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Enantiopure building blocks for the synthesis of 3-methyl-2-alkanols. Diastereoselective methylmetal addition to a chiral 2-methylaldehyde followed by lipase catalysed esterification

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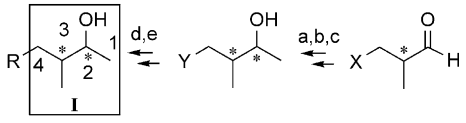
Abstract—The racemic synthetic building block (2*R**,3*R**)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*R**,3*R**)-**2** was obtained in a high diastereomeric ratio [95:5, (2*R**,3*R**)/(2*R**,3*S**)-ratio] by Lewis acid catalysed dimethylzinc addition to racemic 2-methyl-3-(phenylsulfanyl)propanal (*rac*-**1**). Two consecutive acylations with vinyl acetate catalysed by Chirazyme L-2 (immobilised *Candida antarctica* lipase B, CAL-B) led to preferential esterification of three of the four stereoisomers leaving (2*S*,3*S*)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*S*,3*S*)-**2** of 98:2 dr and 98% ee. The stereoisomerically impure acetate of (2*R*,3*R*)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*R*,3*R*)-**2**, obtained in the first CAL-B-catalysed acylation step, was hydrolysed and reesterified using CAL-A (immobilised Novozyme SP 525) as the catalyst, which left (2*R*,3*R*)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*R*,3*R*)-**2** of 98:2 dr and 99% ee as the remaining substrate. The individual enantiomers of 2-methyl-3-(phenylsulfanyl)propanal **1** were prepared from readily available (*S*)- and (*R*)-3-hydroxy-2-methylpropanoic acid methyl ester and reacted with dimethylzinc to give both enantiomers of (2*R**,3*R**)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*R*, 3*R*)- or (2*S*,3*S*)-**2** of both high dr and ee. These products were purified by lipase catalysed acylation to give the enantiomerically and diastereomerically highly pure enantiomers (>99.5:0.5 dr, >99.9% ee). Pure (2*S*,3*S*)-3-methyl-4-(phenylsulfanyl)butan-2-ol (2*S*,3*S*)-**2** was transformed into a potential pheromone precursor isolated from some pine sawflies of the genus *Gilpinia*, (2*S*,3*R*)-3-methylpentadecan-2-ol in 54% yield over eight steps.

1. Introduction

Many natural products such as antibiotics[1] and some pheromones[2] contain the stereoisomerically pure 3-methyl-2-butanol moiety **I** attached to various substituents in the 4-position (Scheme 1). A number of approaches exist for the synthesis of compounds containing this moiety.[1–3] One way of incorporating this moiety in a synthetic target can be to alkylate a stereoisomerically pure intermediate containing a suitable group Y, which subsequently can be removed. Because sulfur containing groups are easy to remove, they are attractive to use as Y-groups. If the Y group is phenylsulfanyl (Y = PhS), the neighbouring methylene carbon can be transformed into an electrophilic one by conversion of the PhS group into a good leaving group, whereas if it is phenylsulfonyl (Y = $PhSO_2$) the same carbon can be rendered nucleophilic by deprotonation.



Scheme 1. General outline describing the incorporation of the stereoisomerically pure 3-methyl-2-butanol moiety **I** in a synthetic target. Reagents and conditions: (a) diastereoselective addition of a methylmetal reagent; (b) enzyme catalysed resolution; (c) transformation of group X (optional); (d) alkylation; (e) removal of Y-group.

We have recently studied the diastereoselectivity in alkylmetal additions to some chiral racemic 2-methylaldehydes and found that titanium tetrachloride catalysed dimethylzinc addition to racemic 2-methyl-3-(phenylsulfanyl)propanal *rac*-**1** (Scheme 2) furnished racemic (2*R**,3*R**)-3-methyl-4-(phenylsulfanyl)-2-butanol (2*R**,3*R**)-**2** in a high diastereomeric ratio (dr), [(2*R**,3*R**)/(2*R**,3*S**)-ratio: ≈95:5].[4] The predominance of (2*R**,3*R**)-**2** is probably due to a cyclic transition state.[4] Thus we have easy access to a synthetic intermediate for the preparation of targets of type **I** in which a suitable group Y (Scheme 1) is already incorporated.

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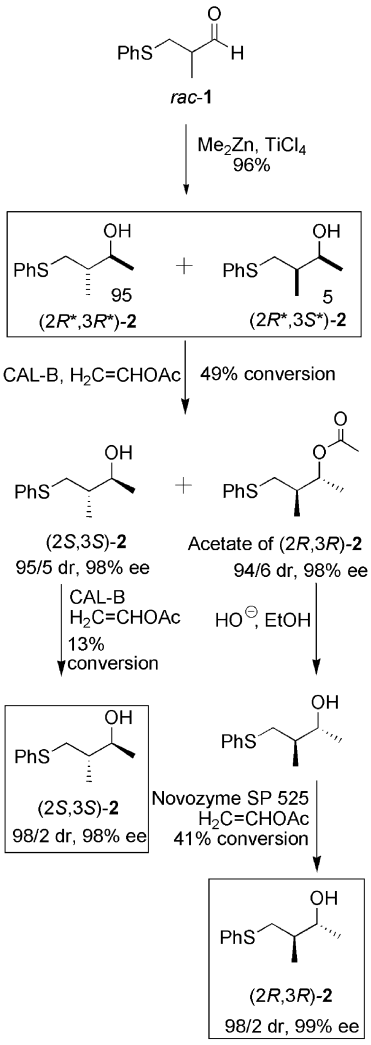


Scheme 2. Preparation of racemic (2*R**,3*R**)-**2** and its enzyme catalysed resolution and diastereoselective purification.

Enantiomerically pure (2*R**,3*R**)-**2** could serve as a synthetic intermediate for the preparation of several pine sawfly sex pheromones, esters of alcohols with the general structure **I** (Scheme 1, R = dimethyl-*n*-alkyl, methyl-*n*-alkyl, or *n*-alkyl). It has earlier been shown that some racemic pine sawfly pheromones can be resolved by lipase catalysed acylation.[2h] We were interested in being able to control the stereochemistry at an earlier stage in the synthetic sequence. Because secondary alcohols are generally easy to resolve by lipase catalysed resolutions,[5,6] we have studied such reactions with the racemic secondary alcohol (2*R**,3*R**)-**2** to see if the products could be obtained in sufficiently high enantiomeric and diastereomic excesses for our needs.

2. Results and discussion

For the synthesis of pure (2*S*,3*R*)-isomers of pine sawfly pheromones, we decided to study the lipase-mediated resolution by transesterification of racemic (2*R**,3*R**)-**2**.

