-trimethyltetradecyl acetate (**1A**) and its propionate analogue (**1P**) are sex pheromones of *Neodiprion lecontei* (North American species) and *Diprion similis* (European species introduced to North America), respectively, and hypothesized a variation of pheromones among species resides in the stereochemistry of alcohol moieties. Subsequent stereochemical studies from 1978 to 1990 have revealed that all *Neodiprion* species so far studied in North America, Japan, China, and Europe used (1*S*,2*S*,6*S*)-**1A** or **1P** as the main pheromone and (1*S*,2*R*,6*R*)-**1A** or **1P** as a synergist or inhibitor,[2] while *Diprion similis* used (1*S*,2*R*,6*R*)-**1P** as the main pheromone.[3,4] Thereafter, (1*S*,2*R*,6*R*)-1,2,6-trimethydodecyl propionate (**2P**)[5] and one of the stereoisomers of 1,2,6,10-tetramethyldodecyl propionate (**3P**)[6] were found to be pheromones of *Diprion pini* and *Microdiprion pallipes*, respectively, by a Swedish group.

Diprion nipponica is a common sawfly in northern Japan. This work began in 1991 on the occasion of heavy defoliation in pine forests of eastern Hidaka, Hokkaido caused by mass outbreaks of *D. nipponica*.[7] After exploring suitable field-test stations where traps fitted with caged verging females could attract sufficient numbers of males, field attraction tests with synthetic pheromones were carried out. However, the results of those studies from 1992 to 1994 were disappointing. None of the known pheromone components or related compounds could attract males of *D. nipponica*. During this period, an indoor breeding technique for the insect was established, and reared virgin females and males became available in 1996. With these insects, the analysis of natural pheromone was carried out by using GC equipped with combined TCD and electroanntenanographic detector (EAD), and by GC-MS.[8] The retention time of an EAD-active compound in an extract of virgin females was found to be much shorter than those of **2P** and **1P**. Mass spectra corresponding to the EAD-active fraction indicated that an ester of propionic acid and a saturated alcohol having 13 carbon atoms (C13 alcohol) is the pheromone. Among several compounds synthesized based on the MS data and on the structural relation with known pheromones, (1*S*,2*R*,6*RS*)-1,2,6-trimethyldecy propionate (**4P**), a 1 to1 mixture of (1*S*,2*R*,6*R*)- and (1*S*,2*R*,6*S*)-**4P** was found to attract a significant number of males of *D. nipponica* in the field attraction test. Being a shorter homologue of the pheromones of *D. similis* and *D. pini,* either (1*S*,2*R*,6*S*)-**4P** or (1*S*,2*R*,6*R*)-**4P** was proposed to be a promising pheromone candidate at this stage.[8] However, a careful analytical study conducted thereafter with synthesized sterochemically pure (1*S*,2*R*,6*R*)-**4P** and (1*S*,2*R*,6*S*)-**4P** showed that their GC and MS data were slightly different from those of the natural product, and suggested that the true pheromone is not either epimer of **4P**, but should be its regioisomers.

This paper deals with our chemical approach for determining the sex pheromone of *D. nipponica* by synthesizing all pheromone candidates of possible regio- and stereoisomers of **4P**.

Results and Discussion

Synthetic Studies. The common structural feature of all

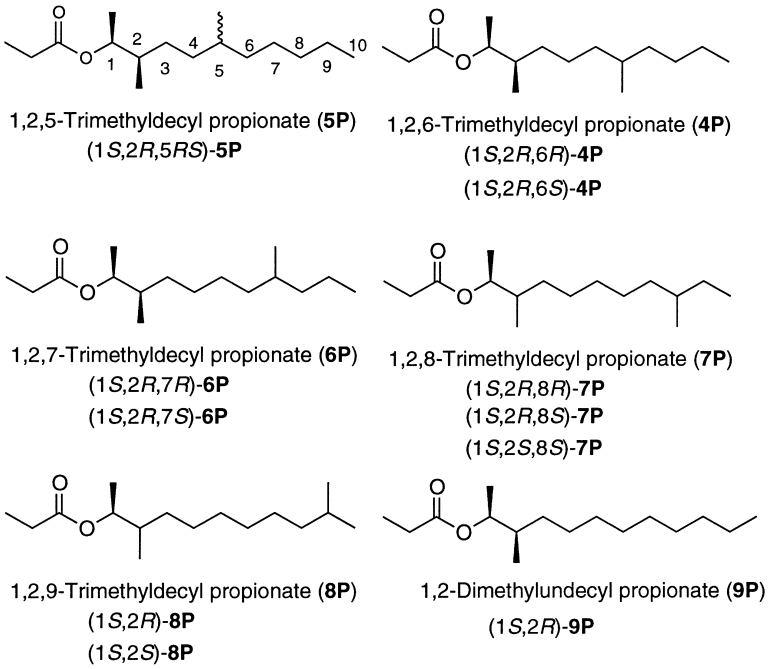
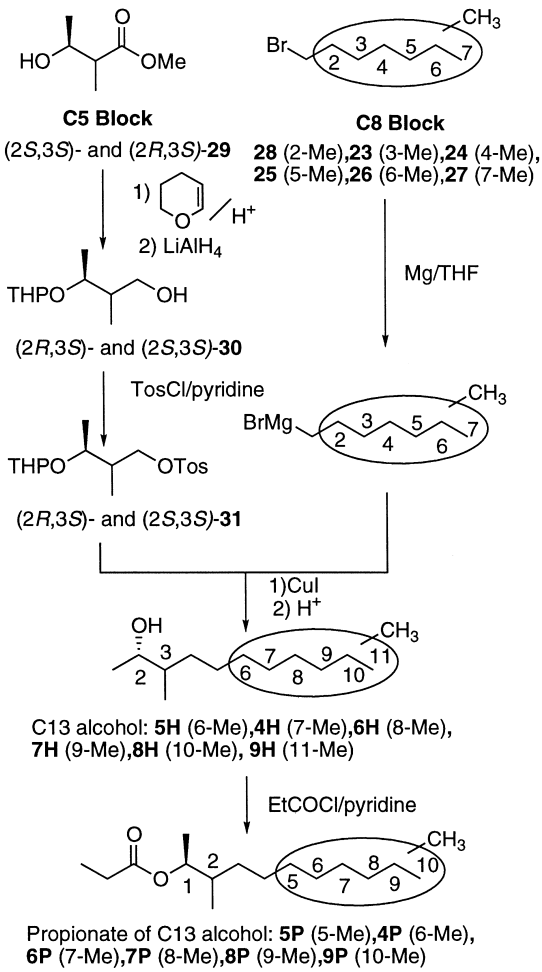


Fig. 1. Structures of pheromone candidates.

