Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 60 (2004) 10659–10669

Diastereoselective addition of organozinc reagents to 2-alkyl-3-(arylsulfanyl)propanals

Michael Larsson, Elodie Galandrin and Hans-Erik Högberg*

Department of Natural and Environmental Sciences, Mid Sweden University, S-851 70 Sundsvall, Sweden

Received 4 June 2004; revised 12 August 2004; accepted 2 September 2004

Available online 1 October 2004

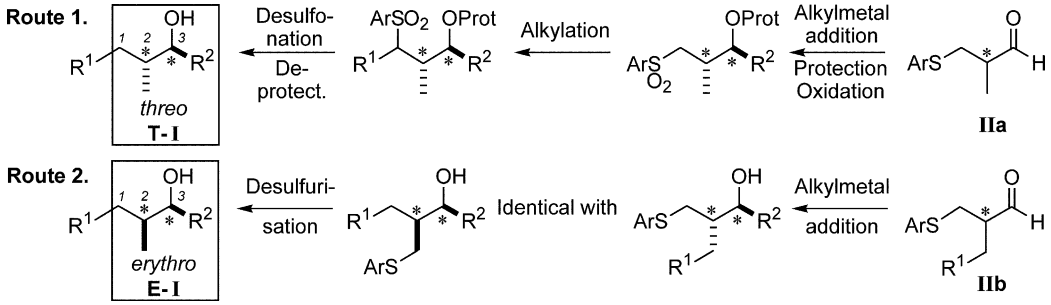
Abstract—The preparation of compounds incorporating the 3-hydroxy-2-methyl-1-alkyl moiety of high diastereomeric purity is described. Such compounds can serve as potential building blocks for the preparation of several kinds of natural products. Diastereoselective synthesis of two potential pine sawfly pheromone components, one the pure racemic *threo*-isomer of 3-methylpentadecan-2-ol and the other the racemic *erythro*-isomer of 3-methyltridecan-2-ol are described. The diastereoselective addition of R_2Zn (R = Me, Et and *n*-Bu) to several 2-alkyl-3-(arylsulfanyl)propanals in the presence of a Lewis acid and CH_2Cl_2 as solvent was studied. An excellent diastereomeric ratio (95/5 *anti*-Cram/Cram) was obtained with 2-[(phenylsulfanyl)methyl]pentanal, 2-[(phenylsulfanyl)methyl]decanal and 2-[(phenylsulfanyl)-methyl]dodecanal and Me_2Zn in the presence of $TiCl_4$.

1. Introduction

A number of natural products, for example, pheromones[1] and antibiotics[2] contain the 3-hydroxy-2-methyl-1-alkyl moiety **I** (either as the *threo*- or *erythro*-form, **T-I** and **E-I**, respectively; Scheme 1). Various approaches are available for the diastereo- and enantioselective synthesis of compounds containing such moieties.[1–3]

The nucleophilic addition of an organometallic reagent to a carbonyl group is one of the most powerful and reliable methods for carbon–carbon bond formation known in organic synthesis. When the carbonyl compound has diastereotopic faces, diastereoselective addition reactions are possible. They usually proceed according to Cram's rule giving the so-called Cram-product [called *erythro*-product (**E**) in this paper].[4] However, for carbonyl compounds incorporating a suitably placed heteroatom (for example O, N or S in the α-, β-, or γ-position), chelation of the organometallic reagent with the carbonyl oxygen and the heteroatom can occur. In such cases, the addition usually proceeds according to Cram's cyclic model, which leads to the so-called *anti*-Cram-product [*threo*-product (**T**)].[4,5]

We are interested in the development of highly stereoselective, preparative methods for a class of natural products



Scheme 1. Generalised synthetic routes to compounds of type **I** containing the stereoisomerically pure 3-hydroxy-2-methyl-1-alkyl moiety. For both routes 1 and 2: R^1 = alkyl group; R^2 = Me, Et or *n*-Bu. *: Marks stereogenic centres (relative or absolute configurations).

Keywords: Diastereoselective additions; Dimethylzinc; Titanium tetrachloride; Chelation; Pheromones.
* Corresponding author. Tel.: +46 60 148704; fax: +46 60 148802; e-mail: hans-erik.hogberg@kep.mh.se

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.09.005

Table 1. Diastereomeric ratios (dr) obtained when reacting Me_2Zn (2 M in toluene, 1.6 equiv) with aldehydes **1a–g** (1 equiv) mixed with added $TiCl_4$ (1 equiv) at −78; +10 °C in CH_2Cl_2[a]

Entry	Aldehyde	R^1	Dr[b] *threo/erythro*	Product	Yield (%)[c]
1	**1a**	Ph	95/05	**2a**	90
2	**1b**	*p*-Tolyl	94/06	**2b**	75
3	**1c**	*p*-ClC_6H_4	90/10	**2c**	32[d]
4	**1d**	*p*-$MeOC_6H_4$	80/20	**2d**	33[d]
5	**1e**	*o*-$MeOC_6H_4$	30/70	**2e**	43[e]
6	**1f**	*t*-Bu	81/19	**2f**	29[e]
7	**1g**	*n*-Bu	94/06	**2g**	44[e]

[a] A small amount (~4 vol%) of toluene from the reagent, the volume of the solvent was 8 mL/0.47 mmol of **1**.
[b] Diastereomeric ratio was determined by GC analysis on the butyrate, derived from the products **2a–g** and/or by ^1H NMR spectroscopy.
[c] Isolated yields after reactions to full conversion.
[d] Product recovery incomplete.
[e] Low yield due to formation of by-products.

containing the 3-hydroxy-2-methyl-1-alkyl moiety **I** (Scheme 1, R^1=methyl branched alkyl group or alkyl group, R^2=Me), namely the pine sawfly pheromones.[1] If an efficient and highly diastereoselective addition of an alkyl moiety to chiral aldehydes of type **II** could be accomplished, we would have easy access to useful synthons for further transformation into targets of type **I** (Scheme 1).

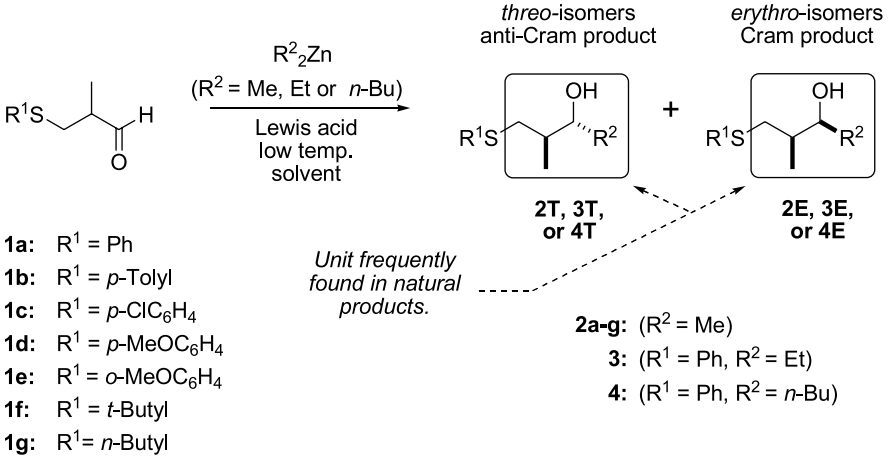
We have earlier screened the reactions of various methylmetal reagents with an aldehyde having a sulfur atom in the β-position, with the sulfur and the carbonyl oxygen serving as chelating centres.[6] Thus, addition of dimethylzinc to 2-methyl-3-(phenylsulfanyl)propanal (**1a**) in the presence of $TiCl_4$ furnished 3-methyl-4-(phenylsulfanyl)butan-2-ol (**2a**) in good yield and high diastereomeric ratio (90%, 95/5 *anti*-Cram/Cram, see entry 1, Table 1).[6] We have also shown that it is possible to prepare stereoisomerically pure 3-methyl-4-(phenylsulfanyl)butan-2-ol (**2a**) from dimethylzinc addition to enantiopure 2-methyl-3-(phenylsufanyl)propanal (**1a**) followed by purification by enzyme catalysed acylation.[7]

In this paper, we describe our efforts to improve the diastereoselectivity in this type of reaction. We have also studied how the diastereoselectivities of additions of other alkylzinc derivatives compare with those of dimethylzinc. Another objective was to see if it was possible to diastereoselectively prepare not only derivatives of type **T-I** via the general Route 1 (Scheme 1) but also **E-I**-ones. In the latter case an alternative sequence of reactions was envisaged (Route 2, Scheme 1).

2. Results and discussion

We first varied the substituents on the sulfur atom in 2-methylpropanals of type **IIa** (Scheme 1) and studied how this affected the diastereoselectivity in methylmetal additions. Therefore, a series of aldehydes **1** were prepared and reacted with dialkylzincs in the presence of various Lewis acids (Scheme 2). Aldehydes **1a–e** with various aryl groups at sulfur and aldehydes **1f** and **1g** with a *tert*-butyl and a *n*-butyl group, respectively, at sulfur were chosen as substrates representing different electronic and steric effects.

The results of the reactions of the arylsulfanylaldehydes **1a–e** with dimethylzinc catalysed by $TiCl_4$ (Table 1) revealed, that an electron withdrawing substituent as well as a donating one in the arylsulfanyl moiety, led to decreased yields and diastereoselectivities (compare entries 3 and 4). The steric effect, however, is more evident (compare entries 6 and 7; products **2f** with a bulky *tert*-butyl group vs **2g** with an *n*-butyl group; dr 81/19 vs 94/06). A probable explanation is that the bulky *tert*-butyl group in **1f** partially hinders chelation between the bulky Lewis acid ($TiCl_4$), sulfur and the carbonyl oxygen. The remarkably



Scheme 2. Diastereoselective addition of R_2Zn (R=Me, Et or *n*-Bu) to racemic aldehydes **1a–g**.

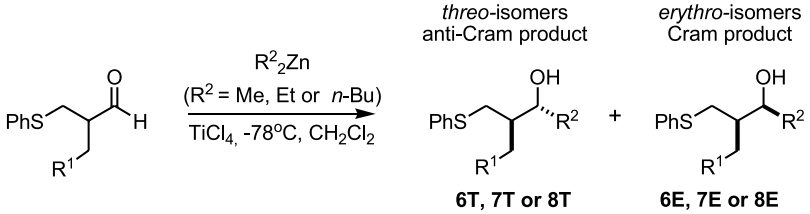
high, and reversed diastereoselectivity observed for the reaction with substrate **1e** to give product **2e** (compare entry 5 with entry 4) with the *erythro* diastereomer in excess (*threo*/*erythro*; 30/70) could probably be explained by assuming that the Lewis acid preferred chelation between oxygen in the 2-methoxyphenyl group and sulfur rather than between sulfur and the carbonyl oxygen. This would lead to an extremely bulky substituent in the aldehyde substrate, which would favour the Cram-product, that is, the *erythro*-one, in excess. In conclusion, when aldehydes **1b–g** were used as substrates, neither the diastereomeric ratios nor the yields in $TiCl_4$-catalysed dimethylzinc additions could be improved by variation of the substituents on sulfur.

