# Synthesis of Chiral Alcohol and Ester Pheromones through Enzyme-Catalysed Hydrolysis using *Pseudomonas fluorescens* Lipase: Preparation of (2*R*,6*S*,10*S*)-6,10-14-Trimethylpentadecan-2-ol and the Propionate of (2*R*,8*R*)-8-Methyldecan-2-ol

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(2*R*,6*S*,10*S*)-6,10,14-Trimethylpentadecan-2-ol [(2*R*,6*S*,10*S*)-**15**], one of the stereoisomers of the sex pheromone of *Corcyra cephalonica* Stainton, was synthesized in highly optically pure form by the hydrolysis of the 2,2,2-trichloroethyl carbonate of (2*RS*,6*S*,10*S*)-6,10,14-trimethylpentadecan-2-ol [(2*RS*,6*S*,10*S*)-**15a**] with *Pseudomonas fluorescens* lipase. The same method led to stereochemically pure (2*R*,8*R*)-8-methyldecan-2-yl propionate [(2*R*,8*R*)-**24**], which is a component of the sex pheromone of *Diabrotica* species.



Enzymatic or microbial transformations have widely been used as a useful means for obtaining chiral synthons or optically active compounds in recent years.[1] It was demonstrated in previous papers from our laboratory that immobilized biocatalysts, such as bakers' yeast[2] and plant-cell cultures[3] entrapped in carrageenan or calcium alginate gels, converted several kinds of keto acids or keto esters into alcohol products with high enantiomeric purities, and showed the advantage of permitting easy separation of products from the catalysts, compared with the use of free biocatalysts. We also reported the asymmetric synthesis of some pheromones, including (*R*)-hexadecan-5-olide,[4] two enantiomers of phoracantholide I,[5] and (5*Z*,13*S*)-tetradec-5-en-13-olide,[6] by a combination of chemical and enzymatic transformations.

We have now extended our investigations of the chemoenzymatic synthesis of pheromones and here present the preparation of two chiral pheromones, (2*R*,6*S*,10*S*)-6,10,14-trimethylpentadecan-2-ol [(2*R*,6*S*,10*S*)-**15**] and the propionate of (2*R*,8*R*)-8-methyldecan-2-ol [(2*R*,8*R*)-**24**], using immobilized *Pseudomonas fluorescens* lipase (IPFL) deposited onto glass beads.

## Results and Discussion

*Synthesis of* (2R,6S,10S)-6,10,14-*Trimethylpentadecan*-2-*ol* [(2R,6S,10S)-**15**].—Compound (2*R*,6*S*,10*S*)-**15** is one of the stereoisomers of the sex pheromone of the rice moth, *Corcyra cephalonica* Stainton.[7]