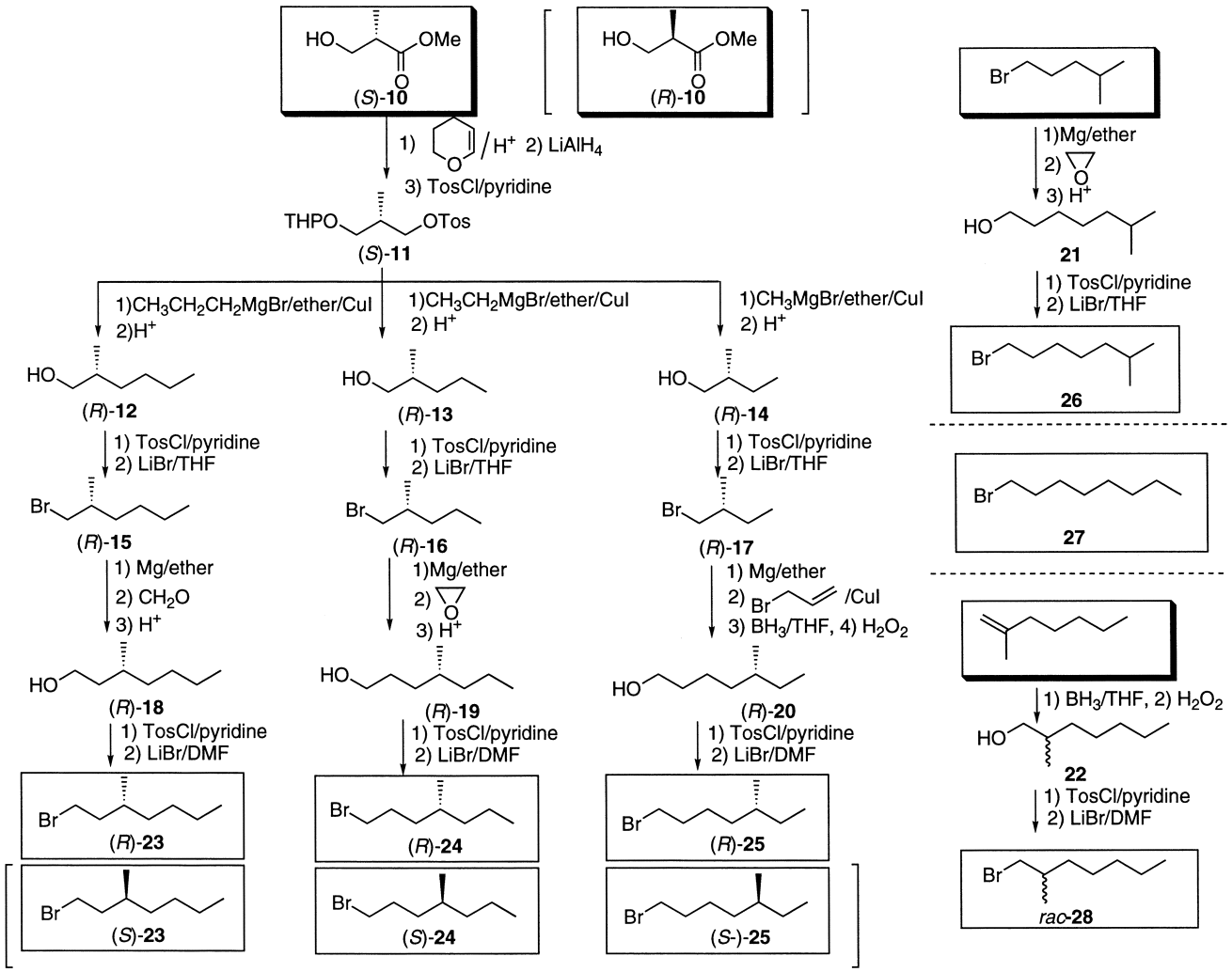
known pheromones of pine sawflies is a branching of methyl groups at the 1, 2, and 6 positions. Judging from the variation of the known pheromone structure, the functionality and their stereochemistries at the 1 and 2 positions are rigorously recognized by the pheromone receptor, and thus they must be an essential unit for pheromone activity in all *Diprion* and *Neodiprion* species. The structure of an alkyl chain, including a number of branched methyl groups and their positions, could be diverse and its recognition with the receptor is rather loose. In fact, we have experienced that (1*S*,2*S*)-1,2-dimethyltetradedyl acetate, a compound lacking the 6-methyl group in **1A**, functioned as a pheromone mimic for *N. sertifer* in a field test.[9] When GC and MS data of the EAD-active compound from the *D. nipponica* extract are taken into account, the pheromone candidates to be synthesized are concentrated to certain stereoisomers of six regioisomers, as listed in the Fig. 1.

Our synthetic procedure for the pheromone candidates is summarized in Scheme 1. C8 blocks **23**–**28** were converted to Grignard reagents, and were coupled with a C5 block **31** derived from methyl 3-hydroxy-2-methybutanoate (**29**) through three steps.[10] A combination of a specified regio- and stereoisomer of the C8 block and a specified stereoisomer of the C5 block gave one of the stereoisomers of C13 alcohols (**4H**, **5H**, **6H**, **7H**, **8H**, and **9H**). The propionates (**4P**, **5P**, **6P**, **7P**, **8P**, and **9P**) derived from the corresponding C13 alcohols, were purified by preparative GC and employed for analytical and field studies.

Optically pure C8 blocks were prepared from (*R*)- and (*S*)-methyl 3-hydroxy-2-methylpropioate (**10**) supplied by the courtesy of Kaneka Co. The procedures used to obtain (*R*)-C8 blocks are shown in Scheme 2. After protection of the hydroxy group in (*S*)-**10**, the ester moiety was reduced with $LiAlH_4$, followed by tosylation of the resulting hydroxy group to give (*S*)-2-methyl-3-tetrahydropyranyloxypropyl tosylate (**11**), which was utilized as a common starting material for the following steps. The coupling of (*S*)-**11** with Grignard reagents



Scheme 1.



Scheme 2.

prepared from bromopropane, bromoethane, and bromomethane gave (*R*)-2-methyl-1-hexanol (**12**), (*R*)-2-methyl-1-pentanol (**13**), and (*R*)-2-methyl-1-butanol (**14**), respectively. Bromides, **15**, **16**, and **17** derived from the above alcohols were converted to the Grignard reagents, which were subjected to reactions with the corresponding counter part to yield (*R*)-3-methyl-1-heptanol (**18**), (*R*)-4-methyl-1-heptanol (**19**), and (*R*)-5-methyl-1-heptanol (**20**), respectively. By the same procedure as mentioned above, (*S*)-isomers were obtained form (*R*)-**10** except for (*S*)-**19**, which was prepared from commercially available (*S*)-**16**. Achiral 6-methyl-1-heptanol (**21**) and *rac*-2-methyl-1-heptanol (**22**) were prepared by one-step reactions from commercially available compounds. C8 blocks, **23**–**26** and **28**, were obtained by bromination of the resulting alcohols via the tosylates. 1-Bromooctane (**27**) was obtained from a commercial source.

Stereochemically pure C5 blocks, (2*S*,3*S*)- and (2*R*,3*S*)-methyl 3-hydroxy-2-methylbutanoate (**29**), were prepared by a method established by our group.[10] The starting material, (*S*)-butyl 3-hydroxybutanoate, was obtained by the enantio-differentiating hydrogenation of methyl acetoacetate over asymmetrically modified Ni and a following optical enrichment.[11]

Determination of the Pheromone by Analytical and Field Studies with Synthetic Pheromone Candidates. Through an analytical study of the extract of virgin females of *D. nipponica* with GC-EAD, the EAD-active material was found to exist in ester fractions of the Florisil column chromatography, and its peak on GC appeared immediately after the peak of isoproyl dodecanoate (**32**). Choosing **32** as an internal standard, the EAD-active material was subjected to a GC-MS analysis. The retention times (rt) of the EAD-active material and **32** were 28.27 and 28.21 min, respectively. The mass spectrum (MS) of the EAD-active material is shown in Fig. 2A.

Based on the results mentioned above, a comparative study with synthetic pheromone candidates and the EAD-active material was carried out with GC-MS. The rt of each compound calibrated with the internal standard (**32**) is listed in Table 1 together with the difference in the rt from the EAD-active material. Among the compounds examined, (1*S*,2*R*,8*R*)- and (1*S*,2*R*,8*S*)-**7P** were found to be identical with the EAD-active material in their rt values. The MS of the synthetic pheromone candidates are shown in Figs. 2B–2D. The EAD-active material and (1*S*,2*R*,8*S*)- and (1*S*,2*R*,8*R*)-**7P** were found to give very compatible spectra with each other, while the spectra of

Table 1. GC Data of Synthetic Pheromone Candidates and EAD Active Material in the Female Extract

	Synthetic compound	Modified rt * calibrated by standard (rt^m)/min	Difference in modified rt and observed rt of sawfly extract ($rt^m - 28.27$)/min
1	(1*S*,2*R*,5*RS*)-**5P**	27.04	−1.23
		27.25	−1.02
2	(1*S*,2*R*,6*S*)-**4P**	27.68	−0.59
3	(1*S*,2*R*,6*R*)-**4P**	27.65	−0.62
4	(1*S*,2*R*,7*S*)-**6P**	27.99	−0.28
5	(1*S*,2*R*,7*R*)-**6P**	27.97	−0.30
6	(1*S*,2*R*,8*S*)-**7P**	28.26	$-0.01 \cong 0$
7	(1*S*,2*R*,8*R*)-**7P**	28.25	$-0.02 \cong 0$
8	(1*S*,2*S*,8*S*)-**7P**	28.11	−0.16
9	(1*S*,2*R*)-**8P**	27.92	−0.35
10	(1*S*,2*R*)-**9P**	29.19	+0.92

*Calibration was carried out by following equation; A × (28.21/B), where A and B are the observed rt of each compound and that of internal standard receptively, listed in Table 4. The figure, 28.21 is the rt of internal standard when EAD active compound appeared at rt 28.27.