2.1. Resolution of racemic (2*R**,3*R**)-2

We screened various lipases in order to achieve resolution and diastereomeric separation of racemic (2*R**,3*R**)-**2** (80:20 dr). Regarding selectivity in position 3, Ohtsuka et al.[6] have earlier shown, that a diastereomeric mixture of (2*R*,3*R*)- and (2*R*,3*S*)-**2** can be separated by using CAL-A-catalysed (Novozyme SP 525) esterification and hydrolysis. Regarding selectivity at position 2, we found that *Candida Antarctica* lipase B (Chirazyme L-2, CAL-B) showed the highest selectivity among the lipases tested. Hence, racemic (2*R**,3*R**)-**2** (95:5 dr) was treated with vinyl acetate in the presence of CAL-B in *n*-heptane over molecular sieves (Scheme 2). Under these conditions, the diastereomers of **2** with (2*R*)-configuration reacted considerably faster than (2*S*)-**2**. At 49% conversion the *E*-value was >500 and a mixture of (2*S*)-isomers of **2** was recovered as the remaining substrate with an unchanged dr and a (2*S*/2*R*)-ratio of >99:1 along with the acetate of (2*R*,3*R*)-**2** (94:6 dr, 2*R*/2*S*-ratio: 99:1).

In addition to its high (2*R*)-selectivity in esterification of compound **2**, CAL-B also showed a slight preference for acylation of the (3*R*)-isomers. Thus, in order to remove traces of the other isomers present in the recovered substrate, slightly impure (2*S*,3*S*)-**2** (≈95:5 dr, 98% ee) was once again subjected to CAL-B and vinyl acetate. Conversions over 13% did not further increase the purity of the remaining substrate. Stopping at this conversion gave (2*S*,3*S*)-**2** [98:2 dr; 98% ee and 37% overall yield from racemic (2*R**,3*R**)-**2**].

It is known that vinyl acetate esterifies (2*R*,3*S*)-**2** twenty times faster than (2*R*,3*R*)-**2** catalysed by Novozyme SP 525.[6] Therefore, the slightly isomerically impure acetate of (2*R*,3*R*)-**2** obtained from the first CAL-B-catalysed esterification was hydrolysed. The resulting alcohol was subjected to vinyl acetate and Novozyme SP 525. The reaction was interrupted at 41% conversion yielding the remaining substrate as highly pure (2*R*,3*R*)-**2** [98:2 dr, 99% ee, overall yield from racemic (2*R**,3*R**)-**2**: 18%].

2.2. Preparation of (2*S*,3*S*)- and (2*R*,3*R*)-2 and their enzyme catalysed purification

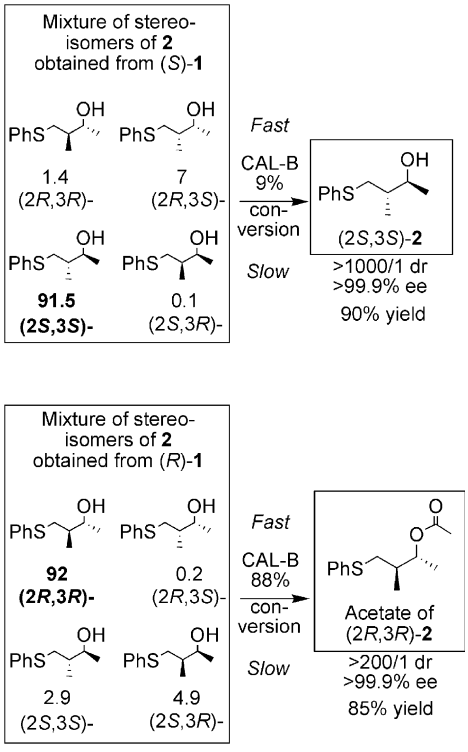
Although lipase catalysed reactions of the slightly diastereomerically impure and racemic (2*R**,3*R**)-**2** furnished both (2*S*,3*S*)-**2** and (2*R*,3*R*)-**2** in quite high diastereomeric ratios and enantiomeric excesses, we were not satisfied with the isomeric purities of these samples, which were too low to be useful for the preparation of the desired highly pure single stereoisomers of pine sawfly pheromones. Clearly, alternative approaches to the pure enantiomers (2*S*,3*S*)- and (2*R*,3*R*)-**2** were needed. We wanted to use lipases for the purification of already enantiomerically and diastereomerically enriched **2**.

If we should have access to enantiomerically pure 2-methyl-3-(phenylsulfanyl)propanal **1**, we could, using our diastereoselective dimethylzinc addition reaction,[4] be able to prepare both (2*S*,3*S*)- and (2*R*,3*R*)-**2** in quite high isomeric purities, provided that no racemisation of

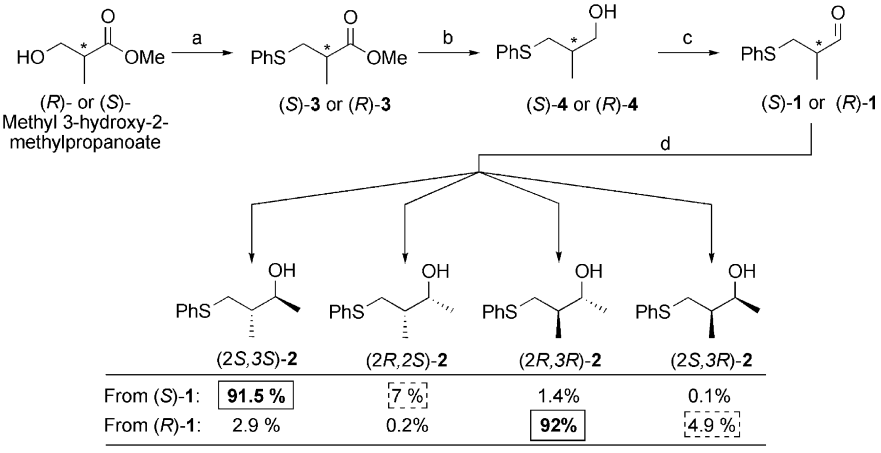
the aldehyde **1** would occur during the reaction sequence. Both enantiomers of the aldehyde **1** have previously been prepared.[7] The method starting from methyl 3-hydroxy-2-methylpropanoate[7b] seemed most advantageous as both enantiomers of this ester are commercially available. Because reaction of enantiopure aldehyde (*S*)-**1** should provide a 95:5 mixture of (2*S*,3*S*)-**2** and (2*R*,3*S*)-**2**, the latter unwanted product should, due to its more reactive (2*R*)-configuration, be easily removed by lipase catalysed acylation. Even if the enantiomeric purity of the aldehyde will be only 90% ee, the product of dimethylzinc addition will contain 90.3% of (2*S*,3*S*)-**2**, 4.7% of (2*R*,3*S*)-**2**, 4.7% (2*R*,3*R*)-**2**, and a very minute amount of 0.3% of (2*S*,3*R*)-**2**. Whereas the two isomers with the (2*R*)-configuration will easily be separated from the major and desired isomer (2*S*,3*S*)-**2** by enzyme-catalysed esterification, the one with (2*S*,3*R*)-configuration will be more difficult to remove completely. However, in the suggested reaction sequence, the latter is produced in an extremely small amount.