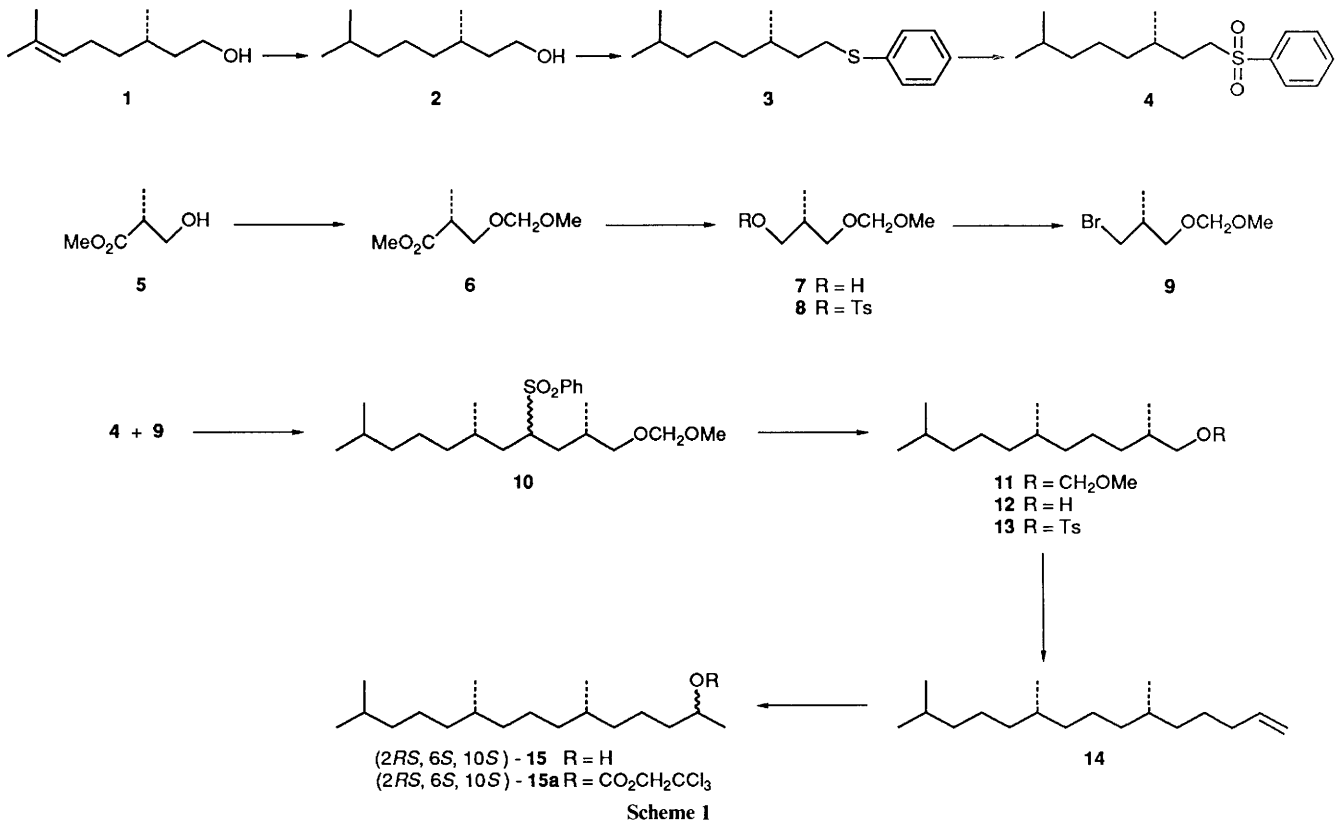
One starting material, (*S*)-β-citronellol **1**, was hydrogenated over 5% Pd/C catalyst to give the saturated alcohol **2**, which was converted into the sulphide **3** by treatment with diphenyl disulphide in the presence of tributylphosphine. Oxidation of compound **3** with *m*-chloroperbenzoic acid (MCPBA) afforded the sulphone **4** in 78% yield from citronellol **1**. The enantiomeric excess (ee) of compound **1** was determined to be at least 98.2% by HPLC analysis after pyridinium dichromate (PDC) oxidation of the alcohol into its carboxylic acid and subsequent condensation with (*R*)-(+)-1-(1-naphthyl)ethylamine to give the diastereoisomeric amide.[8] The other starting material, methyl (*R*)-3-hydroxy-2-methylpropionate **5**, which was determined to be 100% ee by HPLC analysis of the corresponding α-methoxy-α-trifluoromethylphenylacetic acid [(*R*)-MTPA] ester,[9] was protected as the methoxymethyl (MOM) ether **6**, and the latter compound was reduced with $LiAlH_4$ (LAH). The resulting alcohol **7**,[10] was converted, *via* the tosylester **8**, into the bromide **9** in 60% yield from ester **5**. Subsequently, the union of sulphone **4** with bromide **9** in the presence of lithium diisopropylamide (LDA) produced the sulphone **10** in 87% yield. Reductive elimination of the phenylsulphonyl function of compound **10** with Na/Hg (to give compound **11**) and removal of the MOM protective group gave the alcohol **12** in 80% yield, which was converted into the tosyl derivative **13**. Grignard coupling of ester **13** with but-3-en-1-ylmagnesium bromide gave the olefin **14**, and this alkene was transformed into a diastereoisomeric alcohol (2*RS*,6*S*,10*S*)-**15** in 65% yield by treatment with $Hg(OAC)_2$–$NaBH_4$ (Scheme 1).

Before final completion of the synthesis of (2*R*,6*S*,10*S*)-**15**, the enzymatic resolution of pentadecan-2-ol **16** using IPFL was examined (Table 1). The acetate derivative **16b** and the chloroacetate derivative **16c**, both of which were formed from (*RS*)-**16**, were each hydrolysed by IPFL to give (*R*)-**16** with low optical purity. On the other hand, the 2,2,2-trichloroethyl carbonate derivative **16a** was successfully resolved by IPFL to yield (*R*)-**16** of 95% ee. Similarly, enzymatic resolution of the trichloroethyl carbonate derivative prepared from (*RS*)-decan-2-ol afforded (*R*)-decan-2-ol with an optical purity of 93% ee.

As shown in Scheme 2, the synthesis of (2*R*,6*S*,10*S*)-**15** was completed by enzymatic separation of the diastereoisomeric alcohol (2*RS*,6*S*,10*S*)-**15** using IPFL. The alcohol was therefore converted into the 2,2,2-trichloroethyl carbonate derivative (2*RS*,6*S*,10*S*)-**15a**, and the latter was hydrolysed by IPFL in buffered aqueous solution. The resulting alcohol (2*R*,6*S*,10*S*)-**15** showed an optical purity of 91% ee. The optical purity was further enhanced by repetition of the enzymatic hydrolysis using IPFL; the trichloroethyl carbonate (2*R*,6*S*,10*S*)-**15a** derived from (2*R*,6*S*,10*S*)-**15** of 91% ee was resubmitted to the lipase hydrolysis to yield (2*R*,6*S*,10*S*)-**15** of ~100% ee.

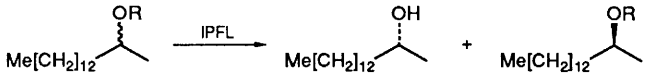
*Synthesis of the* (2R,8R)-8-*Methyldecan*-2-*yl Propionate* [(2R,8R)-**24**].—Compound (2*R*,8*R*)-**24** is a component of the sex pheromone of the western corn rootworm, *Diabrotica virgifera virgifera* Leconte, and also an attractant of some other *Diabrotica* species.[11]

Referring to Scheme 3, methyl hydrogen (*R*)-3-methylglutarate **17** (100% ee)[8] was reduced with borane–methyl sulphide complex to give the alcohol **18** which, after conversion into the mesylester **19**, led to the alcohol **20** after LAH reduction.[12] Subsequently, the alcohol **20** was transformed into its tosyl derivative **21**, and the latter was coupled with pent-4-en-1-ylmagnesium bromide in the presence of $Li_2CuCl_4$ to give the