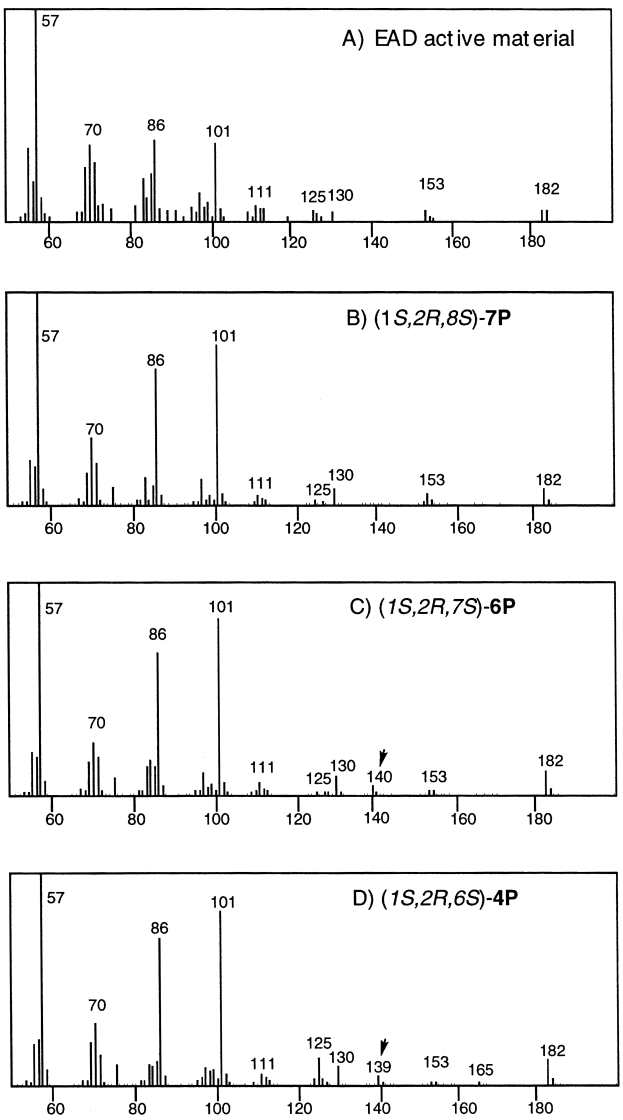


Fig. 2. MS of EAD active fraction of female sawfly extract and synthetic pheromone candidates.

(1*S*,2*R*,6*S*)-**4P** and (1*S*,2*R*,7*S*)-**6P** are slightly different from those of the EAD-active material. Compounds **4P** and **6P** display an additional peak at *m/z* 139–140. This difference was diagnostic to specify the pheromone structure in this study. The peaks *m/z* 182 ($M^+ - C_2H_5CO_2$) and 153 (a fragment caused by fission at the C2–C3 bond) which existed in the EAD-active material were important information at an early stage of this study to postulate the structure at the 1 and 2 positions of the pheromone.

The results of a field bioassay of the synthesized pheromone candidates are summarized in Table 2. Four compounds ((1*S*,2*R*,6*S*)-**4P**, (1*S*,2*R*,7*S*)-**6P**, (1*S*,2*R*,8*S*)-**7P**, and (1*S*,2*R*,8*R*)-**7P** were found to attract males to a trap baited with 10 μg of aliquot. Among them, a trap with (1*S*,2*R*,8*S*)-**7P** caught the largest number of males, and had the ability to attract males even with the low amount of bait (2 μg). The activity of (1*S*,2*R*,8*S*)-**7P** was also proved to be significantly higher than that of the other three compounds by a statistical analysis. Thus, the field study revealed that (1*S*,2*R*,8*S*)-**7P** was only eligible to be the true pheromone, and that the others were pheromone mimics.

The analytical studies specified that the true pheromone should be either (1*S*,2*R*,8*S*)- or (1*S*,2*R*,8*R*)-**7P**. Out of these two epimers, only (1*S*,2*R*,8*S*)-**7P** fulfilled the biological requirement, and thus (1*S*,2*R*,8*S*)-1,2,8-trimethyldecyl propionate was determined to be the true sex pheromone of *D. nipponica*.

The *S* configuration at the 8 position is very acceptable as a natural product, since the *S* configuration of ethyl-methyl-branching of an alkyl chain end was common in natural products: e.g. (2*S*,3*S*)-2-amino-3-methylpentanoic acid (L-isoleucine), (*S*)-2-methyl-1-butanol in fusel oil, (*S*)-6-methyloctanoic acid from "polymyxin", and (*S*)-10-methyldodecanoic acid in wool wax. The present results indicated that the presence of methyl branching at the 6 position in known pheromones of sawflies was not an essential requirement for the sawfly pheromones. The variation of the alkyl end structure has been proved to be more versatile than that expected based on the early studies. The presence of pheromone mimics indicates

Table 2. Field Response of *D. nipponica* (♂) to Traps Baited with Synthetic Pheromone Candidates

No	Date of field bioassay		Aug 12–21, 1997	Aug 13–Sep 3, 1998	Jul 28–Aug 4, 1999	Jul 24–Aug 10, 2000
	Compound	Amount baited on a trap/μg	Mean (catch/trap) ± SE n = 6	Mean (catch/trap) ± SE n = 5	Mean (catch/trap) ± SE* n = 6	Mean (catch/trap) ± SE* n = 5
1	(1*S*,2*R*,6*RS*)-**4P**	10	12.1 ± 4.6	3.8 ± 0.9	—	—
2	(1*S*,2*S*,6*RS*)-**4P**	10	0	—	—	—
3	(1*R*,2*S*,6*RS*)-**4P**	10	0	—	—	—
4	(1*R*,2*R*,6*RS*)-**4P**	10	0	—	—	—
5	(1*S*,2*R*,6*S*)-**4P**	10	—	9.6 ± 3.4	7.2 ± 4.0 [b]	7.2 ± 2.3 [b]
6	(1*S*,2*R*,6*R*)-**4P**	10	—	0	0 [a]	—
7	(1*S*,2*R*,5*RS*)-**5P**	10	—	—	0 [a]	—
8	(1*S*,2*R*,7*S*)-**6P**	10	—	—	0.5 ± 0.1 [a]	4.0 ± 1.6 [a,b]
9	(1*S*,2*R*,7*R*)-**6P**	10	—	—	0 [a]	—
10	(1*S*,2*R*,8*S*)-**7P**	10	—	—	16.5 ± 4.8 [c]	51.4 ± 19.7 [c]
11	(1*S*,2*R*,8*R*)-**7P**	10	—	—	2.0 ± 1.2 [a,b]	14.0 ± 5.3 [b]
12	(1*S*,2*S*,8*S*)-**7P**	10	—	—	—	0 [a]
13	(1*S*,2*R*)-**8P**	10	—	—	0 [a]	—
14	(1*S*,2*S*)-**8P**	10	—	—	0 [a]	—
15	(1*S*,2*R*)-**9P**	10	—	—	—	0 [a]
16	(1*S*,2*R*,6*S*)-**4P**	2	—		0	0.6 ± 0.4
17	(1*S*,2*R*,7*S*)-**6P**	2	—	—	0	—
18	(1*S*,2*R*,8*S*)-**7P**	2	—	—	2.1 ± 1.4	1.6 ± 0.6
19	(1*S*,2*R*,8*R*)-**7P**	2	—	—	0	—

*Means followed by the same letter (a,b, or c) are not significantly different according to Fisher's protected least significant difference ($p < 0.05$).

that the olfactory receptor of *D. nipponica* is not as rigorous as to specify a single compound, but is sufficiently rigorous to avoid interbreeding and to maintain reproductive isolation from an ecological point of view.

Experimental

Instrumental. ^{1}H NMR spectra were recorded at 400 MHz on a JEOL EXcaliber-400 spectrometer with $CDCl_3$ as a solvent. The chemical shifts and coupling constants for new compounds are shown in ppm and Hz, respectively. IR spectra were recorded on a JASCO IR-800 spectrometer. Optical rotation was measured on a Perkin-Elmer 241B polarimeter. Analytical GC for the synthetic study was carried out with a Shimadzu GC-6A (TCD) equipped (pass 1) with a HP-INNOWAX bonded wide-bore silica capillary column (30 m × 0.53 mm) and (pass 2) with a stainless-steel column (2 m × 3 mm) packed with 3% SE-30 on Chromosorb-W. For chiral analysis, a Shimadzu GC-14A equipped with a BETA DEX 225-coated silica capillary column (30 m × 0.25 mm) was employed. Preparative GC was carried out with a Shimadzu GC-6A (TCD) equipped (pass 1) with a stainless-steel column (5 m × 5 mm) packed with 5% NPGS on Chromosorb-W, and (pass 2) with the same stainless steel column (5 m × 5 mm) packed with 5% OV-101 on Chromosorb-W. GC-EAD was carried out with a Hewlett-Packerd 6890 (TCD) equipped with a HP-INNOWAX coated wide bore capillary column (30 m × 0.53 mm). The oven temperatures were fixed at 60 °C for the first 2 min, then elevated at a constant rate (1 °C/min) up to 230 °C. EAD was assembled according to the design reported by Struble et al.[12] GC-MS was carried out with a Hewlett-Packerd 5971A in the electron impact mode (EI, 70 ev). The separation column was a HP-INNOWAX capillary column (30 m × 0.25 mm) and the oven temperatures were controlled by the same program as that applied to GC-EAD.