Thus, the preparation of the building blocks (2*S*,3*S*)-**2** or its enantiomer was conducted as follows (Scheme 3). First we wanted to prepare (*S*)-2-methyl-3-(phenylsulfanyl)propanal (*S*)-**1** from commercially available methyl (*R*)-3-hydroxy-2-methylpropanoate (>99% ee by GC analysis). However, we experienced difficulties with the reproduction of the ee's obtained earlier.[7b] Therefore, to ensure retention of configuration in the reaction sequence leading to enantiomerically enriched **1**, we used a modified method. Thus, methyl (*R*)-3-hydroxy-2-methylpropanoate was treated with diphenyldisulfide to give the corresponding thioether (*S*)-**3** (>97% ee by GC analysis). Reduction of this compound with lithium aluminium hydride gave the alcohol (*S*)-**4** (>97% ee by ^{1}H NMR analysis on its corresponding MTPA-ester, derived from (−)-MTPAC1). Swern oxidation of the alcohol (*S*)-**4** using oxalyl chloride in DMSO and Hünig's base (*N*-ethyldiisopropylamine) was followed by workup with aqueous KH_2PO_4 to ensure that no amine remained and that the pH was neutral. This afforded the corresponding aldehyde (*S*)-**1**. The enantiomeric purity of this was checked by reduction of **1** to **4** and analysis as its MTPA-ester (vide supra). The solution of the aldehyde (*S*)-**1** was reacted with dimethylzinc in the presence of titanium tetrachloride to give the following mixture of stereoisomers of compound **2**: 91.5% of (2*S*,3*S*)-**2**; 7% of (2*R*,3*S*)-**2**; 1.4% of (2*R*,3*R*)-**2**; 0.1% of (2*S*,3*R*)-**2** (Scheme 3).

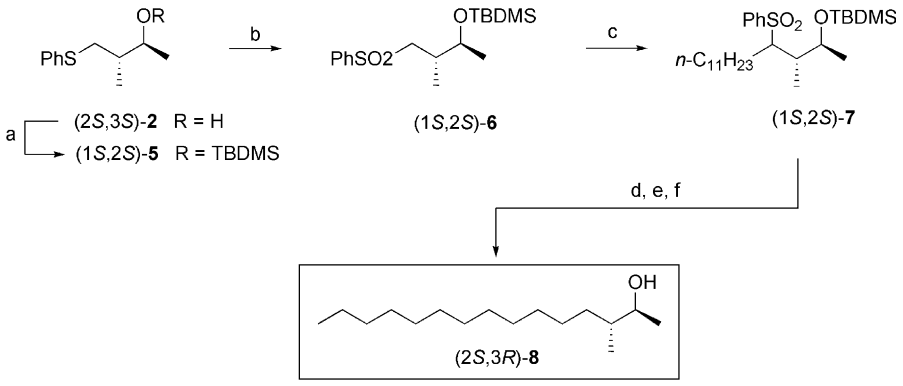
The mixture of the four stereoisomers containing mainly compound (2*S*,3*S*)-**2** was subjected to purification by CAL-B-catalysed esterification with vinyl acetate. After 9% conversion, the slow reacting alcohol (2*S*,3*S*)-**2** was recovered in a very high isomeric purity (>99.9:0.1 dr and >99.9% ee) and in 90% yield based on the starting mixture (Scheme 4). The overall yield was 61% based



Scheme 4. Enzyme catalysed purification of (2*S*,3*S*)- and (2*R*,3*R*)-**2** prepared from methyl (*R*)- or (*S*)-3-hydroxy-2-methylpropanoate.



Scheme 3. Synthesis of the building blocks (2*S*,3*S*)- and (2*R*,3*R*)-**2**. *Stereogenic centre of either (*S*)- or (*R*)-configuration. Reagents and conditions: (a) $(PhS)_2$, $(n\text{-}Bu)_3P$, DMF, 0 °C, rt (95%); (b) $LiAlH_4$, THF (96%); (c) (i) DMSO, oxalyl chloride, −78 °C. (ii) DIPEA, CH_2Cl_2, −78 °C. (iii) Extractive workup with KH_2PO_4; (d) (i) CH_2Cl_2, −78 °C, $TiCl_4$ (1.0 equiv), 10 min, Me_2Zn (1.0 equiv) [75%, over steps (c) and (d)].



Scheme 5. Synthesis of (2*S*,3*R*)-3-methylpentadecan-2-ol (2*S*,3*R*)-**8** from the chiral building block (2*S*,3*S*)-**2**. Reagents and conditions: (a) TBDMSCl, DMF, imidazole (99%); (b) *m*-CPBA, CH_2Cl_2 (88%); (c) (i) THF, DMPU, −40 °C, *n*-BuLi (2.1 equiv), up to 0 °C, cool to −40 °C. (ii) 1-Iodoundecane (1.2 equiv), THF, up to 20 °C (96%); (d) 10% Na–Hg, MeOH, Na_2HPO_4, rt (94%); (e) (i) TBAF, THF, reflux. (ii) Acetyl chloride, pyr, CH_2Cl_2 (84%); (f) (i) RaNi, EtOH, H_2. (ii) KOH/MeOH, rt (82%).

on methyl (*R*)-3-hydroxy-2-methylpropanoate over five steps.

The crude enantiomer, (2*R*,3*R*)-**2**, was prepared in the same manner from methyl (*S*)-3-hydroxy-2-methylpropanoate (>99% ee by GC analysis). The purities of the intermediate products were (*R*)-**3** (>98% ee by GC analysis) and (*R*)-**4** and (*R*)-**1** (both >94% ee by ^{1}H NMR analysis on its corresponding MTPA-ester, from (+)-MTPAC1). Dimethylzinc addition, as described above, furnished the following mixture of stereoisomers of compound **2**; 92% of (2*R*,3*R*)-**2**, 4.9% of (2*S*,3*R*)-**2**, 2.9% of (2*S*,3*S*)-**2**, and 0.2% of (2*R*,3*S*)-**2** (Scheme 3). This mixture of four stereoisomers, containing mainly compound (2*R*,3*R*)-**2**, was subjected to purification by CAL-B-catalysed esterification with vinyl acetate. The reaction was interrupted at 88% conversion. Chromatographic separation furnished the acetate of (2*R*,3*R*)-**2**. Alkaline hydrolysis gave the alcohol (2*R*,3*R*)-**2** in a diastereomeric ratio of >99.5:0.5 and an enantiomeric purity of >99.9% in 74% yield based on the starting mixture (Scheme 4). The overall yield was 43% based on methyl (*S*)-3-hydroxy-2-methylpropanoate over six steps.

