PERKIN 1

Synthesis and lipase catalysed stereoselective acylation of some 3-methylalkan-2-ols, identified as sex pheromone precursors in females of pine sawfly species

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Several 3-methylalkan-2-ols precursors to sex pheromones of *Diprion pini*, *Gilpinia pallida*, *Gilpinia frutetorum*, *Diprion nipponica*, *Macrodiprion nemoralis* and *Microdiprion pallipes* were synthesised as stereoisomeric mixtures in moderate to good yields. The key reaction sequence in the syntheses was the ring opening of either *cis*- or racemic *trans*-epoxybutane using a higher order cyanocuprate as nucleophile followed by a highly efficient lipase catalysed stereoselective acylation of the obtained 3-methylalkan-2-ol. The biologically active species specific stereoisomer was synthesised as a single stereoisomer in high stereoisomeric purity, as one in a mixture of two or as one of four stereoisomers when the appropriate 3-methylalkan-2-ol was stereoselectively acylated using a *Pseudomonas* sp. lipase as catalyst.

Introduction

In the northern hemisphere some pine sawfly species are severe pests on pines.[1] As sex pheromone most of the pine sawfly species employ esters of *erythro*-(2*S*,3*S*,7*S*)- or *threo*-(2*S*,3*R*,7*R*)-3,7-dimethylpentadecan-2-ol **1** (diprionol, see Fig. 1).[2] But lately, several structurally similar sex pheromone precursor alcohols have been identified in females of other pine sawfly species.[3] Actually, structures identified up to now are basically methyl-branched long-chain 3-methyl-2-alcohols see Fig. 1.

We have for a long time been interested in the identification, in the syntheses and in the biological activities of pine sawfly sex pheromones and we have also developed methods for controlling pine sawfly populations using synthetic sex pheromones.[4] As a part of our work concerning sex pheromones of pine sawflies we present herein the syntheses of stereoisomeric mixtures of 3,7-dimethyltridecan-2-ol, of 3,7,11- and of 3,7,9-trimethyltridecan-2-ol (compounds **3**, **4** and **5** respectively, see Fig. 2) by different procedures to those previously published.[3e,5] We also present the syntheses of 3,7-dimethyltetradecan-2-ol and 3-methylpentadecan-2-ol (compounds **6** and **7**, see Fig. 2) two new 3-methylalkan-2-ol structures recently identified from females of the pine sawfly species *Gilpinia pallida*[6] and *Gilpinia frutetorum*[7] respectively.

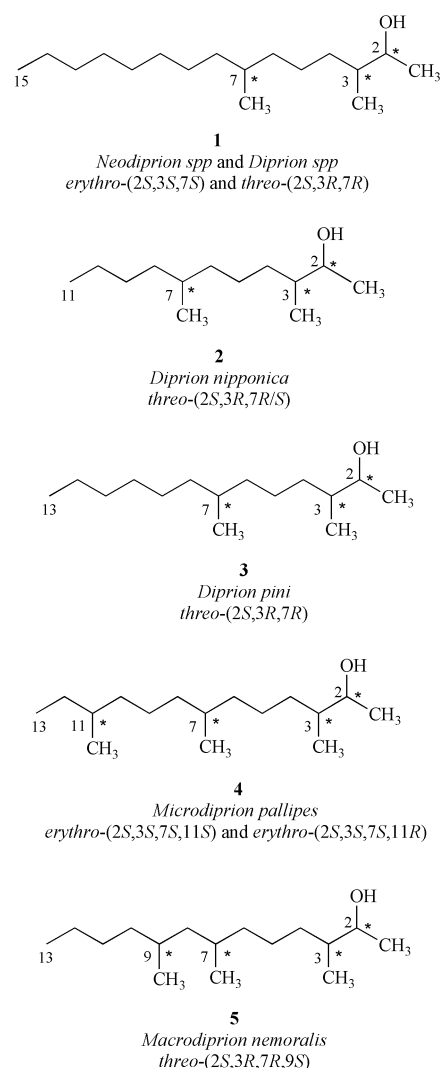

Fig. 1 Methyl-branched long-chain 3-methylalkan-2-ols that during the years have been identified as sex pheromone precursors in females of pine sawfly species.

Results and discussion

Employing essentially the same synthetic methodology previously used by us in the synthesis of *erythro*-3,7-dimethylpentadecan-2-ol as a mixture of the four possible diastereomers,[8] the compound *threo*-**3** as a mixture of four *threo*-stereoisomers was prepared from 4,5-dihydrofuran (as shown in Scheme 1 and Scheme 3).

Accordingly, 2,3-dihydrofuran was reacted with *tert*-butyllithium and alkylated with 1-iodohexane to give 2-hexyl-4,5-dihydrofuran (**8**), which was methylated in a Ni(0) catalysed Grignard reaction and the (*E*)-4-methyldec-3-en-1-ol (**9**) was obtained as a pure diastereomer. Pd/C catalysed hydrogenation gave the saturated alcohol **10** (see Scheme 1). After transformation into the corresponding alkyllithium *via* the iodide **23** by

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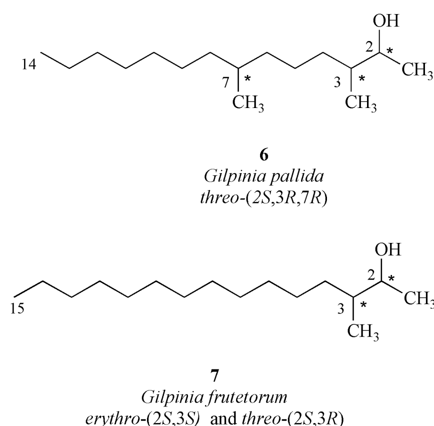
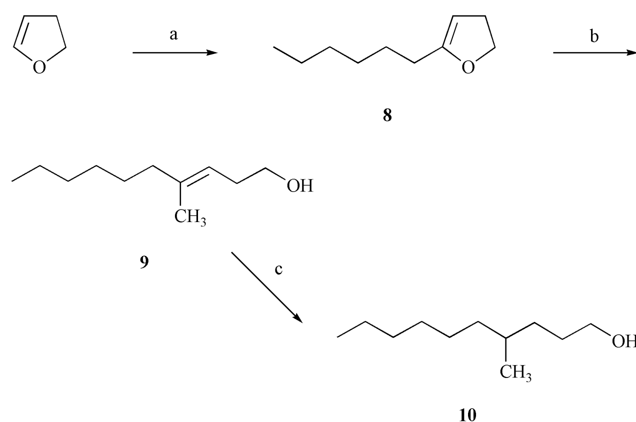


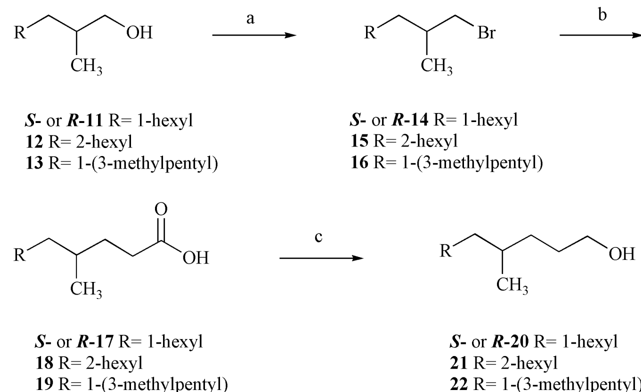
Fig. 2 Two new long-chain 3-methylalkan-2-ols that recently have been found in females of the two pine sawfly species *Gilpinia pallida*[6] and *Gilpinia frutetorum*[7] respectively.