Thus, addition of Me_2Zn to 2-methyl-3-(phenylsulfanyl)-propanal (**1a**) seems to be the most efficient way to a synthetic equivalent for the synthon **2aT** (*threo*-configuration, see Scheme 2) leading to targets of type **T-I** (Route 1, Scheme 1). However, as pointed out above, many natural products also contain the stereoisomerically pure 3-hydroxy-2-methyl-1-alkyl moiety having *erythro*-configuration (**E-I**, shown in Scheme 1, where R^2=Me). Therefore, we were interested to see if we were able to achieve similar diastereoselectivities in methylmetal additions to appropriate aldehydes of type **IIb** (Scheme 1), but in this case furnishing ultimately the desired *erythro*-isomers, **E-I**.

Our previous work shows, that addition of various methylmetal reagents to 2-methyl-3-(phenylsulfanyl)propanal (**1a**), in some cases in the presence of Lewis acids, actually furnish the Cram-products (*erythro*-products), albeit in poor diastereoselectivities.[6] Therefore, we decided to develop an alternative sequence of reactions for achieving the desired products of type **E-I** (Route 2, Scheme 1). Replacement of the methyl group in 2-methyl-3-(phenylsulfanyl)propanal (**1a**, Scheme 2) with an alkyl chain, either straight or methyl-branched, leads to aldehydes of type **5** (Scheme 3). Provided that the *anti*-Cram addition of a methylmetal reagent (e.g., Me_2Zn) to **5**, in the presence of $TiCl_4$, proceeds with a high diastereoselectivity, we shall have easy access to synthons of type **6T**. Removal of the phenylsulfanyl group will lead to a methyl group and will furnish the desired target of type **E-I** (Route 2, Scheme 1).

To investigate such an approach, we prepared three aldehydes of type **5** (Scheme 3) with increasing length of the alkyl chain attached to position 2, one with a moderately long chain (**5a**) and the other two with relatively long chains (**5b** and **5c**). The latter was used in one of the pheromone syntheses described below). First, a crossed aldol condensation of a straight chain aldehyde (pentanal, decanal, or dodecanal) with formaldehyde furnished the corresponding 2-alkylpropenals. Each of them was reacted with thiophenol in a Michael addition reaction. Exposure of the resulting aldehydes **5a–c** to Me_2Zn in the presence of $TiCl_4$ furnished the expected products **6a–c** in good yields and in very good diastereoselectivities (95/5; see entries 1–3, Table 2) in favour of the *threo*-products **6T** (*anti*-Cram-product), independent of the chain length of R^1. The diastereoselectivities observed with aldehydes **1a**, **5a–c** and Me_2Zn are very similar, indicating that exchanging the 2-methyl with longer alkyl groups has limited influence on the reaction. Desulfurisation of the products **6T** by treatment with Raney-Nickel yielded the corresponding compounds of type **E-I** (Route 2, Scheme 1, R^2=Me) with a preserved diastereomeric ratio of 95/5 (*erythro*/*threo*). In order to demonstrate the importance of using a combination of Me_2Zn and $TiCl_4$ in these reactions, MeLi was added in the absence of Lewis acid (entry 4, Table 2). This gave a poor *threo*/*erythro*-diastereoselectivity of 60/40 (*anti*-Cram/Cram). Furthermore, an experiment was performed in which Me_2Zn was added to 2-methylundecanal, in the presence of $TiCl_4$. This yielded a selectivity of 58/42 (*anti*-Cram/Cram). This confirmed the importance of the presence of a good chelating group/atom in the proximity of the electrophilic carbonyl group.

Because the additions of Me_2Zn to the aldehydes **1a**[6] and **5a–c** provided the desired products **2a** and **6a–c** in very good diastereoselectivities, we were interested in exploring if an equally efficient diastereoselective addition of either an ethyl or a *n*-butyl moiety to these aldehydes would be possible (Schemes 2 and 3).



dr: from 81/19 up to 95/5 (T/E)

5a: $R^1 = C_2H_5$
5b: $R^1 = n\text{-}C_7H_{15}$
5c: $R^1 = n\text{-}C_9H_{19}$

6a: $R^1 = C_2H_5$, R^2 = Me
7a: $R^1 = C_2H_5$, R^2 = Et
8a: $R^1 = C_2H_5$, $R^2 = n$-Bu
6b: $R^1 = n\text{-}C_7H_{15}$, R^2 = Me
7b: $R^1 = n\text{-}C_7H_{15}$, R^2 = Et
8b: $R^1 = n\text{-}C_7H_{15}$, $R^2 = n$-Bu
6c: $R^1 = n\text{-}C_9H_{19}$, R^2 = Me

Scheme 3. Diastereoselective addition of R_2Zn (R=Me, Et or *n*-Bu) to racemic aldehydes **5a–c**.

Table 2. Diastereomeric ratios (dr) obtained when reacting alkylmetal reagents (1.5 equiv) with aldehydes **5a–5c** (1 equiv; 0.56 mmol) mixed with added $TiCl_4$ (1.1 equiv) at −78; +10 °C in CH_2Cl_2[a]

Entry[b]	Substrate	Reagent[c]	Major product	R^1	R^2	Dr[d] *threo/erythro*
1	**5a**	Me_2Zn	**6aT**	C_2H_5	Me	95/05
2	**5b**	Me_2Zn	**6bT**	n-C_7H_{15}	Me	95/05
3	**5c**	Me_2Zn	**6cT**	n-C_9H_{19}	Me	95/05
4	**5a**	MeLi[e]	**6aT**	C_2H_5	Me	60/40

[a] The volume of the solvent was 8 mL/0.56 mmol of **5**.
[b] Yields were in range of 80–95%.
[c] The solvents from the reagents are Me_2Zn (2 M in toluene) and MeLi (1.3 M in Et_2O). The solvent from the organometallic reagent constitute about 10 vol% of the reaction media.
[d] Diastereomeric ratio was determined by GC analysis on the trifluoroacetate, derived from the products **6a–6c** and/or by ^{1}H NMR spectroscopy.
[e] No Lewis acid present, Et_2O as solvent.

Whereas Me_2Zn failed to react with the aldehyde **1a** in the absence of Lewis acid,[6] the more reactive (see references cited in Ref. 6) Et_2Zn or Bu_2Zn did react with aldehyde **1a** (conversion <5%) in the absence of Lewis acid. Traces of the desired products **3** or **4**, respectively, were formed [*threo*-products, (*anti*-Cram) in excess]. When Et_2Zn and Bu_2Zn were added to the aldehyde **1a** with $TiCl_4$-catalysis as used for the addition of Me_2Zn, the *anti*-Cram selectivities obtained were lower (65/35; *anti*-Cram/Cram; **3T/3E** and 77/23; *anti*-Cram/Cram; **4T/4E**, respectively, entries 1 and 2, Table 3) than that with Me_2Zn.

A possible explanation for these results is that the $TiCl_4$-chelated substrate underwent a certain degree of alkylzinc to alkyltitanium exchange prior to the alkyl addition to the aldehyde. This should result in some intramolecular addition[8] (e.g., 1,3-intramolecular migration) that would result in a lower diastereoselectivity. In order to see if the selectivity in the addition could be increased, the effects of several variables were further studied. The effect of temperature on the outcome of the reaction was almost negligible, addition of Et_2Zn at −100 °C up to −23 °C gave diastereomeric ratios ranging from 65/35 to 68/32 (*threo/erythro*). Varying the added amount of Bu_2Zn (from 1 up to 10 equiv) had no significant effect [dr from 74/26 to 77/23 (*threo/erythro*)]. Increasing the concentration of $TiCl_4$, from 0.5 to 2.4 equiv (compare entries 2–4, 13, and 14, Table 3), changed the diastereoselectivity from 55/45 (0.5 equiv) to 77/23 (1.2 equiv) (*threo/erythro*). Variations of the concentrations of substrates and reactants did not influence the selectivity much. However, it was clear that the nucleophile should not be added neat to the reaction (compare entries 1, 9, 12 and 15, Table 3). The choice of solvent was important. Reactions in ether solvents, for example, THF or Et_2O, gave a low diastereoselectivity, whereas those in dichloromethane gave the highest one (compare entries 2, 5, 6, 10 and 11, Table 3). Replacing the appropriate dialkylzinc with *n*-BuLi, EtMgCl or BuZnBr in the reaction of the aldehyde **1a** in the presence of $TiCl_4$, resulted in poor diastereoselectivity probably due to

Table 3. Diastereomeric ratios (dr) obtained when reacting alkylmetal reagents with aldehyde **1a** (1 equiv; 0.56 mmol) mixed with added $TiCl_4$ at −78; +10 °C in CH_2Cl_2[a]

Entry[b]	$TiCl_4$ (equiv)	Reagent[c] (equiv)	Conv. (%)	Product	Dr[d] *threo/erythro*
1	(1.2)	Et_2Zn (1.6)	85	**3**	65/35
2	(1.2)	Bu_2Zn (1.6)	90	**4**	77/23
3	(2.4)	Bu_2Zn (1.6)	27	**4**	70/30
4	(0.8)	Bu_2Zn (1.6)	100	**4**	75/25
5	(1.2)[e]	Bu_2Zn (1.6)	90	**4**	57/43
6	(1.2)[f]	Bu_2Zn (1.6)	82	**4**	52/48
7	(1.2)	EtMgCl (1.6)	54	**3**	52/48
8	(1.2)	*n*-BuLi (1.6)	76	**4**	61/39
9	(1.2)	Et_2Zn, (1.6), neat	40	**3**	52/48
10	(1.2)[g]	Et_2Zn (1.6)	94	**3**	62/38
11	(1.2)[h]	Et_2Zn (1.6)	99	**3**	64/36
12	(1.2)[i]	Et_2Zn (1.6)	100	**3**	67/33
13	(0.5)[j]	Bu_2Zn (1.6)	70	**4**	55/45
14	(1.0)	Bu_2Zn (1.0)	84	**4**	77/23
15	(1.2)	Et_2Zn (1.6)[k]	90	**3**	67/33
16	(1.2)	BuZnBr (1.6)	66	**4**	53/47

[a] The volume of the solvent was 8 mL/0.56 mmol of **1a**, unless otherwise stated.
[b] Yields were in range of 15–90%, according to GC.
[c] The solvents from Et_2Zn (1 M) and *n*-BuLi (1.6 M) are *n*-hexane, Bu_2Zn (1 M in *n*-heptane), EtMgCl (2 M) and BuZnBr (0.5 M) in THF. The solvent from the organometallic reagent constitute about 10 vol% of the reaction media.
[d] Diastereomeric ratio was determined by GC analysis on the alcohol products **3** and **4** and/or by ^{1}H NMR spectroscopy.
[e] THF as solvent.
[f] Et_2O as solvent.
[g] CH_2Cl_2/*n*-hexane as solvent (1:1).
[h] CH_2Cl_2/benzene as solvent (1:1).
[i] Double amount of solvent (16 mL).
[j] Double amount of **1a**, due to difficulties in measuring the volume of $TiCl_4$, 20 mL of solvent.
[k] Molarity of 0.2 M in CH_2Cl_2/*n*-hexane; 4/1.