Scheme 1

**Table 1** Enzymatic resolution of (±)-pentadecan-2-ol **16** by immobilized *Pseudomonas fluorescens* lipase




(±)-**16a** – (±)-**16c** (*R*)-**16** (*S*)-**16a** – (*S*)-**16c**

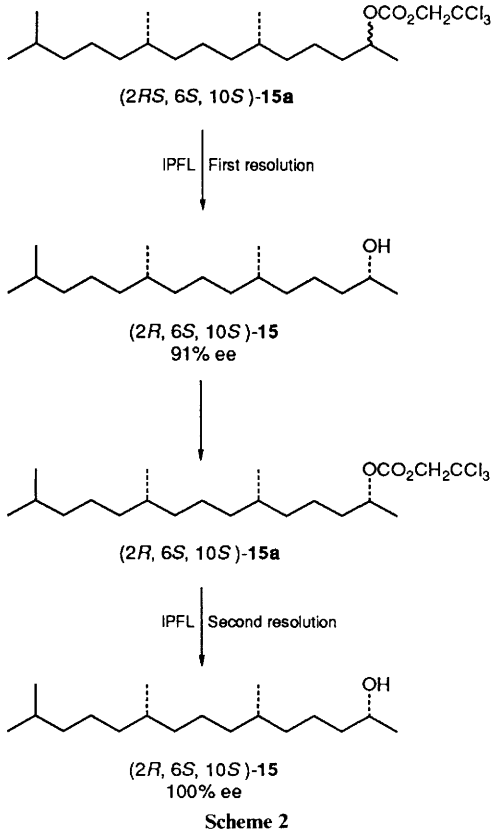
**16** R = H **16a** R = $CO_2CH_2CCl_3$
**16b** R = Ac **16c** R = $COCH_2Cl$

| Substrate | Conversion[a] (%) | Product | Yield (%) | Ee[b] (%) |
|---|---|---|---|---|
| (±)-**16a** | 30 | (*R*)-**16** | 23 | 95 |
| | | (*S*)-**16a** | 42 | 35 |
| (±)-**16b** | 48 | (*R*)-**16** | 40 | 52 |
| | | (*S*)-**16b** | 41 | 54 |
| (±)-**16c** | 45 | (*R*)-**16** | 40 | 54 |
| | | (*S*)-**16c** | 44 | 47 |

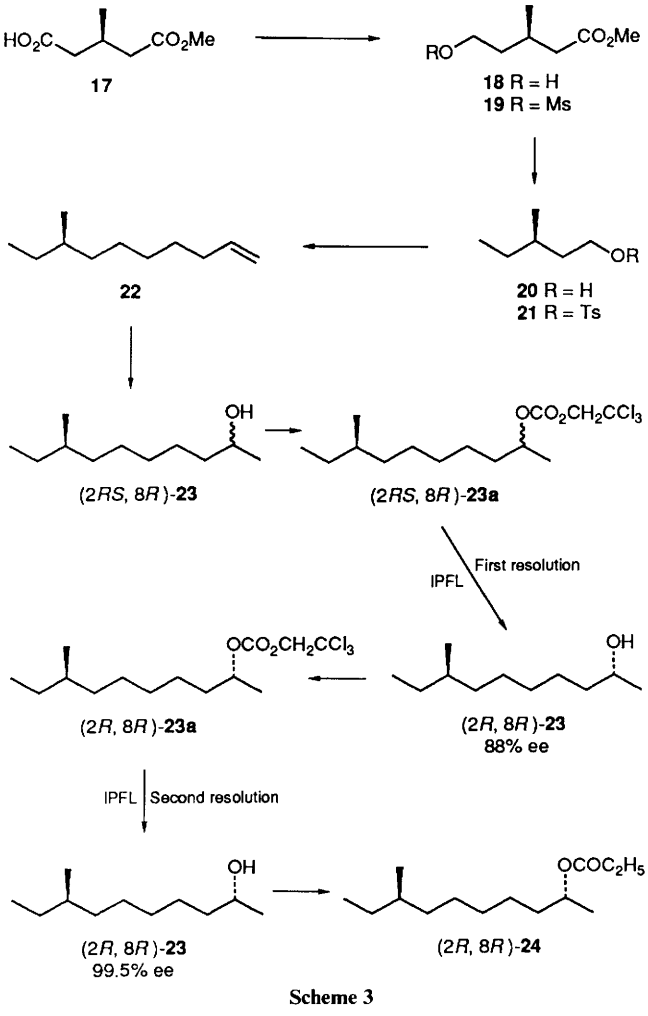
[a] Determined by capillary GLC (PEG-20M 25 m × 0.25 mm column). [b] Enantiomeric excesses of (*S*)-**16a**–(*S*)-**16c** were determined by HPLC analysis after conversion of each ester into the alcohol as described for (*R*)-**16** (see Experimental section).

chiral alkene **22** in 86% yield. Treatment of alkene **22** with $Hg(OAc)_2$–$NaBH_4$ afforded a diastereoisomeric alcohol (2*RS*,8*R*)-**23** in 83% yield, which was then converted into the corresponding trichloroethyl carbonate (2*RS*,8*R*)-**23a**. When ester (2*RS*,8*R*)-**23a** was hydrolysed with IPFL, the alcohol (2*R*,8*R*)-**23** was obtained with an optical purity of 88% ee. This alcohol was immediately converted into it trichloroethyl carbonate derivative **23a**, and the latter was resubmitted to the action of IPFL to yield the alcohol (2*R*,8*R*)-**23** with 99.5% ee. Finally, alcohol (2*R*,8*R*)-**23** of 99.5% ee was transformed into the desired pheromone (2*R*,8*R*)-**24**.