Scheme 1 a) 1) *t*-BuLi THF; 2) 1-iodohexane; b) 1) $(Ph_3P)_2NiCl_2$, benzene; 2) MeMgBr; 3) Add 2-hexyl-4,5-dihydrofuran, Δ 80 °C 5 h; c) Pd/C, H_2 MeOH.

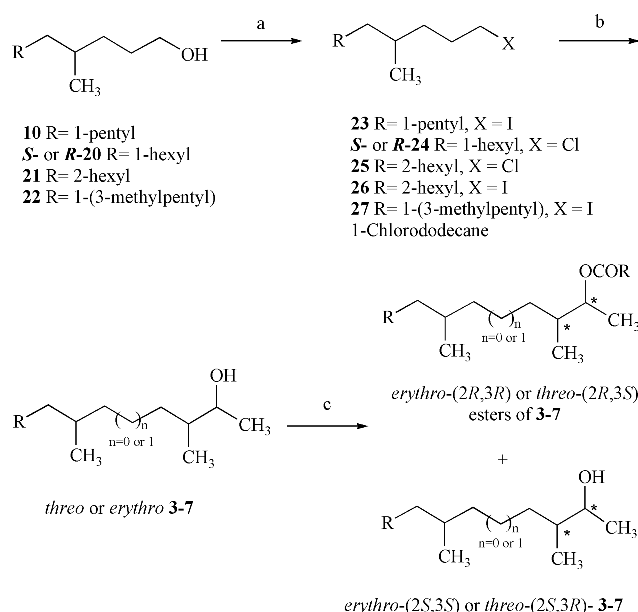
standard methods (see Scheme 3 and Experimental: Method B) the organolithium was added to a solution of Me(CN)CuLi and a mixed higher order cyanocuprate was obtained. This was suitable for ring-opening[8] of *cis*-epoxybutane and furnished the *threo*-3,7-dimethyltridecan-2-ol (*threo*-**3**).

Compounds **4**–**6** were prepared in a similar way as above but starting from (*S*)- or (*R*)-2-methylnonanol (*S*- or *R*-**11**), 2,4-dimethyloctan-1-ol[9] (**12**) or 2,6-dimethyloctan-1-ol[9] (**13**) respectively (see Scheme 2 and Scheme 3). These starting



Scheme 2 a) $P(Ph)_3$, Br_2, CH_2Cl_2; b) 1) Na(s), EtOH; 2) $CH_2(CO_2Et)_2$; 3): KOH, EtOH; 4) 180–200 °C; c) $LiAlH_4$, Et_2O.

alcohols were separately transformed into the corresponding bromides **14**–**16** and in each alkyl bromide the carbon chain was then elongated *via* a malonic ester sequence[10] in analogy with similar recipes. After subsequent lithium aluminium hydride ($LiAlH_4$) reduction of the produced acids **17**–**19** the



Scheme 3 a) $P(Ph)_3$, CCl_4 or $P(Ph)_3$, imidazole, THF–MeCN; b) 1) Li, hexane; 2) add to MeCu(CN)Li, Et_2O, −78 °C; 3) add *cis*- or racemic *trans*-epoxybutane; c) lipase, vinyl ester, heptane, 3 Å.

corresponding alcohols **20**–**22** were obtained (see Scheme 2). From these alcohols the chlorides **24**–**25** or the iodides **23**, **26**–**27** were synthesised using standard methods (see Scheme 3). The desired *threo*- and *erythro*-3-methylalkan-2-ols **4**–**6** were then obtained as above for compound *threo*-**3** but from the ring-opening of *cis*- or *trans*-epoxybutane using the corresponding mixed higher order cyanocuprate prepared from chlorides **24**–**25** (see Scheme 3 and Experimental: Method C) or iodides **23**, **26**–**27** (see Scheme 3 and Experimental: Method B).

Compound **7** was prepared similarly to the ring-opening of *cis*- or *trans*-epoxybutane (see Experimental: Method A) above for *erythro*-7*S*-**6**, *erythro*-**5**, *threo*-7*S*-**6** and *threo*-7*R*-**6**, but from the bis-dodecyl higher order cyanocuprate prepared from 2 equivalents of 1-lithiododecane (obtained from 1-chlorododecane by standard method) and CuCN (see Scheme 3).

Lipases have been used by us and others as catalysts in several successful resolutions[11] and diastereoselections[12] of alkan-2-ols and 3-methyl-2-alcohols. We have shown previously that lipase efficiently catalyses the stereoselective acylation of *erythro*- and *threo*-3,7-dimethylpentadecan-2-ol;[12d] consequently, we applied this strategy to other structurally similar substrates in order to produce stereoisomerically highly pure sex pheromones *e.g.* of pine sawfly species. Recently, Nakamura and Mori published[12a] a synthesis of (2*R*,3*R*,7*R*,11*R*)- (2*S*,3*R*,7*R*,11*R*)-3,7,11-trimethyltridecan-2-ol employing the same lipase catalysed acylation strategy previously applied by us[12d] on the 1 : 1 : 1 : 1-mixture of *erythro*-3,7-dimethylpentadecan-2-ol.

Among the lipases studied herein all except immobilised[13] *Candida rugosa* lipase (CRL) (Table 1, entry 15 and 16, "*E*"[15] = 3 and 10 respectively), showed high or very high *R* preference for the 2-position in the 3-methylalkan-2-ols. The lipase Amano AK (entries 6 and 13, E^{14} = 140 and 80 respectively) showed somewhat lower 2*R*-preference than the lipase Amano PS (entries 3 and 10, *E* = 180) when using substrates *threo*-**7** and *erythro*-**7**. The Amano PS was used crude as received from the supplier but in some cases also used immobilised on two different carriers, Tyonite-200-P (entries 4 and 11) and Diatonite (entries 5, 12 and 18). The 2*R*-preference of these immobilised Amano PS lipases were very high and the reaction rates were higher in all these entries (4, 5, 11, 12 and 18) compared to the ones when the crude Amano PS lipase was