Table 4. Diastereomeric ratios (dr) obtained when reacting Bu_2Zn (1 M in *n*-heptane, 1.6 equiv) with aldehyde **1a** (1 equiv) mixed with various Lewis acids at −78 °C; +10 °C in CH_2Cl_2

Entry	Lewis acid (equiv)	Conv. (%)	Dr[a] *threo/erythro*	Product
1	Ti(O-*i*-Pr)$_4$ (1.1)	0	—	—
2	TiCl(O-*i*-Pr)$_3$ (1.1)	55	55/45	**4**
3	$BF_3{\cdot}OEt_2$ (1.1)	91	46/54	**4**
4	$SnCl_4$ (1.1)	0	—	—
5	LiCl (1.1)	0	—	—
6	$ZrCl_4$ (1.2)	96	46/54	**4**
7	$CeCl_3$ (1.2)	0	—	—
8	Cp_2HfCl_2 (1.2)	95	40/60	**4**
9	$LaCl_3$ (1.2)	0	—	—
10	Cp_2TiCl_2 (1.2)	100	35/65	**4**
11	Cp_2ZrCl_2 (1.2)	89	41/59	**4**

[a] Diastereomeric ratio was determined by GC analysis and/or by ^{1}H NMR spectroscopy on the alcohol product **4**.

decomposition of the cyclic chelate (compare entries 1, 7 and 2, 8 and 16, Table 3). Albeit the yield of the desired product **3** was very low, the best selectivity was obtained when $RTiCl_3$ was added to aldehyde **1a** furnishing **3** in diasteromeric ratios up to 90/10 (*threo/erythro*) along with large amounts of by-products from reduction and elimination.

The results described above indicated that, with Et_2Zn and Bu_2Zn in the presence of the substrate and $TiCl_4$, high diastereoselectivities are not easily obtained. However, chelation seems to have some importance for the outcome of these reactions (compare entries 1 and 2 with entries 7 and 8, respectively).

The influence of the nature of the Lewis acid was also studied. Thus, additions of Bu_2Zn to aldehyde **1a** in the presence of various Lewis acids (Table 4) gave no improvements in terms of the diastereoselectivity or yield. It is worth noting, though, that most of the Lewis acids investigated furnished a slight excess of the Cram product (*erythro*-isomer of **4**). Probably the reaction proceeded via an open chain intermediate resulting in a poor selectivity. R_2Zn (R = Et and *n*-Bu) was also reacted with the aldehydes **5a–b** (Table 5). The diastereoselectivities were substantially increased with these substrates, from a selectivity of 65/35 (Et_2Zn) and 77/23 (Bu_2Zn) (products **3** and **4**, Scheme 2, entries 1 and 2, Table 3) to 87/13 (Et_2Zn) and 87/13 (Bu_2Zn) (products **7a** and **8a**, Scheme 3, entries 1 and 2, Table 5). This indicates that, apart from the effects of chelation, sterical interaction within the substrate also plays an important role in the outcome of the addition.

Finally, using the methods previously described in this and our previous paper[6] as starting points, we have synthesised two compounds, ($2R^*$,$3S^*$)-3-methylpentadecan-2-ol, (**11**, *rac-threo*-isomer), and ($2R^*$,$3R^*$)-3-methyltridecan-2-ol, (**12**, *rac-erythro*-isomer) (Scheme 4). The former is a pheromone component of *Gilpinia socia* and *G. frutetorum*.[9] Both the racemates of **11** and the corresponding *erythro*-isomer have been resolved efficiently by esterification with vinyl acetate or propionate mediated by a lipase from *Pseudomonas* sp. (Amano PS).[10]

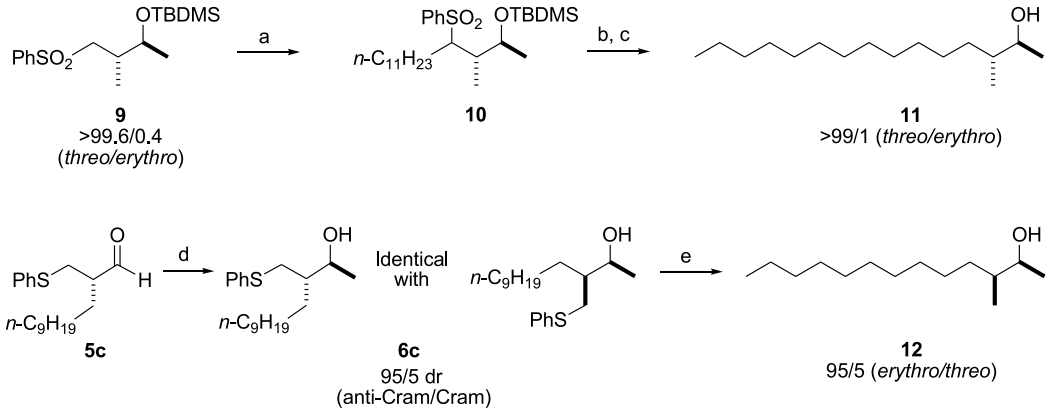
The first synthetic target **11** with *threo*-stereochemistry was prepared from compound **2a**. Oxidation of this to the sulfone followed by recrystallisation of the corresponding 3,5-dinitrobenzoate, hydrolysis and subsequent silylation gave *rac-tert*-butyl-[1,2-dimethyl-3-(phenylsulfonyl)propoxy]-dimethyl-silane, (**9**,[6] *threo/erythro* > 99.6/0.4, Scheme 4). The carbanion of **9** was prepared as earlier reported by us.[6] Alkylation of this with 1-iodoundecane yielded compound **10**. The phenylsulfone moiety and the protective group were removed by treatment with Raney-Ni in 1,4-dioxane under reflux followed by HCl in methanol, to give the desired ($2R^*$,$3S^*$)-3-methylpentadecan-2-ol (**11**, *threo/erythro*, >99/1).

The second synthetic target **12** with *erythro*-stereochemistry was prepared from 3-[(phenylsulfanyl)-methyl]tridecan-2-ol, (**6c**, Scheme 3). Thus, treatment of this compound with Raney-Ni in EtOH at room temperature furnished ($2R^*$,$3R^*$)-3-methyltridecan-2-ol, (**12**, *erythro/threo*, 95/5).

Table 5. Diastereomeric ratios (dr) obtained when reacting alkylmetal reagents (1.5 equiv) with aldehydes **5a–b** (1 equiv; 0.56 mmol) mixed with added $TiCl_4$ (1.1 equiv) at −78; +10 °C in CH_2Cl_2[a]

Entry[b]	Substrate	Reagent[c] (equiv)	Major product	R^1	R^2	Dr[d] *threo/erythro*
1	**5a**	Et_2Zn	**7aT**	C_2H_5	Et	87/13
2	**5a**	Bu_2Zn	**8aT**	C_2H_5	*n*-Bu	87/13
3	**5b**	Et_2Zn	**7bT**	*n*-C_7H_{15}	Et	86/14
4	**5b**	Bu_2Zn	**8bT**	*n*-C_7H_{15}	*n*-Bu	81/19

[a] The volume of the solvent was 8 mL/0.56 mmol of **5**.
[b] Yields were in range of 55–85%.
[c] The solvents from the reagents are Et_2Zn (1 M in *n*-hexane) and Bu_2Zn (1 M in *n*-heptane). The solvent from the organometallic reagent constitute about 10 vol% of the reaction media.
[d] Diastereomeric ratio was determined by GC analysis on the trifluoroacetate, derived from the products **7a–8b** and/or by ^{1}H NMR spectroscopy.



Scheme 4. Synthesis of two potential pine sawfly pheromone components; *threo*-**11** and *erythro*-**12**. Reagents and conditions: (a) 1. THF, DMPU, −40 °C, *n*-BuLi (2.1 equiv), up to 0 °C, cool to −40 °C. 2. 1-Iodoundecane (1.2 equiv, neat), up to 20 °C (93%). (b) Ra-Ni, 1,4-dioxane, reflux (73%). (c) HCl in MeOH, 20 °C (74%). (d) 1. CH_2Cl_2, −78 °C, $TiCl_4$. 2. Me_2Zn. (e) Ra-Ni, EtOH, H_2, 20 °C, 5 days (86%).

3. Experimental

3.1. General experimental procedure

Commercially available chemicals were used without further purification unless otherwise stated Me_2Zn was purchased as a 2.0 M solution in toluene, Et_2Zn (1.0 M) and *n*-BuLi (1.6 M) in *n*-hexane, Bu_2Zn (1.0 M in *n*-heptane), MeLi (1.6 M in Et_2O), EtMgCl (2.0 M) and BuZnBr (0.5 M) in THF. Raney nickel (W-2 type) and $TiCl_4$ were obtained from Fluka and J. T. Baker, respectively. Et_2O ($LiAlH_4$), THF (K, benzophenone), DMPU and CH_2Cl_2 (CaH_2) were distilled from the indicated drying agents and used immediately. 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 of distilled ethyl acetate in distilled cyclohexane as eluent. The progress was followed by GC or thin layer chromatography (TLC) which was performed on silica gel plates (Merck 60 F_{254}, precoated aluminium foil) eluted with ethyl acetate (20–60%) in cyclohexane and developed by spraying with vanillin in sulphuric 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. The diastereomeric ratio (dr) of the alcohols **3** and **4**, the corresponding trifluoroacetates of the alcohols **6a**–**8b** and of the corresponding butyrates of the alcohols **2a**–**g** were determined using a capillary column Factor Four, 30 m, 0.32 mm i.d., d_f=0.25 μm, carrier gas N_2, and/or by ^{1}H NMR spectroscopy. The diastereomeric ratio (dr) of **9** was determined using a capillary column EC-1, 30 m, 0.32 mm i.d., d_f=0.25 μm, carrier gas N_2. Mass spectra were recorded on a Saturn 2000 instrument, operating in the EI mode, coupled to a Varian 3800 GC instrument. Infrared absorption spectra were recorded neat, (KBr plates, Perkin–Elmer 16PC FT-IR). Boiling points are uncorrected, and are given as air-bath temperatures (bath temperature/mbar) in a bulb-to-bulb (Büchi-GKR-51) apparatus. The elemental analyses (C and H) were performed by Mikrokemi AB, SE-752 28 Uppsala, Sweden. 2-Methyl-3-(phenylsulfanyl)propanal (**1a**), 3-methyl-4-(phenylsulfanyl)butan-2-ol (**2a**) and *tert*-butyl-[1,2-dimethyl-3-(phenylsulfonyl)propoxy]-dimethyl-silane (**9**) were prepared using the same procedure as reported by us previously.[6]

