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Sex Pheromone of the Pine Sawfly, *Macrodiprion nemoralis*. Stereoselective Synthesis of the Sixteen Stereoisomers of 3,7,9-Trimethyl-2-tridecyl Acetate

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The sixteen stereoisomers of 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac) were prepared individually, each in over 99.5% stereochemical purity. The syntheses were based on the ring opening of a pure enantiomer of *cis*-3,4-dimethyl-γ-butyrolactone using a pure stereoisomer of 1-lithio-2,4-dimethyloctane, the two stereogenic centres of which were introduced with high selectivity by alkylations of the amide enolates from the appropriate enantiomers of pseudoephedrine. (2*S*,3*R*,7*R*,9*S*)-3,7,9-Trimethyl-2-tridecyl acetate (*SRRS*-**5**Ac) has recently been found to be the major component of the female sex pheromone of *Macrodiprion nemoralis* (Hymenoptera: Diprionidae). A synthetic method for the preparation of a sixteen isomer mixture of **5**Ac is also presented. This mixture has been found to be biologically active in field tests.

As early as 1976, the first examples of diprionid sex pheromones were identified as the acetate and the propionate of the alcohol 3,7-dimethylpentadecan-2-ol (diprionol, Fig. 1) **1** from the North American pine sawflies *Neodiprion lecontei* (Fitch) and *Diprion similis* (Hartig). Since then, several sex pheromones from several other species that occur in eastern North America[1–4] and in Europe, *Neodiprion sertifer*,[5–8] *Diprion pini*,[9,10] and *Microdiprion pallipes*[11] have been identified. *N. sertifer* and several congeneric species use the (2*S*,3*S*,7*S*)-isomer, *SSS*-**1**Ac, as an attractant, while other species employ other stereoisomers, mainly the (2*S*,3*R*,7*R*)-isomer, *SRR*-**1**Ac.[12]

Until the early 1990s it was generally believed that all diprionid pheromones were esters of one or several stereoisomers of diprionol (**1**). However, the sex pheromone of *D. pini* was identified as an ester (propionate and/or acetate in different geographical regions) of one stereoisomer of a chain-shortened diprionol, i.e. (2*S*,3*R*,7*R*/*S*)-dimethyltridecan-2-ol (*SRR*-**2**H), which represents a new type of pine sawfly pheromone.[10] Recently, an even shorter homologue of diprionyl propionate, (2*S*,3*R*,7*R**)-3,7-dimethyl-2-undecyl propionate (*SRR*/*S*-**3**Pr), has been identified from *Diprion nipponica*.[13] *M. pallipes*, on the other hand, employs a hitherto unpresented structural variation containing an additional branching methyl group in its pheromone, 3,7,11-trimethyl-2-tridecyl propionate (**4**Pr).[11] Very recently, we identified the sex pheromone of *Macrodiprion nemoralis* and found yet another structural variation among the pine sawflies. In this case the naturally occurring active compund is (2*S*,3*R*,7*R*,9*S*)-3,7,9-trimethyl-2-tridecyl acetate (*SRRS*-**5**Ac).[14] In field tests *M. nemoralis* males were strongly attracted to a synthetic mixture of the sixteen isomers of 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac).[14] In order to supply the compounds needed for biological tests we prepared first a sixteen-component mixture of all the possible stereoisomers of 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac) and then all the sixteen stereoisomerically pure individual isomers of this acetate. To accomplish this, we employed a synthetic strategy similar to that previously used by us for the pheromones of *N. sertifer*,[15] *D. pini*[10] and *M. pallipes*.[11] The results of our work are presented below.

Results and discussion

Radical bromination of 3-methylthiophene gave the bromide **6**,[16] which was allowed to react with the anion of diethyl methylmalonate to give a diester (see Scheme 1). Basic hydrolysis of this ester followed by decarboxylation of the diacid formed, furnished 2-methyl-3-thiophen-3-ylpropanoic acid (**7**).[17] LAH reduction of this acid gave the racemic 2-methyl-3-thiophen-3-ylpropanol (**8**).[18]

Friedel–Craft acetylation of compound **8** gave a mix-

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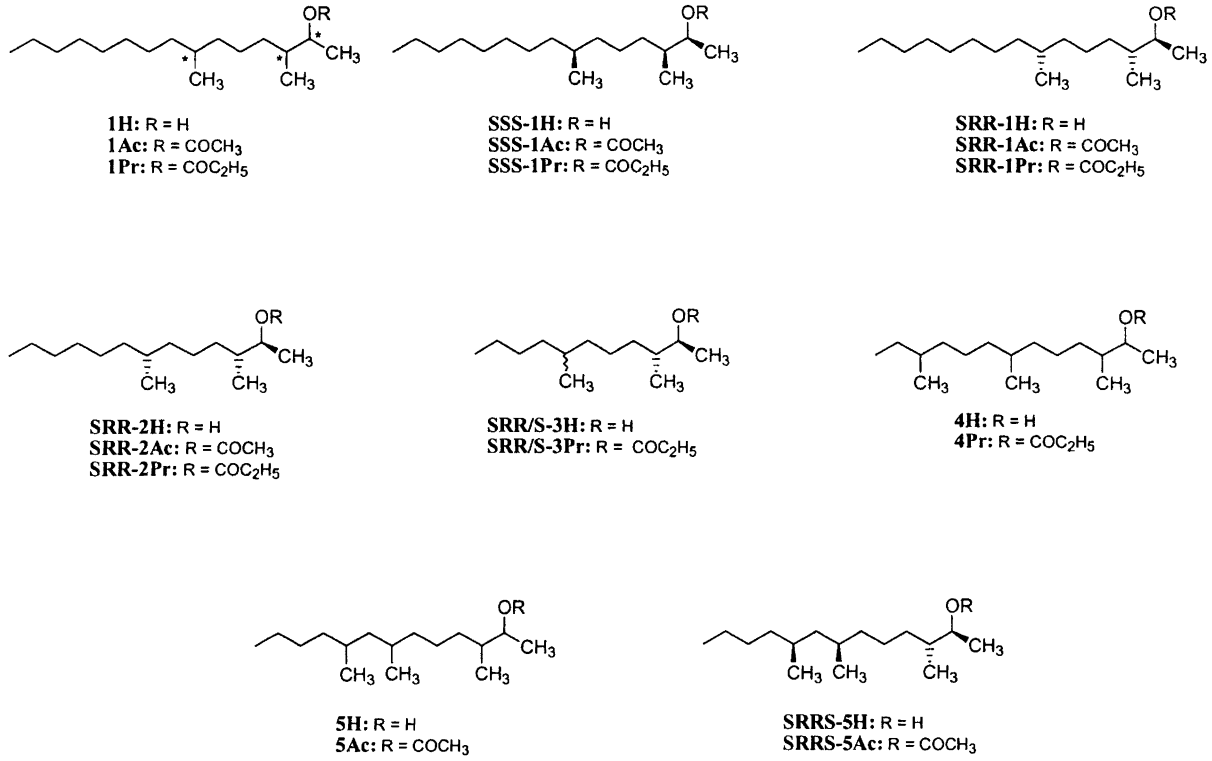
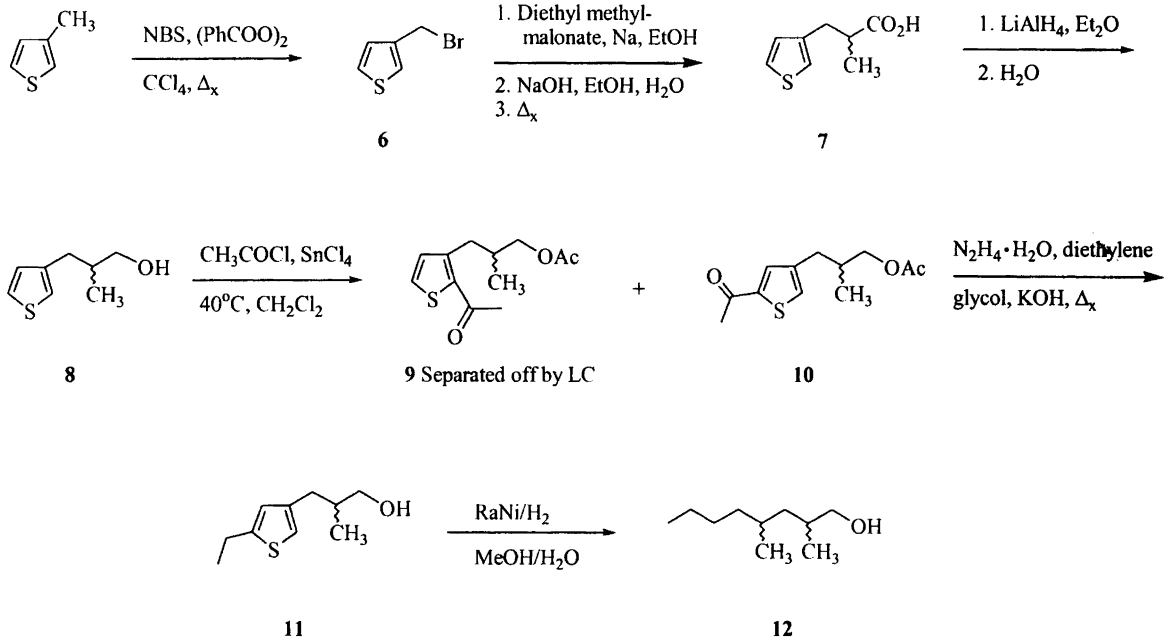