It is worth noting that in the case of the enzymatic resolution process the trichloroethyl carbonate derivatives were each successfully hydrolysed to the alcohol products with relatively high optical purity, while the corresponding acetate or chloroacetate derivatives yielded the products with low optical purity or racemic products. The present two-step resolution method, in which the first resolution of carbonate intermediates gives (*R*)-alcohol products of good to high optical purity and




Scheme 2




**Scheme 3**

the carbonates derived from the products are then submitted to the second resolution, enables us to prepare (*R*)-enantiomers of the desired, optically pure alkan-2-ols.

## Experimental

IR spectra were determined on a Fourier transform Perkin-Elmer 1720 spectrometer. $^1H$ and $^{13}C$ NMR spectra were obtained on Fourier transform Hitachi R-1500 (60 MHz) and Hitachi R-90H (22.63 MHz) spectrometers, respectively, for $CDCl_3$ solutions with $Me_4Si$ as the internal standard *J*-values are given in Hz. Mass spectra were recorded on JEOL JMS-D300 or DX-303HF mass spectrometers, using a direct-insertion probe. GLC was carried out on a Hitachi G-3000 gas chromatograph equipped with a PEG-20M 25 m × 0.25 mm WCOT fused silica capillary column. Optical rotations were measured on a Horiba SEPA-200 high-sensitivity polarimeter. Column chromatography was carried out with 70–230 mesh silica gel (Merck Kieselgel 60 Art. No. 7734) and 230–400 mesh silica gel (Merck Kieselgel 60 Art. No. 9385). Analytical samples were prepared by a combination of column chromatography and micro vacuum distillation with a Kugelrohr distilling apparatus.

*Determination of the C-2 Optical Purity of* (2R,6S,10S)-**15** *and* (2R,8R)-**23**.—The optical purity of alcohols (2*R*,6*S*,10*S*)-**15** and (2*R*,8*R*)-**23** were determined on HPLC analysis of their (*R*)-MTPA esters in comparison with those of alcohols (2*RS*,6*S*,10*S*)-**15** and (2*RS*,8*R*)-**23**, using a Hitachi L-6250 liquid chromatograph equipped with a UV detector [column, Partisil 5 4 × 250 mm; eluent hexane–1,2-dichloroethane–methanol (900:10:0.1); flow rate 1.0 $cm^3$ $min^{-1}$; detection λ 220 nm]. For compound (2*RS*,6*S*,10*S*)-**15**: $t_R$ 38 and 42 min. For compound (2*RS*,8*R*)-**23**: $t_R$ 36 and 40 min.

*Preparation of IPFL Deposited onto Glass Beads.*—Glass beads (0.71–1.19 mm in diameter; 60 g) were impregnated with 0.1 mol $dm^{-3}$ phosphate buffer (pH 7.0) and subsequently dried on a filter paper. After that, *Pseudomonas fluorescens* lipase (Amano Pharmaceutical Co.; 1 g) was added to the beads and the components were mixed completely. The resulting immobilized beads were stored at 5 °C for 12–24 h.

(S)-3,7-*Dimethyloctan*-1-*ol* **2**.—Hydrogenation of (*S*)-(−)-β-citronellol **1** (10.5 g, 66 mmol) in ethanol (35 $cm^3$) was carried out in the presence of 5% Pd/C (3.3 g). Distillation of the product gave compound **2** as a liquid (9.2 g, 88%); b.p. 60–62 °C (0.45 mmHg) [lit.,[13] 62 °C (0.25 mmHg)]; $[\alpha]_D^{20}$ −6.10° (*c* 4.0, MeOH) {lit.,[13] $[\alpha]_D^{25}$ +4.65° (neat) for the (*R*)-enantiomer}.

(S)-3,7-*Dimethyl*-1-*phenylthiooctane* **3**.—To a stirred solution of the alcohol **2** (7.9 g, 50 mmol) and diphenyl disulphide (16.38 g, 75 mmol) in dry $CH_2Cl_2$ (300 $cm^3$) was added tributylphosphine (25.5 $cm^3$) at room temperature and the mixture was stirred for 7 h before being treated with saturated aq. $NH_4Cl$ and then extracted with $CH_2Cl_2$. Usual work-up of the extracts gave a crude product, which was purified by column chromatography on silica gel with hexane, followed by distillation under reduced pressure, to give *compound* **3** as a liquid (12.1 g, 96%); b.p. 111–113 °C (0.5 mmHg); $[\alpha]_D^{20}$ +15.24° (*c* 10.12, MeOH); $\nu_{max}$(neat)/$cm^{-1}$ 3061, 2955, 2927, 1586, 1466, 1441, 1381, 1092, 1027, 892, 738 and 691; $\delta_H$ 0.85–1.58 (19 H, br m), 2.92 (2 H, t, *J* 7) and 7.27 (5 H, br s); $\delta_C$ 137.0 (s), 128.7 (d), 128.6 (d), 125.4 (d), 39.18, 36.89, 36.25, 32.19, 31.45, 27.93, 24.61, 22.66, 22.56 and 19.36 (Found: C, 76.5; H, 10.4. $C_{16}H_{26}S$ requires C, 76.75; H, 10.47%).