3.2. Preparation of starting materials

3.2.1. 3-(*tert*-Butylsulfanyl)-2-methylpropanal (1f). Following the procedure described by Vedejs et al.[11] a mixture of *tert*-butylthiol (5.0 g, 55.4 mmol) and methacrolein (3.88 g, 55.4 mmol) was refluxed with triethylamine (0.5 mL) as catalyst over night. This crude mixture was distilled, furnishing a colourless oil (5.5 g, 62%), 92% pure by GC. Bp 70–80 °C/12 mm Hg. The physical and spectroscopic properties were in accordance with those described in the literature.[11]

3.2.2. 2-Methyl-3-[(4-methylphenyl)sulfanyl]propanal (1b). Similarly, *p*-toluenethiol (5.0 g, 40.3 mmol), methacrolein (2.82 g, 40.3 mmol) and triethylamine (0.5 mL) furnished a colourless oil (3.78 g, 48%) after distillation, 90% pure by GC. Bp 110 °C/0.8 mbar. ^{1}H NMR: δ 1.21 (3H, d, J=7.1 Hz), 2.32 (3H, s), 2.51–2.65 (1H, m), 2.87 (1H, dd, J=7.1, 13.4 Hz), 3.25 (1H, dd, J=6.6, 13.4 Hz), 7.03–7.20 (2H, m), 7.26–7.39 (2H, m), 9.65 (1H, d, J=1.4 Hz). ^{13}C NMR: δ 13.4, 21.0, 35.5, 45.9, 129.9 (2C), 130.9 (2C), 131.5, 137.0, 203.1. MS (EI): *m*/*z* 194 (100) (M^+), 165 (3), 137 (10), 124 (47), 91 (28). IR: 3021, 2969, 2922, 2870, 2817, 2729, 1749, 1734, 1718, 1706, 1700, 1684, 1654, 1647, 1636, 1559, 1540, 1534, 1522, 1516, 1508, 1491, 1473, 1464, 1458, 1436, 1419, 1397, 1092, 1017, 928, 804 cm^{-1}. Anal. Calcd for $C_{11}H_{14}OS$: C 68.0; H 7.3. Found: C 67.9; H 7.2.

3.2.3. 3-[(4-Chlorophenyl)sulfanyl]-2-methylpropanal (1c). Similarly, 4-chlorothiophenol (7.0 g, 48.4 mmol), methacrolein (3.39 g, 48.4 mmol) and triethylamine (0.5 mL) furnished a colourless oil (5.0 g, 48%) after distillation, 97% pure by GC. Bp 118 °C/0.6 mbar. ^{1}H NMR: δ 1.23 (3H, d, J=7.2 Hz), 2.53–2.68 (1H, m), 2.89 (1H, dd, J=7.1, 13.3 Hz), 3.28 (1H, dd, J=6.5, 13.3 Hz), 7.28–7.41 (4H, m), 9.66 (1H, d, J=1.4 Hz). ^{13}C NMR: δ 13.5, 34.9, 45.8, 129.3 (2C), 131.3, (2C), 132.7, 134.0, 202.6. MS (EI): *m*/*z* 216 (36) ($M^{37}Cl)^+$, 214 (100) ($M^{35}Cl)^+$, 185 (2), 157 (5), 144 (14), 109 (8). IR: 2970, 2932, 2876, 2816, 2724, 1724, 1560, 1477, 1458, 1438,

1389, 1096, 1011, 929, 814, 745 cm^{-1}. Anal. Calcd for $C_{10}H_{11}ClOS$: C 55.9; H 5.2. Found: C 55.5; H 5.1.

3.2.4. 3-[(4-Methoxyphenyl)sulfanyl]-2-methylpropanal (1d). Similarly, 4-methoxy-benzenethiol (5.0 g, 35.7 mmol), methacrolein (2.5 g, 35.7 mmol) and triethylamine (0.5 mL) furnished a colourless oil (5.4 g, 72%) after distillation, 98% pure by GC. Bp 125 °C/0.5 mbar. ^{1}H NMR: δ 1.20 (3H, d, J=7.1 Hz), 2.50–2.59 (1H, m), 2.82 (1H, dd, J=7.1, 13.4 Hz), 3.18 (1H, dd, J=6.7, 13.4 Hz), 3.80 (3H, s), 6.78–6.88 (2H, m), 7.34–7.40 (2H, m), 9.64 (1H, d, J=1.5 Hz). ^{13}C NMR: δ 13.4, 36.9, 45.9, 55.3, 114.7 (2C), 125.3, 134.0 (2C), 159.3, 203.2. MS (EI): *m/z* 210 (100) (M^+), 153 (4), 140 (12). IR: 2966, 2935, 2836, 2720, 1724, 1592, 1570, 1495, 1459, 1442, 1406, 1373, 1286, 1247, 1174, 1105, 1031, 928, 827, 639, 626 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_2S$: C 62.8; H 6.7. Found: C 62.8; H 6.8.

3.2.5. 3-[(2-Methoxyphenyl)sulfanyl]-2-methylpropanal (1e). Similarly, 2-methoxy-benzenethiol (10 g, 71.3 mmol), methacrolein (5.87 g, 71.3 mmol) and triethylamine (0.5 mL) furnished a colourless oil (9.0 g, 60%) after distillation, 98% pure by GC. Bp 128 °C/0.5 mm Hg. ^{1}H NMR: δ 1.23 (3H, d, J=7.1 Hz), 2.55–2.64 (1H, m), 2.89 (1H, dd, J=7.2, 13.1 Hz), 3.27 (1H, dd, J=6.5, 13.1 Hz), 3.89 (3H, s), 6.86–6.95 (2H, m), 7.20–7.33 (2H, m), 9.68 (1H, d, J=1.3 Hz). ^{13}C NMR: δ 13.5, 33.1, 45.9, 55.8, 110.7, 121.1, 123.1, 128.2, 131.1, 158.0, 203.2. MS (EI): *m/z* 210 (100) (M^+), 153 (3), 140 (21). IR: 3063, 2967, 2935, 2874, 2836, 2724, 1724, 1578, 1478, 1464, 1433, 1392, 1374, 1295, 1274, 1245, 1182, 1162, 1133, 1072, 1043, 1024, 929, 792, 750, 718, 685 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_2S$: C 62.8; H 6.7. Found: C 62.8; H 6.7.

3.2.6. 3-(Butylsulfanyl)-2-methylpropanal (1g). Similarly, 1-butanethiol (5.0 g, 55.4 mmol), methacrolein (3.88 g, 55.4 mmol) and triethylamine (0.5 mL) furnished a colourless oil (5.3 g, 60%) after distillation, 95% pure by GC. Bp 62–70 °C/1.0 mbar. ^{1}H NMR: δ 0.92 (3H, d, J=7.2 Hz), 1.21 (3H, d, J=6.8 Hz), 1.33–1.69 (5H, m), 2.50–2.61 (3H, m), 2.82–2.97 (1H, m), 9.69 (1H, d, J=1.4 Hz). ^{13}C NMR: δ 13.6, 13.7, 22.0, 31.6, 32.5, 32.8, 46.3, 203.5. MS (EI): *m/z* 160 (43) (M^+), 132 (63), 103 (14), 89 (18), 56 (100). IR: 2959, 2932, 2873, 2718, 1725, 1654, 1560, 1458, 1438, 1420, 1376, 1275, 1225, 1099, 927 cm^{-1}. Anal. Calcd for $C_8H_{16}OS$: C 60.0; H 10.1. Found: C 60.3; H 9.9.

3.2.7. 2-[(Phenylsulfanyl)methyl]pentanal (5a). A mixture of valeraldehyde (4.9 g, 56.4 mmol), 37% aqueous formaldehyde (9.2 g, 0.11 mol) and diethylamine hydrochloride (9.4 g, 84.6 mmol) was stirred at 40 °C for 12 h, followed by the addition of triethylamine (3 mL) and thiophenol (7.0 g, 63.6 mmol) and the reaction was allowed to stir at 70 °C over night. Organic and aqueous phases were extracted. The aqueous phase was extracted with *n*-hexane (3×15 mL) and the combined hexane extract was washed with HCl (20 mL, 2 M, aq.), brine (20 mL), dried ($MgSO_4$), filtered and the solvent was evaporated off. A Colourless oil (5.5 g, 47%) was obtained after chromatography and distillation, 93% pure by GC, which was used immediately without further purification (see Section 3.3.3). Bp 130 °C/0.4 mbar. ^{1}H NMR: δ 0.90 (3H, t, J=7.2 Hz), 1.25–1.38 (2H, m), 1.52–1.76 (2H, m), 2.52–2.59 (1H, m), 3.01 (1H, dd, J=6.0, 13.3 Hz), 3.21 (1H, dd, J=7.7, 13.3 Hz), 7.17–7.37 (5H, m), 9.64 (1H, d, J=2.1 Hz). ^{13}C NMR: δ 14.0, 19.8, 30.6, 32.8, 50.8, 126.6, 129.1 (2C), 130.0 (2C), 135.5, 203.1. MS (EI): *m/z* 208 (100) (M^+), 123 (8), 110 (13).

3.2.8. 2-[(Phenylsulfanyl)methyl]decanal (5b). Similarly, decyl aldehyde (7.6 g, 48.6 mmol) furnished **5b** as a colourless oil (5.1 g, 38%), 84% pure by GC, which was used immediately without further purification (see Section 3.3.3). Bp 210 °C/0.5 mbar. ^{1}H NMR: δ 0.88 (3H, t, J=6.6 Hz), 1.17–1.32 (12H, m), 1.54–1.77 (2H, m), 2.49–2.60 (1H, m), 3.01 (1H, dd, J=6.0, 13.3 Hz), 3.22 (1H, dd, J=7.7, 13.3 Hz), 7.17–7.38 (5H, m), 9.65 (1H, d, J=2.2 Hz). ^{13}C NMR: δ 14.1, 22.6, 26.5, 28.5, 29.2, 29.3, 29.6, 31.8, 32.8, 51.0, 126.6, 129.1 (2C), 130.0 (2C), 135.5, 203.2. MS (EI): *m/z* 278 (35) (M^+), 123 (17), 110 (100).