Fig. 1. Chemical structures of sex pheromone components in Pine sawfly species.

ture of the 2-acylated and 5-acylated esters **9** and **10**, respectively (ratio 35:65; high reaction temperature favoured 5-acylation). Separation on silica gel afforded compound **10**. Huang–Minlon reduction yielded the alcohol **11**, which, on Raney nickel reduction, produced a four-component stereoisomeric mixture of 2,4-dimethyloctan-1-ol (**12**) (*syn*:*anti*, 56:44). The alcohol **12** was transformed into the chloride followed by conversion into the organolithium compound. This was allowed to react with a mixture of all four stereoisomers (*cis*:*trans*, 34:66) of 3,4-dimethyl-γ-butyrolactone (**15**) to give a ketoalcohol, which was reduced without purification using Huang–Minlon conditions to a mixture of sixteen stereoisomers of 3,7,9-trimethyltridecan-2-ol **5H**



Scheme 1. Preparation of a four stereoisomeric mixture of 2,4-dimethyloctan-1-ol.

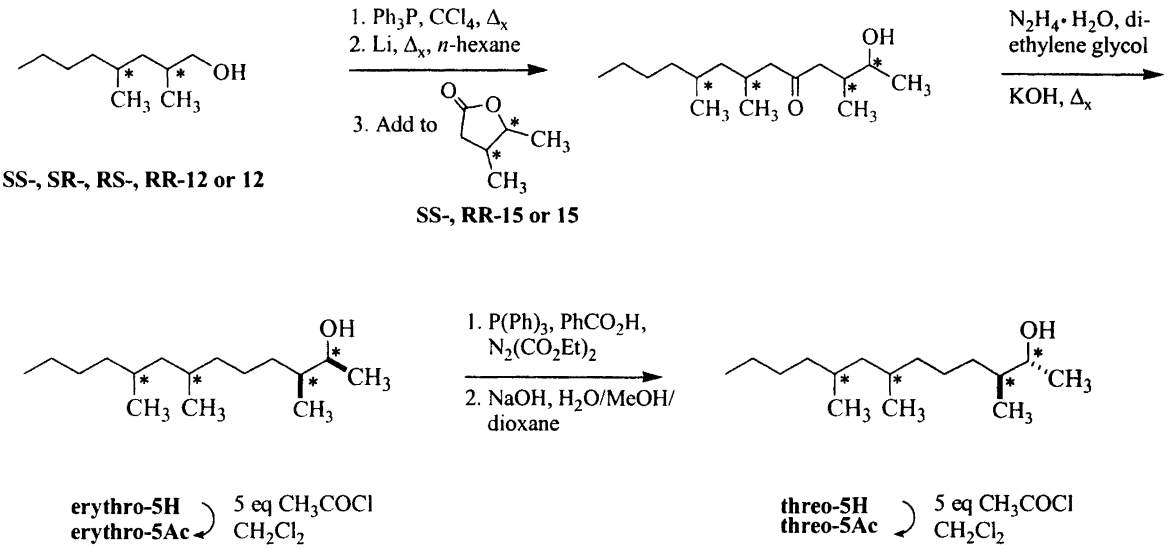
(see Scheme 2). Acylation of this mixture using acetyl chloride furnished 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac).

In order to be able to employ the same lactone ring-opening strategy for the syntheses of each of the sixteen individual stereoisomers in pure forms, all four pure isomers of the alcohol **12** (*SS*-, *SR*-, *RR*- and *RS*-**12**) were needed. We have recently studied enzymatic resolutions by esterification of racemic 2- as well as 4-methylalkanoic acids,[10,19] catalysed by *Candida rugosa* lipase (CRL). When subjected to LAH-reduction, both the esters produced and the remaining acids furnished the corresponding alcohols in excellent enantiomeric purities. However, when we tried to employ this reaction sequence starting from a diastereomeric mixture of 2,4-dimethyloctanoic acid, the diastereoselectivity in the enzymatic esterification reaction was too low to be useful.[20] An alternative approach to the preparation of enantiomerically pure 2-alkylated acyl derivatives is the diastereoselective alkylation of chiral amide enolates formed from chiral amine auxiliaries.[21] Because we needed to prepare all four stereoisomers of the alcohol **12**, an iterative strategy seemed attractive. Therefore, a chiral amine auxiliary available as both pure enantiomers and with proven efficiency in amide alkylation was needed. Pseudoephedrine is available in both enantiomeric forms and has recently been found to be an excellent auxiliary in asymmetric alkylations.[22,23] Therefore the four individual stereoisomers of alcohol **12** should be obtainable in very high stereochemical purities by two consecutive alkylations of the appropriate enantiomer of propionylated pseudoephedrine followed by purification of the products via crystallisation and/or liquid chromatography (see Scheme 3).

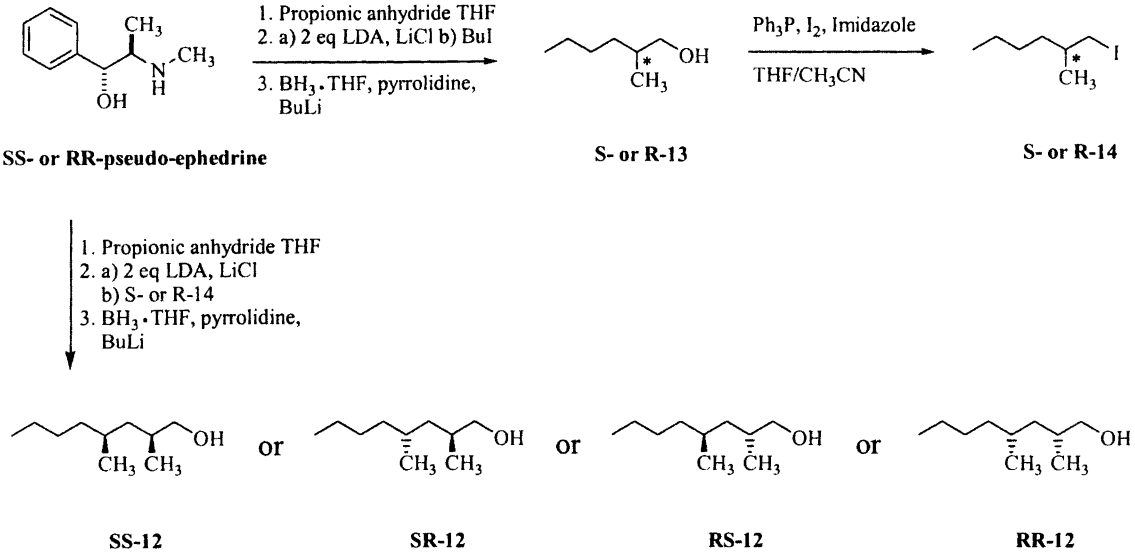
Thus, the appropriate enantiomer of pseudoephedrine was acylated with propionic anhydride and the resulting amide was treated with 2 equiv. of LDA.[22] Alkylation of the resulting *Z*-enolate with 1-iodobutane furnished the crystalline alkylated product in over 95% d.e.

Liquid chromatography followed by recrystallisation from hexane gave one pure diastereomer (>99.5% d.e.), which, after reductive hydrolysis with lithium–borane pyrrolidine complex (LBP), gave (*R*)- or (*S*)-2-methylhexan-1-ol (*S*- or *R*-**13**) respectively, both of >97.5% e.e., i.e. an undesired epimerisation had occurred during the cleavage reaction. In an effort to minimise this epimerisation various cleaving agents were tried such as $ZrOCl_2$ or $FeCl_3$ in refluxing H_2O–dioxane.[23] Unfortunately, all methods used resulted in higher or the same degree of epimerisation. The alcohols, *S*- or *R*-**13** were converted into the corresponding iodoalkanes, *S*- or *R*-**14**. The *Z*-enolate prepared from the appropriate enantiomer of propionylated pseudoephedrine was alkylated with one of the iodides *S*- or *R*-**14** (see Scheme 3). LBP-reduction of the resulting *syn*- and *anti*-pseudoephedrine products yielded the four individual 2,4-dimethyloctan-1-ols, *SS*-, *SR*-, *RS*- or *RR*-**12**, separately. After separation of the *anti*- from the *syn*-products on silica gel each of these was obtained in high stereochemical purities (>99% d.e. and >99.8% e.e., Table 1). The stereochemical purities of the alcohols were determined by GC after oxidation to the acids and derivatisation to the corresponding 1-phenylethyl amides. Because it was possible to obtain practical chromatographic separation of the *syn* and *anti* diastereomers of the alcohol **12**, the problems resulting from epimerisation in the two cleavage reactions were almost eliminated.