Chemicals. Synthesis of C8 Block. (*S*)-2-Methyl-3-tetrahydropyranyloxypropyl Tosylate (11). To a solution of (*S*)-methyl 3-hydroxy-2-methylpropioate (**10**) (40 g) and dehydropyrane (35 g) in 70 mL of ether was added *p*-toluenesulfonic acid (0.2 g) with stirring. After an exothermic reaction completed, the mixture was kept for 5 h at room temperature, washed with aq $NaHCO_3$, and dried over K_2CO_3 overnight. The resulting solution was added to a stirred and ice-cooled suspension of $LiAlH_4$ (18 g) in 1000 mL of ether. The mixture was refluxed for 3 h, cooled down with an ice bath, and hydrolyzed with 33 mL of water. A white precipitate was filtered on a Celite pad and washed with two 200 mL portions of ether. The combined filtrate was concentrated in vacuo. Distillation of the residue gave 53.6 g of a diasteromeric mixture of (*R*)-2-methyl-3-tetrahydropyranyloxypropan-1-ol (90.9%, bp 86–90 °C/6 mm Hg (1 mmHg = 133.322 Pa)). This material (50 g) was added to an ice-cooled solution of *p*-toluenesulfonyl chloride (64 g) in dry pyridine (220 mL) under stirring, and then kept for 4 h to complete the reaction. The mixture was poured into ice-water (500 g) and extracted with three 300 mL portions of ether. The combined extract was washed with aq $CuSO_4$, aq $NaHCO_3$, and brine, successively, and then dried over Na_2SO_4. Evaporation of the solvent from the solution in vacuo gave (*S*)-**11** (93.9 g, 93% crude yield). This material was used for the next step without further purification.

(*R*)-2-Methyl-3-tetrahydropyranyloxypropyl Tosylate (11). By the same method as described above, (*R*)-**10** (25 g) was converted to (*R*)-**11** (61.1 g).

(*R*)-2-Methy-1-hexanol (12). Grignard reagent prepared from 1-bromopropane (15 g) and Mg (3.4 g) in THF (120 mL) was cooled to −50 °C and mixed with CuI (0.5 g). To the solution, (*S*)-**11** (30 g) dissolved in 30 mL of THF was added at −50 °C with stirring. The mixture was allowed to stand over night at room temperature, and was then heated at 40–50 °C for 1 h. After cooling, the reaction mixture was poured in a saturated and ice-cooled aq NH_4Cl solution (100 mL) and allowed to stand for 1 h

under stirring. The insoluble materials in the mixture were filtered on a Celite pad and washed with ether (100 mL). The ethereal layer of the combined filtrate was separated, washed with 100 mL each of aq NH_4Cl, aq $NaHCO_3$, and water, and then dried over K_2CO_3 and concentrated in vacuo. The residue was mixed with methanol (250 mL) containing a small amount of *p*-toluensulfonic acid (ca. 100 mg) and allowed to stand for 5 h at room temperature. After neutralization with sodium methoxide (1 mL of 0.5 M methanol solution), the solution was concentrated in vacuo. The concentrate consisting of **12** and 2-methoxytetrahydropyrane was subjected to fractional distillation under reduced pressure with a Vigreux column to afford crude (*R*)-**12** containing 2-methoxytetrahydropyrane in ca. 5% (7.3 g, 65% yield by calculation) as a fraction of bp 75–82 °C at 45 mmHg. The product was used for the next step without further purification. The preparative GC (NPGS, 70 °C) of a small portion of this material afforded pure (*R*)-**12**: $[\alpha]_D^{20} = 12.2$ (*c* 5.4, MeOH (Ref. 13, $[\alpha]_D^{25} = 2.45$ in ethanol)), GC (BETA DEX 225, 70 °C) 24.9 min, single peak (No peak of the antipode (rt = 26.2 min) was observed.), MS *m/z* ($M^+ - H$), Found: 115.1122, Calcd for $C_7H_{15}O$: 115.1123, IR 3325, 2925, 1460, 1380, 1040 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, $J = 6.8$ Hz, 3H), 0.90 (d, $J = 6.3$ Hz, 3H), 1.05–1.63 (m, 7H), 3.38–3.51 (m, 2H).

(*S*)-2-Methyl-1-hexanol (12). By the same method as described above, (*R*)-**11** (30 g) was converted to (*S*)-**12** containing 2-methoxytetrahydropyrane in ca. 5% (7.7 g, 68% yield by calculation): $[\alpha]_D^{20} = -12.7$ (*c* 5.2, MeOH), GC (BETA DEX 229, 70 °C) 26.2 min, single peak (No peak of the antipode (rt = 24.9 min) was observed.). The other analytical data were identical with those of (*R*)-**12**.

(*R*)-1-Bromo-2-methylhexane (15). Crude (*R*)-**12** (7.1 g) was added to an ice-cooled solution of *p*-toluenesulfonyl chloride (14 g) in dry pyridine (25 mL) under stirring, and was then kept for 4 h to complete the reaction. The mixture was poured into ice-water (50 mL) and extracted with three 50 mL portions of ether. The combined extract was washed with aq $CuSO_4$ solution, aq $NaHCO_3$, and brine, successively, and dried over Na_2SO_4. The solvent was evaporated from the solution in vacuo, and the residue was kept overnight under a high vacuum to give 2-methylhexyl tosylate (16.8 g). This material (16.5 g) was added to a solution of anhydrous LiBr (22 g) dissolved in DMF (150 mL) at 40 °C, and the mixture was stirred overnight at room temperature. The mixture was poured into water (150 mL) and extracted three times with a 150 mL portion of pentane. The combined extract was washed with water, dried over $MgSO_4$, and concentrated. The residue was passed through a short silica gel column with pentane as an eluent. The elute was evaporated in vacuo and distilled under reduced pressure to give (*R*)-**15** (7.3 g, 67% yield): bp 73–78 °C/40 mmHg. The analytical data were compatible with those reported in the literature.[14]

(*S*)-1-Bromo-2-methylhexane (15). By the same method as described above, (*R*)-**12** (7.1 g) was converted to (*S*)-**15** (7.2 g, 66% yield). The analytical data were compatible with those reported in the literature.[14]

(*R*)-3-Methyl-1-heptanol (18). To an ice-cooled solution of Grignard reagent prepared from (*R*)-**15** (6.5 g) and Mg (1 g) in 50 mL of ether, gaseous CH_2O generated from well-dried paraformaldehyde (1.3 g) was introduced by the aid of N_2 stream. After praformaldehyde was consumed, the mixture was heated under reflux for 30 min, then cooled down and poured into ice-suspended aq 2 M HCl (50 mL). The resulting ethereal layer was washed with brine, aq $NaHCO_3$, and brine, successively, and then dried over K_2CO_3 and concentrated in vacuo. Distillation of the residue under reduced pressure gave (*R*)-**18** (3.3 g, 70% yield from **15**): bp 85–86 °C/13 mmHg, $[\alpha]_D^{20} = +3.09$ (*c* 2.14, MeOH), GC (BETA DEX 225, 70 °C) 29.3 min, single peak, (No peak of the antipode (rt = 29.8 min) was observed.), MS *m/z* ($M^+ - H$), Found: 129.1273, Calcd for $C_8H_{17}O$: 129.1279, IR 3350, 2925, 1460, 1370, 1050 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 0.872 (t, $J = 6.8$ Hz, 3H), 0.874 (d, $J = 6.3$ Hz, 3H), 1.11–1.61 (m, 10H), 3.64 – 3.67 (m, 2H).

(*S*)-3-Methyl-1-heptanol (18). By the same method as described above, (*S*)-**15** (6.5 g) was converted to (*S*)-**18** (4.1 g, 86% yield): $[\alpha]_D^{20} = -3.76$ (*c* 2.34, MeOH (Ref. 13, $[\alpha]_D^{25} = -2.76$)), GC (BETA DEX 225, 70 °C) 29.8 min, single peak, (No peak of the antipode (rt = 29.3) was observed.). The other analytical data were identical with those of (*R*)-**18**.

(*R*)-1-Bromo-3-methylheptane (23). (*R*)-**18** (2.1 g) was added to an ice-cooled solution of *p*-toluenesulfonyl chloride (3.9 g) in dry pyridine (8 mL) under stirring and then kept for 4 h to complete the reaction. The mixture was poured into ice-suspended 2 M aq HCl (50 mL) with 50 mL of ether. After being well shaken, the ethereal layer was separated and washed with 50 mL each of 2 M aq HCl, brine, aq $NaHCO_3$, and brine, successively, and then dried over $MgSO_4$ and concentrated in vacuo. The residue was added to a solution of anhydrous LiBr (6.6 g) dissolved in DMF (35 mL) at 40 °C, and the mixture was stirred overnight at room temperature. The mixture was poured into water (35 mL), and extracted three times with a 30 mL portion of pentane. The combined extract was washed with water, dried over $MgSO_4$ and concentrated. The concentrate was passed through a short silica gel column with pentane as an eluent. The elute was concentrated in vacuo and the residue distilled under reduced pressure to give (*R*)-**23** (2.9 g, 50% yield): bp 76–77 °C/22 mmHg, GC (SE-30, 90 °C) 4.1 min (single peak), ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, $J = 6.4$ Hz, 3H), 0.88 (t, $J = 6.3$ Hz, 3H), 1.10–1.30 (m, 6H), 1.55–1.69 (m, 2H), 1.85 (m, 1H), 3.37–3.48 (m, 2H).