3. Synthesis of a potential pheromone precursor present in *Gilpinia* spp

(2*S*,3*R*)-3-Methylpentadecan-2-ol, (2*S*,3*R*)-**8** (Scheme 5) is a probable pheromone precursor, that has been isolated from females of the pine sawflies *G. socia* and *G. frutetorum*.[8] Based on the structures of other known pine sawfly pheromones, the actual *Gilpinia* spp. pheromone is most likely either the acetate or propanoate of (2*S*,3*R*)-**8**.[9] Using the pure building block (2*S*,3*S*)-**2** described in section **2.2** as the starting point, we have synthesised the alcohol (2*S*,3*R*)-**8** using a route similar to that described in our previous paper (Scheme 5).[10]

Treatment of the alcohol (2*S*,3*S*)-**2** with *tert*-butylchlorodimethylsilane (TBDMSCl) gave the silyl ether (1*S*,2*S*)-**5** (Scheme 5). Oxidation of this with MCPBA furnished the sulfone (1*S*,2*S*)-**6**. The carbanion derived from this was alkylated with 1-iodoundecane to yield (1*S*,2*S*)-**7**, whose phenylsulfone unit and TBDMS protective group were removed with sodium amalgam followed by tetrabutylammonium fluoride (TBAF), respectively, to give (2*S*,3*R*)-**8**.[†] In our hands, the sodium amalgam reaction yielded the alcohol (2*S*,3*R*)-**8** contaminated with an elimination product (~15%). NMR-analysis indicated that the double bond in this undesired product was located between the 4- and 5-carbons. Therefore, it should be possible to remove this without epimerisation, provided that the double bond does not migrate towards the alcohol end of the compound, which indeed can happen in some cases.[11–15] However, acetylation of a chiral alcohol seems to prevent such migrations.[16] Therefore, the crude product mixture was acylated and treated with Raney nickel in ethanol under hydrogen. Alkaline hydrolysis followed by chromatography gave, from sulfone (1*S*,2*S*)-**7**, (65%) of the pure pheromone precursor alcohol (2*S*,3*R*)-**8** [>99:1 dr, >99% ee, and 54% total yield based on (2*S*,3*S*)-**2**].

4. Conclusion

Combination of synthesis from an enantiopure starting material, diastereoselective dimethylzinc addition, and enzyme-catalysed purification of the products is a very efficient way to produce some valuable enantiopure synthetic intermediates. By Mitsunobu inversion or related reactions, pure (2*R*,3*S*)- and (2*S*,3*R*)-**2** will probably be easily accessible from the pure (2*S*,3*S*)- and (2*R*,3*R*)-ones, respectively. The synthetic utility of the building block (2*S*,3*S*)-**2** is demonstrated by its conversion into the pheromone precursor alcohol (2*S*,3*R*)-**8**.

5. Experimental

5.1. General

Commercially available chemicals were used without further purification unless otherwise stated. Chirazyme® L-2, carrier fixed, C2, (Lipase B, from *Candida antarc-*

[†] Note that, although the stereochemistry at position 3 is retained when the sulfonyl group is removed, the designation of configuration at position 3 changes from *S* to *R* due to the CIP-priority rules.

tica, CAL-B) was obtained from Roche. Novozyme® SP 525, (immobilised lipase A from *Candida antarctica*, CAL-A) was a gift from Novo Nordisk. Lipases were stored at 4 °C over dry silica gel. Me_2Zn was purchased as a 2.0 M solution in toluene. Raney nickel (W-2 type) and titanium tetrachloride were obtained from Fluka and Baker, respectively. Et_2O ($LiAlH_4$), THF (K, benzophenone), DMPU, CH_2Cl_2, DMF, DMSO and DIPEA (CaH_2) were distilled from the indicated drying agents and stored under argon. (*S*)- and (*R*)-3-hydroxy-2-methylpropanoic acid methyl ester were purchased from Aldrich and Fluka, respectively, $[\alpha]_D^{25} = +26.2$ (*c* 2.3, MeOH) and −26.3 (*c* 2.0, MeOH), respectively. Preparative liquid chromatography (LC) was performed on straight phase silica gel (Merck 60, 230–400 mesh, 0.040–0.063 mm) employing a gradient technique using an increasing concentration (0–100%) of distilled ethyl acetate in distilled cyclohexane as eluent. The diastereomeric ratio (dr) of the alcohols **2** and (2*S*,3*R*)-**8** were determined by gas chromatography (GC, capillary column, factor four, 30 m, 0.32 mm id, $d_f = 0.25$ μm, carrier gas N_2, 10 psi, split ratio 30:1). The enantiomeric purity of (*S*)- and (*R*)-3-hydroxy-2-methylpropanoic acid methyl ester and (*S*)- and (*R*)-2-methyl-3-(phenylsulfanyl)propanoic acid methyl ester **3** were determined by GC (30 m × 0.25 mm id capillary column coated with β-dex 325, $d_f = 0.25$ μm; carrier gas He 22 psi, split ratio 30:1). Program for (*S*)- and (*R*)-3-hydroxy-2-methylpropanoic acid methyl ester: 40 °C, 10 min, 1 °C/min, 150 °C). Retention times (min): 36.6 (*R*-enantiomer) and 40.2 (*S*-enantiomer) and for (*S*)- and (*R*)-**3**: 100 °C, 30 min, 1 °C/min, 160 °C). Retention times (min): 72.4 (*S*-enantiomer) and 72.7 (*R*-enantiomer). 3-Methyl-4-(phenylsulfanyl)butan-2-ol **2** was transformed into its acetate (CH_3COCl, pyridine, CH_2Cl_2) and analysed by GC (capillary column, β-dex 120, 30 m, 0.25 mm id, $d_f = 0.25$ μm, carrier gas He, 20 psi, split 25/1, program: 70 °C/4 min, 4 °C/min, 125 °C/2 min, 0.2 °C/min, 150 °C). Retention times (min) of the four stereoisomers: 125.5 (2*S*,3*R*)-**2**, 126.3 (2*S*,3*S*)-**2**, 129.1 (2*R*,3*S*)-**2**, 130.1 (2*R*,3*R*)-**2**. Mass spectra were recorded on a Saturn 2000 instrument, (EI-mode) coupled to a Varian 3800 GC. NMR spectra were recorded on a Bruker Avance 500 (500 MHz ^1H and 125.8 MHz ^{13}C) spectrometer using $CDCl_3$ as solvent and TMS as internal reference. Boiling points are uncorrected, and are given as air-bath temperatures (bath temperature/mbar) in a bulb-to-bulb (btb, Büchi-GKR-51) apparatus.