The alcohols were then converted via the chlorides into the alkyllithiums which were allowed to react with the desired enantiomer (*RR*-**15** or *SS*-**15**) of *cis*-3,4-dimethyl-γ-butyrolactone, Scheme 2). After Huang–Minlon reduction, each of the eight individual *erythro*-



Scheme 2. Synthetic strategy for the syntheses of the sixteen individual *threo*- and *erythro*-isomers of 3,7,9-trimethyl-2-tridecyl acetate and also for a mixture of isomers.



Scheme 3. Asymmetric synthesis of the optically pure stereoisomers of 2,4-dimethyloctan-1-ol using the two enantiomers of pseudoephedrine as chiral auxiliary.

Table 1. Stereoisomeric composition of the four isomers of 2,4-dimethyloctan-1-ol.[a]

Isomer	*RR*-**12**	*RS*-**12**	*SR*-**12**	*SS*-**12**
SS-**12**	<0.1%	0.4%	<0.1%	>99.5%
RR-**12**	>99.6%	<0.2%	<0.2%	n.d.[b]
SR-**12**	<0.1%	n.d.[b]	>99.8%	<0.1%
RS-**12**	<0.1%	>99.5%	<0.1%	0.3%

[a]Determined by GC analysis after oxidation to the acid and conversion into the (*S*)-1-phenylethylamide derivative.[26] [Capillary column CP-Sil 88, 50 m × 0.25 mm ID, d_f = 0.2 μm, carrier gas He (16 psi), split ratio 1:30, oven temperature programmed from 135 °C (10 min) at 2 °C min^{-1} to 220 °C]. Retention times: *SS*-**12** 86.5 min; *SR*-**12** 88.7 min; *RR*-**12** 89.0 min; *RS*-**12** 91.2 min. [b]Not detectable.

isomers *erythro*-**5**H were obtained separately. The eight *threo*-isomers, *threo*-**5**H, were prepared from the corresponding *erythro*-isomer via Mitsunobu inversion at C-2 followed by basic hydrolysis of the resulting benzoate. The diastereomeric purity of all the individual isomers of *erythro*-**5**H and *threo*-**5**H were confirmed to be >99.5% by GC analysis. Acylation of each of the individual *threo*- and *erythro*-isomers of **5**H using acetyl chloride furnished the sixteen desired 3,7,9-trimethyl-2-tridecyl acetate stereoisomers **5**Ac.

In conclusion we have synthesised each of the sixteen individual stereoisomers 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac), each in very high stereochemical purities (>99.5%). One of these was identified as the major component of the sex pheromone of *M. nemoralis*, namely the (2*S*,3*R*,7*R*,9*S*)-isomer (*SRRS*-**5**Ac). A method for the synthesis of a mixture of isomers of 3,7,9-trimethyl-2-tridecyl acetate (**5**Ac) has also been presented.

Experimental

Commercially available chemicals were used as received, unless otherwise stated. Dry Et_2O ($LiAlH_4$), diethylene glycol (NaOH), diisopropylamine (CaH_2), hexane ($LiAlH_4$), pyrrolidine (Na), and THF (K and benzophenone) were distilled from the indicated drying agents. Acetonitrile and CH_2Cl_2 were dried over molecular sieves 4 Å, LiCl was dried under vacuum at 150 °C for 3 h before use. Reactions sensitive to moisture and/or oxygen were carried out under argon. The molarity of butyllithium was determined by titration using oven dried diphenylacetic acid as the indicator. The (3*S*,4*S*)- and (3*R*,4*R*)-*cis*-dimethyl-γ-butyrolactones used were from the same batches as those used by Bergström *et al.*,[10] i.e. *SS*: >99.9% e.e. and <0.04% *trans*. *RR*: >99.7% e.e. and <0.03% *trans*. Preparative liquid chromatography was performed on straight-phase silica gel (Merck 60, 230–400 mesh, 0.040–0.063 mm, 10–50 g per g of mixture) with an increasing concentration of distilled ethyl acetate in distilled cyclohexane or of distilled Et_2O in distilled pentane as eluents.[24] Thin layer chromatography (TLC) was performed on silica gel plates (Merck 60 F_{254}, pre-coated aluminium foil) using ethyl acetate in cyclohexane as the eluent, and developed by means of ultraviolet irradiation and/or by spraying with vanillin in sulfuric acid and heating at 120 °C. The *syn*:*anti* ratio of the stereoisomers of the alcohol **12** and, unless otherwise stated, the chemical purity of all the other intermediates were determined using a capillary GC column [CP-Sil 19 CB, 30 m × 0.25 mm ID, d_f = 0.25 μm, carrier gas N_2 (15 psi), split ratio 1:30]. The *erythro*:*threo* ratio of the individual isomers of *erythro*-**5**H and *threo*-**5**H were determined using a capillary GC column [DB-WAX, 30 m × 0.32 mm ID, d_f = 0.25 μm, carrier gas He (15 psi),

split ratio 1 : 30]. Melting and boiling points are uncorrected and the latter are, unless otherwise stated, given as air-bath temperatures (bath temp./mbar) in a bulb-to-bulb (Büchi GKR-51) apparatus. Optical rotations were measured in a 1 dm cell using a Perkin Elmer 241 polarimeter. NMR spectra were recorded with tetramethylsilane (^{1}H measurements) or $CDCl_3$ (^{13}C measurements) as internal standard using either a Jeol EX270 (270 MHz ^{1}H and 67.8 MHz ^{13}C) or a Bruker DMX 250 (250 MHz ^{1}H and 62.9 MHz ^{13}C) instrument. Mass spectra were recorded on a Saturn 2000 instrument, operating in the EI or CI (CH_3CN as chemical ionization gas) mode, coupled to a Varian 3800 GC instrument. Exact masses (HRMS) were obtained using a VG-70E mass spectrometer.

2-Methyl-3-thiophen-3-ylpropionic acid (**7**). The method published by Cagniant[17] was used with some modification to synthesise the title compound. 3-Methylthiophene (51.1 g, 0.52 mol), *N*-bromosuccinimide (80.4 g, 0.452 mol) and dibenzoyl peroxide (0.4 g) were heated to reflux in CCl_4 (400 ml). Every 0.1 h dibenzoyl peroxide (0.4 g) was added until the bottom layer of the reaction mixture became transparent. The total amount added was 1.8 g. The mixture was cooled after which the precipitate was filtered off and the organic phase was washed with $NaHCO_3$ (aq. sat. 130 ml) and brine (150 ml), and dried ($MgSO_4$). After concentration the bromide **6**[16] was obtained, 81.6 g (0.462 mol), which was used without further purification in the next step. The bromide **6** was added to sodium diethyl methylmalonate [prepared from diethyl methylmalonate (153.3 g, 0.88 mol) in ethanol (560 ml) and sodium (19.4 g, 0.842 mol) in EtOH, (440 ml)]. The reaction was stirred for 16 h at room temperature, then refluxed for 7 h, neutralised with acetic acid and concentrated to give a residue which was treated with water (200 ml) and *tert*-butyl methyl ether (TBME, 400 ml). The water phase was separated and the product taken up in TBME (4 × 300 ml), and the pooled organic phases were washed with $NaHSO_4$ (aq. sat. 100 ml), Na_2CO_3 (aq. sat. 100 ml) and brine (100 ml), dried ($MgSO_4$) and concentrated to give the crude diester.

The crude diester was hydrolysed with KOH (110 g, 1.968 mol) in H_2O (110 ml) and EtOH (700 ml) under reflux for 7 h. The EtOH was evaporated off and the residue treated with H_2O (200 ml) and washed with TBME (2 × 200 ml). The water phase was acidified to pH 1 with HCl (aq., 250 ml, 6 M) and the diacid was taken up in TBME (5 × 300 ml). Drying ($MgSO_4$) and evaporation of the solvent gave 105 g of the diacid as an oil.

The diacid was decarboxylated at 160 °C for 15 h and after cooling, TBME (300 ml) was added and the organic phase was treated with Na_2CO_3 (aq., 15%, 4 × 100 ml), the pooled aqueous layers were washed with TBME (200 ml). Acidification of the water phase with 6 M HCl, extraction with TBME (4 × 200 ml), washing with H_2O (100 ml), drying ($MgSO_4$), concentration and fractional distillation furnished the pure title acid **7**, 48.2 g (0.172 mol). B.p. 123–125 °C/5.25 mbar, lit.[17] 154 °C/17 mmHg. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.20 (3 H, d, J = 6.6 Hz), 2.69–2.82 (2 H, m), 2.98–3.12 (1 H, m), 6.93 (1 H, dd, J = 1.2, 4.9 Hz), 6.98–7.10 (1 H, m), 7.25 (1 H, dd, J = 2.9, 5.0 Hz), 11.35 (1 H, br). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 16.6, 33.6, 40.7, 121.7, 125.5, 128.3, 139.2, 182.8. MS (EI): *m/z* 170 (35) (M^+), 125 (12), 109 (2), 97 (100).