(*S*)-1-Bromo-3-methylheptane (23). By the same method as described above, (*S*)-**18** (3.7 g) was converted to (*S*)-**23** (3.53 g, 63% yield). The analytical data were identical to those of (*R*)-**23**.

(*R*)-2-Methyl-1-pentanol (13). By the same procedure as that applied to the preparation of **12**, Grignard reagent prepared from bromoethane (12 g) and Mg (2.6 g) in THF (100 mL) was subjected to a reaction with (*S*)-**11** (30 g). Removal of the protecting group from the product gave (*R*)-**13** containing 2-methoxytetrahydropyrane in ca. 5% (7.2 g, 78% yield by calculation) as a fraction at bp 70–76 °C at 45 mmHg. This material was used in the next step without further purification. The preparative GC (NPGS) of a small portion of this material afforded pure (*R*)-**13**: $[\alpha]_D^{20} = 12.3$ (*c* 5.0, MeOH), GC (BETA DEX 225, 65 °C) 17.3 min, single peak, (No peak of the antipode (rt = 19.0 min) was observed.), MS *m/z*, Found: 101.0958, Calcd for $C_6H_{13}O$: 101.0966, IR 3375, 2925, 1450, 1380, 1050 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 0.886 (t, $J = 6.8$ Hz, 3H), 0.895 (d, $J = 6.8$ Hz, 3H), 1.04–1.64 (m, 5H), 3.37–3.52 (m, 2H).

(*S*)-2-Methyl-1-pentanol (13). By the same method as described above, (*S*)-**11** (30 g) was converted to (*S*)-**3** containing 2-methoxytetrahydropyrane in ca. 5% (6.8 g, 74% yield): $[\alpha]_D^{20} = -13.1$ (*c* 5.0, MeOH), GC (BETA DEX 225, 65 °C) 19.0 min, single peak, (No peak of the antipode (rt = 17.3 min) was observed). The other analytical data were identical to those of (*R*)-**13**.

(*R*)-1-Bromo-2-methylpentane (16). By the same procedure as that applied to the preparation of **15**, (*R*)-**13** (6.6 g) was converted to (*R*)-**16** (5.6, 55% yield): bp 77–80 °C/89 mmHg, GC

(SE30, 70 °C) 4.1 min, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.3 Hz, 3H), 0.99 (d, J = 6.8 Hz, 3H) 1.18–1.18 (m, 4H), 1.78 (m, 1H), 3.30 (dd, J = 9.8, 6.3 Hz, 1H), 3.37 (dd, J = 9.8, 4.9 Hz, 1H).

(*S*)-1-Bromo-2-methylpentane (16). By the same method as described above, (*S*)-**13** (6.5 g) was converted to (*S*)-**16** (6.3 g, 60% yield). The analytical data were identical to those of (*R*)-**16**.

(*R*)-4-Methyl-1-heptanol (19). To a Grignard reagent prepared from (*R*)-**16** (5.1 g) and Mg (0.9 g) in 30 mL of ether was added a 20% solution of ethylene oxide in ether (10 mL) with stirring at lower than 5 °C. The reaction mixture was allowed to stand overnight and added into ice-suspended 2 M aq HCl (50 mL). The resulting ethereal layer was washed with brine, aq $NaHCO_3$, and brine successively, dried over K_2CO_3, and then concentrated in vacuo. Distillation of the residue under reduced pressure gave a crude fraction of (*R*)-**19** containing 4,7-dimethlydecane in ca 3%, (2.1 g, 48.4% yield from **16** by calculation): bp 77–80 °C/98 mmHg. This material was used in the next step without further purification. The preparative GC (NPGS) of a small portion of this material afforded pure (*R*)-**19**: GC (BETA DEX 225, 75 °C) 26.0 min, single peak, (No peak of the antipode (rt = 26.3 min) was observed). The $[\alpha]_D^{20}$ value was too small to determine, MS *m/z*, Found: 129.1270, Calcd for $C_8H_{17}O$: 129.1279, IR 3325, 2950, 1460, 1380, 1060 cm^{-1}, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 6.3 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 1.06–1.61 (m, 10H), 3.61 (t, J = 6.3 Hz, 2H).

(*S*)-4-Methyl-1-heptanol (19). By the same method as described above, (*S*)-**16** (4.5 g) was converted to (*S*)-**19** containing 2-methoxytetrahydropyrane in ca. 5%, (1.7 g, 45% yield): GC (BETA DEX 225, 75 °C) 26.3 min, single peak, (No peak of the antipode (rt = 26.0 min) was observed). The $[\alpha]_D^{20}$ value was too small to determine. Other analytical data were identical with those of (*R*)-**19**.

(*R*)-1-Bromo-4-methylheptane (24). (*R*)-**19** containing 5% of 4,7-dimethyldecane (1.6 g) was converted to tosylate by the same procedure as that applied to (*R*)-**18**. The obtained crude tosylate was chromatographed over silica gel. 4,7-Dimethyldecane eluted with hexane was discarded and tosylate eluted with 25% ethyl acetate in hexane was collected. The concentrate of the eluent (2.6 g) was subjected to a reaction with LiBr in DMF by the same method as applied to (*R*)-**18** to give (*R*)-**24** (1.23 g, 53% yield from **19**): bp 77–78 °C/20 mmHg, GC (SE-30, 80 °C) 8.5 min (single peak), ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84, (d, J = 7.3, 3H), 0.86 (t, J = 6.8 Hz, 3H), 1.05–1.45 (m, 7H), 1.83 (m, 2H), 3.61 (t, J = 6.2 Hz, 2H).

(*S*)-1-Bromo-4-methylheptane (24). By the same method as described above, (*S*)-**19** (1.4 g) was converted to (*S*)-**24** (0.75 g, 38% yield). The analytical data were identical to those of (*R*)-**24**.

(*R*)-2-Methyl-1-butanol (14). Grignard reagent prepared from bromomethane (2 M solution in ether, 125 mL) and Mg (6.4 g) was diluted with THF (100 mL) and cooled to −50 °C. To the solution were added CuI (0.5 g) and then a solution of (*S*)-**11** (30 g) in 30 mL of THF with stirring. The mixture was kept for 1 h at −50 °C, allowed to stand overnight at room temperature, and then heated at 40–50 °C for 1 h. By the same work up as that applied to the preparation of **12**, 2-methyl-1-tetrahydropyanylbutane (17.6 g) was obtained from the reaction. This material was mixed with methanol (250 mL) containing a small amount of *p*-toluensulfonic acid (ca. 100 mg), and allowed to stand overnight at room temperature. After neutralization with sodium methoxide (1 mL of 0.5 M methanol solution), the mixture was subjected to fractional distillation under atmospheric pressure with a Vigreux column. A mixture of (*R*)-**14** and 2-methoxytetrahydropyrane in a ratio of 57:43 was obtained (11 g, 76% yield from **11** by calculation) as a fraction of bp 125–130 °C. This material was used in the next step without further purification. The preparative GC (NPGS, 60 °C) of a small portion of this material afforded pure (*R*)-**14**: $[\alpha]_D^{20}$ = 6.45 (*c* 0.95, MeOH), GC (BETA DEX 225, 60 °C) 16.7 min, single peak (No peak of the antipode (rt = 17.6 min) was observed). ^{1}H NMR and IR spectral data were compatible with those of (*S*)-**14** obtained from a commercial source.

(*R*)-1-Bromo-2-methylbutane (17). The mixture of (*R*)-**14** and 2-methoxytetrahydropyrane (10.0 g containing ca. 5.7 g of **14**) was added to an ice-cooled solution of *p*-toluenesulfonyl chloride (15 g) in dry pyridine (30 mL) under stirring and the mixture was kept for 4 h. The mixture was poured into ice-water (50 mL) and extracted with three 50 mL portions of ether. The combined extract was washed with aq $CuSO_4$ solution, aq $NaHCO_3$, brine, and dried over $NaSO_4$. Evaporation of the solvent and 2-methoxytetrahydropyrane from the solution under high vacuum at room temperature gave (*R*)-2-methyllbutyl tosylate (10.2 g, 65% yield). This product was subjected to a reaction with anhydrous LiBr (20 g) in DMF (100 mL) by the same method as that applied to the preparation of **15** to yield (*R*)-**17** (4.3 g, 68% yield): bp 91–93 °C, ^{1}H NMR and IR spectral data were compatible with those of (*S*)-**17** obtained from commercial source.