Table 1

Entry	Substrate	Acyl-donor	Lipase	Conversion[d] (%)	Conversion[e]	Product ratio[f]	Substrate ratio[g]	E^h or "E"[i]
1	*threo*-**7**	Ac	Amano PS	37.0	0.012	99.6 : 0.4	79.1 : 20.9	>400[a]
2		Pr	Amano PS	34.0	0.007	99.5 : 0.5	75.5 : 24.5	>300[a]
3		Pr	Amano PS	37.6	0.012	>99.0 : 1.0	79.5 : 20.5	>180[b]
4		Pr	Amano PS on Tyonite	35.1	0.031	>99.0 : 1.0	76.5 : 23.5	>170[b]
5		Pr	AmanoPS on Diatonite	44.3	0.092	>99.0 : 1.0	89.0 : 11.0	>200[b]
6		Pr	Amano AK	42.9	0.001	98.5 : 1.5	86.5 : 13.5	140[b]
7		Pr	PFL	31.9	0.022	>99.0 : 1.0	73.0 : 27.0	>160[b]
8	*erythro*-**7**	Ac	Amano PS	36.5	0.009	98.8 : 1.2	78.0 : 22.0	150[a]
9		Pr	Amano PS	34.2	0.005	99.0 : 1.0	75.5 : 24.5	160[a]
10		Pr	Amano PS	37.6	0.009	>99.0 : 1.0	79.5 : 20.5	>180[b]
11		Pr	Amano PS on Tyonite	36.4	0.026	>99.0 : 1.0	78.0 : 22.0	>170[b]
12		Pr	Amano PS on Diatonite	37.2	0.083	>99.0 : 1.0	79.0 : 21.0	>180[b]
13		Pr	Amano AK	34.2	0.010	98.0 : 2.0	75.0 : 25.0	80[b]
14		Pr	PFL	30.5	0.025	>99.0 : 1.0	71.5 : 28.5	>150[b]
15	*threo*-**3**	Ac	CRL on polypropene	34.6	0.001	73.0 : 27.0	—	3[c]
16		Bu	CRL on polypropene	40.8	0.003	86.0 : 14.0	—	10[c]
17		Bu	Amano PS	44.1	0.013	97.5 : 2.5	—	90[c]
18		Bu	Amano PS on Diatonite	42.2	0.088	99.4 : 0.6	—	>300[c]
19		Bu	PFL	35.5	0.088	>99.5 : 0.5	—	>300[c]
20[12d]	*threo*-**1**	Ac	Amano PS	39.0	0.019	98.6 : 1.4	—	90[b]
21[12d]	*erythro*-**1**	Ac	Amano PS	39.1	0.014	99.1 : 0.9	—	65[b]
22	*threo*-7*S*-**6**	Ac	Amano PS	36.4	0.011	99.8 : 0.2	78.5 : 21.5	>1000[a]
23	*erythro*-7*S*-**6**	Ac	Amano PS	37.6	0.006	99.0 : 1.0	79.3 : 20.3	180[a]
24	*threo*-7*R*-**6**	Ac	Amano PS	37.6	0.011	99.9 : 0.1	80.1 : 19.9	>2000[a]
25	*threo*-**5**	Pr	Amano PS	31.4	0.005	>99.0 : 1.0	72.4 : 27.6	>300[a]
26	*erythro*-**5**	Pr	Amano PS	36.1	0.006	97.0 : 3.0	76.5 : 23.5	54[a]
27	*threo*-**4**	Pr	Amano PS	35.3	0.008	99.8 : 0.2	77.2 : 22.8	>900[a]
28	*erythro*-**4**	Pr	Amano PS	35.2	0.006	98.9 : 1.1	76.6 : 23.4	160[a]

The enantiomeric ratios (entries 1–14) or the diastereomeric ratios (entries 15–28) were analysed as follows.[a] The formate esters on a β-dex-column. [b] The MTPA-esters using ^{19}F NMR. [c] The MTPA-esters on a BP-A-column. [d] The conversion ξ at each point was obtained from ee_s and ee_p according to $\xi = ee_s/(ee_s + ee_p)$ except in entries 15–21 were the conversions were measured by GC. [e] Given as % h^{-1} mg^{-1} lipase and $mmol^{-1}$ substrate. [f] Product ratios entries 1–7 2*R*3*S* : 2*S*3*R*, entries 8–14 2*R*3*R* : 2*S*3*S*, entries 15–19 2*R*3*S*7*R*/*S* : 2*S*3*R*7*R*/*S*, entry 20 2*R*3*S*7*R*/*S* : 2*S*3*R*7*R*/*S*, entry 21 2*R*3*R*7*R*/*S* : 2*S*3*S*7*R*/*S*, entry 22 2*R*3*S*7*S* : 2*S*3*R*7*S*, entry 23 2*R*3*R*7*S* : 2*S*3*S*7*S*, entry 24 2*R*3*S*7*R* : 2*S*3*R*7*R*, entry 25 2*R*3*S*7*R*/*S*9*R*/*S* : 2*S*3*R*7*R*/*S*9*R*/*S*, entry 26 2*R*3*R*7*R*/*S*9*R*/*S* : 2*S*3*S*7*R*/*S*9*R*/*S*, entry 27 2*R*3*S*7*R*/*S*11*R*/*S* : 2*S*3*R*7*R*/*S*11*R*/*S*, entry 28 2*R*3*R*7*R*/*S*11*R*/*S* : 2*S*3*S*7*R*/*S*11*R*/*S*. [g] Substrate ratios entries 1–7 2*S*3*R* : 2*R*3*S*, entries 8–14 2*S*3*S* : 2*R*3*R*, entries 15–19 2*S*3*R*7*R*/*S* : 2*R*3*S*7*R*/*S*, entry 20 2*S*3*R*7*R*/*S* : 2*R*3*S*7*R*/*S*, entry 21 2*S*3*S*7*R*/*S* : 2*R*3*R*7*R*/*S*, entry 22 2*S*3*R*7*S* : 2*R*3*S*7*S*, entry 23 2*S*3*S*7*S* : 2*R*3*R*7*S*, entry 24 2*S*3*R*7*R* : 2*R*3*S*7*R*, entry 25 2*S*3*R*7*R*/*S*9*R*/*S* : 2*R*3*S*7*R*/*S*9*R*/*S*, entry 26 2*S*3*S*7*R*/*S*9*R*/*S* : 2*R*3*R*7*R*/*S*9*R*/*S*, entry 27 2*S*3*R*7*R*/*S*11*R*/*S* : 2*R*3*S*7*R*/*S*11*R*/*S*, entry 28 2*S*3*S*7*R*/*S*11*R*/*S* : 2*R*3*R*7*R*/*S*11*R*/*S*. [h] The *E*-values were calculated from the ee_p and the conversion ξ using the equation deduced by Chen *et al.*[14] [i] The "*E*"-values were calculated as the lipases preference for 2*R*-isomers over 2*S*-isomers or *vice versa*.[15]

used. In addition, *Pseudomonas fluorescens* (PFL) also showed high 2*R*-preference (entries 7, 14, *E* = 160 and 150 respectively and entry 19 "*E*" >300) and among the highest reaction rates, see Table 1. When using PFL, the conversion was 30–40% after three to five hours, to be compared to the use of Amano PS that required 20–48 hours to reach the same degree of conversion. Reactions catalysed by CRL were the slowest ones and the time required to reach the same conversion as above was 95–200 hours. hours.

Comparing the selectivity of the Amano PS lipase for all the *erythro*- and *threo*-3-methylalkan-2-ols (entries analysed as formate esters) showed that all the *threo*-3-methylalkan-2-ols displayed somewhat higher "*E*"- and *E*-values than the corresponding *erythro* ones, see Table 1. When using different acyl donors *e.g.* vinyl acetate, vinyl propionate or vinyl butyrate (catalysed by Amano PS lipase, entries 1, 2 and 8, 9 or by CRL, entries 15 and 16) to acylate different 3-methylalkan-2-ols very small differences were noted. Consequently, as the *E*-values are high in entries 1, 2, 8 and 9 and the fact that the reaction rates also were similar, the preferred acyl donor to use is the one that produces the biologically active ester in the pine sawfly species[2–4] of interest.