3.2.9. 2-[(Phenylsulfanyl)methyl]dodecanal (5c). Similarly, dodecyl aldehyde (6.6 g, 36.0 mmol) furnished **5c** as a colourless oil (2.5 g, 23%), 94% pure by GC, which was used immediately without further purification (see Section 3.3.3). ^{1}H NMR: δ 0.88 (3H, t, J=6.9 Hz), 1.24 (16H, br s), 1.54–1.77 (2H, m), 2.49–2.61 (1H, m), 3.01 (1H, dd, J=6.0, 13.3 Hz), 3.22 (1H, dd, J=7.7, 13.3 Hz), 7.18–7.39 (5H, m), 9.65 (1H, d, J=2.2 Hz. MS (EI): *m/z* 306 (28) (M^+), 123 (12), 110 (100).

3.3. General procedures for the alkylmetal addition reactions

3.3.1. 3-Methyl-4-[(4-methylphenyl)sulfanyl]butan-2-ol (2b), 4-[(4-chlorophenyl)sulfanyl]-3-methylbutan-2-ol (2c), 4-[(4-methoxyphenyl)sulfanyl]-3-methylbutan-2-ol (2d), 4-[(2-methoxyphenyl)sulfanyl]-3-methylbutan-2-ol (2e), 4-(*tert*-butylsulfanyl)-3-methylbutan-2-ol (2f) and 4-(butylsulfanyl)-3-methylbutan-2-ol (2g). Entries 2–7, Table 1. The appropiate aldehyde (0.47 mmol) was dissolved in freshly distilled CH_2Cl_2 (8 mL) and cooled to −78 °C. $TiCl_4$ (50 μL, 0.47 mmol) was added dropwise via a syringe. An orange viscous solution was obtained and this was kept at −78 °C. After stirring for 0.5 h, Me_2Zn [0.38 mL, 2 M in toluene, 0.75 mmol] was added dropwise followed by stirring at −78 °C. After stirring over night, at which point the temperature had reached 10 °C, water (5 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (3×15 mL) and the combined Et_2O extract was washed with $NaHCO_3$ (20 mL, sat. aq.), dried (Na_2SO_4), filtered and the solvent was evaporated off. A colourless oil was obtained after LC.

3.3.2. 2-Methyl-1-(phenylsulfanyl)pentan-3-ol (3) and 2-methyl-1-(phenylsulfanyl)heptan-3-ol (4). Tables 3 and 4. The Lewis acid (from 0.28 mmol up to 1.34 mmol; see specific entries in Tables 3 and 4) was added to a precooled, −78 °C, solution of 2-methyl-3-(phenylsulfanyl)propanal (**1a**, 0.1 g, 0.56 mmol) in freshly distilled dry solvent (8.0 mL). An orange viscous solution was obtained and this was kept at −78 °C. After stirring for 1 h, the alkylmetal reagent solution (from 0.56 mmol up to 0.90 mmol; see specific entries in Tables 3 and 4) was added. After stirring over night, at which point the temperature had reached 10 °C, water (5 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O

(3×15 mL) and the combined Et_2O extract was washed with $NaHCO_3$ (20 mL, sat. aq.), dried (Na_2SO_4), filtered and the solvent was evaporated off, furnishing the product.

3.3.3. 3-[(Phenylsulfanyl)methyl]hexan-2-ol (6a, $R^1=C_2H_5$, $R^2=Me$), 4-[(phenylsulfanyl)methyl]heptan-3-ol (7a, $R^1=C_2H_5$, $R^2=Et$), 4-[(phenylsulfanyl)methyl]nonan-5-ol (8a, $R^1=C_2H_5$, $R^2=n$-Bu), 3-[(phenylsulfanyl)methyl]undecan-2-ol (6b, $R^1=n$-C_7H_{15}, $R^2=Me$), 4-[(phenylsulfanyl)methyl]dodecan-3-ol (7b, $R^1=n$-C_7H_{15}, $R^2=Et$), 6-[(phenylsulfanyl)methyl]tetradecan-5-ol (8b, $R^1=n$-C_7H_{15}, $R^2=n$-Bu) and 3-[(phenylsulfanyl)methyl]tridecan-2-ol (6c, $R^1=n$-C_9H_{19}, $R^2=Me$). *(a)* Tables 2 and 5, *with the exception of entry 4* (Table 2). $TiCl_4$ (0.07 mL, 0.62 mmol) was added to a precooled, −78 °C, solution of the appropiate aldehyde (0.56 mmol) in freshly distilled dry CH_2Cl_2 (8.0 mL). An orange viscous solution was obtained and this was kept at −78 °C. The mixture was stirred at that temperature for 1 h, followed by the addition of the R_2Zn solution (0.84 mmol; see specific entries in Table 2). After stirring over night, at which point the temperature had reached 10 °C, water (5 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (3×15 mL) and the combined Et_2O extract was washed with $NaHCO_3$ (20 mL, sat. aq.), dried (Na_2SO_4), filtered and the solvent was evaporated off, furnishing the product.

(b) Entry 4 (Table 2). The differences from above are; no Lewis acid is present, the alkylmetal reagent is MeLi (1.3 M in Et_2O) and the reaction is performed in Et_2O.

3.4. Description of specific compounds

3.4.1. 3-Methyl-4-[(4-methylphenyl)sulfanyl]butan-2-ol (2b). Entry 2, Table 1, *threo/erythro*, **2bT/2bE**, 94/06. LC furnished a colourless oil. Bp 120 °C/0.4 mbar. ^{1}H NMR: δ 1.00 (0.18H, d, J=6.9 Hz), 1.02 (2.82H, d, J=6.8 Hz), 1.17 (3H, d, J=6.3 Hz), 1.64 (1H, d, –OH, J=4.8 Hz), 1.68–1.84 (1H, m), 2.31 (3H, s), 2.76 (1H, dd, J=8.0, 12.8 Hz), 3.04–3.12 (0.06H, m), 3.14 (0.94H, dd, J=4.8, 12.8 Hz), 3.75 (0.94H, dquint, J=4.9, 6.3 Hz), 3.91–4.00 (0.06H, m), 7.08–7.11 (2H, m), 7.25–7.30 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.6*, 15.4, 20.3, 21.0, 38.1, 39.1*, 40.1, 69.6*, 71.1, 129.7 (2C), 129.8 (2C), 133.0, 136.0. MS (EI): m/z 210 (100) (M^+), 193 (8), 165 (3), 137 (6), 124 (10), 91 (5). IR: 3385, 2975, 2932, 1654, 1560, 1508, 1492, 1458, 1420, 1400, 1377, 1320, 1124, 1087, 1025, 1012, 932, 846, 811, 668 cm^{-1}. Anal. Calcd for $C_{12}H_{18}OS$: C 68.5; H 8.6. Found: C 68.7; H 8.7.

3.4.2. 4-[(4-Chlorophenyl)sulfanyl]-3-methylbutan-2-ol (2c). Entry 3, Table 1, *threo/erythro*, **2cT/2cE**, 90/10. LC furnished a colourless oil. Bp 135 °C/1.1 mbar. ^{1}H NMR: δ 1.02 (0.3H, d, J=6.9 Hz), 1.03 (2.7H, d, J=6.8 Hz), 1.19 (0.3H, d, J=6.4 Hz), 1.20 (2.7H, d, J=6.3 Hz), 1.49 (1H, d, –OH, J=4.8 Hz), 1.70–1.81 (1H, m), 2.75 (1H, dd, J=8.3, 12.8 Hz), 3.08–3.15 (0.1H, m), 3.20 (0.9H, dd, J=4.4, 12.8 Hz), 3.74 (0.9H, dquint, J=4.9, 6.3 Hz), 3.91–4.03 (0.1H, m), 7.22–7.30 (4H, m). ^{13}C NMR: δ 15.4, 20.6, 37.5, 40.2, 71.1, 129.0 (2C), 130.2 (2C), 131.7, 135.6. MS (EI): m/z 232 (36) ($M^{37}Cl)^+$, 230 (100) ($M^{35}Cl)^+$, 213 (8), 185 (3), 157 (7), 144 (16), 108 (14), 86 (11), 71 (21). Anal. Calcd for $C_{11}H_{15}ClOS$: C 57.3; H 6.6. Found: C 57.7; H 6.7.

3.4.3. 4-[(4-Methoxyphenyl)sulfanyl]-3-methylbutan-2-ol (2d). Entry 4, Table 1, *threo/erythro*, **2dT/2dE**, 80/20. LC furnished a colourless oil. Bp 165 °C/0.8 mbar. ^{1}H NMR: δ 0.99 (0.6H, d, J=6.9 Hz), 1.01 (2.4H, d, J=6.8 Hz), 1.16 (3H, d, J=6.3 Hz), 1.60 (1H, d, –OH, J=5.6 Hz), 1.64–1.80 (1H, m), 2.72 (1H, dd, J=7.9, 12.8 Hz), 2.98–3.06 (0.2H, m), 3.07 (0.8H, dd, J=4.8, 12.8 Hz), 3.72–3.78 (0.8H, m), 3.79 (3H, s), 3.86–4.03 (0.2H, m), 6.81–6.87 (2H, m), 7.33–7.39 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.6*, 15.3, 20.3, 39.6*, 39.7, 40.1, 55.3, 69.6*, 71.1, 114.6 (2C), 126.9, 132.8 (2C), 158.8. MS (EI): m/z 226 (100) (M^+), 209 (6), 181 (3), 153 (9), 140 (32), 125 (13), 107 (6). IR: 3422, 2970, 1595, 1578, 1497, 1458, 1304, 1252, 1174, 1089, 1026, 829, 668 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2S$: C 63.7; H 8.0. Found: C 64.3; H 8.0.

3.4.4. 4-[(2-Methoxyphenyl)sulfanyl]-3-methylbutan-2-ol (2e). Entry 5, Table 1, *threo/erythro*, **2eT/2eE**, 30/70. LC furnished a colourless oil. Bp 150 °C/0.5 mbar. ^{1}H NMR: δ 1.03 (2.1H, d, J=6.9 Hz), 1.05 (0.9H, d, J=6.8 Hz), 1.19 (2.1H, d, J=6.4 Hz), 1.20 (0.9H, d, J=6.3 Hz), 1.58 (1H, d, –OH, J=4.9 Hz), 1.71–1.86 (1H, m), 2.77 (0.7H, dd, J=7.3, 12.5 Hz), 2.75–2.83 (0.3H, m), 3.08 (0.7H, dd, J=6.5, 12.5 Hz), 3.09–3.16 (0.3H, m), 3.75–3.85 (0.3H, m), 3.90 (3H, s), 3.96–4.07 (0.7H, m), 6.84–6.96 (2H, m), 7.15–7.34 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.8, 15.7*, 20.2, 20.3*, 35.8, 35.9*, 39.0, 40.1*, 55.8, 69.7, 71.1*, 110.5, 121.1, 124.8, 127.0, 127.2*, 129.3, 129.6*, 157.3. MS (EI): m/z 226 (100) (M^+), 209 (8), 181 (3), 153 (6), 140 (23), 125 (8), 107 (3). IR: 3367, 2973, 1586, 1479, 1436, 1379, 1274, 1240, 1132, 1071, 1021, 793, 755 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2S$: C 63.7; H 8.0. Found: C 64.1; H 8.1.