5.2. General procedures for the lipase-catalysed reactions

Screening of lipases for different selectivity was made using a diastereomeric mixture of 3-methyl-4-(phenylsulfanyl)butan-2-ol [80:20 dr, (2*R**,3*R**)/(2*R**,3*S**)] a lipase and molecular sieves (3 Å) in *n*-heptane. The reaction was started by the addition of vinyl acetate. The reactions were performed on a shaking board at 25 °C. Samples were taken at intervals and filtered through a pad of $MgSO_4$ and rinsed with *n*-heptane before GC-analysis, which was used to assess the conversion of the alcohol in relation to the amount of ester produced.

5.3. Synthesis of (2*R*,3*R*)- and (2*S*,3*S*)-isomers of 2 from *rac*-1

5.3.1. (2*R,3*R**)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*R**,3*R**)-2.** 2-Methyl-3-(phenylsulfanyl)propanal *rac*-**1** (5.1 g, 28.3 mmol) was dissolved in distilled CH_2Cl_2 (200 mL), stirred and cooled to −70 °C under Ar. Then $TiCl_4$ (3.4 mL, 31 mmol) was added dropwise via a syringe. An orange viscous solution was obtained and this was kept stirring at −70 °C. After 1 h, Me_2Zn (21 mL, 2 M in toluene, 42 mmol) was added dropwise, followed by stirring at −70 °C. After stirring overnight and when the temperature had reached 10 °C, water (90 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (3 × 100 mL) and the combined organic extract was washed with $NaHCO_3$ (2 × 100 mL, aq, satd), dried (Na_2SO_4), filtered and the solvent was evaporated off. Purification by LC furnished a yellowish oil (5.4 g, 96%), 99% pure and 95:5 dr by GC.

5.3.2. (2*R*,3*R*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*R*,3*R*)-2. *Method 1*. Chirazyme L-2 (CAL-B) (1.17 g, 65 mg/mmol) and molecular sieves (3 Å) were added to a solution of racemic (2*R**,3*R**)-**2** (from Section 5.3.1, 95:5 dr, 3.51 g, 17.9 mmol) in heptane (30 mL, 1.7 mL/mmol) and stirred for 2 h at room temperature, followed by addition of vinyl acetate (30 mL, 0.33 mol). After reaching 49% conversion the mixture was filtered and the solid collected was rinsed with *n*-heptane. The solvent was evaporated off and the product, the acetate of crude (2*R*,3*R*)-**2**, was separated from the remaining substrate alcohol by LC, furnishing a colourless oil (2.0 g, 47%), >99% pure, 94:6 dr, and 98% ee by chiral GC.

The isolated acetate of slightly isomerically impure (2*R*,3*R*)-**2** (1.9 g, 8.0 mmol) was stirred with KOH/MeOH (100 mL, 2.4 M) at room temperature overnight. The reaction was quenched by the addition of water (50 mL) and Et_2O (70 mL). The aqueous phase was extracted with Et_2O (3 × 50 mL) and the combined Et_2O-extract was washed with $NaHCO_3$ (2 × 100 mL, aq, satd), dried ($MgSO_4$), filtered and the solvent was evaporated off furnishing an alcohol containing mainly (2*R*,3*R*)-**2** (1.4 g, 87%), >99% (sum of isomers) by GC contaminated by minor amounts of other isomers of **2**.

CAL-A (Novozyme SP 525, 93 mg, 1.1 g/mmol) and molecular sieves (3 Å) were added to a solution of the mixture containing mainly alcohol (2*R*,3*R*)-**2** (85 mg, 0.4 mmol) in *n*-heptane (1.5 mL, 3.7 mL/mmol) and stirred for 2 h, followed by the addition of vinyl acetate (0.2 mL, 2.2 mmol). After 41% conversion, the mixture was filtered and the solid collected was washed with *n*-heptane. The solvent was evaporated off and the remaining alcohol was separated from the ester product using LC. The alcohol fractions were concentrated in vacuo to give an oil [40 mg, 42%, 18% overall from racemic (2*R**,3*R**)-**2**], 99% pure by GC, 98:2 dr, and 99% ee by chiral GC of its acetate.

5.3.3. (2*S*,3*S*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*S*,3*S*)-2. *Method 1*. A solution of the recovered alcohol substrate, (2*S*,3*S*)-**2**, obtained by LC from the first

esterification step (Section 5.3.2) was concentrated in vacuo to give a colourless oil (1.7 g, 49%), 98% pure by GC, 95:5 dr, and 98% ee by chiral GC of its acetate.

This recovered substrate (1.53 g, 7.81 mmol) in heptane (13 mL, 1.7 mL/mmol), Chirazyme L-2 (CAL-B, 0.25 g, 165 mg/mmol) and molecular sieves (3 Å) were stirred for 2 h, followed by the addition of vinyl acetate (13 mL, 140 mmol). After 13% conversion the mixture was filtered and the remaining solid was rinsed with *n*-heptane. The solvent was evaporated off and the remaining alcohol was separated from the ester produced by LC. The fractions containing alcohol were concentrated in vacuo to give an oil [1.2 g, 76%, 37% overall yield from racemic (2*R**,3*R**)-**2**], >99% pure by GC, 98:2 dr, and 98% ee by chiral GC of its acetate.

5.4. Synthesis of (2*S*,3*S*)- and (2*R*,3*R*)-2 from methyl (*R*)- and (*S*)-3-hydroxy-2-methylpropanoate

5.4.1. (*S*)-2-Methyl-3-(phenylsulfanyl)propanoic acid methyl ester (*S*)-3. Tri-*n*-butylphosphine (22.5 mL, 90.2 mmol) was added to a mixture of methyl (*R*)-3-hydroxy-2-methylpropanoate (8.9 g, 75.2 mmol) (>99% ee) and diphenyl disulfide (19.7 g, 90.2 mmol) in DMF (125 mL) at 0 °C (cf. Ref. 7b). After stirring for 4 h, at which point the temperature had reached 20 °C, water (50 mL) and Et_2O (150 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O (3 × 75 mL) and the combined Et_2O-extract was washed with brine (50 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. A colourless oil (15.0 g, 95%) was obtained after LC, 98% pure by GC and with an enantiomeric excess of >97% (GC). Bp 180 °C/1.0 mbar. $[\alpha]_D^{25} = -63.6$ (*c* 1.6, $CHCl_3$). ^{1}H NMR: δ 1.27 (3H, d, *J* = 7.1 Hz), 2.70 (1H, app. sextet, *J* = 7.0 Hz), 2.93 (1H, dd, *J* = 7.0 and 13.4 Hz), 3.27 (1H, dd, *J* = 7.1 and 13.4 Hz), 3.66 (3H, s), 7.18–7.22 (1H, m), 7.26–7.31 (2H, m), 7.35–7.38 (2H, m). ^{13}C NMR: d 16.7, 37.4, 39.7, 51.8, 126.5, 129.0 (2C), 130.1, (2C), 135.7, 175.4. MS (EI): *m*/*z* 210 (100) (M^+), 179 (8), 150 (23), 123 (95), 109 (32).