2-Methyl-3-thiophen-3-ylpropanol (**8**). The method of Cagniant *et al.*[18] was used with some modification to synthesise the title compound. 2-Methyl-3-thiophen-3-ylpropionic acid (9.94 g, 58 mmol) was dissolved in dry Et_2O (50 ml) and added drop by drop to a solution of $LiAlH_4$ (2.19 g, 58 mmol) in dry Et_2O (275 ml) at 0 °C. The mixture was stirred at room temperature for 2 h, then heated to reflux for 1 h. After cooling to 0 °C the reaction was quenched by sequential addition of H_2O (1.1 ml), NaOH (aq. 15%, 1.1 ml) and H_2O (2.2 ml) and then heated to reflux for 1 h. After cooling, the solid was filtered off and washed with Et_2O (50 ml) followed by evaporation of the solvent and drying ($MgSO_4$). The remaining oil was chromatographed and fractionally distilled (b.p. 120–123 °C/12 mbar, lit.[18] 132–133 °C/15 mmHg) to give 7.35 g (48 mmol) of the title alcohol (**8**) as a colourless GC-pure oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.91 (3 H, d, J = 6.8 Hz), 1.86–2.01 (2 H, m), 2.47 (1 H, dd, J = 7.8, 14.0 Hz), 2.75 (1 H, dd, J = 6.2, 14.0 Hz), 3.44 (1 H, dd, J = 6.0, 10.6 Hz), 3.50 (1 H, dd, J = 6.0, 10.6 Hz), 6.90–6.95 (2 H, m), 7.24 (1 H, dd, J = 3.0, 4.7 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 17.0, 34.4, 37.5, 68.0, 121.5, 125.7, 129.1, 141.3. MS (CI): *m/z* 157 (100) $(M+H)^+$, 139 (55), 124 (1), 111 (3), 97 (8).

2-Methyl-3-(2-acetylthiophen-3-yl)propyl acetate (**9**) *and 2-methyl-3-(5-acetylthiophen-3-yl)propyl acetate* (**10**). 2-Methyl-3-thiophen-3-ylpropanol (4.05 g, 26 mmol) and freshly distilled acetyl chloride (4.09 g, 52 mmol) were stirred at 40 °C in dry CH_2Cl_2 (75 ml). To the mixture was added drop by drop $SnCl_4$ (20.7 g, 81 mmol). Stirring was continued until TLC showed no remaining starting material. The reaction was quenched by addition of HCl (aq., 6 M, 30 ml) and then poured into water (60 ml). The organic phase was separated and the water phase extracted with CH_2Cl_2 (4 × 100 ml). From the pooled organic phases was obtained after drying ($MgSO_4$) and concentration a mixture of the two products **9** and **10**. Separation by chromatography and bulb-to-bulb distillation gave 1.46 g of 2-methyl-3-(2-acetylthiophen-3-yl)propyl acetate **9** and 2.72 g (11.3 mmol) of the desired product, 2-methyl-3-(5-acetylthiophen-3-yl)propyl acetate **10**, both pure by GC.

9: ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.95 (3 H, d, J = 6.8 Hz), 2.06 (3 H, s), 2.10–2.30 (1 H, m), 2.55 (3 H, s), 2.91 (1 H, dd, J = 7.6, 13.4 Hz), 3.10 (1 H, dd, J = 6.9,

13.4 Hz), 3.91 (1 H, dd, J=6.2, 10.8 Hz), 3.96 (1 H, dd, J=5.8, 10.8 Hz), 6.97 (1 H, d, J=5.0 Hz), 7.42 (1 H, d, J=5.0 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 17.0, 20.9, 29.8, 33.7, 33.8, 68.8, 129.5, 132.2, 135.9, 147.9, 171.2, 190.9. MS (EI): *m/z* 241 (73) $(M+H)^+$, 181 (80), 165 (71), 151 (53), 138 (100), 125 (19), 97 (10). (HRMS, EI): (M^+) 240.0827. $C_{12}H_{16}O_3S$ requires 240.0820.

10: ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.95 (3 H, d, J= 6.8 Hz), 2.07 (3 H, s), 2.08–2.19 (1 H, m), 2.50 (1 H, dd, J=7.8, 14.2 Hz), 2.54 (3 H, s), 2.74 (1 H, dd, J=6.2, 14.2 Hz), 3.91 (1 H, dd, J=6.2, 10.9 Hz), 3.97 (1 H, dd, J=6.3, 10.9 Hz), 7.26–7.28 (1 H, m), 7.52 (1 H, d, J= 1.4 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 16.5, 20.8, 26.7, 33.7, 34.0, 68.3, 130.0, 133.6, 141.4, 144.2, 170.9, 190.5. MS (EI): *m/z* 241 (9) $(M+H)^+$, 180 (100), 165 (56), 137 (92), 125 (8), 97 (43). (HRMS, EI): (M^+) 240.0828. $C_{12}H_{16}O_3S$ requires 240.0820.

2-Methyl-3-(5-ethylthiophen-3-yl)propanol (**11**). 2-Methyl-3-(5-acetylthiophen-3-yl)propyl acetate (1.80 g, 7.5 mmol) was heated with KOH (2.25 g, 40 mmol) and hydrazine hydrate (1.2 g, 24 mmol) in distilled diethylene glycol (18 ml) at 170 °C for 1 h and then at 210 °C for 2 h. The mixture was cooled to room temperature and water (75 ml) was added. Extraction with Et_2O (4 × 50 ml), drying ($MgSO_4$), evaporation of the solvent and bulb-to-bulb distillation (b.p. 175 °C/0.01 mbar) gave 0.94 g (5 mmol) of the title alcohol pure by GC. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.93 (3 H, d, J=6.8 Hz), 1.29 (3 H, t, J=7.5 Hz), 1.43 (1 H, s), 1.85–2.00 (1 H, m), 2.41 (1 H, dd, J=7.6, 14.0 Hz), 2.66 (1 H, dd, J=6.5, 14.0 Hz), 2.81 (2 H, dq, J=1.0, 7.5 Hz), 3.47 (1 H, dd, J=6.0, 10.6 Hz), 3.54 (1 H, dd, J=6.0, 10.6 Hz), 6.62 (1 H, d, J=1.0 Hz), 6.71 (1 H, d, J= 1.0 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 15.9, 16.7, 23.4, 34.4, 37.0, 67.8, 118.3, 125.1, 140.5, 147.4. MS (CI): *m/z* 185 (100) $(M+H)^+$, 167 (17), 139 (45), 125 (47). (HRMS, EI): (M^+) 184.0921. $C_{10}H_{16}OS$ requires 184.0922.

2,4-Dimethyloctan-1-ol (**12**). 2-Methyl-3-(5-ethylthiophen-3-yl)propanol (0.54 g, 2.9 mmol) was dissolved in methanol (30 ml) and water (1 ml). Four teaspoons of Raney nickel were added and the mixture was stirred under hydrogen (1 atm) at 50 °C for 6 h. The Raney nickel was filtered off and washed with MeOH (5 × 30 ml). After concentration and chromatography a mixture of diastereomers (*syn*:*anti*, 56:44) of 2,4-dimethyloctan-1-ol (**12**) (0.25 g, 1.6 mmol) was obtained. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.8–1.8 (20 H, m), 3.33–3.56 (2 H, m). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 14.1, 16.3, 17.3, 19.4, 20.3, 23.0, 29.1, 29.3, 29.8, 30.0, 33.1, 33.2, 36.3, 37.7, 40.6, 41.0, 68.4, 69.1.

3,7,9-Trimethyltridecan-2-ol (**5H**). From compound **12** (1.5 g, 9.5 mmol) above, a mixture of stereoisomers of 2,4-dimethyl-1-chlorooctane was prepared as described below for (2*S*,4*R*)-2,4-dimethyl-1-chlorooctane. After concentration, chromatography and bulb-to-bulb distillation, 2,4-dimethyl-1-chlorooctane was obtained (1.3 g, 7.4 mmol, b.p. 75 °C/2.5 mbar). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.83–0.93 (6 H, m), 0.99 (3 H, t, J=6.6 Hz), 1.03–1.55 (9 H, m), 1.82–1.99 (1 H, m), 3.33–3.53 (2 H, m). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 14.1, 17.5, 18.4, 19.4, 20.1, 23.0, 29.0, 29.2, 29.9, 30.0, 32.8, 33.1, 36.4, 37.4, 41.6, 41.7, 51.3, 52.0.