Using *erythro*-**5** as substrate (entry 26) resulted in an "*E*"-value of 54 which is low compared to the *threo*-**5** (entry 25, *E* > 300) and also to other *threo*- and *erythro*-substrates (see Table 1). To increase the 2*R*-preference for this substrate the reaction conditions have to be optimised, for instance, change to another lipase. However, in order to obtain this product mixture of 2*R*-esters with higher 2*R*-purity, it is of course also possible to use an additional lipase catalysed acylation step or a lipase catalysed hydrolysis step.

When using *threo*-7*S*-**6** and *threo*-7*R*-**6** (Table 1, entries 22 and 24 respectively) as substrates the recorded reaction rates were similar and the selectivity of the lipase was very high in both cases ("*E*" > 1000 and > 2000 respectively). Thus, it is not possible to judge if the lipase differentiated between the 7*R*- and 7*S*-configuration in the two substrates *threo*-7*R*-**6** and *threo*-7*S*-**6** respectively.

Conclusion

In conclusion we have presented an efficient lipase catalysed acylation method for the preparation of stereoisomeric mixtures or of highly pure stereoisomers of several 3-methylalkan-2-ol structures. The 2*R*-preference of the lipases Amano PS, PFL and Amano AK are very high for some of the tested 3-methylalkan-2-ols, thus, it is possible to produce both the remaining 2*S*-substrate and the product 2*R*-ester in highly pure stereoisomeric forms in the same lipase catalysed acylation sequence.

Experimental

Commercially available chemicals were used without further purification unless otherwise stated. The *cis*- and racemic *trans*-epoxybutanes were obtained from Aldrich and analysed by GC to be of >99.95% diastereoisomeric purity. PFL and CRL were purchased from Sigma, Amano AK, Amano PS, Amano PS on Diationite and Amano PS on Tyonite-200-P were obtained from Amano Pharmaceutical Co. Ltd. The lipases were all stored at 4 °C over silica gel. Dry diethyl ether was distilled from $LiAlH_4$ and the alkyl halides were distilled prior to use and stored under argon. In the coupling reactions the solvents were degassed by argon for about 1 h prior to use. Li (s) was washed with *n*-heptane and was flattened by hammering and cut in very thin pieces prior to use. Preparative liquid chromatography (LC) was performed on normal phase silica gel (Merck 60, 230–400 mesh, 0.040–0.063 mm) employing a gradient technique using an increasing concentration of distilled ethyl acetate in distilled cyclohexane (0 ⟶ 100%), as eluent. To monitor the progress of the reactions thin layer chromatography (TLC) was performed on silica gel plates (Merck 60 F_{254}, pre-coated aluminium foil) eluted with ethyl acetate (20–40% ethyl acetate in cyclohexane) and developed by spraying with vanillin in sulfuric acid and heated at 120 °C. NMR spectra were recorded on a Bruker DMX 250 (250 MHz ^{1}H and 62.9 MHz ^{13}C) spectrometer using $CDCl_3$ as solvent and TMS as internal reference. Optical rotations were measured on a Perkin Elmer 241 polarimeter using a 1 dm cell and are given in units of 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a Saturn 2000 instrument, unless otherwise stated operating in the EI mode, coupled to a Varian 3800 GC instrument. Exact masses (HRMS) were obtained using a VG-70E mass spectrometer at 7.000 resolution and 70 eV. IR-spectra were recorded neat between NaCl plates using a Perkin Elmer 782 infrared spectrometer. Unless otherwise stated, conversions and purity were monitored by a 30 m × 0.32 mm ID capillary column coated with EC-1 d_f = 0.25 µm, carrier gas N_2, 12 psi, split ratio 1 : 50.

2-Hexyl-4,5-dihydrofuran (8)

The title compound was prepared using a method analogous to that described for other substituted dihydrofurans.[8,16] To 2,3-dihydrofuran (18.1 g, 0.259 mol) in dry THF (115 ml) *t*-BuLi (100 ml of a 1.7 M solution in pentane, 0.170 mol) was added dropwise during 2 h, while maintaining the temperature below −40 °C. The mixture was allowed to reach −5 °C during 1 h then cooled to −20 °C and 1-iodohexane (30 g, 0.142 mol, stored over dry K_2CO_3 and 3 Å mol sieves) was added within 0.5 h. The reaction mixture was allowed to reach 20 °C during 16 h. After cooling to 0 °C it was poured into saturated NH_4Cl (400 ml, aq) and Et_2O (400 ml). The aqueous phase was extracted with Et_2O (3 × 200 ml), the combined organic extracts were washed with brine (400 ml) and dried 0.25 h ($MgSO_4$). Removal of the solvent and distillation (75 °C/12 mm Hg) afforded the 2-hexyl-4,5-dihydrofuran (18 g, 117 mmol, 95% pure according to GC) as an oil. This compound was unstable and decomposed when exposed to light, heat, acids and long storage in the freezer. n_D^{20} 1.453. IR: 2974, 2920, 2830, 1696, 1660, 1444, 1354, 1120, 1002, 715 cm^{-1}. ^{1}H NMR: δ 0.88 (3 H, t, *J* = 6.8), 1.2–2.8 (12 H, m), 3.9–4.3 (3 H, m).

(*E*)-4-Methyldec-3-en-1-ol (9)

MeMgBr (2.1 ml of a 3 M solution in dry Et_2O, 6.3 mmol) was added dropwise to $(PPh_3)_2NiCl_2$ (1.53 g, 2.3 mmol), which was stirred at 20 °C in dry benzene (100 ml). After 0.25 h additional MeMgBr (97.9 ml, 3 M in Et_2O, 0.294 mol) was added followed by 2-hexyl-4,5-dihydrofuran (18 g, 0.110 mol, stored over 4 Å mol sieves) in dry benzene (12 ml). The mixture was concentrated to one fifth[8,16] of the original volume in order to remove ether and then the solvent volume was reconstituted with dry benzene. Then the mixture was refluxed at 80 °C (bath temp) for 4.5 h. After cooling to 0 °C the solution was carefully poured into a stirred solution of NH_4Cl (400 ml, sat. aq.) at −20 °C. Stirring was continued until the colour of the solution was stable (0.25 h). The organic layer was separated and the aqueous phase was extracted with Et_2O (3 × 200 ml). The pooled organic extracts were dried ($MgSO_4$), filtered and the solvent evaporated off. The residue was chromatographed to give the title alcohol (*E*)-4-methyldec-3-en-1-ol (15.4 g, 0.100 mol, 97% purity according to GC and with no detected amount of *Z*-diastereomer by ^{1}H NMR). The analytical and spectroscopic data were identical with those in the literature.[17]

4-Methyldecan-1-ol (10)

The unsaturated alcohol **9** from above (15.4 g, 100 mmol) and Pd/C (5%, 1.33 g) in methanol (240 ml, pre-dried over 3 Å mol. sieves) was stirred under H_2 at ambient temperature and pressure for 24 h. The catalyst was filtered off, washed with dry methanol and the solvent was evaporated off to give the saturated alcohol 4-methyldecan-1-ol (13.4 g, 87 mmol). The analytical and spectroscopic data were identical with those in the literature.[18]

(*S*)-4-Methylundecanoic acid (*S*-17)