5.4.2. (*R*)-2-Methyl-3-(phenylsulfanyl)propanoic acid methyl ester (*R*)-3. Similarly, methyl (*S*)-3-hydroxy-2-methylpropanoate (1.0 g, 8.47 mmol) (>99% ee) gave (*R*)-**3** (1.5 g, 85%), >99% pure by GC and with an enantiomeric excess of >98% (GC). Bp 180 °C/0.9 mbar. $[\alpha]_D^{25} = +61.3$ (*c* 1.6, $CHCl_3$) {lit.[17] $[\alpha]_D^{22} = +66.6$ (*c* 1, $CHCl_3$)}. ^{1}H NMR, ^{13}C NMR and MS (EI) spectral data match those of (*S*)-**3**.

5.4.3. (*S*)-2-Methyl-3-(phenylsulfanyl)propan-1-ol (*S*)-4. The title compound was prepared following the method described by Tashiro and Mori,[18] (*S*)-**3** (from Section 5.4.1, 14.5 g, 69.0 mmol) gave 12.1 g (96%) of (*S*)-**4**, after LC, >99% pure by GC (>97% ee by ^{1}H NMR analysis on its corresponding MTPA-ester, derived from (−)-MTPACl). Bp 170 °C/0.95 mbar. $[\alpha]_D^{25} = +15.3$ (*c* 2.0, $CHCl_3$). ^{1}H NMR: δ 1.04 (3H, d, *J* = 6.9 Hz), 1.77 (1H, br s, –OH), 1.90–1.99 (1H, m), 2.83 (1H, dd, *J* = 6.9 and 12.9 Hz), 3.06 (1H, dd, *J* = 6.4 and 12.9 Hz), 3.59 (1H, dd, *J* = 6.1 and 10.8 Hz), 3.62 (1H, dd, *J* = 5.4 and 10.8 Hz), 7.15–7.18 (1H, m), 7.26–7.29 (2H, m), 7.33–7.36 (2H, m). ^{13}C NMR: d 16.5, 35.5, 37.4, 66.8, 125.9, 128.9 (2C), 129.0 (2C), 136.8. MS (EI): *m*/*z* 182 (71) (M^+), 164 (7), 151 (6), 135 (4), 123 (32), 110 (100).

5.4.4. (*R*)-2-Methyl-3-(phenylsulfanyl)propan-1-ol (*R*)-4. Similarly, (*R*)-**3** (from Section 5.4.2, 1.2 g, 5.71 mmol) gave (*R*)-**4** (1.0 g, 98%), 99% pure by GC (>94% ee by ^{1}H NMR analysis on its corresponding MTPA-ester, from (+)-MTPAC1). Bp 160 °C/0.7 mbar. $[\alpha]_D^{25} = -15.0$ (*c* 2.4, $CHCl_3$) {Lit.[17] $[\alpha]_D^{23} = -13$ (*c* 2.2, $CHCl_3$)}. ^{1}H NMR, ^{13}C NMR and MS (EI) spectral data match those of the enantiomer (Section 5.4.3).

5.4.5. (2*S*,3*S*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*S*,3*S*)-2. A solution of DMSO (6.2 mL, 86.9 mmol) in dry CH_2Cl_2 (50 mL) was added to a stirred solution of oxalyl chloride (6.0 mL, 68.3 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C under Ar, and the mixture was stirred at the same temperature for 30 min. The alcohol (*S*)-**4** (from Section 5.4.3, 11.3 g, 62.1 mmol) in dry CH_2Cl_2 (80 mL) was added dropwise to the mixture, and stirring was continued at the same temperature for 2 h. *N*-Ethyldiisopropylamine (54.1 mL, 310 mmol) was then added and the reaction mixture allowed to slowly reach −10 °C (4 h). Water (150 mL) was added, and the two layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phase was washed repeatedly with portions (50 mL) of a KH_2PO_4-solution (1 M, aq, pH ≈ 5), until GC examination revealed that no residual base was present in the organic phase. After additional washes with water (100 mL), brine (100 mL) and drying over Na_2SO_4, the organic phase was filtered and stored in CH_2Cl_2 (500 mL) in the freezer. The (*S*)-2-methyl-3-(phenylsulfanyl)propanal (*S*)-**1** so obtained (>97% ee, determined through $NaBH_4$-reduction of a sample to the corresponding alcohol and analysis on its MTPA-ester by ^{1}H NMR as in Section 5.4.3) was brought to the next step without further purification.

$TiCl_4$ (6.1 mL, 55.9 mmol) was added dropwise via a syringe to the solution of the aldehyde (*S*)-**1** (10.1 g, 55.9 mmol) in CH_2Cl_2 (900 mL) at −78 °C. An orange viscous solution was obtained and this was kept at −78 °C. After stirring for 10 min, Me_2Zn (27.9 mL, 2 M in toluene, 55.9 mmol) was added dropwise followed by stirring at −78 °C. After 35 min, water (100 mL) was added and the mixture allowed to reach room temperature, additional water (100 mL) was added and the two phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL) and the combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off, furnishing a yellowish oil (9.1 g, 75%) after LC, 98% pure by GC, 93:07 dr and 97% ee by chiral GC of its acetate.

5.4.6. (2*S*,3*S*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*S*,3*S*)-2. *Method 2.* A sample of the alcohol (2*S*,3*S*)-**2** (from Section 5.4.5, 6.5 g, 33.2 mmol) was mixed with *n*-heptane (60 mL, 1.8 mL/mmol), CAL-B

(1.54 g, 46.5 mg/mmol), and mol. sieves (3 Å). Vinyl acetate (60 mL, 649 mmol) was added and the reaction was stopped at 9% conversion. LC furnished the unreacted alcohol (2*S*,3*S*)-**2** as an oil (5.9 g, 90%) >99% pure by GC, >99.9:0.1 dr and >99.9% ee by chiral GC of its acetate. Bp 125 °C/0.35 mbar. $[\alpha]_D^{25} = +55.0$ (*c* 1.8, $CHCl_3$), $[\alpha]_{578}^{25} = +57.3$ (*c* 2.0, $CHCl_3$) and $[\alpha]_{546}^{25} = +65.3$ (*c* 2.0, $CHCl_3$). ^{1}H NMR: δ 1.03 (3H, d, $J = 6.9$ Hz), 1.19 (3H, d, $J = 6.3$ Hz), 1.66 (1H, s, –OH), 1.75–1.83 (1H, m), 2.79 (1H, dd, $J = 8.1$ and 12.8 Hz), 3.20 (1H, dd, $J = 4.6$ and 12.8 Hz), 3.76 (1H, app. quint, $J = 6.3$ Hz), 7.14–7.18 (1H, m), 7.25–7.29 (2H, m), 7.34–7.36 (2H, m). ^{13}C NMR: d 15.4, 20.4, 37.3, 40.2, 71.1, 125.8, 128.9 (4C), 137.0. MS (EI): *m*/*z* 196 (92) (M^+), 179 (5), 163 (10), 149 (16), 123 (50), 110 (100).