1-Lithio-2,4-dimethyloctane was prepared using a method used for other alkyllithiums from the literature.[25] Lithium (1.6 g, 0.23 mol) was cut into small pieces and refluxed for 5 min in hexane (11 ml, degassed of oxygen by argon). The solvent was removed and another 11 ml of freshly distilled and degassed hexane was added. Distilled 2,4-dimethyl-1-chlorooctane (1.3 g, 7.4 mmol) was added slowly (5 min) via syringe at reflux temperature. GC analysis indicated full conversion after 15 min. The mixture was cooled to −78 °C and slowly added (15 min) via syringe to a −78 °C solution of freshly distilled 3,4-dimethyl-γ-butyrolactone (**15**) (0.67 g, 5.9 mmol) in Et_2O (15 ml, degassed of oxygen by argon). After 4 h at −78 °C, the reaction was quenched with NH_4Cl (6 ml, sat. aq.) and the resulting mixture extracted with Et_2O (5 × 10 ml). The organic layer was dried (Na_2SO_4) and concentrated. Column chromatography of the residue afforded 1.0 g (3.9 mmol) of a keto alcohol intermediate which was immediately reduced under Huang–Minlon conditions as above for the acetate **10**. The crude product alcohol was chromatographed and distilled (b.p. 110–125 °C/0.4 mbar) to give a sixteen stereoisomeric mixture of **5H** (0.67 g, 2.8 mmol) as a colourless oil in chemical purity >99% (GC). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.80–1.57 (33 H, m), 3.66 (1 H, quint, J=5.9 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 14.2, 14.6, 19.3, 19.4, 19.5, 20.2, 20.3, 23.1, 24.5, 24.6, 24.7, 29.2, 29.3, 30.0, 30.1, 32.8, 32.9, 33.0, 36.5, 36.6, 37.1, 37.2, 37.7, 38.2, 38.3, 39.8, 40.1, 44.8, 45.0, 45.1, 45.3, 71.3, 71.5, 71.7, 71.8.

3,7,9-Trimethyl-2-tridecyl acetate (**5Ac**). 0.2 g (0.8 mmol) of the mixture of alcohols **5H** was stirred overnight in CH_2Cl_2 (20 ml) with acetyl chloride (0.316 g, 4 mmol) at ambient temperature. Evaporation of the solvent, chromatography and distillation (120–135 °C/0.4 mbar) gave the sixteen-component mixture of stereoisomers of the acetate **5Ac** (0.224 g, 0.8 mmol >98% pure by GC) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.80–1.70 (32 H, m), 2.03 (3 H, s), 4.75–4.88 (1 H, m). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 14.6, 14.9, 15.0, 16.2, 16.3, 17.3, 19.8, 19.9, 20.0, 20.6, 20.7, 21.7, 21.8, 23.4, 23.5, 24.7, 24.8, 24.9, 29.6, 29.7, 30.3, 30.4, 33.3, 33.4, 36.9, 37.4, 37.5, 37.6, 37.7, 38.1, 38.5, 38.6, 45.2, 45.3, 45.5, 45.7, 74.7, 74.8.

(2S) and (2R)-2-methylhexan-1-ol (S- *and* R-**13**). (*S*,*S*)- and (*R*,*R*)-*N*-(2-hydroxy-1-methyl-2-phenylethyl)-*N*-methylpropionamide were prepared following the procedure reported by Myers *et al.*[22] Yield 87%, m.p. for

the (*S,S*)- and (*R,R*)-propionamides 112–113 °C, lit.[22] (*S,S*) 114–115 °C. $[\alpha]_D^{25}$ +102.6 (*c* 1.42, MeOH), (*R,R*) $[\alpha]_D^{25}$ −101.1 (*c* 1.48, MeOH). NMR data for (*S,S*)- and (*R,R*)-amides were similar to those in the literature.[22] MS (CI): *m/z* 222 $(M+H)^+$ (100), 204 (42), 148 (5).

(2*S*)-*N*-[(1*R*,2*R*)- and (2*R*)-*N*-[(1*S*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2-dimethylhexanamides were prepared following the procedure reported by Myers *et al.*[22] with the exception that the crude products were purified by flash column chromatography and then crystallised from hexane three times. GC analysis of the corresponding TMS-ether[23] indicated a diastereomeric excess >99.5% for both enantiomers. [Column DB-5, 30 m × 0.25 mm i.d., d_f=0.25 μm, carrier gas helium (15 psi) column temperature programmed from 80 to 250 °C at 2 °C min^{-1}, retention times: (2*S*)-[1*R*,2*R*] 107.4 min; (2*R*)-[1*R*,2*R*] 106.2 min. Yield 78%, chemical purity >99% by GC, m.p. for the (*S,S*)- and (*R,R*)-hexanamides 67–68 °C lit. (*S,S*)[23] 66–67 °C. (*S,S*) $[\alpha]_D^{25}$ −61.3 (*c* 1.75, MeOH) and (*R,R*) $[\alpha]_D^{25}$ +62.0 (*c*=1.42, MeOH). NMR data for both enantiomers were similar to those in the literature.[22] MS (CI): *m/z* 278 $(M+H)^+$ (100), 260 (63), 148 (62).

The preparation of the title compounds followed the procedure reported by Myers *et al.*[22] except that the crude reaction mixture, after being quenched with 3 M HCl was purified by column chromatography. This resulted in an 83% yield and a chemical purity >99% by GC. Oxidation to the acids and GC analysis of the corresponding (*R*) or (*S*)-phenyl-ethyl amide derivative as described[26] indicated an enantiomeric excess of 97.5% for both enantiomers of **13**. [Column DB-5, 30 m × 0.25 mm i.d., d_f=0.25 μm, carrier gas helium (15 psi) column temperature programmed from 100 to 250 °C at 2 °C min^{-1}, retention times: (*SR*) 38.4 min; (*SS*) 37.2 min. *S*-**13** $[\alpha]_D^{25}$ −13.6 (*c* 2.57, MeOH), lit.[27] $[\alpha]_D^{25}$ −14.2 (*c* 0.31, MeOH), *R*-**13** $[\alpha]_D^{25}$ +13.2 (*c* 2.34, MeOH), lit.[28] $[\alpha]_D^{23.4}$ +14.5 (*c* 2.25, MeOH). ^{1}H NMR (250 MHz): δ 0.90 (3 H, t, *J*=6.7 Hz), 0.91 (3 H, d, *J*=6.7 Hz), 1.05–1.49 (7 H, m), 1.53–1.65 (1 H, m), 3.42 (1 H, dd, *J*=6.5, 10.5 Hz), 3.52 (1 H, dd, *J*=5.8, 10.5 Hz). ^{13}C NMR data for both enantiomers of **13** were similar to those in the literature.[27] MS (CI): *m/z* 170 $(M+C_3H_4N)^+$ (2), 158 $(M+C_2H_4N)^+$ (2), 115 $(M-H)^+$ (2), 99 (100).

*(2S) and (2R)-2-methyl-1-iodohexane (*S-**14** *and* R-**14***)* were prepared according to Marshall *et al.*[29] Yield 83%, *S*-**14** with >99% chemical purity by GC, $[\alpha]_D^{25}$ +3.20 (*c* 1.44, MeOH), lit.[30] $[\alpha]_D^{23}$ +2.80 (*c* 3.76, MeOH), *R*-**14** with >98% chemical purity by GC, $[\alpha]_D^{25}$ −3.05 (*c* 3.48, MeOH), lit.[28] $[\alpha]_D^{22}$ −3.23 (*c* 3.53, MeOH). ^{1}H NMR (250 MHz): δ 0.90 (3 H, t, *J*=6.8 Hz), 0.98 (3 H, d, *J*=6.8 Hz), 1.15–1.50 (7 H, m), 3.17 (1 H, dd, *J*=5.9, 9,6 Hz), 3.24 (1 H, dd, *J*=4.5, 9.5 Hz). ^{13}C NMR (62.9 MHz): δ 14.1, 18.2, 20.6, 22.7, 29.1, 34.7, 36.1. MS (EI): *m/z* 127 (6), 99 (5), 57 (100).

*Representative procedure for preparation of 2,4-dimethyl-octan-1-ols (*SS-, SR-, RS- *and* RR-**12***). Synthesis of (2*R,4S*)-2,4-dimethyloctan-1-ol* RS-**12**. (2*R*,4*S*)-*N*-[(1*S*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2,4-trimethyloctanamide was prepared from (*S,S*)-*N*-(2-hydroxy-1-methyl-2-phenylethyl)-*N*-methylpropionamide (14.2 g, 64 mmol) and (*S*)-2-methyl-1-iodohexane *S*-**14** (6.9 g, 30 mmol) following procedure B described in Ref. 23 for other alcohols with the following exceptions. The reaction was performed at room temperature when the electrophile *S*-**14** was added. The crude product was filtered from the crystalline starting material before the column chromatography purification. Thus, we obtained 9.3 g (29 mmol) of the octanamide as a highly viscous oil with chemical purity >99% by GC. $[\alpha]_D^{25}$ +63.8 (*c* 0.96, MeOH). ^{1}H NMR (250 MHz) (asterisk denotes minor rotamer peaks): δ 0.82 (3 H, d, *J*=6.0 Hz), 0.88 (3 H, t, *J*=6.6 Hz), 0.95–1.45 (9 H, m), 1.06 (3 H, d, *J*=6.7 Hz), 1.13 (3 H, d, *J*=7.0 Hz), 2.69 (1 H, sextet, *J*=6.7 Hz), 2.85 (2 H, s), 2.91* (1 H, s), 4.02–4.16* (0.2 H, m), 4.30–4.47 (0.8 H, m), 4.54–4.73 (2 H, m), 7.22–7.40 (5 H, m). ^{13}C NMR (62.9 MHz) (asterisk denotes minor rotamer peaks): δ 14.0*, 14.1, 14.4, 15.4*, 17.0, 17.3*, 17.6*, 19.6, 22.7*, 22.9, 23.1*, 29.1, 29.2*, 29.6*, 30.3, 33.2, 33.8*, 34.2, 36.6*, 36.9, 37.2*, 41.0*, 41.1, 58.1*, 59.3, 75.3*, 77.2, 126.3, 126.9*, 127.5, 128.3, 128.4*, 128.7*, 141.0*, 142.6, 178.3*, 179.3*, 179.6. MS (CI): *m/z* 320 (100) $(M+H)^+$, 303 (12), 302 (10), 148 (52).