(S)-3,7-*Dimethyl*-1-*phenylsulphonyloctane* *4*.—To a stirred and cooled (−25 °C) solution of sulphide **3** (5.1 g, 20 mmol) in dry $CH_2Cl_2$ (50 $cm^3$) was added a solution of MCPBA (9.32 g, 54 mmol) in dry $CH_2Cl_2$ (120 $cm^3$), and the mixture was allowed to warm gradually to room temperature while being stirred. The mixture was treated with saturated aq. $NaHCO_3$ and then extracted with $CH_2Cl_2$. Usual work-up of the extracts gave a yellow liquid, which was purified by column chromatography on silica gel (180 g) with hexane–ethyl acetate (10:1) to give *compound* **4** as a liquid (5.35 g, 93%); $[\alpha]_D^{20}$ +8.16° (*c* 2.65, MeOH); $\nu_{max}$(neat)/$cm^{-1}$ 3066, 2955, 2928, 2869, 1587, 1466, 1088, 790, 742 and 690; $\delta_H$ 0.86–1.71 (19 H, br m), 3.10 (2 H, t, *J* 7) and 7.56–8.01 (5 H, m); $\delta_C$ 139.2 (s), 133.4 (d), 129.1 (d), 128.0 (d), 54.42 (t), 39.03, 36.56, 31.86, 29.18, 27.88, 24.45, 22.60, 22.50 and 19.15; *m*/*z* (EI) 282 ($M^+$, 3%), 250 (2), 197 (2), 169 (30), 143 (100), 142 (27), 141 (16), 140 (84), 85 (27), 70 (57) and 57 (45) (Found: C, 68.1; H, 9.2. $C_{16}H_{26}O_2S$ requires C, 68.05; H, 9.28%).

(S)-3-*Methoxymethoxy*-2-*methylpropan*-1-*ol* **7**.—Compound **7** was prepared from methyl (*R*)-3-hydroxy-2-methylpropionate **5** according to the reported procedure.[10] This alcohol was found to be pure by GLC analysis and was used without purification in the next step of the synthesis.

(R)-1-*Bromo*-3-*methoxymethoxy*-2-*methylpropane* **9**.—Tosyl-ester **8**, which was prepared from alcohol **7** (15.1 g, 0.11 mol) and *p*-TsCl (26.7 g, 0.14 mol) in dry pyridine (90 $cm^3$), was added to a suspension of LiBr (19.1 g, 0.22 mol) and $NaHCO_3$ (18.5 g, 0.22 mol) in dry butan-2-one (350 $cm^3$). The mixture was heated under reflux for 4 h, diluted with diethyl ether, and worked up in the usual manner. The crude product obtained was purified by

column chromatography on silica gel (190 g) with hexane–ethyl acetate (10:1) to give the bromide **9** as a liquid (16.42 g, 74%); $[\alpha]_D^{20}$ −9.14° (*c* 2.89, MeOH); $\nu_{max}$(neat)/cm$^{-1}$ 2933, 2883, 2824, 1460, 1387, 1260, 1233, 1217, 1142, 1113, 1046, 969, 923 and 825; $\delta_H$ 1.10 (3 H, d, *J* 5), 2.12 (1 H, m), 3.36 (3 H, s), 3.50 (4 H, overlapped) and 4.62 (2 H, s).

(2S,4RS,6S)-1-*Methoxymethoxy*-2,6,10-*trimethyl*-4-*phenylsulphonylundecane* **10**.—To a stirred and cooled (−50 °C) solution of the sulphone **4** (7.7 g, 27 mmol), the bromide **9** (16.15 g, 82 mmol), and hexamethylphosphonic triamide (HMPA) (56 cm$^3$) in dry tetrahydrofuran (THF) (600 cm$^3$) under nitrogen was added LDA freshly prepared from 1.6 mol dm$^{-3}$ BuLi (53 cm$^3$, 82 mmol) in hexane (Aldrich) and *N*,*N*-diisopropylethylamine (8.43 g, 82 mmol) in dry THF (60 cm$^3$). The mixture was warmed up quickly to −30 °C while being stirred. After being stirred for 4 h, the mixture was diluted with saturated aq. $NH_4Cl$ and the THF was evaporated off under reduced pressure. The residue was extracted with diethyl ether, washed successively with water and brine, dried and concentrated. The crude product obtained was purified by column chromatography on silica gel (310 g) with hexane–ethyl acetate (8:1) to give *compound* **10** as a liquid mixture of diastereoisomers (9.35 g, 87%); $\nu_{max}$(neat)/cm$^{-1}$ 3066, 2955, 1586, 1466, 1448, 1385, 1367, 1305, 1216, 1147, 1111, 1086, 1046, 922, 765, 738 and 693; $\delta_H$ 0.80–1.88 (19 H, br m), 3.29 (6 H, br s) and 4.55 (2 H, br s); $\delta_C$ 137.9 (s), 133.3 (d), 128.9 (d), 96.47, 96.38, 72.72 (t), 60.52, 60.43, 55.10 (q), 27.86, 22.62 and 22.53; *m*/*z* (EI) 367 ($M^+ - OCH_3$ 2%), 353 ($M^+ - CH_2OCH_3$, 6), 337 ($M^+ - OCH_2OCH_3$, 5), 257 ($M^+ - SO_2C_6H_5$, 9) and 45 (100) (Found: C, 66.2; H, 9.8. $C_{22}H_{38}O_4S$ requires C, 66.30; H, 9.61%).