5.4.7. (2*R*,3*R*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*R*,3*R*)-2. In a similar way (see Section 5.4.5), (*R*)-**4** (0.3 g, 1.50 mmol) gave the intermediate aldehyde (*R*)-2-methyl-3-(phenylsulfanyl)propanal (*R*)-**1**, which was immediately transformed into (2*R*,3*R*)-**2** (0.2 g, 70%), 99% pure by GC, 95:05 dr, and 94% ee by chiral GC of its acetate.

5.4.8. (2*R*,3*R*)-3-Methyl-4-(phenylsulfanyl)butan-2-ol (2*R*,3*R*)-2. *Method 2*. A sample of the alcohol (2*R*,3*R*)-**2** from Section 5.4.7. (123 mg, 0.63 mmol) was mixed with *n*-heptane (1.5 mL, 2.4 mL/mmol), CAL-B (33 mg, 52 mg/mmol), and mol. sieves (3 Å). Vinyl acetate (1.5 mL, 16 mmol) was added and the reaction was stopped at 88% conversion. Workup and LC furnished the acetate of (2*R*,3*R*)-**2** (127 mg, 85%), >99% pure by GC (>99.5:0.5 dr and >99.9% ee by chiral GC). The acetate of (2*R*,3*R*)-**2** was hydrolysed (see Section 5.3.2) to give the alcohol (2*R*,3*R*)-**2** in 87% yield (74% overall yield). Bp 150 °C/0.55 mbar. $[\alpha]_{578}^{25} = -54.7$ (*c* 3.0, $CHCl_3$) and $[\alpha]_{546}^{25} = -62.4$ (*c* 3.0, $CHCl_3$) {lit.[6] $[\alpha]_D^{20} = -49.5$ (*c* 0.41, $CHCl_3$)}. ^{1}H NMR, ^{13}C NMR and MS (EI) spectral data match those of (2*S*,3*S*)-**2**.

5.5. Synthesis of a probable pheromone precursor, (2*S*,3*R*)-8, from (2*S*,3*S*)-2

5.5.1. (1*S*,2*S*)-*tert*-Butyl-[1,2-dimethyl-3-(phenylsulfanyl)propoxy]-dimethylsilane (1*S*,2*S*)-5. *tert*-Butylchlorodimethylsilane (2.4 g, 16.0 mmol) was added to a mixture of (2*S*,3*S*)-**2** from Section 5.4.6 (2.9 g, 14.5 mmol) and imidazole (1.1 g, 16.0 mmol) in DMF (25 mL) at room temperature. After stirring overnight, water (30 mL) and Et_2O (75 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O (1 × 50 mL) and the combined Et_2O extract was washed with HCl (25 mL, 1 M, aq), brine (25 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. A colourless oil (4.5 g, 99%) was obtained after LC, 99% pure by GC. Bp 145 °C/0.3 mbar. $[\alpha]_{578}^{25} = +41.1$ (*c* 2.0, $CHCl_3$) and $[\alpha]_{546}^{25} = +46.8$ (*c* 2.0, $CHCl_3$) {lit.[1b] $[\alpha]_D^{21} = +39$ (*c* 0.305, $CHCl_3$)}. ^{1}H NMR: δ 0.03 (3H, s), 0.05(3H, s), 0.88 (9H, s), 1.00 (3H, d, $J = 6.8$ Hz), 1.11 (3H, d, $J = 6.2$ Hz), 1.71–1.79 (1H, m), 2.62 (1H, dd, $J = 9.1$ and 12.8 Hz), 3.20 (1H, dd, $J = 4.4$ and 12.8 Hz), 3.75 (1H, app. quint, $J = 6.0$ Hz), 7.12–7.18 (1H, m), 7.23–7.27 (2H, m), 7.31–7.33 (2H, m). ^{13}C NMR: d 4.7, 4.2, 15.5, 18.2, 20.5, 26.0 (3C), 36.8, 40.6, 71.5, 125.5, 128.5 (2C), 128.9 (2C), 137.6. MS (EI): *m*/*z* 309 (2) $(M - H)^+$, 295 (8), 253 (100), 211 (7), 167 (35), 143 (12), 123 (10).

5.5.2. (1*S*,2*S*)-*tert*-Butyl-[1,2-dimethyl-3-(phenylsulfonyl)propoxy]-dimethylsilane (1*S*,2*S*)-6. *m*-Chloroperbenzoic acid (8.1 g, 36.3 mmol) was added to a solution of (1*S*,2*S*)-**5** from Section 5.5.1 (4.3 g, 14.5 mmol) in CH_2Cl_2 (100 mL) at 0 °C. After stirring overnight, $NaHCO_3$ (75 mL, aq, satd) and Et_2O (150 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O (2 × 50 mL) and the combined Et_2O-extract was washed with brine (50 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. A colourless oil (4.4 g, 88%) was obtained after LC, 98% pure by GC. Bp 230 °C/0.35 mbar. $[\alpha]_{578}^{25} = +16.0$ (*c* 2.6, $CHCl_3$) and $[\alpha]_{546}^{25} = +18.1$ (*c* 2.6, $CHCl_3$) {lit.[1b] $[\alpha]_D^{22} = +15.0$ (*c* 0.225, $CHCl_3$)}. ^{1}H NMR: δ −0.02 (3H, s), 0.00 (3H, s), 0.82 (9 H, s), 1.01 (3H, d, $J = 6.2$ Hz), 1.09 (3H, d, $J = 6.8$ Hz), 1.96–2.03 (1H, m), 2.82 (1H, dd, $J = 9.2$ and 14.4 Hz), 3.33 (1H, dd, $J = 2.6$ and 14.4 Hz), 3.64 (1H, dq, $J = 4.4$ and 6.2 Hz), 7.54–7.58 (2H, m), 7.62–7.66 (1H, m), 7.90–7.93 (2H, m). ^{13}C NMR: δ −4.8, −4.1, 17.1, 18.1, 20.9, 25.9 (3C), 36.2, 58.5, 71.6, 128.0 (2C), 129.4 (2C), 133.6, 140.2. MS (EI): *m*/*z* 343 (4) $(M + H)^+$, 327 (9), 285 (100), 199 (13), 159 (11), 135 (28).