3.4.5. 4-(*tert*-Butylsulfanyl)-3-methylbutan-2-ol (2f). Entry 6, Table 1, *threo/erythro*, **2fT/2fE**, 81/19. LC furnished a colourless oil. ^{1}H NMR: δ 1.00 (3H, d, J=6.9 Hz), 1.19 (3H, d, J=6.3 Hz), 1.33 (9H, s), 2.18 (1H, s, –OH), 1.67–1.81 (1H, m), 2.41–2.48 (0.19H, m), 2.50 (0.81H, dd, J=7.2, 11.7 Hz), 2.69 (1H, dd, J=5.3, 11.7 Hz), 3.69–3.79 (0.81H, m), 3.86–3.98 (0.19H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 14.1*, 16.0, 20.2*, 20.4, 30.9 (3C), 31.0*, 31.9, 32.0*, 39.8*, 40.7, 42.0, 70.3*, 71.5. MS (EI): m/z 176 (53) (M^+), 159 (7), 131 (8), 119 (12), 103 (14), 87 (54), 71 (36), 57 (100).

3.4.6. 4-(Butylsulfanyl)-3-methylbutan-2-ol (2g). Entry 7, Table 1, *threo/erythro*, **2gT/2gE**, 94/06. LC furnished a colourless oil. Bp 95 °C/1.4 mbar. ^{1}H NMR: δ 0.92 (3H, t, J=7.2 Hz), 0.99 (3H, d, J=6.9 Hz), 1.18 (3H, d, J=6.3 Hz), 1.33–1.86 (5H, m), 1.95 (1H, d, –OH, J=4.4 Hz), 2.39–2.56 (3H, m), 2.68 (1H, dd, J=5.4, 12.7 Hz), 3.74 (0.94H, dquint, J=4.5, 6.3 Hz), 3.90–3.96 (0.06H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.7, 15.7, 20.4, 22.0, 31.7, 32.5, 36.0*, 36.3, 39.3*, 40.3, 70.1*, 71.5. MS (EI): m/z 176 (65) (M^+), 159 (19), 131 (12), 103 (14), 87 (34), 71 (100), 57 (11). IR: 3356, 2977, 2937, 2877, 1706, 1458, 1448, 1379, 1345, 1321, 1294, 1125, 1100,

1048, 1007, 948, 907, 846 cm^{-1}. Anal. Calcd for $C_9H_{20}OS$: C 61.3; H 11.4. Found: C 61.1; H 11.3.

3.4.7. 2-Methyl-1-(phenylsulfanyl)pentan-3-ol (3). Entry 1, Table 3; *threo/erythro*, **3T/3E**, 65/35. LC furnished a colourless oil. Bp 140 °C/0.5 mbar. ^1H NMR: δ 0.91–0.99 (3H, m), 1.00 (1.05H, d, $J=6.7$ Hz), 1.05 (1.95H, d, $J=6.9$ Hz), 1.33–1.67 (3H, m), 1.75–1.90 (1H, m), 2.80 (0.65H, dd, $J=8.4$, 12.8 Hz), 2.85 (0.35H, dd, $J=7.1$, 13.0 Hz), 3.10 (0.35H, dd, $J=6.9$, 12.8 Hz), 3.23 (0.65H, dd, $J=4.2$, 12.7 Hz), 3.44–3.51 (0.65H, m), 3.66–3.73 (0.35H, m), 7.13–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 10.0, 10.6*, 13.1*, 15.9, 26.9, 27.4*, 36.9, 37.4*, 37.8*, 38.4, 74.8*, 76.5, 125.7, 128.8 (2C), 128.9 (2C), 137.1. MS (EI): *m/z* 210 (100) (M^+), 193 (28), 163 (8), 123 (25), 110 (32), 100 (30). IR: 3406, 3058, 2964, 2932, 2876, 1584, 1480, 1458, 1438, 1378, 1302, 1272, 1245, 1186, 1091, 1069, 1026, 972, 897, 738, 690 cm^{-1}. Anal. Calcd for $C_{12}H_{18}OS$: C 68.5; H 8.6. Found: C 68.5; H 8.8.

3.4.8. 2-Methyl-1-(phenylsulfonyl)pentan-3-ol (sulfonyl of 3). *m*-Chloroperbenzoic acid (0.57 g, 2.54 mmol) was added to a solution of **3** (0.21 g, 1.01 mmol) in CH_2Cl_2 (7 mL) at 0 °C. The mixture was allowed to reach room temperature over night, $NaHCO_3$ (10 mL, sat. aq.) was added and the aqueous phase was extracted with Et_2O (3× 15 mL) and the combined Et_2O extract was washed with $NaHCO_3$ (15 mL, sat. aq.), brine (15 mL), dried (Na_2SO_4), filtered and the solvent was evaporated off, furnishing a yellowish oil (0.20 g, 81%) after LC (EtOAc gradient in cyclohexane), 99% pure by GC. Bp 235 °C/0.6 mbar. (*threo/erythro*, 65/35). ^1H NMR: δ 0.91 (1.95H, t, $J=7.4$ Hz), 0.94 (1.05H, t, $J=7.4$ Hz), 1.02 (1.05H, d, $J=7.0$ Hz), 1.14 (1.95H, d, $J=6.9$ Hz), 1.27–1.57 (2H, m), 1.85 (1H, br s, OH), 2.09–2.20 (0.65H, m), 2.26–2.35 (0.35H, m), 2.94 (0.65H, dd, $J=8.5$, 14.2 Hz), 2.97 (0.35H, dd, $J=6.9$, 14.1 Hz), 3.32–3.47 (1.65H, m), 3.65–3.71 (0.35H, m), 7.53–7.69 (3H, m), 7.91–7.95 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 9.79, 10.6*, 13.6*, 17.4, 26.5*, 27.2, 33.4*, 34.1, 58.6, 59.6*, 74.8*, 76.4, 127.8 (2C), 129.3 (2C), 133.6, 140.0. MS (EI): *m/z* 243 (34) $(M+H)^+$, 225 (32), 213 (12), 200 (30), 182 (7), 143 (75), 125 (43), 100 (19), 78 (100), 59 (90). The ^1H NMR and ^{13}C NMR spectral data were similar to those reported in the literature for the *erythro*-isomer.[12]

3.4.9. 2-Methyl-1-(phenylsulfanyl)heptan-3-ol (4). Entry 3, Table 3; *threo/erythro*, **4T/4E**, 70/30. LC furnished a colourless oil. Bp 180 °C/0.9 mbar. ^1H NMR: δ 0.88–0.93 (3H, m), 1.00 (0.9H, d, $J=6.9$ Hz), 1.05 (2.1H, d, $J=6.9$ Hz), 1.23–1.58 (7H, m), 1.74–1.88 (1H, m), 2.79 (0.7H, dd, $J=8.4$, 12.7 Hz), 2.84 (0.3H, dd, $J=7.1$, 12.9 Hz), 3.10 (0.3H, dd, $J=6.9$, 12.8 Hz), 3.22 (0.7H, dd, $J=4.3$, 12.7 Hz), 3.51–3.58 (0.7H, m), 3.74–3.79 (0.3H, m), 7.12–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.2*, 14.1, 15.9, 22.7*, 22.7, 28.0, 28.4*, 33.7, 34.2*, 36.9, 37.7*, 38.7, 73.3*, 75.1, 125.7, 128.9 (4C), 137.1. MS (EI): *m/z* 238 (100) (M^+), 221 (14), 163 (15), 151 (14), 128 (34), 123 (57), 110 (100), 86 (88), 69 (49), 58 (47). IR: 3406, 3059, 2957, 2932, 2871, 1584, 1481, 1466, 1458, 1438, 1378, 1272, 1115, 1090, 1026, 1001, 978, 897, 737, 690, 670 cm^{-1}. Anal. Calcd for $C_{14}H_{22}OS$: C 70.5; H 9.3. Found: C 70.6; H 9.4.

3.4.10. 2-Methyl-1-(phenylsulfonyl)heptan-3-ol (sulfonyl of 4). Oxidation of **4** was performed as above to give a colourless oil after LC. Bp 260 °C/1.2 mbar (*threo/erythro*, 70/30). ^1H NMR: δ 0.85–0.92 (3H, m), 1.02 (0.9H, d, $J=7.0$ Hz), 1.15 (2.1H, d, $J=6.9$ Hz), 1.18–1.48 (6H, m), 1.82 (1H, br s, OH), 2.06–2.21 (0.7H, m), 2.25–2.34 (0.3H, m), 2.90–3.01 (1H, m), 3.33–3.46 (1.7H, m), 3.73–3.79 (0.3H, m), 7.53–7.69 (3H, m), 7.91–7.95 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 13.7*, 14.0, 17.4, 22.6, 27.7, 28.3*, 33.3*, 33.7*, 34.1, 34.5, 58.5, 59.5*, 73.3*, 75.0, 127.8 (2C), 129.3 (2C), 133.6, 140.0. MS (EI): *m/z* 271 (7) $(M+H)^+$, 253 (11), 228 (10), 213 (12), 170 (4), 156 (7), 143 (42), 125 (23), 87 (48), 78 (40), 69 (100). IR: 3510, 3066, 2957, 2933, 2872, 1466, 1459, 1448, 1406, 1381, 1304, 1147, 1086, 999, 986, 749, 689 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_3S$: C 62.2; H 8.2. Found: C 62.5; H 8.1.

3.4.11. 3-[(Phenylsulfanyl)methyl]hexan-2-ol (6a, $R^1=C_2H_5$, $R^2=Me$). Entry 1, Table 2; *threo/erythro*, **6aT/6aE**, 95/05. LC furnished a colourless oil. ^1H NMR: δ 0.90 (3H, t, $J=6.9$ Hz), 1.20 (3H, d, $J=6.3$ Hz), 1.17–1.55 (4H, m), 1.61–1.71 (1H, m), 1.71 (1H, s, –OH), 2.86–3.15 (2H, m), 3.94 (0.95H, app. quint, $J=6.2$ Hz), 4.02–4.16 (0.05H, m), 7.13–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 14.3, 15.3*, 19.7, 20.2, 20.6, 31.3*, 31.8, 34.5, 34.7*, 43.9*, 44.5, 68.8*, 69.1, 125.8, 128.9 (2C), 129.0 (2C), 137.1. MS (EI): *m/z* 224 (100) (M^+), 207 (20), 123 (27), 110 (50), 85 (15).