(2S,6S)-1-*Methoxymethoxy*-2,6,10-*trimethylundecane* **11**.—A solution of the sulphone **10** (6.37 g, 16 mmol) in dry MeOH (150 cm$^3$) was added to Na(Hg) prepared from Na (7.4 g) and Hg (115 g), and the mixture was stirred overnight at room temperature. After filtration, the filtrate was concentrated under reduced pressure and diluted with diethyl ether. Usual work-up of the ethereal solution gave a crude product, which was purified by column chromatography on silica gel (140 g) with hexane–ethyl acetate (40:1) to give *compound* **11** as a liquid (3.47 g, 84%); $\nu_{max}$(neat)/cm$^{-1}$ 2930, 1465, 1241, 1151, 1114, 1051 and 925; $\delta_H$ 0.82–1.57 (27 H, br m), 3.31–3.36 (5 H, overlapped) and 4.62 (2 H, s); $\delta_C$ 96.50 (t), 73.33 (t), 54.97 (q), 39.36, 37.32, 33.94, 33.48, 32.75, 27.96, 24.79, 24.36, 22.68, 22.59, 19.66 and 17.11 (Found: C, 74.2; H, 13.3. $C_{16}H_{34}O_2$ requires C, 74.36; H, 13.26%).

(2S,6S)-2,6,10-*Trimethylundecan*-1-*ol* **12**.—To a solution of the ether **11** (2.84 g, 11 mmol) in MeOH (30 cm$^3$) was added conc. HCl (25 cm$^3$), and the mixture was heated under reflux for 8 h while being stirred. After cooling, the mixture was concentrated and diluted with diethyl ether. Usual work-up of the ethereal solution gave a crude product, which was purified by column chromatography on silica gel (90 g) with hexane–ethyl acetate (10:1) to give *compound* **12** as a liquid (2.26 g, 96%); $[\alpha]_D^{20}$ −9.01° (*c* 1.42, MeOH); $\nu_{max}$(neat)/cm$^{-1}$ 3334, 2955, 2927, 2871, 1467, 1384, 1367, 1170, 1055, 1011 and 735; $\delta_H$ 0.82–1.87 (28 H, br m) and 3.48 (2 H, br s) (Found: C, 78.2; H, 14.0. $C_{14}H_{30}O$ requires C, 78.43; H, 14.11%).

(6R,10S)-6,10,14-*Trimethylpentadec*-1-*ene* **14**.—4-Bromobut-1-ene (4.96 g, 37 mmol) was treated with Mg (0.87 g, 36 mmol) in dry diethyl ether (20 cm$^3$) under argon to give the corresponding Grignard reagent. To this ethereal solution at −40 °C was added a THF solution (15 cm$^3$) of the tosyl **13** prepared from alcohol **12** (2.78 g, 13 mmol) and *p*-TsCl (3.81 g, 20 mmol), followed by a 0.1 mol dm$^{-3}$ THF solution of $Li_2CuCl_4$ (0.75 cm$^3$). The mixture was then allowed to warm to room temperature over a period of 6 h while being stirred, and was stirred overnight. The mixture was then poured into saturated aq. $NH_4Cl$ and extracted with diethyl ether. Usual work-up of the extract gave a yellow liquid, which was purified by column chromatography on silica gel (80 g) with hexane to give *compound* **14** as a liquid (2.29 g, 70%); $[\alpha]_D^{20}$ −1.09° (*c* 1.02, MeOH); $\nu_{max}$(neat)/cm$^{-1}$ 3078, 2955, 2927, 2869, 1642, 1463, 1378, 1367, 994, 910 and 788; $\delta_H$ 0.81–2.07 (33 H, br m), 4.83–5.09 (2 H, m) and 5.52–5.91 (1 H, m); $\delta_C$ 139.2 (d), 114.1 (t), 39.40 (t), 37.46, 37.32, 36.55, 34.19, 32.82, 32.71, 28.01, 26.46, 24.84, 24.49, 22.75, 22.65 and 19.77 (Found: C, 85.5; H, 14.35. $C_{18}H_{36}$ requires C, 85.63; H, 14.37%).

(2RS,6S,10S)-6,10,14-*Trimethylpentadecan*-2-*ol* [(2RS,6S,10S)-**15**].—A solution of alkene **14** (2.10 g, 8.3 mmol) in THF (90 cm$^3$) was added to a stirred solution of $Hg(OAc)_2$ (10.52 g, 33 mmol) in water (30 cm$^3$). The mixture was stirred for 1.5 h at room temperature and then cooled to 0 °C. To the cooled solution was added 3.0 mol dm$^{-3}$ NaOH (30 cm$^3$), followed by a solution of $NaBH_4$ (1.48 g, 39 mmol) in 3.0 mol dm$^{-3}$ NaOH (30 cm$^3$). After being stirred overnight at room temperature, the mixture was diluted with water and filtered; the filtrate was extracted with diethyl ether. Usual work-up of the extract gave a crude product, which was purified by column chromatography on silica gel (80 g) with hexane to give *compound* **15** as a liquid mixture of diastereoisomers (1.46 g, 65%); $\nu_{max}$(neat)/cm$^{-1}$ 3348, 2955, 2927, 2869, 1463, 1377, 1245, 1123, 1078, 953, 857, 788 and 737; $\delta_H$ 0.82–1.42 (37 H, br m) and 3.77–3.85 (1 H, br m); *m*/*z* (EI) 252 ($M^+ - H_2O$, 14%), 210 (2), 196 (6), 182 (6), 167 (4), 140 (7), 126 (32), 111 (27), 97 (46), 83 (31), 71 (56), 69 (53), 57 (100) and 43 (22): *m*/*z* (CI, isobutane) 327 [$(M + C_4H_9)^+$, 17%] and 253 [$(M + H - H_2O)^+$, 100] (Found: C, 79.9; H, 14.1. $C_{18}H_{38}O$ requires C, 79.92; H, 14.16%).