Data for (2*S*,4*R*)-*N*-[(1*R*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2,4-trimethyloctanamide. Chemical purity >99% by GC, $[\alpha]_D^{25}$ −62.3 (*c* 1.12, MeOH). NMR and MS data were similar to the enantiomer above.

Data for (2*R*,4*R*)-*N*-[(1*S*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2,4-trimethyloctanamide. Chemical purity >99% by GC, $[\alpha]_D^{25}$ +54.5 (*c* 1.00, MeOH). ^{1}H NMR (250 MHz) (asterisk denotes minor rotamer peaks): δ 0.77 (3 H, d, *J*=6.4 Hz), 0.89 (3 H, t, *J*=6.2 Hz), 0.95–1.50 (8 H, m), 1.07 (3 H, d, *J*=6.8 Hz), 1.15 (3 H, d, *J*=7.0 Hz), 1.63–1.98 (1 H, m), 2.71 (1 H, sextet, *J*=6.7 Hz), 2.86 (2 H, s), 2.91* (1 H, s), 4.04–4.18* (0.2 H, m), 4.30–4.48 (0.8 H, m), 4.52–4.83 (2 H, m), 7.21–7.40 (5 H, m). ^{13}C NMR (62.9 MHz) (asterisk denotes minor rotamer peaks): δ 14.1, 14.4, 15.4*, 17.9, 18.6*, 19.7, 20.0*, 23.0, 23.1*, 26.8*, 29.1, 29.3*, 30.5, 30.6*, 33.3, 34.1, 36.9, 37.0*, 41.5, 41.7*, 58.1*, 59.6, 75.2*, 77.2, 126.2, 126.9*, 127.5, 128.3, 128.4*, 128.7*, 142.6, 142.7*, 179.3. MS (CI): *m/z* 320 (100) $(M+H)^+$, 303 (9), 302 (8), 148 (4).

Data for (2*S*,4*S*)-*N*-[(1*R*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2,4-trimethyloctanamide. Yield 93% and chemical purity >99% by GC, $[\alpha]_D^{25}$ −53.7 (*c* 1.38, MeOH). NMR and MS data were similar to the enantiomer above. (HRMS, EI): $(M+H)^+$ 320.2563. $C_{20}H_{34}O_2N$ requires 320.2590.

The title alcohol *RS*-**12** was prepared from (2*R*,4*S*)-*N*-[(1*S*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*,2,4-trimethyloctanamide (9.3 g, 29 mmol) following the same

procedure as described above for the alcohols *S*-**13** and *R*-**13**. The crude product (GC analysis of the crude product indicated a ratio of *syn*:*anti* 1:50, column temperature programmed from 70 to 250 °C at 1 °C min^{-1}, retention times: *syn* isomer 34.2 min; *anti* isomer 35.2 min) was further diastereomerically enriched through LC separations [SiO_2; Et_2O in pentane (0–100%) + 0.3% MeOH as the eluent] to give 2.0 g (13 mmol, *anti*:*syn*, 250:1, see Table 1 for the stereoisomeric composition) and 1.9 g (12 mmol, *anti*:*syn*, 20:1) of *RS*-**12**. B.p. 90 °C/3 mbar, $[\alpha]_D^{25}$ +25.4 (*c* 1.26, $CHCl_3$). ^1H NMR (250 MHz): δ 0.84 (3 H, d, *J* = 6.6 Hz), 0.89 (3 H, t, *J* = 6.6 Hz), 0.89 (3 H, d, *J* = 6.6 Hz), 0.95–1.80 (11 H, m), 3.40 (1 H, dd, *J* = 6.8, 10.4 Hz), 3.49 (1 H, dd, *J* = 5.8, 10.4 Hz). ^{13}C NMR: δ 14.1, 16.3, 19.4, 23.0, 29.3, 29.9, 33.2, 37.7, 40.7, 69.1. MS (EI): *m*/*z* 157 (1) $(M-H)^+$, 140 (2), 125 (2), 111 (4), 98 (9), 83 (63), 70 (100).

*(2S,4R)-2,4-Dimethyloctan-1-ol (*SR-**12**). $[\alpha]_D^{25}$ −26.1 (*c* 0.97, $CHCl_3$). See Table 1 for the stereoisomeric composition. NMR, MS and b.p. data were similar to the enantiomer *RS*-**12**. The alcohol *SR*-**12** was converted into (2*S*,4*R*)-2,4-dimethyloctanoic acid following the procedure reported for other alcohols by Lundh *et al.*[19] The acid was obtained as a colourless oil (84%) with a chemical purity >99% by GC. $[\alpha]_D^{25}$ +14.9 (*c* 1.00, MeOH), lit.[27] $[\alpha]_D^{25}$ +6.5 (*c* 0.05, MeOH). NMR and MS data were similar to those given in the literature.[27]

*(2S,4S)-2,4-Dimethyloctan-1-ol (*SS-**12**). Crude *syn*:*anti* 35:1, yield 82%. After purification by LC >200:1 (see Table 1 for the stereoisomeric composition) 42% yield and a chemical purity >98% by GC. B.p. 92 °C/2.5 mbar. $[\alpha]_D^{25}$ −13.2 (*c* 5.1, $CHCl_3$). ^1H NMR (250 MHz): δ 0.87 (3 H, d, *J* = 6.5 Hz), 0.90 (3 H, t, *J* = 6.5 Hz), 0.92 (3 H, d, *J* = 6.7 Hz), 0.97–1.55 (10 H, m), 1.62–1.80 (1 H, m), 3.37 (1 H, dd, *J* = 6.9, 10.4 Hz), 3.52 (1 H, dd, *J* = 5.2, 10.4 Hz). ^{13}C NMR: δ 14.1, 17.3, 20.4, 23.0, 29.1, 30.0, 33.1, 36.4, 41.1, 68.4. MS (EI): *m*/*z* 157 (3) $(M-H)^+$, 140 (3), 125 (2), 111 (5), 98 (11), 83 (75), 70 (100). (HRMS, EI): $(M-H_2O)^+$ 140.1581. $C_{10}H_{22}O$ requires 140.1565.

The alcohol *SS*-**12** was oxidised to (2*S*,4*S*)-2,4-dimethyloctanoic acid as above for the *SR*-**12** isomer to give the acid in chemical purity >99% by GC. B.p. 100 °C/0.6 mbar. $[\alpha]_D^{25}$ +21.8 (*c* 1.21, MeOH), lit.[27] $[\alpha]_D^{25}$ +8.4 (*c* 0.09, MeOH). NMR and MS data were similar to those given in the literature.[27]

*(2R,4R)-Dimethyloctan-1-ol (*RR-**12**). Chemical purity by GC >99%, $[\alpha]_D^{25}$ +13.3 (*c* 1.84, $CHCl_3$) (see Table 1 for the stereoisomeric composition). NMR, MS and b.p. data were similar to those of enantiomer *SS*-**12**.

Representative procedure for the preparation of 2,4-dimethyl-1-chlorooctanes. Synthesis of (2S,4R)-2,4-dimethyl-1-chlorooctane. Prepared via the procedure reported by Hedenström *et al.*,[31] but from (2*S*,4*R*)-2,4-dimethyloctan-1-ol *SR*-**12** (0.71 g, 4.5 mmol), with the following modification. Triphenylphosphine in excess was quenched by the addition of MeOH (1 ml) instead of EtOH. The crude product was distilled to give the chloride (0.75 g, 4.3 mmol) as a colourless oil in chemical purity >99% (GC). B.p. 75 °C/2.5 mbar. $[\alpha]_D^{25}$ −18.5 (*c* 0.63, hexane). MS (EI): *m*/*z* 121 (16), 119 (49), 83 (100), 69 (25). ^1H NMR (250 MHz): δ 0.85 (3 H, d, *J* = 6.5 Hz), 0.88–0.94 (3 H, m), 0.98 (3 H, d, *J* = 6.6 Hz), 1.07–1.35 (8 H, m), 1.38–1.54 (1 H, m), 1.81–1.99 (1 H, m), 3.37 (1 H, dd, *J* = 6.4, 10.5 Hz), 3.46 (1 H, dd, *J* = 5.3, 10.5 Hz). ^{13}C NMR (62.9 MHz): δ 14.1, 17.5, 19.4, 23.0, 29.2, 30.0, 33.2, 37.4, 41.6, 52.0.