To a stirred solution of triphenylphosphine (7.2 g, 27 mmol) in dichloromethane (11 ml) at −5 °C bromine (1.4 ml, 28 mmol) was added dropwise. After 1 h (*S*)-2-methylnonanol[6] (3.5 g, 22 mmol 98% ee) in dichloromethane (2 ml) was added dropwise. After 1 h the main part of the solvent was evaporated off and the residue was treated with pentane to precipitate triphenylphosphine oxide. The mixture was filtered through a plug of silica gel followed by evaporation of the solvent to give the (*S*)-1-bromo-2-methylnonane as an oil (3.0 g, 13.6 mmol) pure by GC. The enantiomeric purity was determined by GC using a 30 m × 0.25 mm ID capillary column coated with β-dex 225, d_f = 0.25 µm, carrier gas He, 15 psi, split ratio 1 : 100 (GC programme: 90 °C (20 min), 0.5 °C min^{-1}, 120 °C). Retention time/min: 59.1 (*S*-enantiomer) and 60.1 (*R*-enantiomer). The analytical and spectroscopic data were identical with those in the literature.[19]

Sodium (0.35 g, 14 mmol) was added gradually in small pieces to 9 ml of absolute ethanol under argon. Diethyl malonate (2.5 ml, 15 mmol) was added over a period of 10 min. The mixture was refluxed for five minutes and (*S*)-1-bromo-2-methylnonane[6] (2.9 g, 13.2 mmol) from above was added at room temperature over a period of 0.25 h. After refluxing for 40 h and neutralisation with four drops of glacial acetic acid, the ethanol was evaporated off. Water (10 ml) was added, the organic phase separated and the aqueous phase extracted with Et_2O (3 × 25 ml). The combined organic phases were washed (10 ml sat. sodium chloride solution), dried ($MgSO_4$) and concentrated to an oil, which was hydrolysed with a solution of potassium hydroxide (4.0 g, 71 mmol) in ethanol (40 ml, 95%) during reflux for 16 h. Ethanol was evaporated off and water (30 ml) was added. The mixture was washed with Et_2O (2 × 30 ml). The remaining water phase was acidified to pH 1 at 0 °C with 6 M HCl and extracted with Et_2O (3 × 15 ml). The

combined organic phases were washed with sat. sodium chloride solution (50 ml), dried ($MgSO_4$) and evaporated to dryness. The diacid (3.4 g, 14 mmol) was heated to 190 °C for 1 h and the crude acid was dissolved in aqueous sodium carbonate solution (20 ml, 10%) and washed with Et_2O (15 ml). The carbonate phase was acidified (pH 1–2) with 6 M HCl and the organic phase separated followed by extraction of the water phase with Et_2O (7 × 15 ml). The combined organic phases were washed with sat. sodium chloride solution (15 ml), dried ($MgSO_4$), evaporation of the solvent gave an oil which after distillation (bp 140 °C/0.73 mbar) (lit. 158–162 °C/12 Torr)[20] gave the title acid *S*-**17** (1.9 g, 9.5 mmol, 98.9% purity by GC). $[\alpha]_D^{25}$ +0.43 (neat). IR: 2925, 2855, 1711, 1458, 1414, 1379, 1284, 1216, 940, 723 cm^{-1}. ^1H NMR: δ 0.85–0.91 (6 H, m), 1.14–1.52 (14 H, m), 1.63–1.73 (2 H, m), 1.7 (1 H, m), 2.28–2.39 (2 H, m). ^{13}C NMR: δ 14.1, 19.2, 22.7, 26.9, 29.3, 29.9, 31.6, 31.9, 31.9, 32.3, 36.6, 180.7. MS: *m*/*z* 201 (M^+, 12%), 182 (1), 171 (11), 143 (89), 125 (5), 101 (25), 85 (100), 73 (90), 57 (95), 41 (81).

(*R*)-4-Methylundecanoic acid (*R*-17)

Similarly prepared *via* the above malonic ester sequence but from (*R*)-1-bromo-2-methylnonane[6] was the title acid (0.285 g, 1.4 mmol, 99.7% purity by GC). $[\alpha]_D^{25}$ −0.33 (neat). Physical and spectral data were identical to those of the enantiomer above.

4,6-Dimethyldecanoic acid (18)

Similarly prepared using the above malonic ester sequence but from 1-bromo-2,4-dimethyloctane[9] was the title acid (13.3 g, 66.4 mmol, >99% purity by GC). Bp 90–92 °C/1.0 mbar. n_D^{20} 1.4420. MS: *m*/*z* 200 (M^+, 1%), 183 (1), 165 (10), 143 (7), 125 (7), 101 (100), 88 (35), 73 (40), 55 (49). IR: 2958, 2927, 1711, 1457, 1414, 1380, 1287, 1216, 943, 668 cm^{-1}. ^1H NMR: δ 0.80–1.77 (21 H, m), 2.24–2.46 (2 H, m). ^{13}C NMR: δ 14.2, 19.1, 19.5, 19.8, 20.1, 23.0, 23.1, 29.1, 29.3, 29.6, 29.7, 29.9, 30.0, 31.4, 31.7, 31.9, 32.4, 36.5, 37.5, 44.4, 44.7, 180.6. Anal. calcd. $C_{12}H_{24}O_2$: C 72.0%, H 12.1%. Found: C 72.1%, H 12.3%.

4,8-Dimethyldecanoic acid (19)

Similarly prepared *via* the above malonic ester sequence but from 1-bromo-2,6-dimethyloctane[9] was the title acid (13.3 g, 66.4 mmol) in >98% purity by GC. Bp 91 °C/0.5 mbar. ^1H NMR: δ 0.82–0.90 (9 H, m), 1.02–1.53 (13 H, m), 1.59–1.79 (1 H, m). ^{13}C NMR: δ 11.4, 11.4, 19.2, 19.2, 19.2, 19.3, 24.3, 29.4, 29.5, 31.6, 31.7, 31.9, 31.9, 32.3, 32.3, 34.4, 36.8, 36.8, 36.9, 37.0, 180.7. MS: *m*/*z* 200 (M^+, 5%), 171 (12), 143 (95), 125 (6), 111 (15), 101 (26), 85 (85), 73 (86), 55 (100), 41 (85). IR data were identical to those in the literature.[21]

(*S*)-4-Methylundecanol (*S*-20)

The (*S*)-4-methylundecanoic acid from above (1.72 g, 8.6 mmol) was dissolved in dry Et_2O (25 ml) and slowly added to $LiAlH_4$ (0.367 g, 9.7 mmol) in dry Et_2O (20 ml) under argon. The mixture was stirred at 20 °C for 3 h and then quenched with water (0.35 ml), 15% NaOH (0.35 ml) and water (0.35 ml). After refluxing for 1 h the mixture was filtered, dried ($MgSO_4$), concentrated and distilled bulb-to-bulb to yield the title alcohol as a colourless oil (1.38 g, 7.4 mmol) with a chemical purity by GC of 98.6%. Bp 126 °C/1.1 mbar. $[\alpha]_D^{25}$ −2.3 (*c* 1.0, $CHCl_3$). n_D^{20} 1.453, MS: *m*/*z* 168 (M^+ − 18, 1%), 140 (10), 125 (48), 97 (45), 84 (45), 69 (100), 41 (69). IR: 3330, 2925, 2854, 2360, 1466, 1378, 1058, 897, 722, 668 cm^{-1}. ^1H NMR: δ 0.88 (6 H, t, *J* = 6.6 Hz), 1.1–1.6 (18 H, m), 3.6 (2 H, t, *J* = 6.6 Hz). ^{13}C NMR: δ 14.1, 19.6, 22.7, 27.0, 29.4, 29.9, 30.3, 31.9, 32.6, 32.9, 37.0, 63.5. HRMS calculated for $C_{12}H_{26}O{\cdot}H_2O$: 168.1878. Observed: 168.1889.