*The* 2,2,2-*Trichloroethyl Carbonate of* (RS)-*Pentadecan*-2-*ol* [(RS)-**16a**].—The alcohol (*RS*)-**16** (1.5 g, 6.6 mmol) was treated with a solution of 2,2,2-trichloroethyl chloroformate (3.18 g, 15 mmol) in diethyl ether (20 cm$^3$) in the presence of pyridine (0.5 cm$^3$). Usual work-up of the mixture and subsequent purification by column chromatography on silica gel (30 g) with hexane gave compound (*RS*)-**16a** as a liquid (2.61 g, 98%); $\nu_{max}$(neat)/cm$^{-1}$ 2926, 2855, 1758, 1380, 1254, 1122, 1064, 963, 911, 819, 786 and 734; $\delta_H$ 4.80 (3 H, overlapped).

*Enzymatic Resolution of Carbonate* (RS)-**16a**.—A mixture of carbonate (*RS*)-**16a** (2 g, 5 mmol), IPFL prepared from *P. fluorescens* lipase (3 g) and glass beads (180 g), and 0.1 mol dm$^{-3}$ phosphate buffer (350 cm$^3$) was shaken for 24 h at room temperature. After filtration, the filtrate was extracted with diethyl ether and the extract was worked up. Purification by column chromatography on silica gel (30 g) gave the alcohol (*R*)-**16** (0.26 g, 23%); $[\alpha]_D^{21}$ −8.90° (*c* 1.01, pentane). The optical purity of the product was estimated to be 95% ee by HPLC analysis of the corresponding (*R*)-MTPA ester in comparison with that of (*RS*)-**16** as described for (2*R*,6*S*,10*S*)-**15** and (2*R*,8*R*)-**23**. $t_R$ 24 min (2.5%) and $t_R$ 26 min (97.5%).

*The* 2,2,2-*Trichloroethyl Carbonate of* (2RS,6S,10S)-6,10,14-*Trimethylpentadecan*-2-*ol* [(2*RS*,6*S*,10*S*)-**15a**].—Compound (2*RS*,6*S*, 10*S*)-**15** (1.4 g, 5.2 mmol) was treated with 2,2,2-trichloroethyl chloroformate (2.6 g, 12 mmol) in diethyl ether in the presence of pyridine (0.5 cm$^3$). Usual work-up of the reaction mixture gave a crude product, which was purified by column chromatography on silica gel (30 g) with hexane to give the carbonate **15a** as a liquid (2.1 g, 92%); $\nu_{max}$(neat)/cm$^{-1}$ 2927, 2868, 1758, 1380, 1255, 1124, 1064, 964, 914, 819, 785 and 733; $\delta_H$ 4.77 (3 H, overlapped).

*Enzymatic Resolution of Carbonate* (2RS,6S,10S)-**15a**.—A mixture of (2*RS*,6*S*,10*S*)-**15a** (1 g, 2.24 mmol), IPFL prepared from *P. fluorescens* lipase (2 g) and glass beads (120 g), and 0.1 mol $dm^{-3}$ phosphate buffer (250 $cm^3$) was shaken for 94 h at room temperature. GLC analysis indicated that conversion was ~40%. After filtration, the filtrate was extracted with diethyl ether and the extract was worked up. Purification by column chromatography as described for alcohol (2*RS*,6*S*,10*S*)-**15** gave one of its isomers, (2*R*,6*S*,10*S*)-**15** (0.21 g, 35%), with 91% ee; $[\alpha]_D^{24}$ −6.38° (*c* 3.5, pentane). The structure was characterized on the basis of spectral data.

*Enzymatic Optical Enhancement of Alcohol* (2*R*,6*S*,10*S*)-**15**.—Compound (2*R*,6*S*,10*S*)-**15a** (0.15 g, 0.33 mmol), which was prepared from the alcohol (2*R*,6*S*,10*S*)-**15** of 91% ee, was added to a mixture of IPFL prepared from *P. fluorescens* lipase (0.3 g) and 0.1 mol $dm^{-3}$ phosphate buffer (120 $cm^3$), and the mixture was shaken for 8 h at room temperature. GLC showed a conversion of *ca.* 40%. Column chromatography gave the desired pheromone [(2*R*,6*S*,10*S*)-**15** (0.033 g, 33%) with 100% ee; $[\alpha]_D^{24}$ −7.72° (*c* 1.23, pentane).