(*R*)-5-Methyl-1-heptanol (20). Grignard reagent prepared from (*R*)-**17** (4.0 g) and Mg (0.78 g) in 20 mL of ether was cooled to −50 °C and mixed with CuI (0.1 g). To the solution was added 3-bromo-1-propene (3.2 mL) dissolved in 10 mL of ether with stirring. The mixture was kept for 1 h at −50 °C, allowed to stand over night at room temperature, and then mixed with an ice-cooled saturated aq. solution of NH_4Cl (70 mL). The separated ethereal layer was washed with 70 mL portions of saturated aq. solution of NH_4Cl, aq $NaHCO_3$, brine, successively, and dried over $MgSO_4$. From the resulting solution of 5-methyl-1-heptene, ether was carefully distilled off through a Vigreux column under atmospheric pressure. To a solution of the residue in 25 mL of THF was added a 1 M solution of BH_3 in THF (27 mL), and the mixture was allowed to stand at room temperature for 5 h, and was then cooled with an ice-bath. To this mixture, 30 mL of a 1 M aq solution of NaOH was added, followed by 3.5 mL of a 35% solution of H_2O_2. After stirring for 2 h at room temperature, the mixture was extracted twice with 50 mL portions of ether. The combined extracts were washed with brine, dried over K_2CO_3, and concentrated in vacuo. Distillation of the residue under reduced pressure gave (*R*)-**20** (2.39 g, 69% yield): bp 90–92 °C/26 mmHg, $[\alpha]_D^{20}$ = −7.16 (neat), GC (SE-30, 80 °C) 7.9 min. MS *m/z* (M^+ − H), Found: 129.1277, Calcd for $C_8H_{17}O$: 129.1279, IR 3350, 2920, 1460, 1370, 1060 cm^{-1}, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 7.3 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H), 1.09–1.57 (m, 10H), 3.63 (t, J = 6.3 Hz, 2H).

(*S*)-5-Methyl-1-heptanol (20). By the same method as described above, commercial (*S*)-1-bromo-2-methylbutane (**17**) (5.0 g) was converted to (*S*)-**20** (2.7 g, 62% yield), $[\alpha]_D^{20}$ = 6.94 (neat (Ref. 13, $[\alpha]_D^{24}$ = 2.99)). The analytical data were identical to those of (*R*)-**20**. This compound has recently become commercially available from TCI Co.

(*R*)-1-Bromo-5-methylheptane (25). This compound (2.1 g, 74% yield) was obtained from (*R*)-**20** (1.9 g) by the same procedure as that employed for the preparation of **23**: bp 78 °C/20 mmHg, GC (SE-30, 90 °C) 4.2 min (single peak), ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 6.4 Hz, 3H), 0.88 (t, J = 6.3 Hz, 3H), 1.10–1.30 (m, 6H), 1.15–1.69 (m, 2H), 1.85 (m, 1H), 3.37–3.48

(m, 2H).

(*S*)-1-Bromo-5-methylheptane (25). By the same method as described above, (*S*)-**20** (1.4 g) was converted to (*S*)-**25** (0.75 g, 38% yield). The analytical data were identical with those of (*R*)-**25**.

6-Methyl-1-heptanol (21). Commercial 1-bromo-4-methylpentane (5.5 g) was converted to Grignard reagent with Mg (1 g) in ether (50 mL). To the ice-cooled Grignard reagent was added a 20% solution of ethylene oxide in ether (22 mL) with stirring. The mixture was kept stirring overnight at room temperature, and then worked up in the same manner as that applied to the preparation of **16** to yield crude **21** containing ca. 5% of 2,9-dimethyldecane (1.58 g, 34% yield by calculation): bp 84–89 °C/15 mmHg (Ref. 13, 87–89 °C/14 mmHg). This material was used for the next step without further purification.

1-Bromo-6-methylheptane (26). This compound was obtained from **21** (1.5 g) by the same procedure as that employed for the preparation of **24**. **26** (1.35 g, 61% yield by calculation): bp 77–78 °C/20 mmHg, GC (3% SE-30, at 90 °C) 4.3 min (single peak), ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (d, J = 6.8 Hz, 6H), 1.15–1.30 (m, 2H), 1.32–1.42 (m, 4H), 1.51 (m, 2H), 1.84 (septet, J = 6.3 Hz, 1H) 3.39 (t, J = 6.8 Hz, 2H).

***rac*-2-Methyl-1-heptanol (22).** A solution of BH_3 (1 M in THF, 32 mL) was added to commercial 2-methyl-1-heptene (3.2 g) diluted with 25 mL of THF with stirring at 5 °C. The mixture was allowed to stand at room temperature for 5 h, and was then cooled with an ice bath. To this mixture, 30 mL of 3 M aq NaOH was added, followed by 20 mL of 30% H_2O_2. After stirring at room temperature for 2 h, the mixture was extracted twice with 50 mL portions of ether. The combined extracts were washed with brine, dried over K_2CO_3, and concentrated in vacuo. Distillation of the residue under reduced pressure gave **22** (4.0 g, yield 95%): bp 83–90 °C/15 mmHg. The analytical data were compatible with those reported in literatures.[15]

***rac*-1-Bromo-2-methylheptane (28).** This compound was obtained from **22** (3.5 g) by the same procedure as that employed for the preparation of **24**. **28** (3.9 g, 74% yield): bp 77–78 °C/ 20 mmHg. The analytical data were compatible with those reported in the literature.[6]

Synthesis of C5 Block. Methyl (2*S*,3*S*)-3-Hydroxy-2-methylbutanoate and Methyl (2*R*,3*S*)-3-Hydroxy-2-methylbutanoate (29). These compounds were prepared by the same procedure reported before from optically pure (*S*)-butyl 3-hydroxybutanoate (100 g, $[\alpha]_D^{20}$ = 14.6 (neat)).[9] (2*S*,3*S*)-**29** (14.8 g): $[\alpha]_D^{20}$ = 36.8 (*c* 5.0, MeOH), (2*R*,3*S*)-**29** (6.2 g): $[\alpha]_D^{20}$ = −14.3 (*c* 5.0, MeOH).

(2*R*,3*S*)-2-Methyl-3-tetrahydropyranyloxybutyl Tosylate (31) and (2*S*,3*S*)-2-Methyl-3-tetrahydropyranyloxybutyl Tosylate (31). These compounds were obtained from **29** by the same procedure as that applied to the preparation of **11**. (2*R*,3*S*)-**31** (21.7 g, 67%) was obtained from (2*S*,3*S*)-**29** (12.5 g) via (2*R*,3*S*)-2-methyl-3-tetrahydropyranyloxybutanol (**30**) (bp 86–90 °C/6 mmHg, Found: C, 63.91, H, 10.91%; Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%). This compound (20.5 g, 60 mmol) was made up to a 1 M solution in THF and used for the coupling reaction. (2*S*,3*S*)-**31** (7.7 g, 71% yield) was obtained from (2*R*,3*S*)-**29** (4.2 g) via (2*S*,3*S*)-**30** (bp 86–90 °C/6 mmHg, Found: C, 63.78 H, 10.89%; Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%). This compound was made up to a 1 M solution in THF and used for the coupling reaction.

Coupling of C5 and C8 Blocks. Preparation of C13 Alcohols (4H–9H). All C13 alcohols were obtained by cross coupling of C5 and C8 blocks. The common procedure was as follows: Grignard reagent was prepared from C8 block (1 g, 5.1 mmol) and Mg (0.15 g, 1.2 equiv) in 5 ml of THF. The Grignard reagent was cooled to −70 °C and mixed with a catalytic amount of CuI (ca. 5 mg) under stirring. To the solution, a 1 M solution of the C5 block in THF (5 mL, 5 mmol) was added. The mixture was kept at −70 °C for 1 h, followed by stirring overnight at room temperature. The mixture was poured into an ice-cooled saturate aq solution of NH_4Cl (20 mL) with 10 ml of ether. The separated ethereal layer was washed with 20 mL portions of aq $NaHCO_3$, brine successively, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was mixed with methanol (10 mL) containing *p*-toluenesulfonic acid (ca. 1 mg) and allowed to stand over night. After removing methanol from the mixture, the residue was dissoluble in ether (15 mL) and washed with aq $NaHCO_3$, brine, dried over K_2CO_3, and concentrated in vacuo. The residue was dissolved in hexane (5 mL) and chromatographed over a silica gel column. Evaporation of the solvent from a fraction eluted with 15% of ethyl acetate in hexane in vacuo gave a C13 alcohol. Synthetic data of each C13 alcohol are listed in Table 3.

Preparation of C13 Propionates (4P–9P). All C13 alcohols listed in Table 3 were converted to propionate by the common procedure and employed for a field bioassay. A C13 alcohol (0.1 mL, 86.5 mg) and pyridine (0.1 mL) were mixed with ether (2 mL) and cooled with an ice-bath. To this solution was added propionyl chloride (0.06 mL) under stirring. The mixture was allowed to stand overnight at room temperature, and was then poured into ice-suspended water (2 mL). The ethereal layer was washed with solutions of 2 M aq HCl, aq $NaHCO_3$, and brine, successively, and dried over $MgSO_4$. The solvent was removed, and the residue was purified by preparative GC (OV-101, 150 °C). The GC-purified material was made up to a 1 mg/mL hexane solution, and stored in sealed glass ampoules (1 mL each) as a stock solution for bioassays. The analytical data of each purified material are listed in Table 4.