3.4.12. 4-[(Phenylsulfanyl)methyl]heptan-3-ol (7a, $R^1=C_2H_5$, $R^2=Et$). Entry 1, Table 5; *threo/erythro*, **7aT/7aE**, 87/13. LC furnished a colourless oil. Bp 190 °C/2.8 mbar. ^1H NMR: δ 0.90 (3H, t, $J=7.0$ Hz), 0.95 (3H, t, $J=7.2$ Hz), 1.27–1.62 (6H, m), 1.64 (1H, s, –OH), 1.67–1.77 (1H, m), 2.98 (1H, dd, $J=6.5$, 12.6 Hz), 3.12 (1H, dd, $J=5.0$, 12.6 Hz), 3.62 (0.87H, dt, $J=4.5$, 8.4 Hz), 3.78 (0.13H, dt, $J=3.2$, 6.6 Hz), 7.13–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 10.4, 10.8*, 14.3, 20.2, 20.7*, 26.8*, 27.3, 30.7*, 32.2, 34.3, 35.2*, 42.4*, 42.6, 74.3*, 74.5, 125.8, 128.9 (2C), 129.0 (2C), 137.2. MS (EI): *m/z* 308 (100) (M^+), 291 (28), 249 (12), 169 (65), 123 (53), 110 (82). MS (EI): *m/z* 238 (100) (M^+), 221 (58), 123 (5), 110 (8). IR: 3416, 3059, 2959, 2931, 2872, 1584, 1480, 1464, 1438, 1378, 1304, 1090, 1069, 1026, 998, 973, 738, 690 cm^{-1}. Anal. Calcd for $C_{14}H_{22}OS$: C 70.5; H 9.3. Found: C 70.5; H 9.5.

3.4.13. 4-[(Phenylsulfanyl)methyl]nonan-5-ol (8a, $R^1=C_2H_5$, $R^2=n$-Bu). Entry 2, Table 5; *threo/erythro*, **8aT/8aE**, 87/13. LC furnished a colourless oil. Bp 195 °C/0.3 mbar. ^1H NMR: δ 0.90 (6H, t, $J=7.0$ Hz), 1.21–1.55 (10H, m), 1.61 (1H, s, –OH), 1.63–1.75 (1H, m), 2.97 (1H, dd, $J=6.5$, 12.6 Hz), 3.10 (1H, dd, $J=5.0$, 12.6 Hz), 3.70 (0.87H, dt, $J=4.6$, 7.6 Hz), 3.83–3.90 (0.13H, m), 7.13–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 14.1, 14.3, 20.3, 20.7*, 22.7, 28.3, 28.5*, 30.7*, 32.2, 33.6*, 34.1, 34.3, 35.2*, 42.8*, 43.0, 72.7*, 73.0, 125.8, 128.9 (2C), 129.0 (2C), 137.2. MS (EI): *m/z* 266 (100) (M^+), 249 (73), 123 (5), 110 (11). IR: 3422, 3059, 2957, 2931, 2871, 1584, 1480, 1466, 1458, 1438, 1378,

1089, 1026, 738, 690 cm^{-1}. Anal. Calcd for $C_{16}H_{26}OS$: C 72.1; H 9.8. Found: C 72.0; H 10.0.

3.4.14. 3-[(Phenylsulfanyl)methyl]undecan-2-ol (6b, R^1=*n*-C_7H_{15}, R^2=Me). Entry 2, Table 2; *threo*/*erythro*, **6bT/6bE**, 95/05. LC furnished a colourless oil. ^{1}H NMR: δ 0.88 (3H, t, J=6.8 Hz), 1.21 (3H, d, J=6.3 Hz), 1.18–1.48 (14H, m), 1.60–1.68 (1H, m), 1.67 (1H, s, –OH), 2.86–3.15 (2H, m), 3.94 (0.95H, app. quint, J=6.2 Hz), 4.05–4.20 (0.05H, m), 7.14–7.38 (5H, m). MS (EI): *m*/*z* 294 (100) (M^+), 277 (18), 184 (21), 163 (13), 123 (51), 110 (83), 85 (29), 71 (42).

3.4.15. 4-[(Phenylsulfanyl)methyl]dodecan-3-ol (7b, R^1=*n*-C_7H_{15}, R^2=Et). Entry 3, Table 5; *threo*/*erythro*, **7bT/7bE**, 86/14. LC furnished a colourless oil. Bp 270 °C/0.8 mbar. ^{1}H NMR: δ 0.88 (3H, t, J=6.6 Hz), 0.95 (3H, t, J=7.4 Hz), 1.26 (12H, br s), 1.37–1.60 (4H, m), 1.67 (1H, s, –OH), 1.61–1.75 (1H, m), 2.97 (1H, dd, J=6.5, 12.6 Hz), 3.12 (1H, dd, J=4.9, 12.6 Hz), 3.62 (0.86H, dt, J=4.3, 8.4 Hz), 3.78 (0.14H, dt, J=3.2, 6.5 Hz), 7.13–7.37 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 10.4, 10.8*, 14.1, 22.7, 26.8*, 27.1, 27.3, 27.5*, 28.4*, 29.3, 29.5, 29.9 (2C), 31.9, 34.3, 35.2*, 42.7*, 42.9, 74.3*, 74.5, 125.8, 128.9 (2C), 129.0 (2C), 137.0*, 137.2. MS (EI): *m*/*z* 308 (100) (M^+), 291 (28), 249 (12), 169 (65), 123 (53), 110 (82). IR: 3422, 3059, 2957, 2926, 2855, 1584, 1480, 1459, 1438, 1376, 1088, 1026, 738, 690 cm^{-1}. Anal. Calcd for $C_{19}H_{32}OS$: C 74.0; H 10.5. Found: C 74.4; H 10.7.

3.4.16. 6-[(Phenylsulfanyl)methyl]tetradecan-5-ol (8b, R^1=*n*-C_7H_{15}, R^2=*n*-Bu). Entry 4, Table 5; *threo*/*erythro*, **8bT/8bE**, 81/19. LC furnished a colourless oil. Bp 300 °C/0.35 mbar. ^{1}H NMR: δ 0.85–0.93 (6H, m), 1.26 (16H, br s), 1.30–1.49 (4H, m), 1.58 (1H, s, –OH), 1.61–1.73 (1H, m), 2.97 (1H, dd, J=6.5, 12.6 Hz), 3.11 (1H, dd, J=5.0, 12.6 Hz), 3.71 (0.81H, dt, J=4.6, 7.4 Hz), 3.84–3.90 (0.19H, m), 7.13–7.39 (5H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ 14.0*, 14.1 (2C), 22.6*, 22.7 (2C), 27.1, 27.5*, 28.3, 28.4*, 28.5*, 29.2*, 29.3, 29.5, 29.8, 29.9, 31.8*, 31.9, 34.2, 34.3, 43.0*, 43.2, 72.8*, 73.0, 125.8, 128.9 (2C), 129.0 (2C), 129.7*, 137.2. MS (EI): *m*/*z* 336 (100) (M^+), 319 (62), 110 (11).

3.4.17. 3-[(Phenylsulfanyl)methyl]tridecan-2-ol (6c, R^1=*n*-C_9H_{19}, R^2=Me). Entry 3, Table 2; *threo*/*erythro*, **6cT/6cE**, 95/05. A yellowish oil which was used without further purification (see Section 3.4.19). ^{1}H NMR: δ 0.88 (3H, t, J=6.8 Hz), 1.21 (3H, d, J=6.3 Hz), 1.18–1.48 (18H, m), 1.59–1.68 (1H, m), 1.59 (1H, s, –OH), 2.86–3.15 (2H, m), 3.94 (0.95H, app. quint, J=6.2 Hz), 4.01–4.14 (0.05H, m), 7.14–7.37 (5H, m). ^{13}C NMR: δ 14.1, 20.7, 22.7, 26.9, 27.0, 29.4, 29.6 (3C), 29.9, 31.9, 34.5, 44.7, 69.2, 125.8, 128.9 (2C), 129.0 (2C), 137.1. MS (EI): *m*/*z* 322 (100) (M^+), 305 (8), 277 (14), 212 (25), 197 (13), 163 (13), 123 (50), 110 (85), 71 (55).