(R)-8-*Methyldec*-1-*ene* **22**.—5-Bromopent-1-ene (7.56 g, 51 mmol) was treated with Mg (1.58 g, 66 mmol) in dry diethyl ether (40 $cm^3$) under argon. To the resulting Grignard reagent solution at −60 °C was added a THF solution of the tosyl ester **21** formed from (*R*)-3-methylpentan-1-ol **20**[12] (2.62 g, 25 mmol) and *p*-TsCl (5.6 g, 29 mmol), followed by a 0.1 mol $dm^{-3}$ THF solution of $Li_2CuCl_4$ (1.3 $cm^3$). The mixture was then allowed to warm to room temperature during 2 h and was stirred for 12 h. Usual work-up gave a yellow liquid, which was purified by distillation to give the *alkene* **22** as a liquid (3.43 g, 86%); b.p. 67–70 °C (26 mmHg); $[\alpha]_D^{20}$ −10.64° (*c* 1.8, pentane); $\nu_{max}$(neat)/$cm^{-1}$ 3078, 2962, 2927, 2856, 1642, 1463, 1378, 993 and 910; $\delta_H$ 0.87–2.09 (19 H, br m), 4.83–5.09 (2 H, m) and 5.52–5.93 (1 H, m); $\delta_H$ 139.0 (d), 114.0 (t), 36.65, 34.48, 29.57, 29.09, 27.01, 19.24 and 11.40; *m*/*z* (EI) 154 ($M^+$, 3%), 125 ($M^+ - C_2H_5$, 30), 97 (21), 83 (67), 70 (100), 55 (75), 41 (60) and 29 (30) (Found: C, 85.55; H, 14.4. $C_{11}H_{22}$ requires C, 85.63; H, 14.37%).

(2RS,8R)-8-*Methyldecan*-2-*ol* [(2RS,8R)-**23**].—This alcohol was prepared from alkene **22** (2.81 g, 18 mmol) according to the procedure described for compound (2*RS*,6*S*,10*S*)-**15**. Column chromatography on silica gel (60 g) with hexane–ethyl acetate (30:1) gave the title alcohol as a liquid (2.62 g, 83%); $\delta_C$ 67.92 (d), 39.49, 36.78, 34.54, 30.27, 29.61, 27.28, 26.05, 23.39, 19.26 and 11.44 (q). The IR and $^1H$ NMR spectra were identical with those previously reported.[14]

*The* 2,2,2-*Trichloroethyl Carbonate of* (2RS,8R)-8-*Methyldecan*-2-*ol* [(2RS,8R)-**23a**].—Compound (2*RS*,8*R*)-**23** (2.5 g, 14.4 mmol) was treated with 2,2,2-trichloroethyl chloroformate (3.6 g, 17 mmol). Column chromatography on silica gel (50 g) with hexane–ethyl acetate (30:1) gave the corresponding carbonate as a liquid (4.8 g, 96%); $\nu_{max}$(neat)/$cm^{-1}$ 2959, 2931, 2859, 1757, 1458, 1380, 1254, 1123, 1062, 963, 909, 819, 785 and 734; $\delta_H$ 4.77 (3 H, overlapped); $\delta_C$ 153.6 (s), 94.82 (s), 76.85 (d), 76.50 (t), 36.51, 35.78, 34.35, 29.71, 29.47, 26.95, 25.29, 19.80, 19.19 and 11.38 (q).

*Enzymatic Resolution of the Carbonate* (2RS,8R)-**23a**.—A mixture of compound (2*RS*,8*R*)-**23a** (2 g, 5.75 mmol), IPFL prepared from *P. fluorescens* lipase (3 g) and glass beads (180 g), and 0.1 mol $dm^{-3}$ phosphate buffer (350 $cm^3$) was shaken for 30 h at room temperature. GLC showed a conversion of 32%. Column chromatography as described for the alcohol (2*RS*,8*R*)-**23** gave one of the isomers, (2*R*,8*R*)-**23** (0.27 g, 28%), with 88% ee; $[\alpha]_D^{24}$ −12.05° (*c* 1.65, $CHCl_3$).

*Enzymatic Optical Enhancement of the Alcohol* (2R,8R)-**23**.—Compound (2*R*,8*R*)-**23a** (0.3 g, 0.86 mmol), which was formed from the alcohol (2*R*,8*R*)-**23** of 88% ee, was added to a mixture of IPFL prepared from *P. fluorescens* lipase (0.45 g) and 0.1 mol $dm^{-3}$ phosphate buffer (150 $cm^3$), and the mixture was shaken for 3 h at room temperature; the conversion reached 30%. Column chromatography gave compound (2*R*,8*R*)-**23** (0.034 g, 23%) with 99.5% ee; $[\alpha]_D^{24}$ −14.91° (*c* 1.81, $CHCl_3$) {lit.,[14] $[\alpha]_D^{23.5}$ −14.9° (*c* 1.01, $CHCl_3$); lit.,[15] $[\alpha]_D^{22}$ −13.86° (*c* 12.5, $CHCl_3$)}.

*The Propionate of* (2R,8R)-8-*Methyldecan*-2-*ol* [(2R,8R)-**24**].—The propionate was synthesized from (2*R*,8*R*)-**23** (0.03 g, 0.17 mmol) of 99.5% ee according to the reported procedure.[14] Column chromatography and subsequent micro-vacuum distillation gave the desired pheromone (2*R*,8*R*)-**24** (0.035 g, 87%); $[\alpha]_D^{24}$ −8.02° (*c* 1.18, $CHCl_3$) {lit.,[14] $[\alpha]_D^{23}$ −7.57° (*c* 1.05, $CHCl_3$), lit.,[15] $[\alpha]_D^{26}$ −7.967° (*c* 15, $CHCl_3$)}. The IR, $^1H$ NMR and mass spectra were identical with those previously reported.[14]

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