Biomaterials and Analysis. Breeding of Insects. In the late summer of 1965, larvae were collected at Apoi Mountain, eastern Hidaka Hokkaido. The larvae were fed on fresh pine blanches (*Pinus strobus*) until forming cocoons. The cocoons were held during the winter at outdoor temperature. In late spring, large female cocoons and small male cocoons were separated and the individuals were kept in plastic boxes. The cocoons in plastic boxes were stored indoor under regulated temperature to let the adults emerge around mid summer. The females used for the extraction were stored in a freezer within a few hours after emergence. The males used for EAD were collected shortly after emergence and stored at 10 °C for 3 to 5 days before testing.

Preparation and Analysis of Female Extract. The whole bodies of 30 females were immersed in 20 mL of hexane and kept 2 days in a refrigerator. After removing the insects, the extract was filtered and concentrated to 100 µL. The concentrated extract was chromatographed over Florisil with an ether/hexane eluent following a procedure reported by Carroll.[16] A 0.3 female equivalent aliquot of each fraction was subjected to GC–EAD analysis using an antenna of one of the males. The EAD-active material was found in the fraction of 5% ether in hexane (corresponding to ester fraction). After selecting isopropyl dodecanoate (**32**) as a suitable internal standard for monitoring the rt of the EAD-active material in the GC system, all other of active fractions (25 female equivalent) were fractionated by the same GC system. The fraction corresponding to the EAD-active material accompanying **32** as the internal standard was subjected to a GC-MS analysis.

Table 3. Syntheses and Properties of the Alcoholic Parts (**4H**–**9H**) of the Pheromone Candidates

No	Materials and amount of use		Product of	$[\alpha]_D^{20}$	Elemental analysis	^{1}H NMR (400 MHz, $CDCl_3$)
	C8 block	C5 block	C13 alcohol	(*c* in MeOH)	Calcd for $C_{13}H_{28}O$; C,77.92; H,14.08	
	(g, mmol)	(1 M solution/mL)	(g, yield from C5 block)		Found:	
1	*rac*-**28** (0.56, 2.9)	(2*R*,3*S*)-**31** (2.2)	(2*S*,3*R*,6*RS*)-3,6-dimethyl-2-undecanol (**5H**) (0.10, 23%)	—	C,77.68; H,14.40	δ 0.82–0.88 (d, J = 6.8 Hz, 6H), 0.99–1.48 (m, 17H), 1.11 (d, J = 6.8 Hz, 3H), 3.64–3.66 (m, 1H)
2	(*R*)-**23** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*,7*R*)-3,7-dimethyl-2-undecanol (**4H**) (0.16, 16%)	20.3 (2.8)	C,77.58; H,14.30	δ 0.83 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 7.0 Hz, 3H) 1.10 (d, J = 6.8 Hz, 3H), 1.01–1.52 (m, 14H), 3.64 (m, 1H)
3	(*S*)-**23** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*,7*S*)-3,7-dimethyl-2-undecanol (**4H**) (0.28, 28%)	22.7 (2.6)	C,77.83; H,14.56	δ 0.83 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H) 1.10 (d, J = 6.8 Hz, 3H), 1.02–1.51 (m, 14H), 3.64 (m, 1H)
4	(*R*)-**24** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*,8*R*)-3,8-dimethyl-2-undecanol (**6H**) (0.33, 33%)	18.6 (3.8)	C,77.84; H,14.74	δ 0.83 (d, J = 6.8 Hz, 3H), 0.85–0.87 (m, 6H), 1.11 (d, J = 6.7 Hz, 3H) 1.03–1.48 (m, 14H), 3.63 (m, 1H)
5	(*S*)-**24** (0.7, 3.6)	(2*R*,3*S*)-**31** (4.0)	(2*S*,3*R*,8*S*)-3,8-dimethyl-2-undecanol (**6H**) (0.17, 21%)	23.2 (3.3)	C,77.58; H,14.30	δ 0.82 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H) 1.10 (d, J = 6.8 Hz, 3H), 1.03–1.45 (m, 14H), 3.65 (m, 1H)
6	(*R*)-**25** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*,9*R*)-3,9-dimethyl-2-undecanol (**7H**) (0.25, 25%)	11.9 (4.2)	C,77.94; H,14.29	δ 0.83 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H) 1.10 (d, J = 6.8 Hz, 3H), 1.00–1.50 (m, 14H), 3.64 (m, 1H)
7	(*S*)-**25** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*,9*S*)-3,9-dimethyl-2-undecanol (**7H**) (0.59, 59%)	29.1 (3.4)	C,77.53; H,14.62	δ 0.83 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 7.0 Hz, 3H) 1.10 (d, J = 6.8 Hz, 3H), 1.01–1.52 (m, 14H), 3.64 (m, 1H)
8	(*S*)-**25** (0.19, 1.0)	(2*S*,3*S*)-**31** (1.0)	(2*S*,3*S*,9*S*)-3,9-dimethyl-2-undecanol (**7H**) (0.03, 15%)	—[a]	—[a]	δ 0.81–0.85 (m, 6H), 0.86 (d, J = 6.8 Hz, 3H), 1.13 (d, J = 6.4 Hz, 3H), 1.08–1.52 (m, 14H), 3.69 (m, 1H)
9	**26** (0.65, 3.3)	(2*R*,3*S*)-**31** (3.5)	(2*S*,3*R*)-3,10-dimethyl-2-undecanol (**8H**) (0.31, 44%)	20.4 (4.9)	C,77.83; H,14.50	δ 0.84 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 1.10 (d, J = 6.4 Hz, 6H) 1.24–1.51 (m, 14H), 3.64 (m, 1H)
10	**26** (0.65, 3.3)	(2*S*,3*S*)-**31** (3.5)	(2*S*,3*S*)-3,10-dimethyl-2-undecanol (**8H**) (0.22, 31%)	−17.9 (2.0)	C,77.63; H,14.20	δ 0.84 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 1.13 (d, J = 6.4 Hz, 6H) 1.24–1.51 (m, 14H), 3.64 (m, 1H)
11	**27** (1.00, 5.1)	(2*R*,3*S*)-**31** (5.0)	(2*S*,3*R*)-3-methyl-2-dodecanol (**9H**) (0.57, 57%)	20.4 (2.5)	C,77.53; H,14.62	δ 0.84 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 6.8 Hz, 3H), 1.10 (d, J = 6.4 Hz, 3H) 1.04–1.49 (m, 17H), 3.64 (m, 1H)

a) An amount of the sample was insufficient for analyses

Field Tests. Stock solutions of pheromone candidates (1 mg/mL in hexane) were each diluted 10 times with hexane. The desired amount of the resulting solution (100 μg/mL in hexane) of each compound was loaded onto a cotton-roll dispenser (1 × 4 cm, Nitiei Co.). By 100 μL or 20 μL loading, a dispenser baited with 10 μg or 2 μg of pheromone candidate was prepared.