(*R*)-4-Methylundecanol (*R*-20)

Similarly prepared from (*R*)-4-methylundecanoic acid was the title alcohol (0.280 g, 1.27 mmol) with a chemical purity of 98.5% by GC. Bp 150 °C/3.0 mbar. $[\alpha]_D^{25}$ +1.5 (*c* 1.1, $CHCl_3$). Other spectroscopic and analytical data were identical to those of (*S*)-4-methylundecanol.

4,6-Dimethyldecan-1-ol (21)

Similarly prepared from 4,6-dimethyldecanoic acid was the title alcohol (12.2 g, 65.2 mmol) in >99% purity by GC. Bp 65 °C/0.9 mbar. n_D^{20} 1.453. IR: 3345, 2980, 2927, 2847, 2364, 2346, 1376, 1056, 827, 668 cm^{-1}. ^1H NMR: δ 0.80–1.62 (24 H, m), 3.63 (2 H, t, *J* = 6.7 Hz). ^{13}C NMR: δ 14.2, 19.4, 19.5, 20.2, 20.3, 23.0, 23.1, 29.2, 29.3, 29.9, 30.0, 30.0, 30.2, 30.3, 32.7, 33.8, 36.5, 37.7, 44.8, 45.1, 63.5, 63.5. MS: *m*/*z* 140 (M^+ − 46, 3%), 125 (24), 111 (34), 97 (6), 83 (31), 69 (100), 57 (31), 56 (28), 55 (49). Anal. calcd. $C_{12}H_{26}O$: C 77.4%, H 14.1%. Found: C 77.4%, H 14.2%.

4,8-Dimethyldecan-1-ol (22)

Similarly prepared from 4,8-dimethyldecanoic acid was the title compound (3.60 g, 19.3 mmol, >98% purity by GC). Bp 69 °C/1 mbar. The analytical and spectroscopic data were identical with those in the literature.[21–22]

(*S*)-1-Chloro-4-methylundecane (*S*-24)

General procedure for the preparation of chlorides[8]. The appropriate alcohol, in this case 4-methylundecan-1-ol (1.36 g, 7.3 mmol), was mixed with triphenylphosphine (8.2 g, 30.8 mmol) and CCl_4 (1.4 ml, 14.8 mmol) and refluxed for 3 h. EtOH (0.12 ml) was poured into the reaction mixture which was immediately subjected to a flash chromatography and bulb-to-bulb distillation to give a colourless oil (1.2 g, 5.9 mmol) as the product. Chemical purity by GC >99%. Bp 112 °C/0.58 mbar. Lit. 116–117 °C/10 Torr.[23] $[\alpha]_D^{25}$ +0.6 (*c* 3.0, hexane). ^1H NMR: δ 0.86–0.91 (6 H, m), 1.18–1.56 (15 H, m), 1.82–1.70 (2 H, m), 3.52 (2 H, t, *J* = 6.8 Hz). ^{13}C NMR: δ 14.1, 19.6, 22.7, 27.0, 29.4, 29.9, 30.3, 31.9, 32.3, 34.2, 36.9, 45.6. MS: *m*/*z* 205 (M^+, 2%), 191 (6), 177 (5), 163 (2), 147 (5), 133 (8), 105 (61), 97 (15), 85 (45), 69 (100).

*(R)-1-Chloro-4-methylundecane (**R-24**).* Similarly prepared from (*R*)-4-methylundecanol was the title compound (0.21 g, 0.99 mmol) with >98% purity by GC. $[\alpha]_D^{25}$ −1.3 (*c* 0.3, hexane). NMR, MS and bp data were similar to those of the enantiomer above.

*1-Chloro-4,6-dimethyldecane (**25**).* Similarly prepared from 4,6-dimethyldecan-1-ol was the title chloride (12.1 g, 59.1 mmol) with >99% purity by GC. Bp 122 °C/10 mmHg. IR: 2957, 2626, 2872, 2362, 1462, 1379, 788, 727, 688, 656. ^1H NMR: δ 0.78–1.82 (23 H, m), 3.5 (2 H, t, *J* = 6.8 Hz). ^{13}C NMR: δ 14.1, 14.2, 19.4, 19.5, 20.2, 20.2, 23.1, 23.1, 29.2, 29.3, 29.6, 29.6, 30.0, 30.0, 30.2, 30.3, 34.0, 35.1, 36.5, 37.6, 44.7, 45.0, 45.5, 45.5. MS (CI, CH_3CN): *m*/*z* 248 (M^+ + 43, 1%), 171 (1), 147 (9), 133 (10), 119 (10), 111 (20), 99 (14), 85 (100), 71 (99), 57 (2). Anal. calcd. $C_{12}H_{26}Cl$: C 70.4%, H 12.3%. Found: C 70.6%, H 12.4%.

1-Iodo-4-methyldecane (23)

General procedure for the preparation of iodides[24]. The appropriate alcohol, in this case 4-methyldecan-1-ol (16.0 g, 92.7 mmol), was stirred in a mixture of dry THF–MeCN (120 ml : 40 ml) with triphenylphosphine (34.1 g, 130 mmol) and imidazole (9.46 g, 139 mmol) at −10 °C when I_2 (37.7 g, 148 mmol) was added in small portions. After stirring for 0.5 h MeOH (1.6 g, 50 mmol) was added and stirring was continued for 0.5 h. $Na_2S_2O_3$ (100 ml, sat.) was added and the product extracted into Et_2O (4 × 100 ml). After drying ($MgSO_4$), evaporation of the solvent, LC and distillation the title compound (19.8 g, 69.5 mmol) was obtained with a chemical purity of >97.5% by GC. Bp 72 °C/0.7 mbar. The identity of the compound was checked by NMR and the iodide was used in the next step without further characterisation.

*1-Iodo-4,6-dimethyldecane (**26**).* Similarly prepared as above but from 4,6-dimethyldecan-1-ol the title compound (0.67 g, 2.26 mmol) was obtained with a chemical purity by GC of >97%. Bp 96 °C/0.9 mbar. The identity of the compound was checked by NMR and the iodide was used in the next step without further characterisation.

*1-Iodo-4,8-dimethyldecane (**27**).* Similarly prepared as above but from 4,8-dimethyldecan-1-ol the title compound (4.90 g, 16.6 mmol) was obtained with a chemical purity by GC of >95%. Bp 100 °C/0.9 mbar. The identity of the compound was checked by NMR and the iodide was used in the next step without further characterisation.