5.5.3. (1*S*,2*S*)-(3-Benzenesulfonyl-1,2-dimethyl-tetradecyloxy)-*tert*-butyl-dimethylsilane (1*S*,2*S*)-7. To a mixture of (1*S*,2*S*)-**6** from Section 5.5.2. (0.6 g, 1.75 mmol) and DMPU (2.1 mL, 17.5 mmol) in dry degassed THF (15 mL) a solution of *n*-BuLi (3.1 mL, 3.68 mmol, 1.2 M) was added at −40 °C. After 1 h the reaction was allowed to reach 0 °C (10 min), followed by cooling to −40 °C. 1-Iodoundecane (0.5 mL, 2.10 mmol) in dry degassed THF (1 mL) was added dropwise and the reaction was allowed to reach room temperature overnight. The reaction was quenched with NH_4Cl (5 mL, aq, satd) and EtOAc (20 mL) and the phases were separated. The aqueous phase was extracted with EtOAc (4 × 25 mL) and the combined organic extract was washed with brine (25 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. A colourless oil (0.83 g, 96%) was obtained after LC, 98% pure by GC with a diastereomeric ratio of 89:11. Bp 300 °C/0.5 mbar. $[\alpha]_{578}^{25} = +7.8$ (*c* 1.6, $CHCl_3$) and $[\alpha]_{546}^{25} = +8.8$ (*c* 1.6, $CHCl_3$). ^{1}H NMR: δ 0.00 (2.67H, s), 0.02 (2.67H, s), 0.14 (0.33H, s), 0.20 (0.33H, s), 0.84 (8.01H, s), 0.88 (0.99H, s), 0.87–0.90 (3H, m), 0.97 (3H, d, $J = 7.0$ Hz), 1.04 (3H, d, $J = 6.1$ Hz), 1.17–1.42 (18H, m), 1.61–1.68 (1H, m), 1.81–1.91 (1H, m), 2.04–2.10 (1H, m), 3.47–3.50 (0.89H, m), 3.57 (1H, dq, $J = 6.1$ and 7.0 Hz), 4.40–4.46 (0.11H, m), 7.52–7.55 (2H, m), 7.60–7.63 (1H, m), 7.86–7.90 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ −4.66, −4.15*, −3.61, −3.31*, 11.7*, 11.8, 14.3, 18.1, 18.2*, 21.9, 22.5*, 22.8, 24.3, 26.0 (3C), 26.1*, 26.8*, 28.2*, 28.9*, 29.1, 29.2*, 29.4, 29.5, 29.6, 29.7 (2C), 29.7*, 30.2, 32.0, 39.7, 44.2*, 63.1*, 64.2, 70.4*, 71.2, 128.7 (2C), 129.0*, 129.1 (2C), 133.3*, 133.4, 139.7, 140.6*. MS (EI): *m*/*z* 497 (2) $(M + H)^+$, 481 (11), 439 (100), 365 (79), 341

(11), 297 (10), 217 (4), 199 (14), 159 (15), 135 (12), 103 (18).

5.5.4. (2*S*,3*R*)-3-Methylpentadecan-2-ol (2*S*,3*R*)-8. A solution of (1*S*,2*S*)-**7** from Section 5.5.3 (0.3 g, 0.60 mmol) in dry MeOH (5 mL) was added dropwise to a prestirred mixture of 10% Na(Hg) (1.12 g, 4.8 mmol) and dry Na_2HPO_4 (0.69 g, 4.8 mmol) at room temperature. After 1 h, the mixture was diluted and filtered through a pad of Celite/silica gel with Et_2O (8 × 5 mL). The filtrate was washed with water (30 mL), brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. This gave crude (1*S*,2*R*)-*tert*-butyl-(1,2-dimethyl-tetradecyloxy)-dimethylsilane (0.2 g, 94%) as a colourless oil; purity of >90% (GC), which was contaminated with an elimination product (~15%). This crude product was employed in the next step without any further purification. TBAF (5.1 mL, 5.06 mmol, 1 M in THF) was added to the protected alcohol (0.16 g, 0.44 mmol) in THF (5 mL) at room temperature and the mixture was refluxed overnight. The reaction was quenched by the addition of water (10 mL) and Et_2O (20 mL). The aqueous phase was extracted with Et_2O (3 × 25 mL) and the combined Et_2O-extract was washed with water (25 mL), brine (25 mL), dried ($MgSO_4$) and concentrated in vacuo. A colourless oil (0.1 g, 96%) was obtained after LC. Acetyl chloride (1.5 mL, 21 mmol) and pyridine (3 mL) were added to a solution of this oil (68 mg, 0.28 mmol) in CH_2Cl_2 (5 mL) and the solution was stirred overnight. The reaction was quenched by HCl (25 mL, 2 M, aq) and Et_2O (20 mL). The aqueous phase was extracted with Et_2O (2 × 25 mL) and the combined Et_2O-extract was washed with $NaHCO_3$ (25 mL), dried ($MgSO_4$) and concentrated in vacuo. A colourless oil (0.07 g, 88%) of (1*S*,2*R*)-1,2-dimethyltetradecyl acetate was obtained as an oil after LC, 99% pure by GC (if the ~15% unsaturated product is included). This acetate (0.35 mg, 0.12 mmol) in EtOH (1.5 mL) was subjected to a suspension of Raney nickel (W-2) in EtOH (3 mL) and stirred under H_2 at room temperature overnight. The catalyst was filtered off through a pad of Celite/silica gel and the solids were rinsed with Et_2O (7 × 10 mL). The filtrate was concentrated to give the saturated (1*S*,2*R*)-1,2-dimethyltetradecyl acetate (0.03 g, 86%). This was subjected to alkaline hydrolysis with KOH/MeOH (3 mL, 2.4 M) and stirred for 2 h at room temperature. Water (10 mL) and Et_2O (20 mL) were added and the phases were separated. The aqueous phase was extracted with Et_2O (4 × 15 mL) and the combined Et_2O-extract was washed with brine (20 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. After LC the title compound was obtained as a colourless oil (0.02 g, 95%) 99% pure by GC and <0.1% of the corresponding (2*S*,3*S*)-isomer. Bp 160 °C/0.45 mbar. $[\alpha]_{578}^{25} = +18.3$ (*c* 2.2, *n*-hexane) and $[\alpha]_{546}^{25} = +20.8$ (*c* 2.2, *n*-hexane) {lit.[19] $[\alpha]_D^{20} = +16.0$ (*c* 5, hexane)}. ^{1}H NMR: δ 0.89 (3H, d, $J = 6.8$ Hz), 0.88–0.92 (3H, m), 1.14 (3H, d, $J = 6.3$ Hz), 1.28–1.54 (23H, m), 1.48 (1H, s, –OH), 3.68 (1H, app. quint, $J = 6.3$ Hz). ^{13}C NMR: δ 14.1, 14.5, 19.3, 22.7, 27.3, 29.4, 29.7 (5C), 30.0, 32.0, 32.6, 40.1, 71.8. MS (EI): *m*/*z* 241 (4) $(M - H)^+$, 227 (8), 194 (13), 181 (5), 166 (8), 152 (7), 139 (14), 125 (25), 111 (41), 97 (58), 83 (44), 69 (50), 57 (62), 45 (100).

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