3.4.18. (2R^*,3S^*)-3-Methylpentadecan-2-ol (11). To a solution of **9**, *threo*/*erythro*>99.6/0.4 (0.38 g, 1.11 mmol) and DMPU (1.34 mL, 11.1 mmol) in dry degassed THF (10 mL) a solution of *n*-BuLi (1.50 mL, 2.33 mmol, 1.55 M) was added at −40 °C. After 5 min the reaction was allowed to reach 0 °C followed by cooling to −40 °C. 1-Iodoundecane (0.31 mL, 1.33 mmol) was added neat and the reaction was allowed to reach room temperature overnight. The reaction was quenched with NH_4Cl (10 mL, sat. aq.) and the aqueous phase was extracted with Et_2O (4×15 mL) and the combined Et_2O extract was washed with HCl (10 mL, 2 M, aq.), brine (20 mL), dried (Na_2SO_4). filtered and the solvent was evaporated off. A colourless oil of (1R^*,2R^*)-[3-(phenylsulfonyl)1,2-dimethyl-tetradecyloxy]-*tert*-butyl-dimethyl-silane (**10**) (0.54 g, 93%) was obtained after chromatography, 95% pure by GC with a diastereomeric ratio of 84/16, which was used without further purification. ^{1}H NMR: δ 0.00 (2.52H, s), 0.02 (2.52H, s), 0.14 (0.48H, s), 0.20 (0.48H, s), 0.84 (7.56H, s), 0.88 (1.44H, s), 0.80–0.92 (3H, m), 0.96 (3H, d, J=7.0 Hz), 1.04 (3H, d, J=6.1 Hz), 1.08–1.30 (18H, m), 1.58–2.10 (3H, m), 3.46–3.59 (1.84H, m), 4.38–4.48 (0.16H, m), 7.50–7.65 (3H, m), 7.85–7.91 (2H, m). ^{13}C NMR (asterisk denotes minor diastereomer peaks): δ −4.67, −4.16*, −3.60, −3.30*, 11.7*, 11.8, 14.3, 18.1, 22.0, 22.5*, 22.8, 24.3, 26.0 (3C), 26.1*, 26.8*, 28.1*, 28.9*, 29.1, 29.4, 29.5, 29.6, 29.7, 29.8, 30.2, 32.1, 39.7, 44.1*, 63.0*, 64.2, 70.4*, 71.2, 128.7 (2C), 129.0*, 129.1 (2C), 133.3*, 133.4, 139.6, 140.5*. MS (EI): *m*/*z* 439 (100), 365 (88), 355 (23), 297 (10), 217 (4), 199 (22), 159 (25), 135 (18), 103 (28). A suspension of a large excess of Raney Ni (W-2) in 1,4-dioxane (3 mL) was added to a refluxing solution of **10** (0.02 g, 0.04 mmol) in 1,4-dioxane (1.5 mL). The reaction was refluxed for 2 h. Raney-Ni was filtered off through a pad of Celite-silica gel and the solids were rinsed with CH_2Cl_2. The filtrate was concentrated and distilled (bp 145 °C/1.7 mbar) to give *tert*-butyl-(1,2-dimethyl-tetradecyloxy)-dimethyl-silane (0.01 g, 73%) as a colourless oil; purity of >99% (GC). ^{1}H NMR: δ 0.03 (3H, s), 0.03 (3H, s), 0.82 (3H, d, J=6.7 Hz), 0.81–0.91 (3H, m), 0.88 (9H, s), 1.02 (3H, d, J=6.2 Hz), 1.13–1.46 (23H, m), 3.64 (1H, dq, J=5.0, 6.2 Hz). ^{13}C NMR: δ −4.8, −4.4, 14.1, 14.4, 18.1, 19.3, 22.7, 25.9 (3C), 27.4, 29.4, 29.7 (5C), 30.0, 31.9, 32.7, 40.3, 72.0. MS (EI): *m*/*z* 355 (8) $(M-H)^+$, 341 (42), 299 (100), 159 (37), 103 (22), 75 (30). This compound (0.01 g, 0.03 mmol) was subjected to a solution of HCl in MeOH (1.5 mL, 3 vol%) at room temperature and allowed to stir over night. The reaction was quenched with water (4 mL) and 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. A colourless oil of **11** (0.06 g, 74%) was obtained after chromatography and distillation (bp 110 °C/0.5 mbar), 98% pure by GC. ^{1}H NMR: δ 0.87 (3H, d, J=6.8 Hz), 0.81–0.91 (3H, m), 1.12 (3H, d, J=6.3 Hz), 1.16–1.55 (24H, m), 3.66 (1H, dq, J=5.6, 6.2 Hz). ^{13}C NMR: δ 14.1, 14.5, 19.3, 22.7, 27.3, 29.4, 29.7 (5C), 30.0, 31.9, 32.5, 40.0, 71.8. MS (EI): *m*/*z* 241 (34) $(M-H)^+$, 224 (18), 194 (27), 182 (8), 166 (19), 155 (21), 138 (33), 125 (69), 111 (100), 97 (75), 85 (91), 71 (62), 57 (50), 45 (63). The ^{1}H NMR was similar to that reported in the literature for the diastereomerically pure *threo* isomer[13] and for the enantiomerically pure *erythro* isomer, (2*S*,3*S*)-3-methylpentadecan-2-ol,[14] except for the peak at 3.66 ppm, where our alcohol displayed a doublet of quartets (J=5.6, 6.2 Hz), whereas a doublet of quartets (J=4.2, 6.4 Hz) at 3.69 ppm was reported.

3.4.19. (2R^*,3R^*)-3-Methyltridecan-2-ol (12). A solution

of **6c** (0.08 g, 0.25 mmol) in absolute EtOH (5 mL, saturated with H_2) was added via a syringe to a suspension of a large excess of Raney-Ni (W-2) in EtOH (5 mL, saturated with H_2). The reaction was then allowed to stir for 5 days under an atmosphere of H_2. The work-up procedure was performed as above and a colourless oil of **12** (0.05 g, 86%) was obtained after chromatography and distillation (bp 120 °C/0.9 mbar, lit.[15] 100 °C/0.2 Torr), 96% pure by GC. ^{1}H NMR: δ 0.87 (3H, t, J=7.0 Hz), 0.88 (3H, d, J=6.6 Hz), 1.15 (3H, d, J=6.4 Hz), 1.09–1.49 (19H, m), 1.33 (1H, s, –OH), 3.60–3.67 (0.05H, m), 3.71 (0.95H, dq, J=4.3, 6.3 Hz). ^{13}C NMR: δ 14.1 (2C), 20.3, 22.7, 27.4, 29.4, 29.7 (3C), 30.0, 31.9, 32.7, 39.8, 71.4. MS (EI): m/z 213 (8) $(M-H)^+$, 199 (12), 183 (8), 166 (17), 154 (10), 139 (15), 125 (22), 111 (41), 97 (42), 83 (34), 71 (38), 57 (62), 45 (100). The ^{1}H NMR was similar to those reported in the literature for the diastereomerically pure *erythro* isomer of 3-methylpentadecan-2-ol,[13] for the diastereomerically pure *erythro* isomer of (2R^*,3R^*)-3-methylnonan-2-ol[16] and for the enantiomerically pure *erythro* isomer, (2*S*,3*S*)-3-methylpentadecan-2-ol.[14]

Acknowledgements

The authors thank Mid Sweden University and EU (Objective 1 the Region of South Forest Counties) for financial support.

References and notes

1. (a) Byström, S.; Högberg, H.-E.; Norin, T. *Tetrahedron* **1981**, *37*, 2249–2254. (b) Mori, K. The Synthesis of Insect Pheromones 1979–1989. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed. John Wiley & Sons: Ottawa, 1992; Vol. 9, pp 98–130. (c) Giblin-Davis, R. M.; Gries, R.; Gries, G.; Pena-Rojas, E.; Pinzon, I.; Pena, J. E.; Perez, A. L.; Pierce, H. D.; Oehlschlager, A. C. *J. Chem. Ecol.* **1997**, *23*, 2287–2298. (d) Tai, A.; Higashiura, Y.; Kakizaki, M.; Naito, T.; Tanaka, K.; Fujita, M.; Sugimura, T.; Hara, H.; Hayashi, N. *Biosci. Biotechnol. Biochem.* **1998**, *62*, 607–608. (e) Karlsson, S.; Hedenström, E. *Acta Chem. Scand.* **1999**, *53*, 620–630. (f) Nakamura, Y.; Mori, K. *Eur. J. Org. Chem.* **1999**, 2175–2182. (g) Larsson, M.; Nguyen, B.-V.; Högberg, H.-E.; Hedenström, E. *Eur. J. Org. Chem.* **2001**, 353–363 and references cited therein.
2. (a) Tanner, D.; Somfai, P. *Tetrahedron* **1987**, *43*, 4395–4406. (b) Takle, A.; Kocienski, P. *Tetrahedron* **1990**, *46*, 4503–4516. (c) Harada, T.; Matsuda, Y.; Imanaka, S.; Oku, A. *J. Chem. Soc., Chem. Commun.* **1990**, *22*, 1641–1643. (d) Yamamoto, K.; Shiinoki, Y.; Furukawa, J.; Nakamura, S. *Chem. Pharm. Bull.* **1991**, *39*, 1436–1439. (e) Sunazuka, T.; Obata, R.; Zhuorong, L.; Takamatsu, S.; Komiyama, K.; Omura, S. *Tetrahedron Lett.* **1994**, *35*, 2635–2636. (f) Middleton, R. F.; Foster, G.; Cannell, R. J. P.; Sidebottom, P. J.; Taylor, N. L.; Noble, D.; Todd, M.; Dawson, J.; Lawrence, G. C. *J. Antibiot.* **1995**, *48*, 311–316. (g) Makino, K.; Kimura, K.-I.; Nakajima, N.; Hashimoto, S.-I.; Yonemitsu, O. *Tetrahedron Lett.* **1996**, *37*, 9073–9076. (h) Evans, D. A.; Kim, A. S. *Tetrahedron Lett.* **1997**, *38*, 53–56. (i) Marino, S. D.; Iorizzi, M.; Palagiano, E.; Zollo, F.; Roussakis, C. *J. Nat. Prod.* **1998**, *61*, 1319–1327. (j) Kozmin, S. A. *Org. Lett.* **2001**, *3*, 755–758.
3. (a) Baker, R.; Boyes, R. H. O.; Broom, D. M. P.; Devlin, J. A.; Swain, C. J. *J. Chem. Soc. Chem. Commun.* **1983**, 829–831. (b) Mori, K.; Kiyota, H.; Rochat, D. *Liebigs Ann. Chem.* **1993**, *8*, 865–870. (c) Mori, K.; Kiyota, H.; Malosse, C.; Rochat, D. *Liebigs Ann. Chem.* **1993**, *11*, 1201–1204. (d) Koutek, B.; Streinz, L.; Romanuk, M. *Collect. Czech. Chem. Commun.* **1998**, *63*, 899–954. (e) Karlsson, S.; Högberg, H.-E. *Synthesis* **2000**, 1863–1867.
4. Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828–5835.
5. Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245–1249.
6. Larsson, M.; Högberg, H.-E. *Tetrahedron* **2001**, *57*, 7541–7548.
7. Larsson, M.; Andersson, J.; Liu, R.; Högberg, H.-E. *Tetrahedron: Asymmetry* **2004**, *15*, 2907–2915.
8. Safont, V. S.; Moliner, V.; Olivia, M.; Castillo, R.; Andrés, J.; González, F.; Carda, M. *J. Org. Chem.* **1996**, *61*, 3467–3475.
9. Anderbrant, O.; Östrand, F.; Lyytikäinen-Saarema, P.; Bergström, G.; Wassgren, A.-B.; Högberg, H.-E.; Hedenström, E.; Nguyen, B.-V.; Larsson, M.; Karlsson, S.; Varama, M.; Sierpinski, A.; Kolk, A.; Slusarski, S.; Bystrowski, K.; Herz, A.; Heitland, W.; Auger-Rosenberg, M.-A.; Geri, C.; Baronio, P.; Baldassari, N. Final report of the project PHERODIP supported by the European Community, FAIR1-CT95-0399 and IC20-CT96-0090: pine sawfly pheromones for sustainable management of European forests, **1999**; pp 93–96.
10. Hedenström, E.; Edlund, H.; Lund, S.; Abersten, M.; Persson, D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1810–1817.
11. Vedejs, E.; Buchanan, R. A.; Conrad, P. C.; Meier, G. P.; Mullins, M. J.; Schaffhausen, J. G.; Schwartz, C. E. *J. Am. Chem. Soc.* **1989**, *111*, 8421–8430.
12. Carretero, J. C.; Dominguez, E. *J. Org. Chem.* **1992**, *57*, 3867–3873.
13. Magnusson, G. *Tetrahedron* **1978**, *34*, 1385–1388.
14. Hedenström, E.; Högberg, H.-E.; Wassgren, A.-B.; Bergström, G.; Löfqvist, J.; Hansson, B.; Anderbrant, O. *Tetrahedron* **1992**, *48*, 3139–3146.
15. Matt, J.; Gunther, E. P. *J. Am. Chem. Soc.* **1955**, *77*, 3655–3656.
16. Sakai, T.; Matsumoto, S.; Hidaka, S.; Imajo, N.; Tsuboi, S.; Utaka, M. *Bull. Chem. Soc. Jpn* **1991**, *64*, 3473–3475.