***erythro*-(2*R**,3*R**,7*S*)-3,7-Dimethyltetradecan-2-ol (*erythro*-7*S*-6)**

Method A for the preparation of *erythro*- and *threo*-3-methylalkan-2-ols. The alkyllithium was prepared by modifying the method used for other alkyllithiums in the literature.[25] Accordingly, lithium (0.98 g, 140 mmol) was cut into small pieces and refluxed for 0.12 h in *n*-hexane (4 ml, degassed of oxygen by argon). The solvent was removed, another 4 ml of freshly distilled and degassed *n*-hexane was added and heated to reflux. Distilled (*S*)-1-chloro-4-methylundecane (***S*-24**) (0.60 g, 2.9 mmol) was added slowly (0.12 h) *via* a syringe into the reaction flask and the reaction mixture was refluxed for 2 h. Methyllithium (2.30 ml, 2.30 mmol, 1 M) was added dropwise to a mixture of CuCN [0.202 g, 2.30 mmol, predried at 105 °C and then dried by azeotropic evaporation of dry toluene (4 ml) at 40 °C under reduced pressure] and dry Et_2O (5 ml) at −78 °C. The solution was allowed to reach 0 °C and then cooled to −78 °C followed by dropwise addition of *S*-4-methylundecanyllithium. After the addition of alkyllithium, the reaction mixture was allowed to reach 0 °C and then cooled to −78 °C. *trans*-2,3-Epoxybutane (0.40 g, 0.50 ml) was injected. The temperature was allowed to slowly reach 20 °C during 48 h. Saturated NH_4OH–NH_4Cl (25 ml, 10% NH_3) was added followed by vigorous stirring until the water layer turned blue. The mixture was extracted with Et_2O (5 × 15 ml), washed with water (15 ml) and saturated sodium chloride solution (15 ml), dried ($MgSO_4$), filtered and concentrated. The residue was purified by LC and distilled (bp 170 °C/1.4 mbar) to give the title alcohol (0.30 g, 1.24 mmol) with a chemical purity by GC of >96%. $[a]_D^{25}$ +0.20 (*c* 4.1, hexane). The analytical and spectroscopic data were similar with those in the literature for *erythro*-(2*S*,3*S*,7*S*)-3,7-dimethyltetradecan-2-ol.[26a]

threo-(2R,3S*,7S)-3,7-Dimethyltetradecan-2-ol (threo-7S-**6**).* Similarly prepared using the above Method A but from *S*-1-chloro-4-methylundecane (***S*-24**) and *cis*-2,3-epoxybutane was the title alcohol (0.051 g, 0.21 mmol) with a chemical purity by GC of >98%. $[a]_D^{25}$ +0.25 (*c* 1.0, hexane). The analytical and spectroscopic data were similar to those above for *erythro-7S*-**6**.

threo-(2R,3S*,7R)-3,7-Dimethyltetradecan-2-ol (threo-7R-**6**).* Similarly prepared using the above Method A but from *R*-1-chloro-4-methylundecane (***R*-24**) and *cis*-2,3-epoxybutane was *threo*-7*R*-**6** (0.25 g, 0.98 mmol) with a chemical purity by GC of >98%. $[a]_D^{25}$ +0.20 (*c* 1.0, hexane). The analytical and spectroscopic data were identical to those above for *threo*-7*S*-**6**.

*erythro-3,7,9-Trimethyltridecan-2-ol (erythro-**5**).* Similarly prepared using the above Method A but from 1-chloro-4,6-dimethyldecane (**25**) and *trans*-2,3-epoxybutane was the title compound (0.080 g. 0.33 mmol) with a chemical purity by GC of >98%. The analytical and spectroscopic data were similar with those in the literature.[5b]

***threo*-3,7-Dimethyltridecan-2-ol (*threo*-3)**

Method B for the preparation of *erythro*- and *threo*-3-methylalkan-2-ols. The alkyllithium was prepared by modifying the method used for other alkyllithiums in the literature.[8,27] Accordingly, *tert*-butyllithium (50 ml 1.5 M in pentane, 75 mmol) was added drop by drop for 1.5 h to 4-methyl-1-iodododecane (8.46 g, 30 mmol) in Et_2O (30 ml, degassed of oxygen by argon) at −78 °C. Methyllithium (18.0 ml, 28.9 mmol, 1 M) was added dropwise to CuCN [(2.59 g, 28.9 mmol), pre-dried at 105 °C and then dried by azeotropic evaporation of dry toluene (120 ml) at 40 °C under reduced pressure] and dry Et_2O (24 ml) at −78 °C. The solution was allowed to reach 0 °C and then cooled to −78 °C followed by dropwise addition of 4-methyldodecanyllithium. After the addition of alkyllithium, the reaction mixture was allowed to reach room temperature for 1 h and then cooled to −78 °C. *cis*-2,3-Epoxybutane (2.09 g, 2.53 ml, 28.9 mmol) was injected. The temperature was allowed to slowly reach 20 °C during 24 h. Saturated NH_4OH–NH_4Cl (250 ml, 10% NH_3) was added followed by vigorous stirring until the water layer turned blue. The mixture was extracted with Et_2O (3 × 125 ml), washed with NH_4OH–NH_4Cl (2 × 100 ml, 10% NH_3) and brine (2 × 100 ml), dried ($MgSO_4$), filtered and concentrated. The residue was purified by LC and distilled (bp 110 °C/0.7 mbar) to give the title alcohol (4.0 g, 16.5 mmol) with a chemical purity by GC of >98%. The analytical and spectroscopic data of the title compound were similar to those in the literature.[3e]

*threo-3,7,11-Trimethyltridecan-2-ol (threo-**4**).* Similarly prepared using the above Method B but from 1-iodo-4,8-dimethyldecane and *cis*-2,3-epoxybutane was the title compound (0.065 g, 0.27 mmol) with a chemical purity by GC of >98%. The analytical and spectroscopic data were similar to those in the literature.[5a,12a]

*erythro-3,7,11-Trimethyltridecan-2-ol (erythro-**4**).* Similarly prepared using the above Method B but from 1-iodo-4,8-dimethyldecane and *trans*-2,3-epoxybutane was compound *erythro*-**4** (0.081 g, 0.33 mmol) with a chemical purity by GC of >98%. The analytical and spectroscopic data were similar to those in the literature.[5a,12a]

*threo-3,7,9-Trimethyltridecan-2-ol (threo-**5**).* Similarly prepared using the above Method B but from 1-iodo-4,6-dimethyldecane (**26**) and *cis*-2,3-epoxybutane was the title alcohol (0.10 g, 0.41 mmol) with a chemical purity by GC of >96%. The analytical and spectroscopic data were similar to those in the literature.[5b]