Table 4. ^{1}H NMR and GC-MS Data of Pheromone Candidates

No	Compound	^{1}H NMR (400 MHz, $CDCl_3$)	GC-MS	
			Retention time and that of internal standard (in parentheses)	Major fragments in EI mode
1	(1*S*,2*R*,5*RS*)-1,2,5-trimethyldecyl propionate (**5P**)	δ 0.81–0.88 (m, 9H), 1.00–1.37 (m, 20H), 2.29 (q, J = 7.2 Hz, 2H), 4.78–4.82 (m, 1H)	23.16 and 23.34 (24.16)	*m/z* 57, 69, 86, 101, 112, 130, 153, 165, 182
2	(1*S*,2*R*,6*R*)-1,2,6-trimethyldecyl propionate (**4P**)	δ 0.82 (d, J = 6.8 Hz, 3H), 0.85 (t, J = 7.5 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 7.5 Hz, 3H), 1.13 (t, J = 7.5 Hz, 3H), 1.05–1.40 (m, 13H), 1.63 (m, 1H), 2.28 (q, J = 7.5 Hz, 2H), 4.80 (m, 1H)	28.57 (29.15)	*m/z* 57, 70, 86, 101, 111, 125, 140, 158, 165, 182
3	(1*S*,2*R*,6*S*)-1,2,6-trimethyldecyl propionate (**4P**)	δ 0.82 (d, J = 6.8 Hz, 3H), 0.85 (t, J = 7.5 Hz, 3H), 0.85 (t, J = 7.5 Hz, 3H) 0.87 (d, J = 6.8 Hz, 3H), 1.12 (t, J = 7.5 Hz, 3H), 1.02–1.35 (m, 13H), 1.63 (m, 1H), 2.28 (q, J = 7.5 Hz, 2H), 4.78 (m, 1H)	28.60 (29.15)	See Fig. 2D
4	(1*S*,2*R*,7*R*)-1,2,7-trimethyldecyl propionate (**6P**)	δ 0.82 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.85 (t, J = 7.5 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H), 1.11 (t, J = 7.5 Hz, 3H), 1.01–1.48 (m, 13H), 1.63 (m, 1H), 2.29 (q, J = 7.5 Hz, 2H), 4.79 (m, 1H)	28.90 (29.15)	*m/z* 57, 70, 86, 101, 111, 130, 139, 158, 182
5	(1*S*,2*R*,7*S*)-1,2,7-trimethyldecyl propionate (**6P**)	δ 0.82 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.5 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H), 1.12 (t, J = 7.5 Hz, 3H), 1.00–1.38 (m, 13H), 1.63 (m, 1H), 2.28 (q, J = 7.5 Hz, 2H), 4.79 (m, 1H)	28.92 (29.15)	See Fig. 2C
6	(1*S*,2*R*,8*R*)-1,2,8-trimethyldecyl propionate (**7P**)	δ 0.81–0.86 (m, 9H), 1.11 (d, J = 6.3 Hz, 3H), 1.12 (t, J = 7.3 Hz, 3H), 1.07–1.34 (m, 14H), 2.28 (q, J = 7.5 Hz, 2H), 4.80 (m, 1H)	24.17 (24.14)	*m/z* 57, 70, 86, 101, 111, 130, 153, 182
7	(1*S*,2*R*,8*S*)-1,2,8-trimethyldecyl propionate (**7P**)	δ 0.81–0.86 (m, 9H), 1.12 (d, J = 6.3 Hz, 3H), 1.07–1.33 (m, 17H), 2.28 (q, J = 7.4 Hz, 2H), 4.80 (m, 1H)	28.65 (28.60)	See Fig. 2B
8	(1*S*,2*S*,8*S*)-1,2,8-trimethyldecyl propionate (**7P**)	δ 0.82 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H), 1.12 (t, J = 7.3 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.06–1.40 (m, 17H), 2.28 (q, J = 7.3 Hz, 2H), 4.82 (m, 1H)	28.49 (28.59)	*m/z* 57, 70, 86, 101, 111, 130, 153, 182
9	(1*S*,2*R*)-1,2,9-trimethyldecyl propionate (**8P**)	δ 0.79 (d, J = 6.8 Hz, 6H), 0.80 (d, J = 6.8 Hz, 3H), 1.07 (t, J = 7.5 Hz, 3H), 1.00–1.28 (m, 17H), 2.28 (q, J = 7.5 Hz, 2H), 4.79 (m, 1H)	23.89 (24.14)	*m/z* 57, 70, 86, 101, 121, 130, 153, 167, 182
10	(1*S*,2*S*)-1,2,9-trimethyldecyl propionate (**8P**)	δ 0.79 (d, J = 6.8 Hz, 6H), 0.81 (d, J = 6.8 Hz, 3H), 1.07 (t, J = 7.5 Hz, 3H), 1.09 (d, J = 6.4 Hz, 3H), 0.98 –1.26 (m, 14H), 2.23 (q, J = 7.5 Hz, 2H), 4.77 (m, 1H)	23.74 (24.14)	*m/z* 57, 70, 86, 101, 121, 130, 153, 167, 182
11	(1*S*,2*R*)-1,2-trimethylundecyl propionate (**9P**)	δ 0.85 (d, J = 6.8 Hz, 3H), 1.12 (t, J = 7.6 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H), 1.03–1.33 (m, 20H), 2.29 (q, J = 7.2 Hz, 2H), 4.77–4.83 (m, 1H)	25.07 (24.23)	*m/z* 57, 70, 86, 101, 111, 130, 153, 182

The field attraction of males to pheromone candidates was tested on Apoi Mountain, Hidaka, Hokkaido, Japan. The test areas were mixed stands of *Pinus parviflora* var, *Picea glehenii*, and *Rhododendron spp*. The sawfly attacked those *P. parviflora* in the previous summer. A cockroach trap supplied by Earth Pharmaceutical Co. was used throughout the field tests. A cotton-roll dispenser baited with a synthetic compound was placed at the center of the sticky surface of the trap. The baited traps were randomly used and attached to pine branches 1.5–2 m high and about 10 m apart. The dates of test period and the results are listed in Table 2 in the text.

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References

1 D. M. Jewett, F. Matsumura, and H. C. Coppel, *Science*, **192**, 51 (1976).

2 a) A. Tai, M. Imaida, and T. Oda, *Chem. Lett.*, **1978**, 61. b) K. Mori, S. Tamada, and S. Matsui, *Tetrahedron Lett.*, **1978**, 901.

c) F. Matsumura, A. Tai, H. C. Coppel, and M. Imaida, *J. Chem. Ecol.*, **5**, 237 (1979). d) T. Kikukawa, A. Tai, and M. Imaida, *Chem. Lett.*, **1982**, 1799. e) T. Kikukawa, F. Matsumura, J. Olaifa, M. Kraemer, H. C. Coppel, and A. Tai, *J. Chem. Ecol.*, **9**, 673 (1983). f) J. Orlaifa, T. Kikukawa, F. Matsumura, and H. C. Coppel, *Environ. Entomol.*, **13**, 1274 (1984). g) J. Orlaifa, F. Matsumura, and H. C. Coppel, *J. Chem. Ecol.*, **13**, 1395 (1987). h) J. Orlaifa, T. Kikukawa, F. Matsumura, and H. C. Coppel, *J. Chem. Ecol.*, **14**, 1131 (1987). i) A. Tai, N. Morimoto, M. Yoshikawa, T. Sugimura, and T. Kikukawa, *Agric. Biol. Chem.*, **54**, 1753 (1988).

3 T. Kikukawa, F. Matsumura, M. Kraemer, H. C. Coppel, and A. Tai, *J. Chem. Ecol.*, **5**, 301 (1982).

4 For reviews, see: a) A. Tai, *Gendai Kagaku*, No. **8**, 16 (1985). b) A. Tai, *Nippon Nogei Kagaku Kaishi*, **64**, 1741 (1990).

5 G. Bergström, A.-B. Wassgern, O. Anderbrant, J. Fägerhag, H. Edlund, E. Hedenström, H.-E. Högberg, C. Geri, M. A. Auger, M. Varsma, S. B. Hansson, and J. Löfqvist, *Experientia*, **51**, 370 (1995).

6 G. Bergström, A.-B. Wassgern, O. Anderbrant, S. A. Ochieng, F. Östrand, B. S. Hansson E. Hedenström, H.-E. Högberg, *Naturwissenschaften*, **85**, 244 (1998).

7 Y. Higashiura, *Forest Protection*, **266**, 26 (1988).

8 A. Tai, Y. Higashiura, M. Kakizaki, T. Naito, K. Tanaka, M. Fujita, T. Sugimura, H. Hara, and N. Hayashi, *Biosci. Biotechnol. Biochem.*, **62**, 607 (1998).

9 A. Tai, T. Sugimura, T. Kikukawa, T. Naito, Y. Nishimoto, and N. Morimoto, *Biosci. Biotechnol. Biochem.*, **56**, 1711 (1992).

10 a) A. Tai, N. Morimoto, M. Yoshikawa, K. Uehara, T. Kikukawa, and T. Sugimura, *Agric. Biol. Chem.*, **54**, 1751 (1990). b) A. Tai and M. Imaida, *Bull. Chem. Soc. Jpn.*, **51**, 1114 (1978).

11 a) A. Tai, T. Kikukawa, T. Sugimura, Y. Inoue, S. Abe, T. Osawa, and T. Harada, *Bull. Chem. Soc. Jpn.*, **67**, 2473 (1994). b) T. Kikukawa, Y. Iizuka, T. Sugimura, T. Harada, and A. Tai, *Chem. Lett.*, **1981**, 1267.

12 D. E. Struble, and H. Arn, "Combined gas chromatography and electroantennographic recording in insect olfactory responses" in "Techniques in Pheromone Research," ed by H. E. Hummel and T. A. Miller ed., Springer-Verlag (1984), pp. 161–178.

13 J. Buckingham, "Dictionary of Organic Compounds," 5th ed., Chapman Hall, New York (1982).

14 H. Tamagawa, H. Takigawa, and K. Mori, *Eur. J. Org. Chem.*, **5**, 973 (1999).

15 H.-E. Högberg, E. Hedenström, J. Fägerhag, and S. Servi, *J. Org. Chem.*, **57**, 2052 (1992).

16 K. K. Carroll, *J. Lipid Res.*, **141**, 135 (1961).