(2R,4S)-2,4-Dimethyl-1-chlorooctane. Chemical purity by GC >98%, $[\alpha]_D^{25}$ +19.0 (*c* 0.72, hexane). NMR, MS, and b.p. data were similar to those of the enantiomer above.

(2R,4R)-2,4-Dimethyl-1-chlorooctane. Chemical purity by GC >99%, $[\alpha]_D^{25}$ −0.4 (*c* 0.76, hexane). B.p. 70 °C/2.5 mbar. MS (EI): *m*/*z* 121 (16), 119 (49), 83 (100), 69 (25). ^1H NMR (250 MHz): δ 0.87 (3 H, d, *J* = 6.4 Hz), 0.89–1.55 (12 H, m), 1.00 (3 H, d, *J* = 6.6 Hz), 1.85–1.97 (1 H, m), 3.38 (1 H, dd, *J* = 6.4, 10.6 Hz), 3.50 (1 H, dd, *J* = 4.5, 10.6 Hz). ^{13}C NMR (62.9 MHz): δ 14.1, 18.4, 20.1, 23.0, 29.0, 30.0, 32.9, 36.4, 41.7, 51.3.

(2S,4S)-2,4-Dimethyl-1-chlorooctane. Yield 88% and chemical purity by GC >99%, $[\alpha]_D^{25}$ +0.3 (*c* 2.79, hexane). NMR, MS, and b.p. data were similar to the enantiomer above. (HRMS, EI): $(M^{35}Cl-C_4H_9)^+$ 119.0625 and $(M^{37}Cl-C_4H_9)^+$ 121.0597. $C_6H_{12}Cl$ requires 119.0627 and 121.0625 respectively.

Preparation of the eight pure erythro-*3,7,9-trimethyltridecan-2-ols (*erythro-**5H**) followed the protocol above for 3,7,9-trimethyltridecan-2-ol but from the appropriate lactone and alkyl chloride in 40–46% overall yield based on the lactone. The diastereomeric purity of all the individual isomers of *erythro*-**5H** were confirmed to be >99.5% by GC analysis. For spectral and physical data see Table 2.

Representative procedure for the Mitsunobu reaction. (2S,3R,7R,9S)-3,7,9-trimethyltridecan-2-ol. The title compound was prepared using the procedure described in Högberg *et al.*[15] but from (2*R*,3*R*,7*R*,9*S*)-3,7,9-trimethyltridecan-2-ol (0.11 g, 0.46 mmol), which gave a pure benzoate ester that was directly hydrolysed to the corresponding alcohol (reflux overnight in a 1:1:1 mixture of 1.2 M KOH in H_2O–MeOH–dioxane). The crude reaction mixture was extracted with Et_2O (5 × 6 ml), dried (Na_2SO_4), concentrated and chromatographed. Distillation gave the desired *SRRS*-alcohol, *threo*-**5H** (60 mg, 0.25 mmol) as a colourless oil of chemical purity >99% by GC. All other threo-isomers were obtained in

Table 2. Spectral and physical data for the stereoisomers of 3,7,9-trimethyltridecan-2-ol.

Isomer of **5H**	^{1}H NMR 270 MHz	^{13}C NMR 67.8 MHz	MS CI; CH_3CN	$[\alpha]_{546}^{25}$ *c* 1.0 hexane	B.p. °C/mbar
S,S,S,S	0.82 (6 H, d, J=6.6 Hz), 0.89 (3 H, d, J=6.6 Hz), 0.89 (3 H, t, J=6.6 Hz), 0.92–1.55 (18 H, m), 1.15 (3 H, d, J=6.3 Hz), 3.70 (1 H, dq, J=4.3, 6.3 Hz).	14.1 (2 C), 19.4, 19.5, 20.3, 23.0, 24.7, 29.3, 30.0 (2 C), 32.9, 37.7, 38.2, 39.8, 45.0, 71.4.	296 (3) $(M+C_3H_4N)^+$, 169 (6), 155 (11), 141 (18), 127 (26), 111 (28), 99 (70), 85 (100).	+4.1	120/0.4
R,R,R,R	Same as above	Same as above	Same as above	−4.1	Same as above
S,S,S,R	0.84 (6 H, d, J=6.6 Hz), 0.89 (3 H, d, J=6.9 Hz), 0.89 (3 H, t, J=6.6 Hz), 0.92–1.56 (18 H, m), 1.15 (3 H, d, J=6.3 Hz), 3.70 (1 H, dq, J=4.3, 6.3 Hz).	14.1, 14.2, 20.2, 20.3 (2 C), 23.1, 24.6, 29.2, 30.0 (2 C), 32.9, 36.6, 37.1, 39.8, 45.3, 71.5.	296 (8) $(M+C_3H_4N)^+$, 169 (6), 155 (12), 141 (17), 127 (23), 113 (40), 99 (43), 85 (100).	−15.6	110/0.4
R,R,R,S	Same as above	Same as above	Same as above	+16.6	Same as above
S,S,R,R	0.82 (6 H, d, J=6.6 Hz), 0.89 (3 H, d, J=6.9 Hz), 0.89 (3 H, t, 6.6 Hz), 0.95–1.51 (18 H, m), 1.15 (3 H, d, J=6.3 Hz), 3.71 (1 H, dq, J=4.3, 6.3 Hz).	14.2 (2 C), 19.5, 19.6, 20.3, 23.0, 24.8, 29.3, 30.0, 30.1, 33.0, 37.7, 38.3, 39.8, 44.8, 71.4.	296 (1) $(M+C_3H_4N)^+$, 169 (7), 155 (15), 141 (23), 127 (27), 113 (57), 99 (74), 85 (100).	−35.8	130/0.5
R,R,S,S	Same as above	Same as above	Same as above	+35.7	Same as above
S,R,R,R	0.82 (6 H, d, J=6.6 Hz), 0.87 (3 H, d, J=6.9 Hz), 0.88 (3 H, t, J=6.9 Hz), 0.95–1.55 (18 H, m), 1.12 (3 H, d, J=6.3 Hz), 3.66 (1 H, quint, J=6.3 Hz).	14.1, 14.5, 19.3, 19.4, 19.5, 23.0, 24.6, 29.3, 30.0 (2 C), 32.8, 37.7, 38.2, 40.1, 45.0, 71.8.	296 (1) $(M+C_3H_4N)^+$, 169 (12), 155 (25), 141 (35), 127 (55), 113 (52), 99 (80), 85 (100).	+2.2	110/0.4
R,S,S,S	Same as above	Same as above	Same as above	−2.1	Same as above
S,R,S,S	0.82 (3 H, d, J=6.6 Hz), 0.82 (3 H, d, J=6.3 Hz), 0.87 (3 H, d, J=6.9 Hz), 0.89 (3 H, t, J=6.9 Hz), 0.91–1.58 (18 H, m), 1.12 (3 H, d, J=6.3 Hz), 3.66 (1 H, quint, J=6.3 Hz).	14.2, 14.6, 19.3, 19.5, 19.6, 23.0, 24.7, 29.3, 30.1 (2 C), 32.9, 37.7, 38.3, 40.1, 44.8, 71.8.	296 (8) $(M+C_3H_4N)^+$, 169 (5), 155 (11), 141 (18), 127 (28), 113 (33), 99 (65), 85 (100).	+43.2	115/0.4
R,S,R,R	Same as above	Same as above	Same as above	−42.3	Same as above
S,R,S,R	0.84 (6 H, d, J=6.6 Hz), 0.87 (3 H, d, J=6.9 Hz), 0.87–1.57 (21 H, m), 1.12 (3 H, d, J=6.3 Hz), 3.66 (1 H, quint, J=6.3 Hz).	14.2, 14.6, 19.3, 20.3 (2 C), 23.1, 24.5, 29.2, 30.0 (2 C), 33.0, 36.5, 37.2, 40.1, 45.1, 71.8.	296 (12) $(M+C_3H_4N)^+$, 169 (3), 155 (12), 141 (22), 127 (22), 113 (38), 99 (82), 85 (100).	+18.0	112/0.4
R,S,R,S	Same as above	Same as above	Same as above	−19.2	Same as above
S,R,R,S	0.84 (6 H, d, J=6.6 Hz), 0.87 (3 H, d, J=6.6 Hz), 0.87–1.55 (21 H, m), 1.13 (3 H, d, J=6.3 Hz), 3.66 (1 H, quint, J=6.3 Hz).	14.2, 14.5, 19.4, 20.2, 20.3, 23.1, 24.5, 29.2, 30.0 (2 C), 32.8, 36.6, 37.1, 40.0, 45.3, 71.8.	296 (3) $(M+C_3H_4N)^+$, 169 (8), 155 (22), 141 (44), 127 (46), 113 (45), 99 (80), 85 (100).	+23.3	110/0.4
R,S,S,R	Same as above	Same as above	Same as above	−23.3	Same as above
S,S,R,S	0.84 (6 H, d, J=6.6 Hz), 0.89 (3 H, d, J=6.6 Hz), 0.89 (3 H, t, J=6.6 Hz), 0.89–1.55 (18 H, m), 1.15 (3 H, d, J=6.3 Hz), 3.71 (1 H, dq, J=4.3, 6.3 Hz).	14.2 (2 C), 20.3 (3 C), 23.1, 24.6, 29.2, 30.0 (2 C), 33.0, 36.5, 37.2, 39.8, 45.1, 71.4.	296 (1) $(M+C_3H_4N)^+$, 169 (7), 155 (18), 141 (28), 127 (38), 113 (65), 99 (68), 85 (100).	−14.2	110/0.4
R,R,S,R	Same as above	Same as above	Same as above	+15.7	Same as above