***erythro*-3-Methylpentadecan-2-ol (*erythro*-7)**

Method C for the preparation of *erythro*- and *threo*-alkan-2-ols. Lithium (0.49 g, 70 mmol) was cut into small pieces and refluxed for 5 min in *n*-hexane (75 ml, degassed of oxygen by argon). The solvent was removed, another 100 ml of freshly distilled and degassed *n*-hexane was added and allowed to reflux. Distilled 1-chlorododecane (33 ml, 28.4 g, 139 mmol) was added slowly (0.15 h) *via* a syringe into the refluxing mixture in the reaction flask. After 3 h no 1-chlorododecane remained according to GC. To a mixture of CuCN [(5.5 g, 61 mmol), predried at 105 °C and then dried by azeotropic evaporation of toluene (100 ml, dry and degassed) at 30 °C under reduced pressure] and dry Et_2O (100 ml) at −78 °C the dodecyllithium was added dropwise (1 h). After 1 h *trans*-2,3-epoxybutane (4.5 g, 5.6 ml, 62 mmol) was injected at −78 °C. The temperature was allowed to slowly reach 20 °C (20 h). A saturated ammonium chloride solution with 10% ammonia (550 ml) was added followed by vigorous stirring until the water layer turned blue. The mixture was extracted with Et_2O (5 × 150 ml), washed with water (100 ml), sodium chloride solution (100 ml, sat. aq), dried ($MgSO_4$) and then the solvent was evaporated off *in vacuo*. The residue was purified by LC and distilled (bp 149 °C/4.2 mbar) to yield the alcohol *erythro*-**7** as an oil. (8.23 g, 34 mmol, >99% pure by GC). The analytical and spectroscopic data were similar to those in the literature.[26]

threo-3-Methylpentadecan-2-ol (threo-7). Similarly prepared using the above Method C but from 1-chlorododecane and *cis*-2,3-epoxybutane was the title alcohol *threo*-**7** (6.28 g, 26 mmol, >99% pure by GC). Bp 125 °C/0.3 mbar. The analytical and spectroscopic data were similar to those in the literature.[26b]

Lipase catalysed acylation of different *erythro*- and *threo*-3-methylalkan-2-ols

General method. *erythro*- (or *threo*)-3-methylalkan-2-ol, *n*-heptane (4.3 ml per mmol alcohol), lipase (160 mg per mmol alcohol) and molecular sieves (3 Å) were stirred for 2 h in a sealed flask and vinyl ester (4.8 mmol per mmol alcohol) was added to start the reaction. The conversion was monitored by periodic withdrawal of samples. When the reaction reached the desired conversion (~35%), the mixture was filtered and the solid remaining on the filter was washed with *n*-pentane. The solvent was evaporated and the product 2*R*-ester and the remaining 2*S*-alkanol substrate were separated by LC. The esters and the alcohols were in this way obtained on a 1–20 gram scale chemically pure by GC without any trace of the remaining alcohol or the product ester respectively. The stereoisomeric purity of the obtained compounds were analysed as below and for the stereoisomeric purities see Table 1.

The remaining substrate 2*S*-3-methylalkan-2-ols and the product 2*R*-esters from the above lipase catalysed acylation sequence for *threo*-**7**, *erythro*-**7**, *threo*-7*S*-**6**, *erythro*-7*S*-**6**, *threo*-7*R*-**6**, *threo*-**5**, *erythro*-**5**, *threo*-**4**, *erythro*-**4** were all analysed as formate ester on a β-dex 325 or on a β-dex 120 GC-column. The product 2*R*-propionate or 2*R*-acetate ester (30–40 mg) was reduced by $LiAlH_4$[28] in Et_2O. The obtained 2*R*-alcohol or the 2*S*-substrate alcohol (10 mg) was then dissolved in formic acid and stirred at room temperature overnight. The formic acid was evaporated and the residue was purified by LC and the stereoisomeric purity was determined using a Varian 3300 gas chromatograph equipped with 30 m × 0.25 mm ID capillary column coated with β-dex 325 or β-dex 120, d_f = 0.25 µm, carrier gas He, 15 psi, split ratio 1 : 100. *threo*-**7**: β-dex 325 (GC programme: 150 °C isothermal). Retention time/min: 90.3 (2*S*3*R*), 103.4 (2*R*3*S*). *erythro*-**7**: β-dex 325 {(GC programme: 155 °C (40 min), 0.5 °C min^{-1}, 180 °C)}. Retention time/min: 68.1 (2*S*3*S*), 69.8 (2*R*3*R*). *threo*-7*S*-**6**: β-dex 120 (GC programme: 150 °C isothermal). Retention time /min: 50.8 (2*S*3*R*7*S*), 53.1 (2*R*3*S*7*S*). *erythro*-7*S*-**6**: β-dex 120 (GC programme: 150 °C isothermal). Retention time/min: 50.0 (2*S*3*S*7*S*), 53.2 (2*R*3*R*7*S*). *threo*-7*R*-**6**: β-dex 120 (GC programme: 150 °C isothermal). Retention time/min: 51.2 (2*S*3*R*7*R*), 53.1 (2*R*3*S*7*R*). *threo*-**5**: β-dex 325 {(GC programme: 135 °C (0 min), 0.5 °C min^{-1}, 170 °C)}. Retention time/min: 54.2 (2*S*3*R*7*R*/*S*9*R*/*S*), 55.2 (2*R*3*S*7*R*/*S*9*R*/*S*), 56.2 (2*S*3*R*7*R*/*S*9*R*/*S*), 57.2 (2*R*3*S*7*R*/*S*9*R*/*S*). *erythro*-**5**: β-dex 325 {(GC programme: 135 °C (0 min), 0.5 °C min^{-1}, 170 °C)}. Retention time /min: 54.2 (2*S*3*S*7*R*/*S*9*R*/*S*), 55.3 (2*R*3*R*7*R*/*S*9*R*/*S*), 56.2 (2*S*3*S*7*R*/*S*9*R*/*S*), 57.3 (2*R*3*R*7*R*/*S*9*R*/*S*). *threo*-**4**: β-dex 120 {(GC programme: 150 °C (60 min), 4 °C min^{-1}, 170 °C)}. Retention time/min: 43.0 (2*S*3*R*7*R*/*S*11*R*/*S*), 44.9 (2*R*3*S*7*R*/*S*11*R*/*S*). *erythro*-**4**: β-dex 120 {(GC programme: 150 °C (60 min), 4 °C min^{-1}, 170 °C)}. Retention time/min: 42.7 (2*S*3*S*7*R*/*S*11*R*/*S*), 45.1 (2*R*3*R*7*R*/*S*11*R*/*S*). For the stereoisomeric purity see Table 1.

The remaining substrate 2*S*-3-methylalkan-2-ols and the product 2*R*-esters from the above lipase catalysed acylation sequence for *threo*-**7** and *erythro*-**7** were all analysed as MTPA-esters and analysed by ^{19}F NMR. The product 2*R*-esters (30–40 mg) were reduced by $LiAlH_4$[28] in diethyl ether and the obtained 2*R*-alcohols or the substrate 2*S*-alcohols were reacted with the chloride derived from (*S*)-(−)-MTPA following the method described by Lund *et al.*[12d] For the stereoisomeric purity see Table 1.

The remaining substrate 2*S*-3-methylalkan-2-ol and the product 2*R*-ester from the above lipase catalysed acylation sequence for *threo*-**3** were analysed as MTPA-esters using a BP-A GC-column. Using the same method as above except that the chloride from (*R*)-(+)-MTPA was used in the preparation of the (*R*)-MTPA-esters. The diastereomeric purity was analysed on a BP-A column using a Varian 3300 gas chromatograph equipped with 30 m × 0.25 mm ID capillary column coated with BP-A, d_f = 0.25 µm, carrier gas He, 15 psi, split ratio 1 : 100, {(GC programme: 150 °C (20 min), 3 °C min^{-1}, 180 °C)}. Retention time/min: 93.7 (minor diastereomer, 2*S*3*R*7*S*), 94.9 (major and minor diastereomers 2*R*3*S*7*S* and 2*S*3*R*7*R*) and 96.6 (major diastereomer 2*R*3*S*7*R*). For the stereoisomeric purity see Table 1.

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