48–58% yield and chemical purities >99% by GC except for the *RSSS*-isomer which was obtained in 96% chemical purity. The diastereomeric purity of the individual isomers of *threo*-**5H** were confirmed to be >99.5% by GC analysis. (HRMS, EI): $(M-H_2O)^+$ 224.2508. $C_{16}H_{32}$ requires 224.2504 for (2*S*,3*R*,7*R*,9*S*)-3,7,9-trimethyltridecan-2-ol; for all other spectral and physical data see Table 2.

The sixteen stereoisomerically pure acetates of 3,7,9-trimethyltridecan-2-ols were prepared as above for

Table 3. Spectral and physical data for the stereoisomers of 3,7,9-trimethyl-2-tridecyl acetate.

Isomer of **5**Ac	^{1}H NMR (270 MHz)	^{13}C NMR (67.8 MHz)	MS CI; CH_3CN
S,S,S,S	0.81 (6 H, d, *J*=6.6 Hz), 0.89 (3 H, t, *J*=6.6 Hz), 0.89 (3 H, d, *J*=6.9 Hz), 0.93–1.63 (17 H, m), 1.16 (3 H, d, *J*=6.3 Hz), 2.03 (3 H, s), 4.83 (1 H, dq, *J*=5.0, 6.3 Hz).	14.1, 14.8, 16.9, 19.4, 19.5, 21.3, 23.0, 24.4, 29.3, 30.0 (2 C), 32.6, 37.5, 37.7, 38.1, 44.9, 74.1, 170.8.	169 (17), 155 (45), 141 (52), 127 (55), 113 (65), 99 (94), 85 (100).
R,R,R,R	Same as above	Same as above	Same as above
S,S,S,R	0.84 (6 H, d, *J*=6.6 Hz), 0.89 (3 H, t, *J*=6.3 Hz), 0.89 (3 H, d, *J*=6.6 Hz), 0.91–1.64 (17 H, m), 1.16 (3 H, d, *J*=6.3 Hz), 2.03 (3 H, s), 4.82 (1 H, dq, *J*=5.0, 6.3 Hz).	14.2, 14.8, 16.9, 20.2, 20.3, 21.3, 23.1, 24.3, 29.2, 30.0 (2 C), 32.6, 36.6, 37.0, 37.6, 45.2, 74.2, 170.8.	338 (5) $(M+C_3H_4N)^+$, 169 (8), 155 (30), 141 (48), 127 (52), 113 (74), 99 (72), 85 (100).
R,R,R,S	Same as above	Same as above	Same as above
S,S,R,R	0.82 (6 H, d, *J*=6.3 Hz), 0.89 (3 H, t, *J*=6.6 Hz), 0.90 (3 H, d, *J*=6.9 Hz), 0.91–1.63 (17 H, m), 1.16 (3 H, d, *J*=6.3 Hz), 2.03 (3 H, s), 4.83 (1 H, dq, *J*=5.0, 6.3 Hz).	14.2, 14.8, 16.9, 19.5 (2 C), 21.3, 23.0, 24.5, 29.3, 30.0 (2 C), 32.7, 37.6, 37.7, 38.2, 44.8, 74.1, 170.8.	338 (2) $(M+C_3H_4N)^+$, 169 (13), 155 (18), 141 (47), 127 (47), 113 (48), 99 (87), 85 (100).
R,R,S,S	Same as above	Same as above	Same as above
S,R,R,R	0.81 (6 H, d, *J*=6.6 Hz), 0.88 (3 H, d, *J*=6.9 Hz), 0.89 (3 H, t, *J*=5.9 Hz), 0.94–1.55 (16 H, m), 1.13 (3 H, d, *J*=6.6 Hz), 1.59–1.72 (1 H, m), 2.03 (3 H, s), 4.80 (1 H, quint, *J*=6.6 Hz).	14.1, 14.6, 15.9, 19.4, 19.5, 21.4, 23.0, 24.5, 29.3, 30.0 (2 C), 32.8, 37.2, 37.6, 38.1, 44.9, 74.4, 170.8.	338 (3) $(M+C_3H_4N)^+$, 169 (8), 155 (20), 141 (31), 127 (45), 113 (65), 99 (68), 85 (100).
R,S,S,S	Same as above	Same as above	Same as above
S,R,S,S	0.81 (3 H, d, *J*=6.6 Hz), 0.82 (3 H, d, *J*=6.6 Hz), 0.87–0.90 (3 H, m), 0.88 (3 H, d, *J*=6.9 Hz), 0.91–1.52 (16 H, m), 1.13 (3 H, d, *J*=6.3 Hz), 1.58–1.72 (1 H, m), 2.03 (3 H, s), 4.81 (1 H, quint, *J*=6.3 Hz).	14.1, 14.6, 15.8, 19.5, 19.6, 21.4, 23.0, 24.5, 29.3, 30.0 (2 C), 32.9, 37.2, 37.7, 38.2, 44.8, 74.3, 170.8.	338 (5) $(M+C_3H_4N)^+$, 169 (5), 155 (15), 141 (25), 127 (34), 113 (52), 99 (42), 85 (100).
R,S,R,R	Same as above	Same as above	Same as above
S,R,S,R	0.83 (6 H, d, *J*=6.3 Hz), 0.88 (3 H, d, *J*=6.6 Hz), 0.88–1.53 (19 H, m), 1.13 (3 H, d, *J*=6.6 Hz), 1.58–1.72 (1 H, m), 2.03 (3 H, s), 4.81 (1 H, quint, *J*=6.6 Hz).	14.2, 14.6, 15.8, 20.3 (2 C), 21.4, 23.1, 24.4, 29.2, 30.0 (2 C), 33.0, 36.5, 37.1, 37.3, 45.1, 74.3, 170.7.	338 (8) $(M+C_3H_4N)^+$, 169 (5), 155 (13), 141 (32), 127 (32), 113 (45), 99 (73), 85 (100).
R,S,R,S	Same as above	Same as above	Same as above
S,R,R,S	0.84 (6 H, d, *J*=6.6 Hz), 0.88 (3 H, d, *J*=6.6 Hz), 0.88–1.39 (17 H, m), 1.14 (3 H, d, *J*=6.3 Hz), 1.40–1.52 (2 H, m), 1.59–1.71 (1 H, m), 2.03 (3 H, s), 4.80 (1 H, quint, *J*=6.3 Hz).	14.2, 14.5, 15.9, 20.2, 20.3, 21.4, 23.1, 24.3, 29.2, 29.9, 30.0, 32.8, 36.6, 37.0, 37.2, 45.2, 74.4, 170.8.	338 (4) $(M+C_3H_4N)^+$, 169 (5), 155 (25), 141 (28), 127 (47), 113 (60), 99 (56), 85 (100).
R,S,S,R	Same as above	Same as above	Same as above
S,S,R,S	0.84 (6 H, d, *J*=6.6 Hz), 0.89 (3 H, t, *J*=6.6 Hz), 0.90 (3 H, d, *J*=6.6 Hz), 0.91–1.63 (17 H, m), 1.16 (3 H, d, *J*=6.6 Hz), 2.03 (3 H, s), 4.83 (1 H, dq, *J*=5.0, 6.6 Hz).	14.2, 14.8, 16.9, 20.3 (2 C), 21.3, 23.1, 24.3, 29.2, 30.0 (2 C), 32.8, 36.5, 37.1, 37.6, 45.1, 74.1, 170.8.	338 (3) $(M+C_3H_4N)^+$, 169 (12), 155 (33), 141 (55), 127 (43), 113 (60), 99 (75), 85 (100).
R,R,S,R	Same as above	Same as above	Same as above

3,7,9-trimethyl-2-tridecyl acetate (**5**Ac). (HRMS, EI): $(M-CH_3CO_2H)^+$ 224.2504. $C_{16}H_{32}$ requires 224.2504 for (2*S*,3*R*,7*R*,9*S*)-3,7,9-trimethyl-2-tridecyl acetate; for all other spectral and physical data see Table 3.

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